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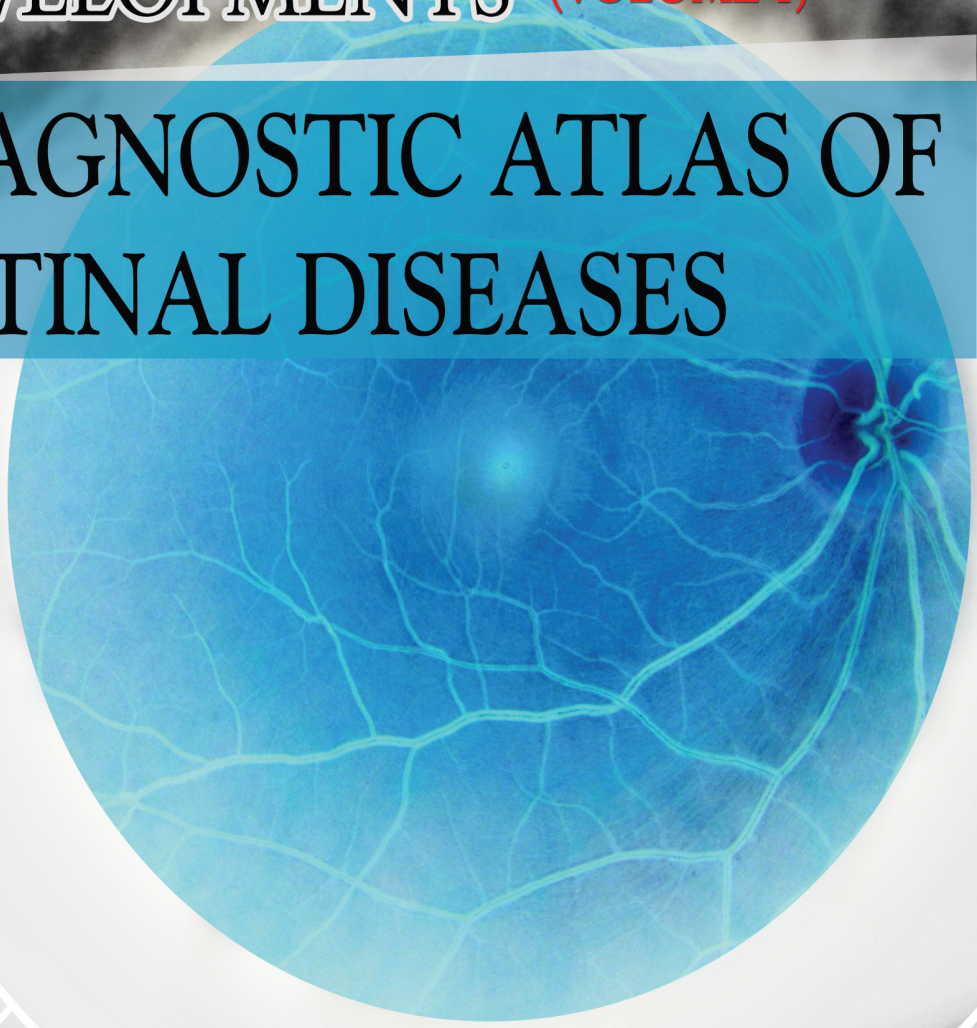
DIAGNOSTIC ATLAS OF RETINAL DISEASES



Editors:
Mitzy E. Torres Soriano
Gerardo García Aguirre
Maximiliano Gordon
Veronica Kon Graversen

Bentham Books

Ophthalmology: Current and Future Developments

Diagnostic Atlas of Retinal Diseases

(Volume 1)

Editors

Mitzy E. Torres Soriano
Unidad Oftalmológica "Dr. Torres López". Centro Médico Cagua, Aragua, Venezuela

Gerardo García Aguirre
Retina Department, Asociación para Evitar la Ceguera en Mexico, Mexico City, Mexico

Co-Editors

Maximiliano Gordon
Centro de la Visión Gordon Manavella, Rosario, Santa Fe, Argentina

Veronica Kon Graversen
University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Ophthalmology: Current and Future Developments

Volume # 1

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FOREWORD

Drs. Torres, García, Gordon and Kon deliver a very useful and practical work that contains, in this volume, a collection of images of retinal vascular diseases and macular diseases. The editors have recruited a vast array of retina specialists from four continents to write the different chapters that constitute this volume. The chapters are structured in such a way that the reader may easily find pearls about the diagnosis, differential and treatment, accompanied by beautiful pictures using different imaging modalities. Our subspecialty has had tremendous advances in recent years regarding diagnostic imaging, and I'm sure ophthalmologists and residents will find this compilation really useful and enjoyable.

Dr. Hugo Quiroz-Mercado
Retina Department
Asociación para evitar la Ceguera en Mexico
Mexico City
Mexico
E-mail: hugoquiroz@yahoo.com

PREFACE

We are honored to contribute to the information and education of ophthalmology students around the world. We have attempted to distill the current knowledge of medical practice and basic science retina research into a diagnostic atlas of retinal diseases. This is a quick-reference atlas eBook of the retina, edited by specialists in the field, essential to any practicing ophthalmologist or resident who has more than a passing interest in diseases and treatment of the retina.

This e-book includes contributors from Mexico, Venezuela, Argentina, Brazil, United States, Denmark, Spain, Italy, Costa Rica and Peru. It is divided into three volumes: Volume I, retinal vascular diseases, choroidal neovascularization related diseases, vitreomacular interface, and other macular disorders; Volume II, traumatic retinopathies, diseases of vitreous, peripheral degenerations, retinal detachment, pediatric retinal diseases, and retinal dystrophies; and Volume III, posterior uveitis, tumors of the retina, and choroid.

This diagnostic atlas eBook of retinal diseases contains full-color, high quality images of the most frequent retinal pathologies with a brief and comprehensive review of retinal diseases. Each chapter includes essentials of diagnosis, differential diagnosis and treatment. The format is concise, well organized, and didactic, without being exhaustive.

We hope and expect that our atlas of retina will facilitate in providing patients with the best possible care.

ACKNOWLEDGEMENTS

We would like to express our gratitude to Judy Soriano, who provided support with english composition and edition.

To our friends and colleagues without whose contribution would not have been possible to realize this project.

We also want to thank the staff of Bentham Science for their help and support and give us the opportunity to publish this eBook.

DEDICATION

This e-book is specially dedicated to Guillermo Manuel Gordon, MD. He inspired us to always work hard and try our best. He was a friend and a recognized ophthalmologist of Rosario-Argentina, who died on May 2nd, 2015.

Dr. Mitzy E. Torres Soriano
Unidad Oftalmológica “Dr. Torres López”,
Centro Médico Cagua,
Aragua,
Venezuela

Dr. Gerardo García Aguirre
Retina Department,
Asociación para Evitar la Ceguera en Mexico,
Mexico City,
Mexico

Dr. Maximiliano Gordon
Centro de la Visión Gordon Manavella,
Rosario, Santa Fe,
Argentina

Dr. Veronica Kon Graversen
University of North Carolina at Chapel Hill,
Chapel Hill, NC,
USA

List of Contributors

Andrés Bastien	Universidad de Buenos Aires-Universidad del Salvador, Retina and Vitreous, Argentina
Aristides J. Mendoza	Retina Department, Centro Oftalmológico de Valencia (CEOVAL), Valencia, Venezuela Retina Department, OftalmoSalud, Arequipa, Peru
Ana Domínguez Yates	Retina Consultants of Charleston, Charleston, South Carolina, USA
Aziz A. Khanifar	Retina Group of Washington, Washington DC, USA
Daniela Roca	Ophthalmology Department, Clínica Ricardo Palma, Lima, Peru
Diego Fernando Mojica	Centro Oftalmológico de Valencia (CEOVAL), Valencia, Venezuela
Daniel D. Kim	Department of Ophthalmology, Henry Ford Health Systems, Detroit, MI, USA
Eleonora Lavaque	Retina Deparmeant, Hospital Oftalmológico Santa Lucia, Buenos Aires, Argentina
Federico Furno Sola	Ophthalmology Service, Sanatorio Mapaci, Rosario, Argentina Grupo Laser Visión, Rosario, Santa Fe, Argentina
Gerardo García Aguirre	Retina Department, Asociación para Evitar la Ceguera en Mexico, Mexico City, Mexico
Guillermo Gordon	Died
Hugo Luglio	Macula D&T, Lima, Peru
Jans Fromow Guerra	Retina Department, Asociación para Evitar la Ceguera en México, IAP, México City, México
Jose A. Roca	Ophthalmology Department, Clínica Ricardo Palma, Lima, Peru
Luis Felipe Rivero	Centro Clínico, de Ojos Maracay, Maracay, Venezuela Centro Oftalmológico Regional Aragua "Filippo Sindoni", Maracay, Venezuela
Luis A. Acabá	Sidney Kimmel College of Medicine, Philadelphia, PA, USA
Liriany Arrieta Ruiz	Unidad Popular de Ojos (UPO), Maracay, Venezuela
Luke B. Lindsell	Retina Group of Washington, Washington DC, USA
Luz Elena Concha del Río	Uveitis Department, Asociación para Evitar la Ceguera en México. I.A.P, Mexico
Luis M. Suarez-Tata	Retina & Vitreous Service, Clínica Oftalmológica El Viñedo, Valencia, Venezuela

Maximiliano Gordon	Centro de la Visión Gordon-Manavella, Rosario, Santa Fe, Argentina
Maria H. Berrocal	Berrocal & Asociados, San Juan, Puerto Rico
Mitzy E. Torres Soriano	Centro de la Visión Gordon-Manavella, Rosario, Santa Fe, Argentina Unidad Oftalmológica "Dr Torres López", Centro Médico Cagua, Aragua, Venezuela
Michael D. Ober	Department of Ophthalmology, Henry Ford Health System, Detroit, MI, USA Retina Consultants of Michigan, Southfield, MI, USA
Michael Larsen	Department of Ophthalmology, Glostrup Hospital and Faculty of Health Sciences, University of Copenhagen, Denmark
Mette K.G. Andersen	Department of Ophthalmology, Glostrup Hospital and Faculty of Health Sciences, University of Copenhagen, Denmark
Manuel Garza León	Department of Medical Sciences, Division of Health Sciences, Universidad de Monterrey, Monterrey, Nuevo León, México
Miguel Pedroza Seres	Uveitis and Ocular Inmunology Department, Instituto de Oftalmología Conde de Valenciana, México, DF. Clínica de Retina, Guadalajara, Jalisco, Mexico
Moravia B. Suarez-Tata	Retina & Vitreous Service, Clínica Oftalmológica El Viñedo, Valencia, Venezuela
Naresh Mandava	Department of Ophthalmology, University of Colorado School of Medicine, Aurora, CO, USA
Nelson Segovia Rodríguez	Retina Department, Grupo de Clínicas IDB, Centro Profesional Arca, Barquisimeto, Venezuela
Paul Baciu	Department of Ophthalmology, Henry Ford Health Systems, Detroit, MI, USA
Raul Velez-Montoya	Retina Department, Asociación para Evitar la Ceguera en México, IAP, Mexico City, Mexico
Rafael Muci Mendoza	Universidad Central de Venezuela, Unidad de Neurooftalmología, Hospital Vargas de Caracas, Venezuela
Rodrigo Lechuga Perezanta	Asociación para Evitar la Ceguera en Mexico, Mexico City, Mexico
Richard Hwang	Vitreoreitnal Disease and Surgery, Department of Ophthalmology, University of Colorado School of Medicine, Aurora, CO, USA
Reinaldo García	Retina & Vitreous Service, Clínica Oftalmológica El Viñedo, Valencia, Venezuela
Silvia Mendoza	Retina Department, Centro Oftalmológico de Valencia (CEOVAL), Valencia, Venezuela

Sandra Zambrano	Centro Oftalmológico de Valencia (CEOVAL), Valencia, Venezuela
Virgilio Morales Cantón	Retina Department, Asociación para Evitar la Ceguera en Mexico, Mexico City, Mexico
Veronica Kon Graversen	University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
Virgil Alfaro	Retina Consultants of Charleston, Charleston, South Carolina, USA
Yogin Patel	Department of Ophthalmology, Henry Ford Health System, Detroit, MI, USA

CHAPTER 1

Non-Proliferative Diabetic Retinopathy

Luis Felipe Rivero[1,2,*] and **Maximiliano Gordon**[3]

[1] *Centro Clínico de Ojos Maracay, Maracay, Venezuela*

[2] *Centro Oftalmológico Regional Aragua "Filippo Sindoni", Maracay, Venezuela*

[3] *Centro de la Visión Gordon-Manavella, Rosario, Santa Fe, Argentina*

Diabetic retinopathy (DR) is the most frequent ocular complication in patients with diabetes mellitus. Its early and moderate stages are called non-proliferative diabetic retinopathy (NPDR). It is characterized clinically by the presence of one or more of the following signs: microaneurysms, intraretinal hemorrhages, intraretinal microvascular anomalies (IRMA), cotton-wool spots (CWS), hard exudates, and venous beading.

ESSENTIALS OF DIAGNOSIS

The hallmark of DR is the development of microaneurysms, which are small dilations of the capillaries due to weakening of their walls and the loss of pericytes [1]. They appear clinically as tiny red dots in the retinal stroma, predominantly in and around the posterior pole. Eventually they may break, leading to the formation of intraretinal hemorrhages. When the broken microaneurysms are located in the most superficial layers of the retina, the hemorrhage will take a flame or splinter-like appearance, oriented along the nerve fiber layer. When they are located in the deeper layers, the hemorrhage will look like a red dot or blot. Clinically, microaneurysms and dot hemorrhages are indistinguishable (Fig. **1**), so they are referred to as hemorrhages and/or microaneurysms (H/Ma). Unless clotted, microaneurysms will show as hyperfluorescent points in a fluorescein angiogram (FA). They may or may not

* **Corresponding author Luis Felipe Rivero:** Centro Clínico de Ojos Maracay, Av. José María Vargas N° 18, Maracay 2101, Edo. Aragua, Venezuela; Tel: +58(243) 241-8324/5243; E-mail: luife2020@hotmail.com

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leak dye depending on the integrity of their walls (Fig. **2**). In an optic coherence tomography (OCT), they appear as hyperreflective rings usually located in the middle retinal layers [2] (Fig. **3**). The smaller intraretinal hemorrhages will hardly show in the FA, while the larger ones block the dye (Fig. **4**). The largest intraretinal hemorrhages may be seen in an OCT as moderately hyperreflective masses located in the inner retinal layers.

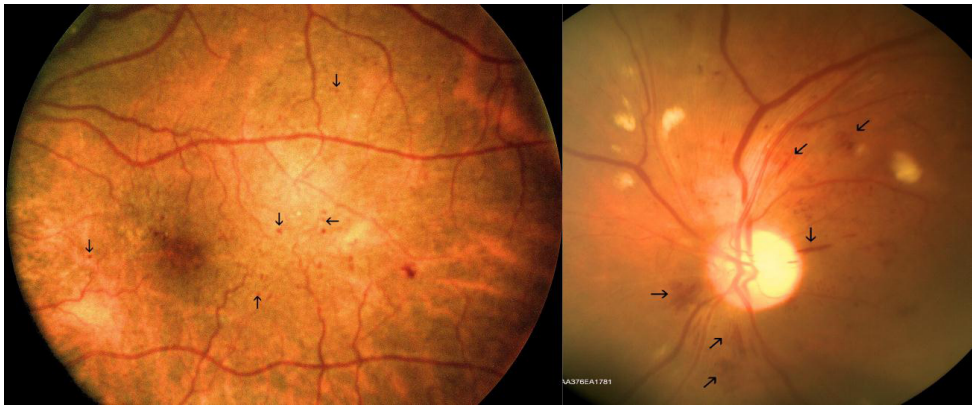

Fig. (1). Intraretinal hemorrhages and microaneurysms. **Left**: Both deep intraretinal hemorrhages and microaneurysms (H/Ma) appear as small red points and dots. Some of them are pointed with arrows. **Right**: Superficial intraretinal hemorrhages have a splinter or flame shape (some of them are pointed with arrows). Note that superficial hemorrhages as well as CWS follow the striations of the nerve fiber layer.

Capillary wall damage will lead to leakage of fluids and macromolecules. These will accumulate in the retinal stroma producing macular edema, which can be observed as areas of thickening of the retina. Lipoproteins diffusing from microaneurysms or weakened capillaries will be trapped at the outer plexiform layer forming the so-called hard exudates. They are irregularly shaped yellow-white spots located slightly deeper in the retina and may coalesce with each other, forming streaks, clusters or a circinate pattern centered on the leaking structure (Fig. **5**). They may accumulate in the center of the fovea forming a dense plaque, which carries a very bad visual prognosis [3]. They are not usually seen on a FA, except when they are extremely dense, causing minimum blockage of the dye. On the OCT they appear as markedly hyperreflective and irregular interstitial images with posterior shadowing (Fig. **6**).

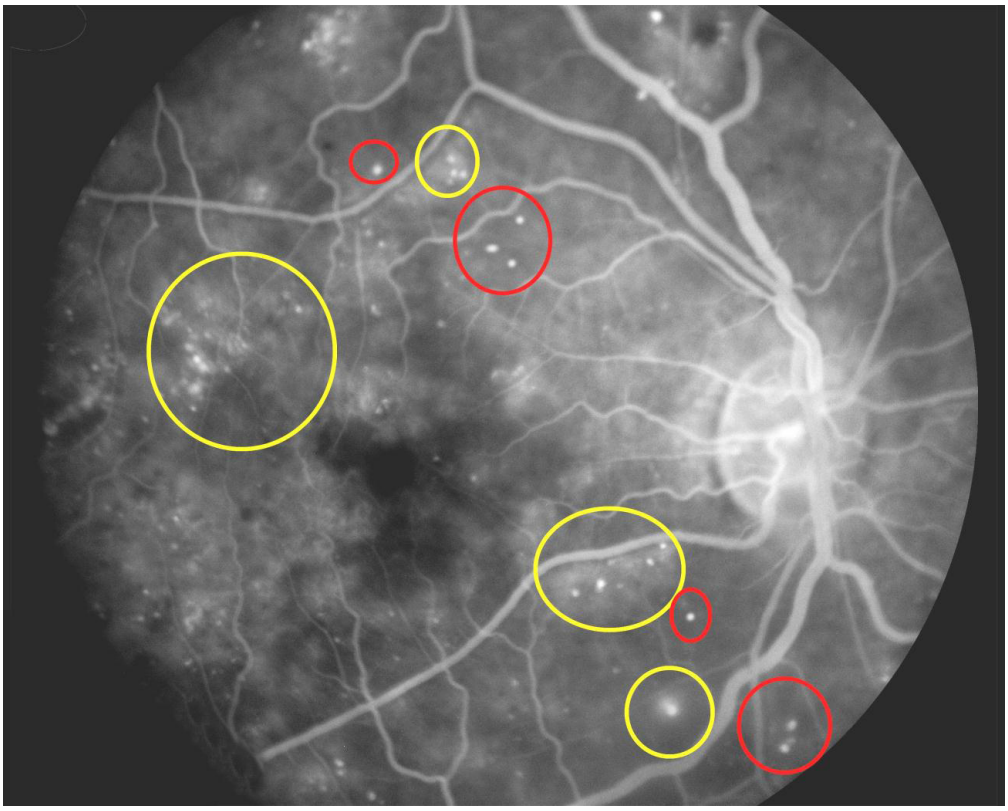

Fig. (2). Fluorescein angiogram showing microaneurysms. They can be observed as well-defined hyper-fluorescent (white) dots, appearing in the early phases of the study. Non-leaking microaneurysms will remain as well-defined dots throughout the angiogram (some are circled in red). Leaking microaneurysms develop a hazy area around them that increases along the study (some are circled in yellow).

As diabetic retinopathy progresses, there will be further damage to the arterioles and capillaries, leading to progressive ischemia. Focal ischemia in the inner layers will result in the arrest of the axoplasmic flow with the subsequent dilation of the axons, constituting the so-called CWS [4]. Clinically they present as small superficial grey-white fluffy spots with feathery borders (Fig. **7**). They are usually located near the temporal arcades and near the disc in the nasal retina. They look hypofluorescent in the FA (Fig. **4**). In an OCT they appear as more or less pronounced focal thickenings of the nerve fiber layer with enhanced hyperreflectivity (Fig. **8**). Over some 6 to 12 months CWS will eventually fade, leaving almost no signs of their former presence but relative scotomata [5] and nicks in the inner retinal layers [6].

CHAPTER 2

Proliferative Diabetic Retinopathy (PDR)

Maria H. Berrocal[1,*] and **Luis A. Acabá**[2]

[1] *Berrocal & Asociados, San Juan, Puerto Rico*

[2] *Sidney Kimmel College of Medicine, Philadelphia, PA, USA*

ESSENTIALS OF DIAGNOSIS

Proliferative diabetic retinopathy (PDR) occurs as a progression of severe diabetic vascular damage and includes intraretinal capillary closure with resultant ischemia and the formation of new vessels (Figs. **1-3**). Severe non-proliferative diabetic retinopathy is the precursor of PDR. It includes diffuse intraretinal hemorrhages in 4 quadrants, venous beading in 2 quadrants or more and intra-retinal microvascular abnormalities (IRMA) in 1 quadrant. The chance of progression to PDR in 1 year is between 15% and 45% [1, 2].

Severe NPDR can be confused with PDR. Fluorescein angiography is the best way to differentiate IRMA from neovascularization as the latter shows significant leakage throughout the study. The evolution of new vessels starts with fine vessels with minimal fibrosis, then an increase in vessel size and fibrous tissue, and then the end stage of PDR which includes regressed vessels and significant fibrovascular proliferation on the posterior hyaloid. Vitreous hemorrhage and sub-hyaloid hemorrhage can result from PDR.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis includes NPDR particularly when many IRMAs are present, other retinovascular diseases like vein occlusions, sickle cell retinopathy,

[*] **Corresponding author Maria H. Berrocal:** 150 Ave De Diego Ste 404, San Juan, 00907, Puerto Rico; Tel: (787) 725-9315; E-mail: mariahberrocal@hotmail.com

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leukemic retinopathy, hypertensive retinopathy, radiation retinopathy, retinal vasculitis, sarcoidosis, and ocular ischemic syndrome. Differences in the clinical picture and fluorescein angiographic appearance are usually sufficient to discriminate bet-ween these entities.

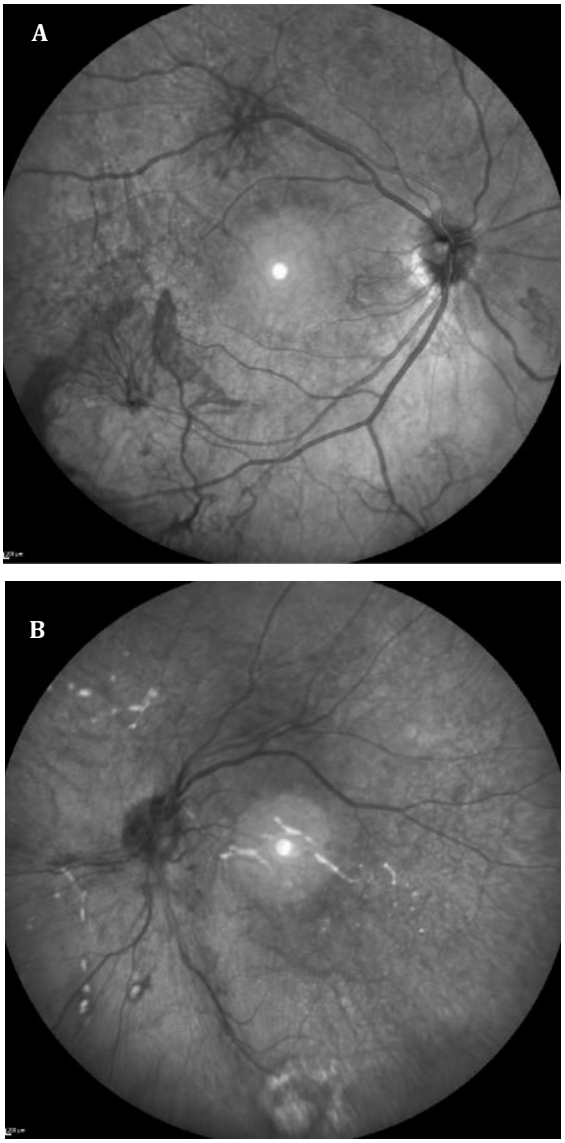

Fig. (1). A. Red-free image of the right eye of a 35 year-old male with prominent neovascularization in the posterior pole; **B**. Red-free image of the left eye in the same patient, showing neovascularization and exudates.

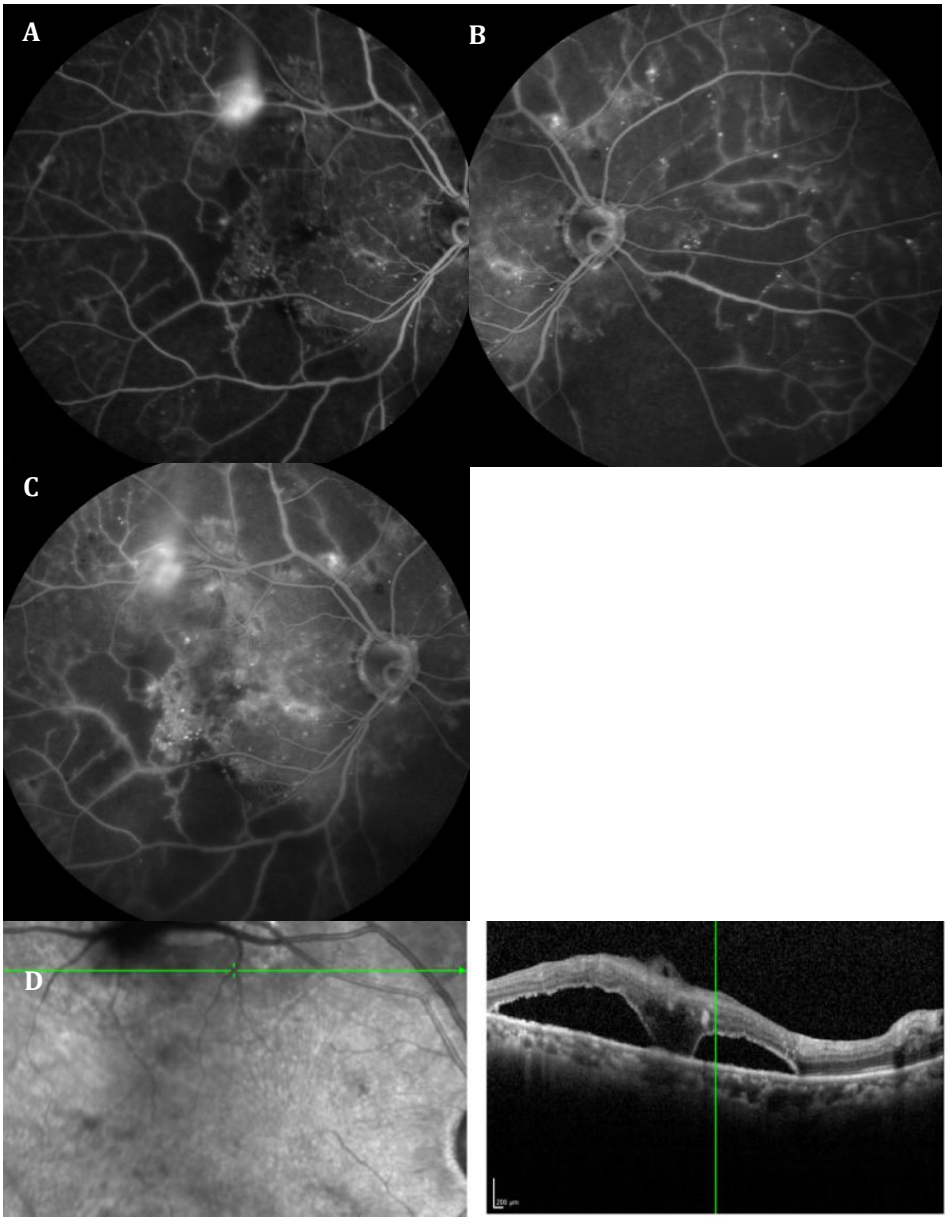

Fig. (2-I). 66-year-old male with type 1 diabetes mellitus and proliferative diabetic retinopathy. **A**. Early fluorescein angiography (FA) of the right eye showing multiple areas of capillary dropout and ischemia, including the foveal area with enlarged foveal avascular zone. One area of NVE is present in the superotemporal arcade; **B**. FA of the nasal retina with severe ischemia and capillary leakage; **C**. Late FA of the same eye, showing diffused leakage in the posterior pole; **D**. OCT of retinal area near neovascularization showing areas of localized tractional retinal detachment.

CHAPTER 3

Diabetic Macular Edema

Maximiliano Gordon[1,2,*] and **Mitzy E. Torres Soriano**[1,2,3]

[1] *Centro de la Visión Gordon-Manavella, Rosario, Santa Fe, Argentina*

[2] *Retina Department, Ophthalmology Service, Hospital Provincial del Centenario, Rosario, Santa Fe, Argentina*

[3] *Unidad Oftalmológica "Dr Torres López", Centro Médico Cagua, Aragua, Venezuela*

Diabetic macular edema (DME) is the main cause of visual loss in diabetic patients. It may present at every stage of diabetic retinopathy.

The systemic risk factors identified for DME are hyperglycemia, arterial hypertension, hyperlipidemia, kidney failure and anemia [1, 2].

ESSENTIALS OF DIAGNOSIS

Diabetic macular edema is diagnosed with a detailed bio-microscopic examination with the slit lamp and indirect ophthalmoscopy.

The Early Treatment Diabetic Retinopathy Study (ETDRS) described DME as retinal thickening or hard exudates (consisting of lipoproteins) within 1 disk diameter of the center of the macula (Figs. **1**, **2**, **4a**, **5a-b**, **6a**, **8**, **11a**).

The term clinically significant macular edema (CSME) indicates the severity of macular edema and is used for treatment guidelines. CSME is characterized by: 1) thickening of the retina within 500 μm of the macular center; 2) hard exudates at the center of the retina or within 500 μm with thickening of adjacent retina; and 3) one or more disc diameters of retinal thickening, part of which is within one disc diameter of the center of the macula [3].

[*] **Corresponding author Maximiliano Gordon:** Centro de la Vision Gordon - Manavella, Montevideo 763, CP 2000, Rosario - Santa Fe, Argentina; Tel: +54 (0341) 4 400 239; E-mail: maximilianogordon19@gmail.com

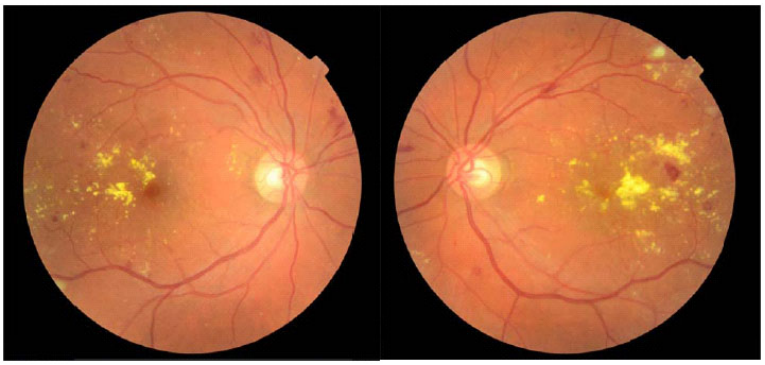

Fig. (1). Fundus photograph of CSME in both eyes. Microaneurysms, hard exudates and retinal hemorrhages are shown.

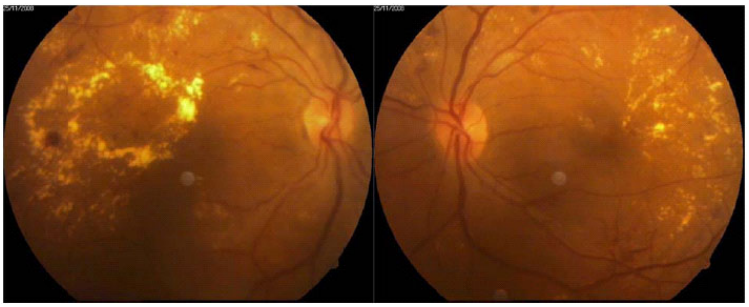

Fig. (2). Fundus photograph of severe and clinically significant diabetic macular edema in both eyes.

In 2002, the American Academy of Ophthalmology proposed an international classification of DME (Table **1**): DME absent: absence of retinal thickening or hard exudates in the posterior pole. DME present: some retinal thickening or hard exudates in the posterior pole.

Table 1. International clinical diabetic macular edema (DME) disease severity scale.

Proposed Disease Severity Level	**Findings observable on Dilated Ophthalmoscopy**
Mild DME	Some retinal thickening or hard exudates in posterior pole but far from the macula center
Moderate DME	Retinal thickening or hard exudates that approach the macular center but without involving it
Severe DME	Retinal thickening or hard exudates involving the macula center

Program and abstracts of the American Academy of Ophthalmology 2002 [4].

Classically, three different types of DME can be observed in fluorescein angiography (FA): 1) focal leakage: well-defined focal area of leakage from micro-aneurysms or dilated capillaries (Figs. **3**-**6**); 2) diffuse leakage: wide-spread leakage from IRMA, retinal capillary bed (Fig. **7**); and 3) diffuse cystoid leakage: diffuse leakage and pooling of dye in the cystic spaces of the macula in the late phase of the angiogram [5]. However, one of the most important utilities of the angiography is to roll out macular ischemia (Fig. **7**). It has long been considered that ischemic changes and microvascular pathologies are key in the development of DME. In diabetic retinopathy, peripheral ischemia leads to an increased production of vascular endothelial growth factor (VEGF), which can result in the breakdown of blood-retinal barriers, thus increasing retinal vessel permeability and causing DME. These areas can be detected using ultra-wide field fluorescein angiography [6].

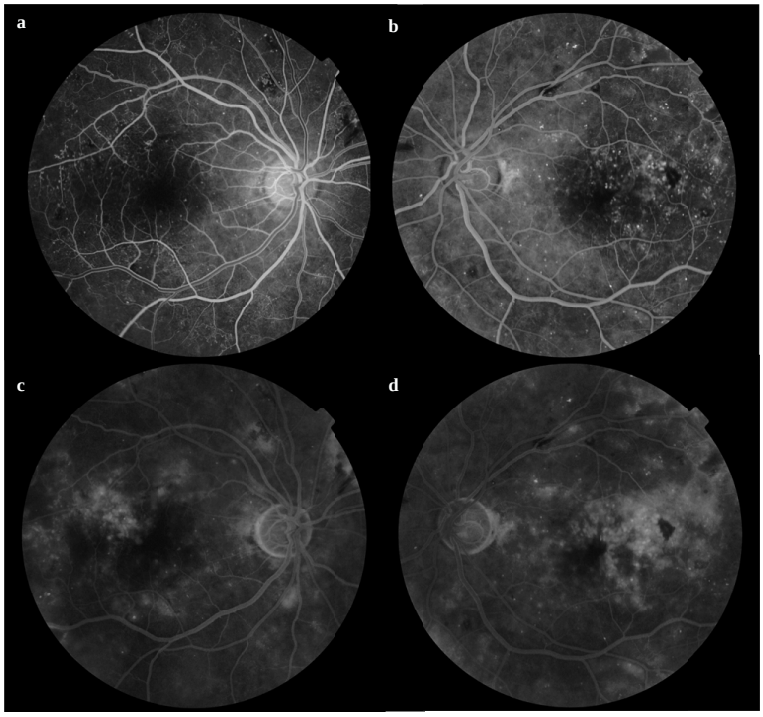

Fig. (3). FA of the same patient as shown in Fig. (**1**). (**a-b**) Multiple hyperfluorescent points due to mycroaneurisms with mild leakage in late phases (**c-d**).

CHAPTER 4

Central Retinal Vein Occlusion

Nelson Segovia Rodríguez*

Retina Department, Grupo de Clínicas IDB, Centro Profesional Arca, Barquisimeto, Venezuela

Central retinal vein occlusion (CRVO), a member of the group of vascular retinal diseases, is a sight-threatening condition that needs to be correctly diagnosed and treated in order to diminish its consequences, which can lead to painful blindness if neovascular glaucoma (NVG) develops. CRVO occurs predominantly in adults of 65 years old and over [1]; the prevalence does not differ by gender [2], and it is predominantly unilateral [3]. Some described systemic risk factors are end-organ damage from hypertension or diabetes, a hypercoagulable state, and a diagnosis of stroke or obstructive sleep apnea [4, 5]. The most described ocular risk factor is glaucoma. Patients with CRVO also show an increased (almost two-fold) incidence in cerebrovascular accidents compared with age and sex-matched controls in a US population [6].

ESSENTIALS OF DIAGNOSIS

Fortunately, this is a relatively easy condition to diagnose based mostly on its clinical features. CRVO commonly presents as a sudden and painless loss of vision. Occasionally, the vision loss occurs gradually, mostly happens at night time in the recumbent position probably by low blood pressure and/or high central venous pressure. The typical fundoscopic features appear in all the four quadrants of the fundus: venous tortuosity and dilation, retinal hemorrhages (scattered superficial and deep), and cotton wool spots (Figs. **1**-**3**). Macular edema and optic disc swelling are also present. All these features are present in varying degrees depending on the severity of the occlusion. Long-standing CRVO should be

* **Corresponding author Nelson Segovia Rodríguez:** Retina Department, Grupo de Clínicas IDB, Centro Profesional Arca, Barquisimeto, Venezuela; Tel: +57(315)5929618; Email: nelsegovia@yahoo.com

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suspected if occluded or sheathed retinal veins are observed, or if vascular anastomoses (known as optociliary collaterals) at the optic disc are detected (Fig. **4**).

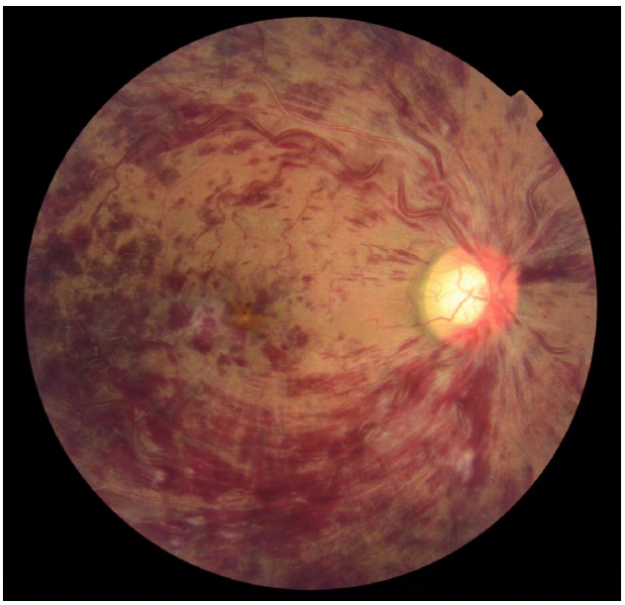

Fig. (1). Central Retinal Vein Occlusion. Fundus photograph shows tortuosity and dilatation of all branches of the central retinal vein, dot and flame-shaped hemorrhages, macular edema and optic nerve head cupping is noted. (Courtesy of Mitzy E. Torres Soriano).

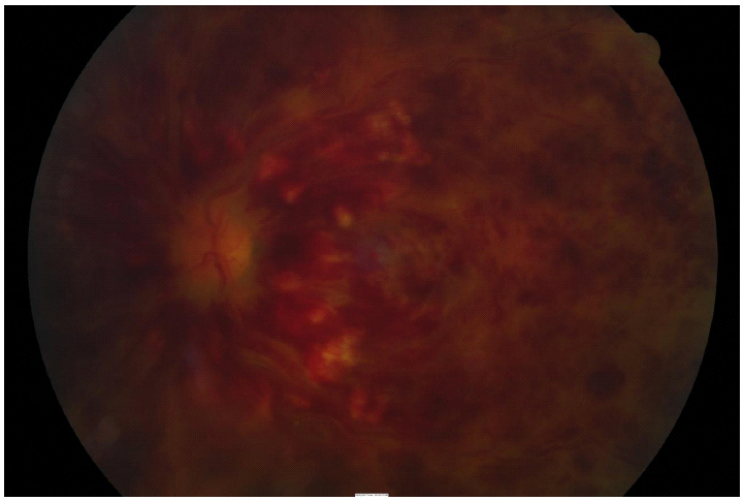

Fig. (2). Fundus photograph showing massive intraretinal hemorrhages, venular tortuosity, cotton wool spots and macular edema, corresponding to an ischemic CRVO.

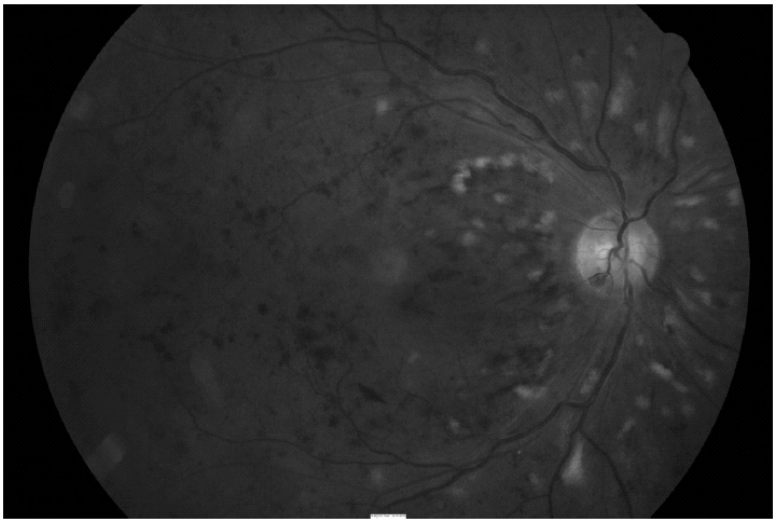

Fig. (3). Red-free photograph shows the typical features of CRVO, corresponding to a non-ischemic CRVO.

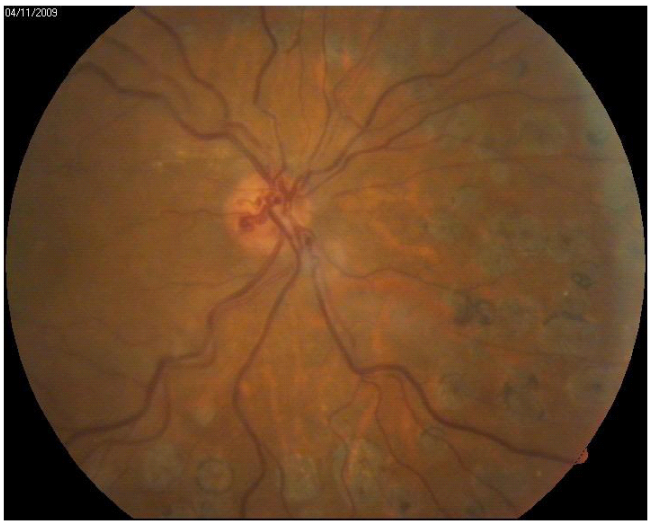

Fig. (4). Eye fundus of a patient with long standing CRVO demonstrating optociliary shunts vessels (optociliary collaterals) in the optic nerve head, and panretinal photocoagulation.

CRVO can be divided into 2 clinical types, ischemic and non-ischemic. Non-ischemic CRVO (Figs. **3**, **5**, **6**) is the most common type, accounting for about 75% CRVO cases. Non-ischemic CRVO is characterized by mild to moderate loss of acuity, usually 20/200 or better, and an absent or mild relative afferent pupillary defect. Conversion to ischemic CRVO occurs in 15% of cases within 4

CHAPTER 5

Branch Retinal Vein Occlusion

Liriany Arrieta Ruiz[1] and **Gerardo García Aguirre**[2,*]

[1] *Unidad Popular de Ojos (UPO), Maracay, Venezuela*

[2] *Retina Department, Asociación para Evitar la Ceguera en Mexico, Mexico City, Mexico*

Branch Retinal Vein Occlusion (BRVO) is a common retinal vascular disease caused by the occlusion of one of the branches of the central retinal vein, affecting only a portion, typically a quadrant, of the posterior pole [1]. It is three times more common than the central retinal vein occlusion, and onset usually occurs in the elderly. There are some risks factors for its development: hypertension, cardiovascular disease, obesity and open angle glaucoma.

ESSENTIALS OF DIAGNOSIS

Patients usually complain of a sudden onset of blurred vision or central visual field defect.

Upon ophthalmologic examination, typical findings include superficial hemorrhages, which are usually flame-shaped, retinal edema, and cotton-wool spots in a sector of retina drained by the affected vein (Figs. **1**-**3**). The horizontal raphe is respected.

In the chronic stage (Fig. **4**), hemorrhages may be absent and macular edema with telangiectatic vessels can be observed, extending across the horizontal raphe. The quadrant most commonly affected is the superotemporal (63%) [2].

* **Corresponding author Gerardo García Aguirre:** Retina Department, Asociación para Evitar la Ceguera en Mexico, Vicente García Torres 46, San Lucas Coyoacan, Mexico City 04030, Mexico; Tel: +52 (55) 10841400; Email: jerry_gar_md@yahoo.com

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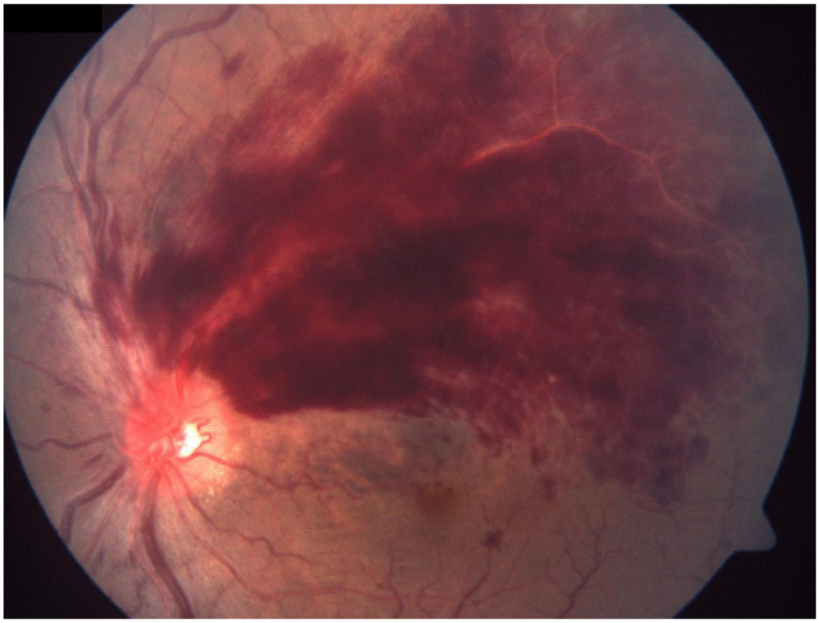

Fig. (1). Flamed-shaped hemorrhages and retinal edema in superior macular area. (Courtesy of Gerardo Garcia Aguirre (Mexico)).

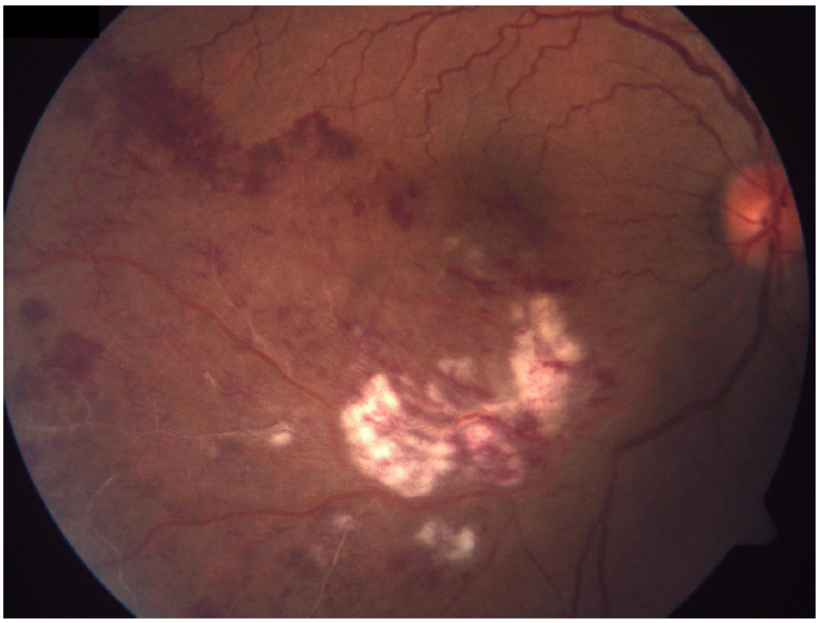

Fig. (2). Retinal hemorrhages, cotton-wool spots and sclerotic vessels in inferotemporal BRVO. (Courtesy of Gerardo Garcia Aguirre (Mexico)).

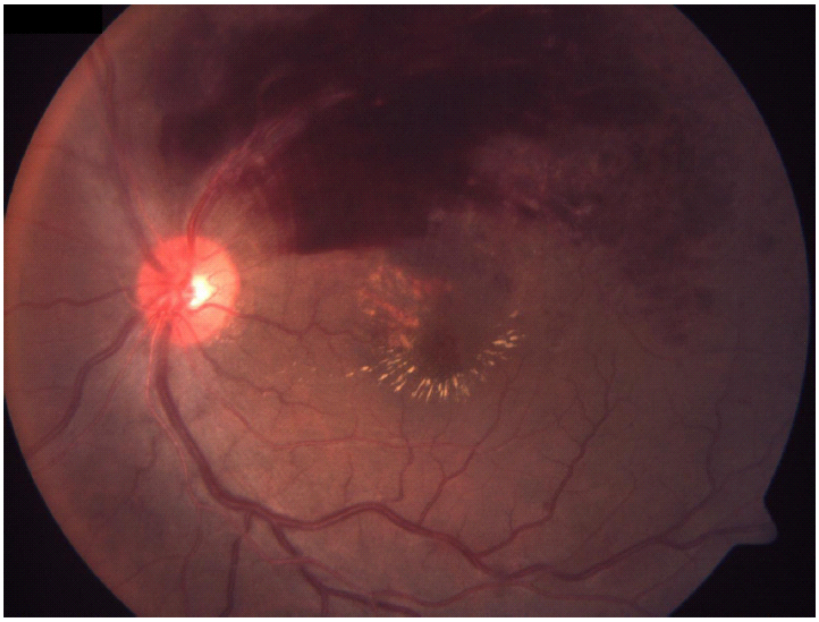

Fig. (3). Intraretinal hemorrhages in the superotemporal area and macular edema. (Courtesy of Gerardo Garcia Aguirre (Mexico)).

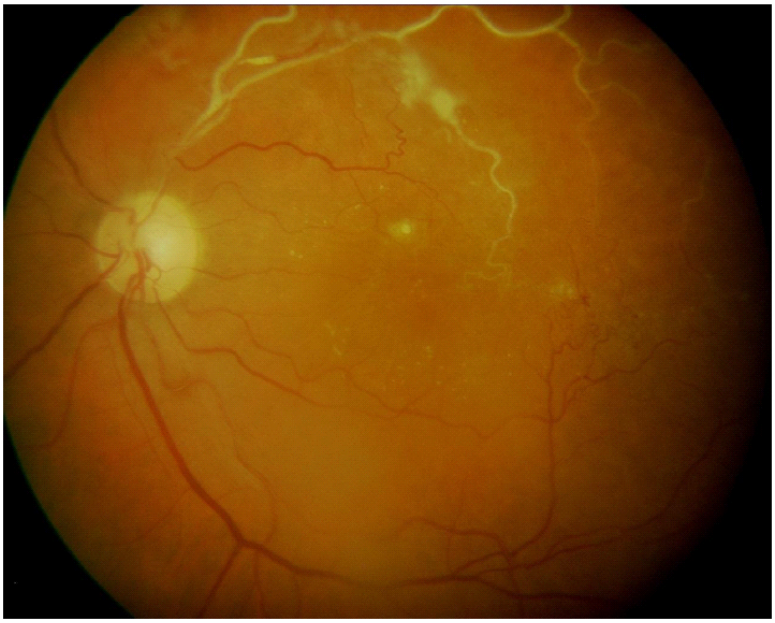

Fig. (4). Left eye: Chronic superior temporal branch retinal vein occlusion, sclerotic vessels and neovascularization. Courtesy of Luis Miguel Suarez Tata MD (Venezuela).

CHAPTER 6

A Three-Dimensional Look into Hypertensive Retinopathy

Rafael Muci Mendoza*

Universidad Central de Venezuela, Unidad de Neurooftalmología, Hospital Vargas de Caracas, Venezuela

ESSENTIALS OF DIAGNOSIS

The amount of arteriolar damage signals the individual prognosis of a hypertensive subject; therefore, any information about its severity will be extremely helpful in a practical way. Arteriolosclerosis is the hardening and narrowing of the arterioles secondary to systemic arterial hypertension [1]. Fundoscopic changes reflect the duration, severity, and the right way to control hypertension, so monitoring the changes in the retina, the choroid, and the optic nerve will help the physician determine the best course of care of the hypertensive patient. "Essential" or "primary" hypertension is a pathological condition characterized by endothelial dysfunction that affects vessel structure and tone, thus causing constriction of blood vessels and narrowing of small arteries and arterioles in the peripheral vascular bed. It is a silent disease and its injurious effect begins many years before organic damage becomes clinically apparent [2, 3]. Arteriosclerosis follows chronic arterial hypertension like a shadow [4]. The amount of arteriolar damage is the essential piece of information that signals the individual prognosis of a hypertensive subject [5, 6]. Retinal arterioles share similar anatomical, physiological and embryological characteristics with cerebral, coronary and renal arterioles. Thus, the ocular fundus and the retina are like doors open to medical curiosity that enable noninvasive, *in vivo* testing of circulation,

* **Corresponding author Rafael Muci Mendoza:** Universidad Central de Venezuela, Unidad de Neurooftalmología, Hospital Vargas de Caracas, Venezuela; Email: rafalemuci@gmail.com

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since a direct fundoscopy allows for easy and bedside observation of the arterioles. This can lead to extremely important data when the resulting information is applied to other arterial territories [2].

When considered individually, the fundoscopic technique gains more importance than a blood pressure check. The reason is that it provides first-hand knowledge to the trained eye about past and future events in the disease natural history, thus providing a *three dimensional look into hypertensive patients*: 1) The acute or insidious damage to the arteries in the past, since the chronic form causes progressive arteriolosclerotic changes, unlike recently diagnosed hypertension; 2) "*Here and now*": the current situation of arteriolar and retinal damage, manifestation of the process activity, probable diastolic blood pressure readings, and, especially, which phase of the evolution process the patient is going through: incorrectly called benign hypertension *vs.* accelerated-malignant hypertension; 3) The possibility of differentiating "secondary" forms of hypertension and primary hypertension, and even the possibility of going deeper into the etiologic diagnosis; 4) Prognosis of the disease in untreated patients; and 5) Objective assessment of the response to different invasive and noninvasive treatments [4].

We consider the following fundoscopic changes of hypertension, which depend on diastolic blood pressure readings:

- Arteriolar signs typical of chronic hypertension. 1) Diffuse constriction that is difficult to observe if it is not in youthful vessels with normal auto regulation (pregnancy toxemia, acute diffuse glomerulonephritis). It is reversible. 2) Focal or localized constriction: apparent notches along the arterioles where caliber narrows and axial reflex is less bright. They are easily visible and constitute morphological wall changes that cannot be reversed with treatment. A significant number of them suggest left ventricular hypertrophy (Fig. **1**). 3) Irreversible generalized arteriolosclerosis: This means long-standing hypertension. It manifests as exaggerated axial reflex over arterioles, copper wiring and silver wiring of arterioles, sheathing of arterioles, and arteriolovenous crossing changes in its four grades of progressive severity: concealment, tapering, deflection with depression and compression (Figs. **1**-**8**).

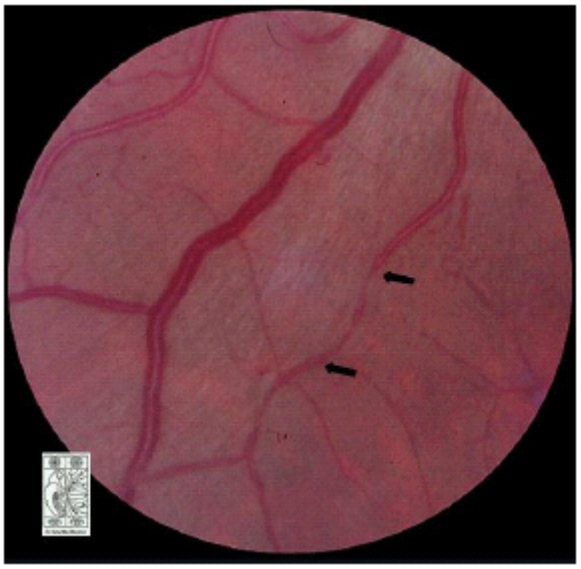

Fig. (1). Hypertensive arteriolosclerosis – time function: Arteriolar narrowing and focal narrowing.

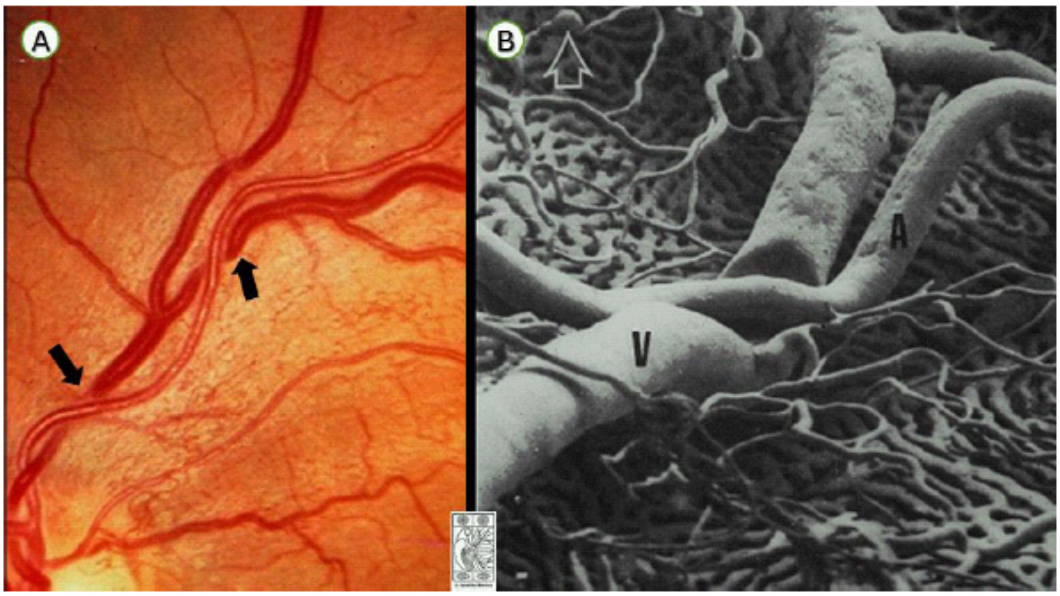

Fig. (2). (**A**) Chronic hypertensive arteriolosclerosis: Copper wiring of arteriole. Abnormal arteriolovenous crossing of higher grade. Notice that the end that is distal from the crossing is wider than the proximal end, which denotes compression. A thin layer of collateral vessels can be seen adjacent to the optic disc. (**B**) Abnormal crossing (scanning microscopy).

CHAPTER 7

Central Retinal Artery Occlusion

Silvia Mendoza[1], Sandra Zambrano[2], Diego Fernando Mojica[2] and **Mitzy E. Torres Soriano[3,*]**

[1] *Retina Department, Centro Oftalmológico de Valencia (CEOVAL), Valencia, Venezuela*

[2] *Centro Oftalmológico de Valencia (CEOVAL), Valencia, Venezuela*

[3] *Centro de la Visión Gordon-Manavella, Rosario-Santa Fe, Argentina*

Central retinal artery occlusion is a vaso-occlusive ischemic disease that causes a sudden painless loss of vision usually irreversible and unilateral. Incidence is 1 to 15 cases per 10,000 it generally occurs in the elderly, and is usually accompanied by an afferent pupillary defect [1 - 3].

The most frequent causes of obstruction of blood flow are:

1. Atherosclerosis: The deposits of cholesterol and other particles form atherosclerotic plaques. They slowly thicken towards the artery lumen causing obliteration or even complete obstruction.
2. Embolism: The ophthalmic artery is the first branch of the internal carotid artery. When the artery lumen narrows by plaques containing cholesterol or other particles, some pieces can break off, blocking the flow of the ophthalmic artery, central retinal artery or one of its branches. The severity of vision loss depends on the area of obstruction.
3. Collagenosis and coagulopathy [3 - 5].

Risk factors: Hypertension, hypercholesterolemia, blood dyscrasias, vasculitis.

[*] **Corresponding author Mitzy E. Torres Soriano:** Centro de la Visión Gordon-Manavella, Montevideo 763, CP 2000, Rosario - Santa Fe, Argentina; Tel: +54 (0341) 4400239; E-mail: mitzytorres@yahoo.com

ESSENTIALS OF DIAGNOSIS

Symptoms

- Sudden painless loss of vision can last for seconds, minutes or be permanent.
- Usually unilateral.
- Loss of the entire visual field if the central retinal artery is affected or partial loss if a branch is affected.
- Most patients have a history of previous episodes of amaurosis fugax.

Fundus Findings

- Whitish discoloration of the retina, due to edema of the inner retinal layers, especially at the posterior pole where the nerve fiber layer and ganglion cell layer are thickest (Figs. **1**-**4**) [1 - 6].

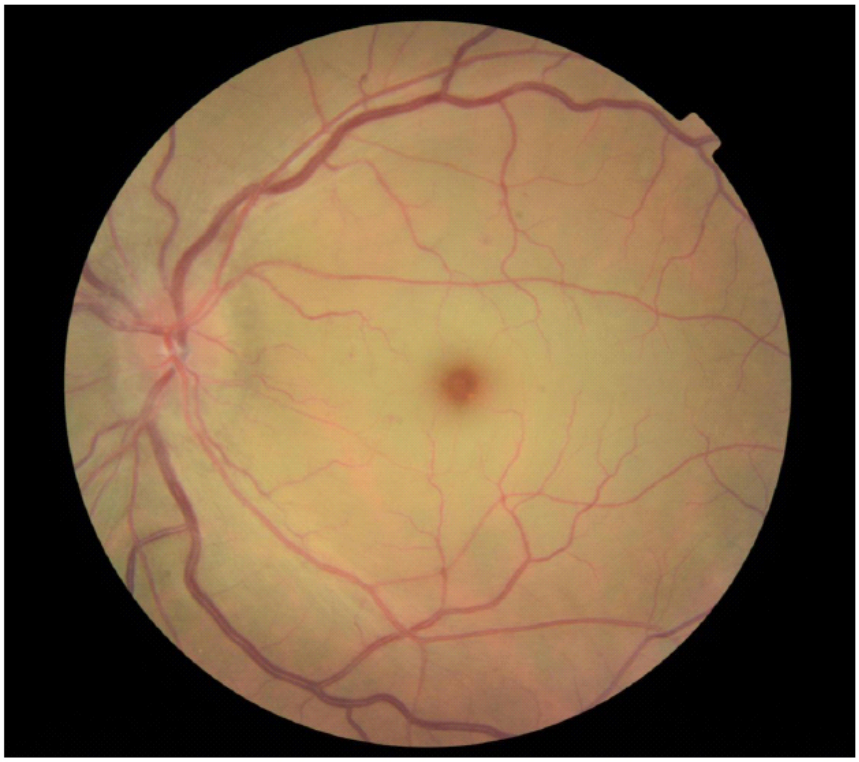

Fig. (1). Central retinal artery occlusion: Note pale retina, narrowed arterioles and “cherry red spot” in macula.

- Cherry-red spot. Visualization of the choroid and retinal pigment epithelium with xanthophyll pigment in the foveal area, surrounded by edematous retina (Figs. **1**-**4**) [1 - 5].
- Retinal arterial attenuation [4].
- Optic disc edema and pallor [4].
- At later stages, fundoscopic findings include optic atrophy, retinal arterial attenuation, cilioretinal collaterals, and macular retinal pigment epithelial changes [4].

Complementary Exams

- Fluorescein angiography: to assess if the arterial obstruction is complete or partial and to determine if there is reperfusion (Figs. **2**, **4**).

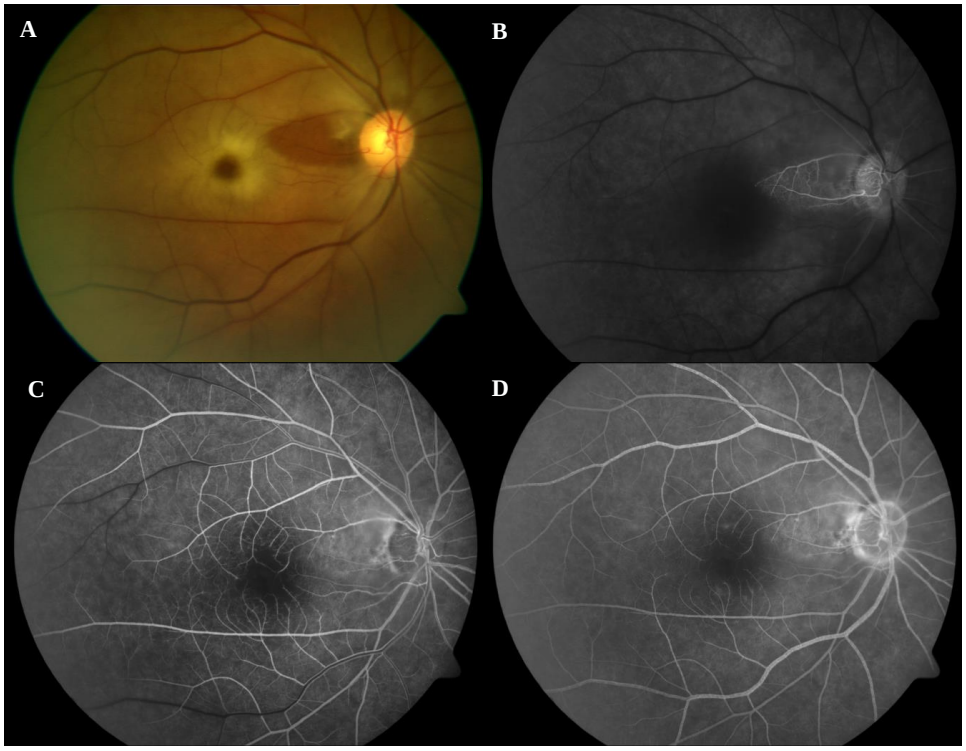

Fig. (2). A. Fundus photograph showing retinal pallor and a cherry-red spot. **B** and **C**. Early to mid stages of the fluorescein angiogram showing significant delay in the vascular filling. There is a small area adjacent to the optic disc that is still perfused by a cilioretinal artery. **D**. Late Phase of the Angiogram.

CHAPTER 8

Branch Retinal Artery Occlusion and Cilioretinal Artery Occlusion

Raul Velez-Montoya*

Retina Department, Asociación para Evitar la Ceguera en México, IAP. Mexico City, Mexico

Branch retinal artery occlusion (BRAO) is an arterial occlusive disease in which the obstruction of blood flow is located after the bifurcation of the central retinal artery in its major branches. The severity of the clinical manifestations will depend on the exact localization of the obstruction which can be found anywhere from the emergence of the major temporal or nasal arcades to the small capillary arterioles [1, 2].

BRAOs are thought to represent 38% of all acute retinal artery obstructions [3]. It is classified according to its visual outcome in *transient* and *permanent* BRAO [2, 4, 5]. Diabetes mellitus, arterial hypertension, ischemic heart disease, and transient ischemic attacks/cerebrovascular accidents are more prevalent in patients with BRAO than the matched US population ($p<0.001$) [2]. Smoking prevalence in female patients with BRAO is higher; although this association has not been proven in male patients. When comparing BRAO with central retinal artery occlusion (CRAO), only diabetes mellitus has a slightly higher prevalence among patients with CRAO [2].

Embolism is the most common cause of BRAO [5, 7]. There are three main types or retinal emboli: calcific (10.5%), cholesterol (74%), and platelet-fibrin (15.5%) [6, 7]. The most common sources of emboli are the carotid artery (plaque) and the heart (valvular lesions, atrial fibrillation, patent foramen ovale, tumors in left

* **Corresponding author Raul Velez-Montoya:** Retina Department, Asociación para Evitar la Ceguera en México, Vicente García Torres, 46. San Lucas Coyoacán, México DF.04030; México; Tel: +52.55.10841400; Fax: +52.55.10841404; Email: rvelezmx@yahoo.com

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atrium and myxoma) [8]. Due to the fact that microemboli are responsible for most BRAO, and the major source of microemboli is an arterial plaque, the absence of an abnormal carotid doppler does not rule out the carotid artery as the source of microemboli [7, 9].

ESSENTIALS OF DIAGNOSIS

Conversely to CRAO patients, in which visual loss can be severe (light perception) at presentation, more than 70% of patients with *permanent* BRAO, seen within 7 days of onset, will have 20/40 or better at the initial visit especially if the affected vessel is the inferior temporal artery. Furthermore, 80% of patients with decreased visual acuity (VA) at presentation (worse than 20/40) will experience an improvement of VA within 1 week after onset. Final VA of 20/40 or better is seen in 89% of patients, and only 3% of eyes experience a worsening of VA during follow-up. The most frequently reported visual field defects are a central scotoma (20%) and inferior central altitudinal defect (13%), which tend to improve in 47% of the cases within 1 week of onset. In patients with *transient* BRAO, VA at presentation of 20/40 or better is seen in more than 90% of cases. The central and peripheral visual field remains normal. Final VA tends to be 20/40 or better in virtually all cases, regardless of VA at onset (even if it was worse than 20/40) [1, 5].

During the acute phase of the disease, an area of retinal pallor corresponding to the area of compromised blood flow and oncotic damage (swelling) can be identified on fundus examination (Figs. **1**, **2**) [10 - 12]. However, the initial pallor is replaced by the normal sheen of the fundus in long-standing cases, making it more difficult to diagnose [10]. If there is enough ischemia, cotton-wool spots will develop 6 to 18 hours after onset, especially if the affected vessel is large enough and close to the posterior pole where the nerve fiber layer is thicker [13, 14]. A retinal emboli is seen in 47% of cases. However, its absence does not rule out an embolic case because it may have disintegrated, migrated and disappeared by the time the eye is examined [15, 16].

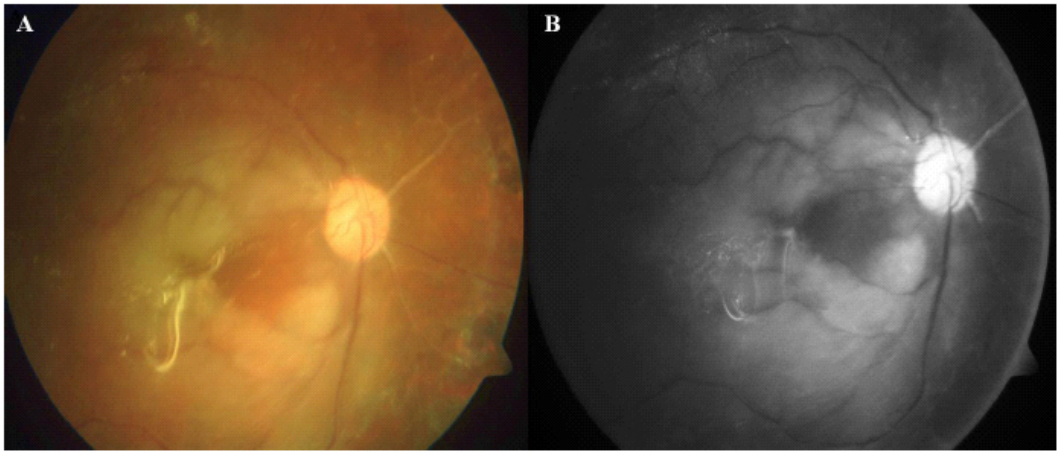

Fig. (1). BRAO on a diabetic patient after pars plana vitrectomy and silicon oil. **A**) Color photograph shows whitening of the posterior pole with normal color of the papillomacular bundle. **B**) Red-free photograph shows more clearly the territory supplied by the cilioretinal artery on the same patient.

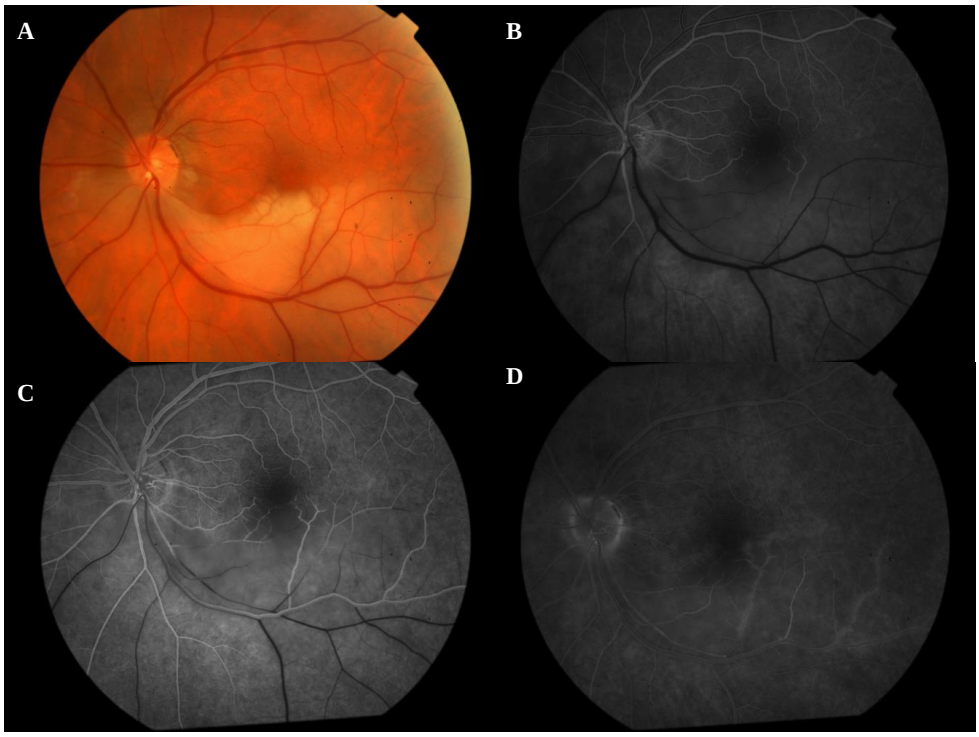

Fig. (2). Acute phase of inferotemporal BRAO. **A**) Fundus photograph shows retinal pallor in inferior macular area. **B** and **C**) FA shows a delay on the vessel filling and transit time. **D**) Cattle trucking and staining of the vessels walls (Courtesy of Natalia Pecce MD, Argentina).

CHAPTER 9

Retinal Arterial Macroaneurysm

Rodrigo Lechuga Perezanta[1] and **Virgilio Morales Cantón**[2,*]

[1] *Asociación para Evitar la Ceguera en Mexico, Mexico City, Mexico*

[2] *Retina Department, Asociación para Evitar la Ceguera en Mexico, Mexico City, Mexico*

The term macroaneurysm was first coined by Robertson, in 1973 making reference to arterial retinal lesions with saccular or fusiform swelling, localized on the first three orders of the retinal arterial tree found mainly at arterial bifurcations [1]. Saccular arterial macroaneurysms are more likely to burst and develop closer to the optic nerve where perfusion pressure is higher. Retinal arterial macroaneurysms are more frequent in women (60 – 80% probably due to hormonal and hereditary factors) with an average age of 69 years and have a strong association with systemic diseases such as arterial hypertension, aterosclerotic disease, hyperlipidemia, polycythemia and cerebrovascular disease. Retinal arterial macroaneurysms have been described in Leber´s miliary aneurysms, Coats´ disease, branch retinal artery occlusion and Eales´ disease among others [1, 2].

Systemic arterial hypertension causes an increase in hydrostatic pressure and may lead to hyaline degeneration of the vascular wall, loss of autoregulation tone and arterial dilatation [2].

Another theory to support that systemic arterial hypertension is a risk factor to the formation of arterial macroaneurysms is Laplace equation, which states that an increase in the transmural pressure is directly proportional to the increased tension of the wall.

Focal embolic damage to the arterial wall is considered to be a part of the

* **Corresponding author Virgilio Morales Cantón:** Retina Department, Asociación para Evitar la Ceguera en Mexico, Vicente García Torres 46, San Lucas Coyoacan, Mexico City, 04030; Mexico; Tel +52 (55) 10841400, Email: vmoralesc@mac.com

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mechanism for lesion formation, which may result in localized ischemia.

ESSENTIALS OF DIAGNOSIS

Most of these lesions appear on the superotemporal arterial branch (51%), followed by the inferotemporal branch (28%). Macroaneurysms affecting the nasal arterial branches may be less frequently diagnosed because patients may not notice the loss of visual acuity until the macula is affected, which could not happen, or a vitreous hemorrhage develops. Usually one macroaneurysm is present, but more lesions have been described affecting the same eye and 10% may be bilateral.

The main symptom is decreased visual acuity as a consequence of exudation, edema or hemorrhage. A characteristic finding is the presence of hemorrhage in different layers including subretinal, intraretinal, sub internal limiting membrane (Figs. **1A**, **2A** and **3A**) or in the vitreous cavity [1, 3]. Hourglass hemorrhages are also a typical finding.

These lesions may develop symptoms when acute or chronic decompensation occurs. Acute decompensation is typically associated with rupture and hemorrhage of the macroaneurysm while chronic decompensation is due to abnormal leakage of plasma constituents across the aneurysmal wall leading to the accumulation of yellow perianeurysmal intraretinal exudates [4].

When the arterial macroaneurysm is visible during fundus examination, the correct diagnosis can be achieved without much trouble, but when massive hemorrhage, exudation or retinal edema are present they suppose a diagnostic challenge. Fluorescein angiography (Figs. **1B**, **2B** and **3B**) is useful to locate the lesion when dense hemorrhage is absent so hyperfluorescence is visible. Macroaneurysm typically shows hyperfluorescence during the early arterial phase of the angiogram but late phase varies from little staining of the vessel wall to marked leakage. The absorption and emission spectrum of indocyanine green are close to infrared range and this allows the dye to be seen through hemorrhage. This makes indocyanine green a good alternative when diagnostic dilemma is present due to dense hemorrhage or exudates [5, 6].

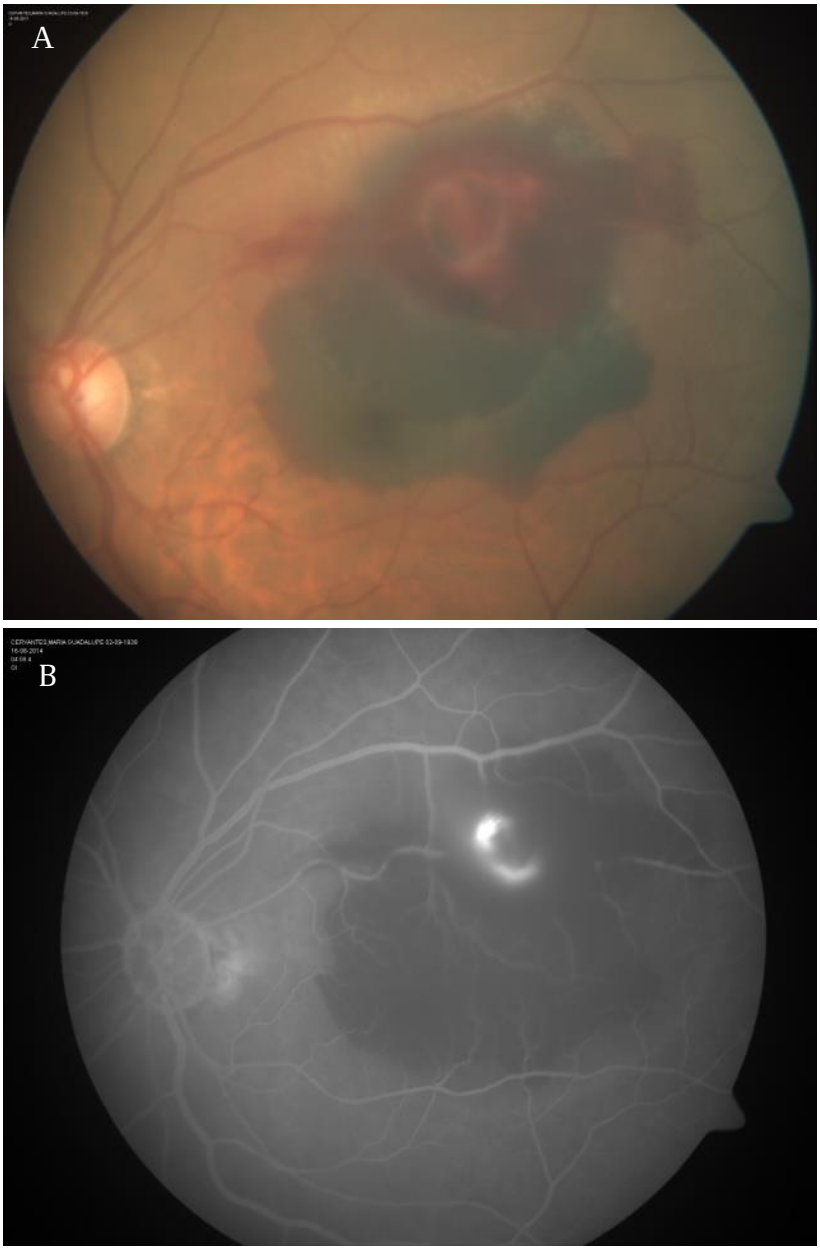

Fig. (1). A 74-year-old female patient complains of floaters and photopsia in her left eye from 8 days ago. Diagnosis of systemic arterial hypertension was made 20 years before. Visual acuity was 20/100, intraocular pressure 16 mmHg, fundus examination revealed subretinal and intraretinal hemorrhage (**A**) and fluorescein angiography showed a hyperfluorescent lesion in the superior temporal arterial vessel in the second branch (**B**). No treatment was performed and visual acuity was recovered to 20/60 three months later.

CHAPTER 10

Macular Telangiectasia

Yogin Patel[1] and **Michael D. Ober**[1,2,*]

[1] *Department of Ophthalmology, Henry Ford Health System, Detroit, MI, USA*

[2] *Retina Consultants of Michigan, Southfield, MI, USA*

Macular telangiectasia (MacTel) was best classified and described by Gass and Blodi as a form of idiopathic juxtafoveolar retinal telangiectasis [1] and is also commonly referred to as idiopathic perifoveal telangiectasia. This is a group of disorders which affects the vasculature of the posterior pole. Numerous classification schemes have been designed to categorize it, most notably, that of Gass and Blodi [1] and an update by Yannuzzi *et al.* [2]. Two major subclassifications are of greatest importance; MacTel type 1 refers to a unilateral presentation with prominent microaneurysms that is often grouped within the spectrum of Coats disease. MacTel type 2 is more often referred to simply as MacTel, and represents an acquired bilateral retinal vascular disorder. For the purposes of this review, we will focus on MacTel type 2.

Different studies quote very different numbers for the prevalence of this condition ranging from as high as 0.1% in the Beaver Dam Eye Study to 0.0045 to 0.022% in the Melbourne collaborative cohort study [3, 4]. The age at onset is usually in the late 40s to early 60s. There may be a slight female predominance depending on the study population quoted.

ESSENTIALS OF DIAGNOSIS

Patients will often present with a pericentral scotoma or metamorphopsia. Visual acuity rarely progresses to legal blindness but visual dysfunction is common. The clinical presentation begins with subtle changes noted in the posterior pole.

* **Corresponding author Michael D. Ober:** Retina Consultants of Michigan, 29201 Telegraph Road, Suite 606, Southfield, MI 48034, USA; Tel: (248) 356-8610; Fax: (248) 356-6473; E-mail: obermike@gmail.com

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Lesions most often begin just temporal to the fovea (Figs. **1A, B**). They may then further evolve to include the larger perifoveal region. The initial presenting change is often a loss of transparency in the retina temporal to the fovea. With time the lesion may evolve to include dilation of capillaries and will likewise spread from their temporal perifoveal origin. Histological studies have demonstrated that the dilated capillaries are mostly located in the deeper retinal layers [1]. Although, Yannuzzi and others have observed the involvement of both the superficial and deep plexus [2]. Later changes include dilated venules, which are often associated with the abnormal capillaries. These vessels tend to increase in diameter as they approach the fovea, in contrast to normal vessels. In addition, these vessels often take characteristic right angle turns, which represent diving of the vessel toward the deeper retinal layers. Associated changes in the RPE include crystalline deposits (Figs. **3A, B**), pigment migration, and hyperplasia following these venules [2]. Over the time, secondary atrophy of the pigment epithelium and neurosensory retina may develop. Some eyes may accumulate vitelliform material under the central macula. Lamellar thinning of the inner retina within the fovea is common and manifests with the development of inner lamellar cystic changes (Fig. **4**). On occasion the atrophic changes may progress to a full thickness macular hole.

Neovascularization is another common later stage development usually preceded by the appearance of the right angle venules and pigmentary changes. As with any neovascularization, it may be associated with hard exudate, edema, and hemorrhage. The neovascularization stems from retinal vessels, but may be indistinguishable from choroidal neovascularization with chorioretinal anastomosis from other etiologies. Late changes may include the formation of a disciform scar.

Multimodal imaging is critical in the diagnosis of MacTel. One of the earliest signs of the disease, even before clinical changes appear, is the loss of the hypofluorescent center in fundus autofluorescence photos which later progress to more pronounced hypoautofluorescence corresponding to RPE atrophy with adjacent granular hyperautofluorescence (Figs. **5A, B**). This has been postulated as a direct result of the depletion in macular pigment [5]. Fluorescein angiography (FA) findings are often diagnostic and include the characteristic telangiectatic

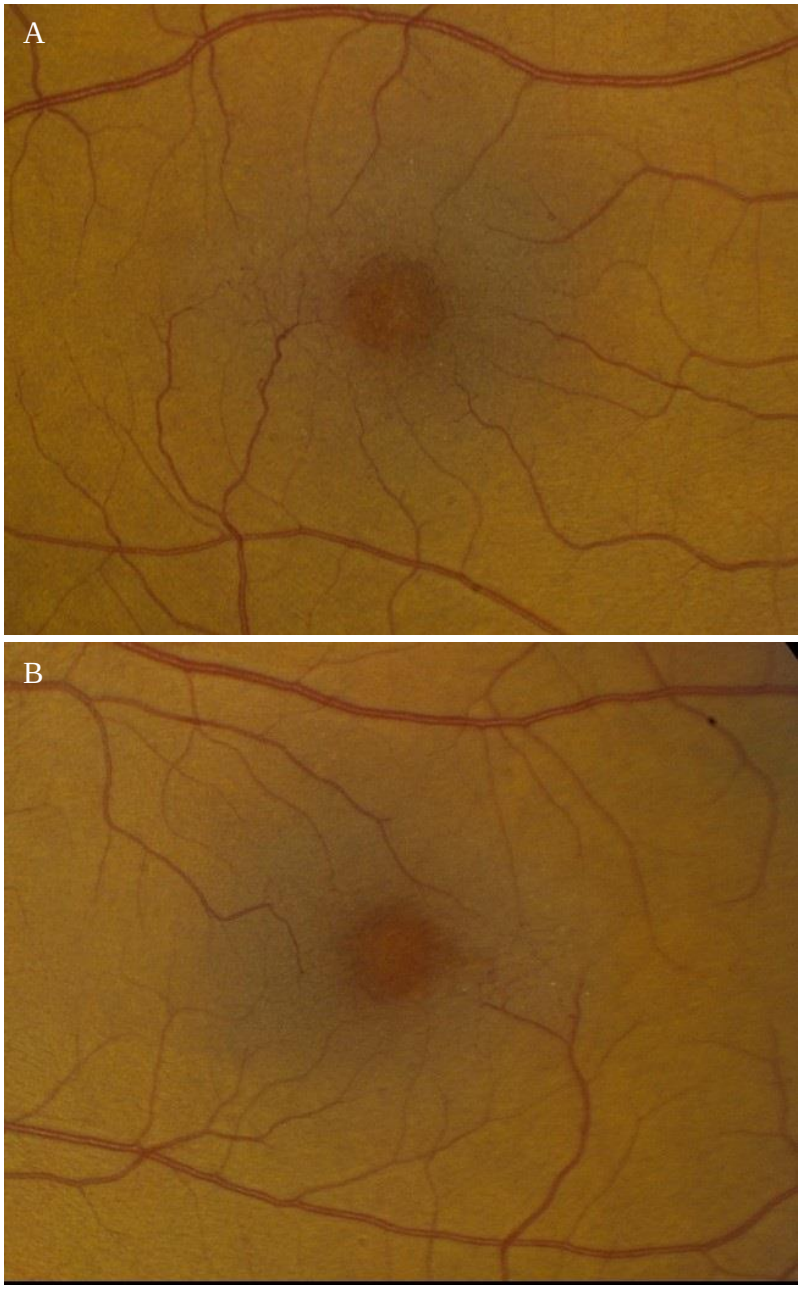

Fig. (1). (**A** and **B**) Color fundus photographs demonstrating the subtle loss of retinal transparency and right angle vessels most notable temporal to both foveae. Retinal pigment epithelial hyperplasia can be seen surrounding the right angle vessels (not shown here). Vessels temporal to the fovea are noted to be of irregular caliber and telangiectatic (Photo Credit: Colin Griffin).

CHAPTER 11

Sickle Cell Retinopathy

Luke B. Lindsell and **Aziz A. Khanifar***

Retina Group of Washington, Washington DC, USA

ESSENTIALS OF DIAGNOSIS

Sickle cell disease is an autosomal recessive condition comprising several different forms of mutated hemoglobin. Patients who are homozygous for the hemoglobin S gene (HbS) have the most severe form of sickle cell anemia. Other genotypes of clinical importance to ophthalmologists include HbSC disease (double heterozygote for HbS and HbC), HbS/b-thal (double heterozygote for HbS and beta-thalassemia), and sickle cell trait (one normal Hb allele and one HbS allele). In general, patients with the more severe genotype of sickle cell disease have less severe ophthalmic manifestations. For example, HbSS has the most critical systemic complications, the ocular manifestations are less severe compared to HbSC disease which has a more moderate systemic course. Although sickle cell trait is relatively asymptomatic, under hypoxic conditions both systemic and ophthalmic consequences can occur [1].

Relative hypoxia causes mutated hemoglobin to polymerize, ultimately altering the morphology of the red blood cell (RBC) to the characteristic sickle shape. These abnormal RBCs occlude terminal arterioles, leading to ischemia and possible tissue infarction [2]. Sickle cell retinopathy is one end-organ manifestation of the disease. Similar to diabetic eye disease, both non-proliferative and proliferative forms occur, and the proliferative disease is associated with more significant visual morbidity [3].

* **Corresponding author Aziz A. Khanifar:** Retina Group of Washington, Washington DC, USA; Tel: (301) 495-2357, Fax: (301) 495-2359; E-mail: azizkhanifar@gmail.com

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Non-proliferative sickle cell retinopathy is characterized by several possible findings:

1. Vascular tortuosity – more common in HbSS disease (Fig. **1**).
2. Salmon patch hemorrhages – located between the internal limiting membrane (ILM) and retinal surface ("blowout" of occluded arteriole) [4] (Fig. **2**).
3. Intraretinal hemorrhages (Fig. **1**).
4. Iridescent spots – small schisis cavity in area of resolved intraretinal hemorrhage. Hemosiderin-laden macrophages appear as glistening spots [4] (Fig. **3**).
5. Black sunburst – flat areas of hyperpigmentation resulting from intraretinal hemorrhage infiltrating the subretinal space and damaging the retinal pigment epithelium (RPE) (Fig. **4**).

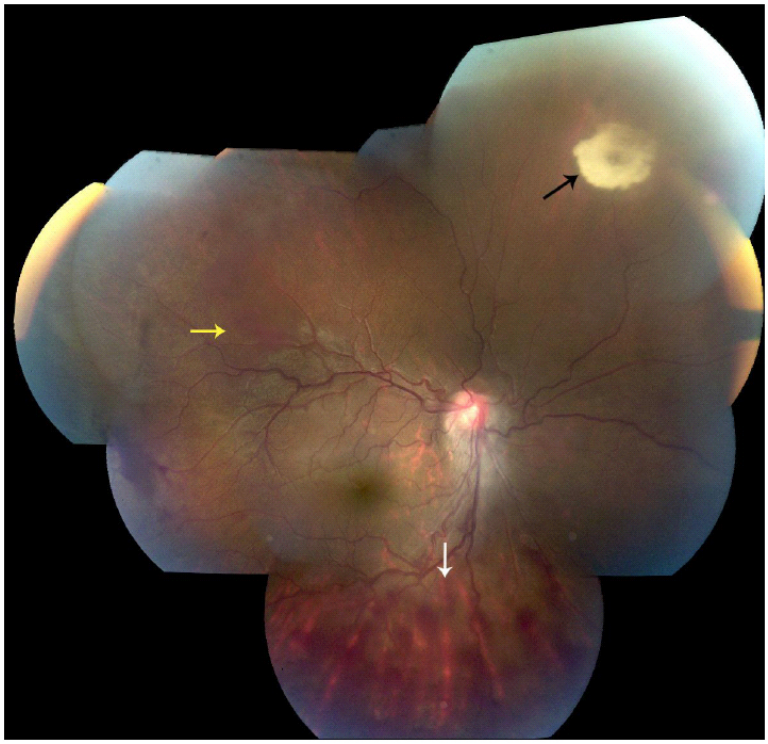

Fig. (1). Color photo montage. Resolving intraretinal hemorrhage that will become a sunburst or possibly iridescent spots (black arrow). Faint resolving salmon patch hemorrhage (yellow arrow). Vitreous hemorrhage (white arrow). Vascular tortuosity is also evident.

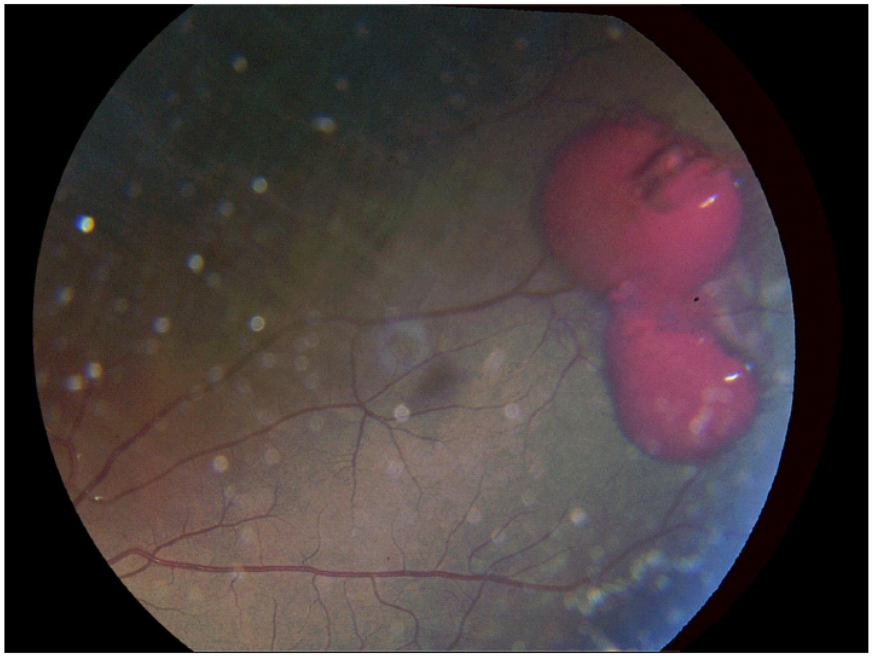

Fig. (2). Color photo. Large peripheral salmon patch.

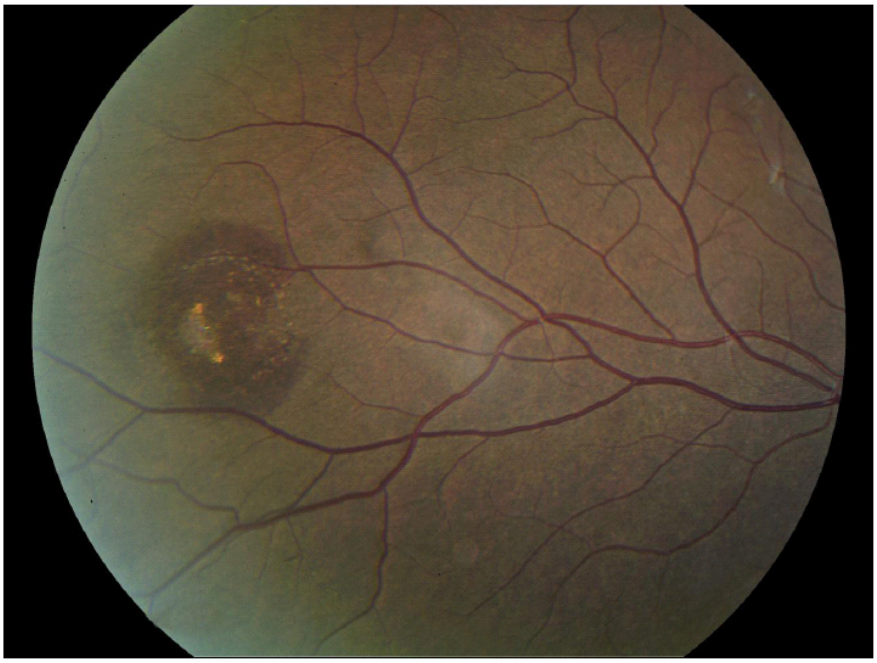

Fig. (3). Color photo. Iridescent spots.

CHAPTER 12

Radiation Retinopathy

Veronica Kon Graversen*

University of North Carolina at Chapel Hill, NC, USA

Radiation retinopathy (RR) is the result of ultra-structural impairment of the vascular endothelial cells and pericytes of the retina and choroid after exposure to ionizing radiation [1]. Several factors influence the development of retinopathy, including the type of radiation received (external-beam irradiation *versus* local radioactive plaque therapy), total dosage and fraction size schemes used, concomitant systemic vascular diseases, simultaneous chemotherapy, and pregnancy [2, 3]. These factors determine the interval to onset and severity of the disease. The dose required to produce retinopathy is variable, but it is generally accepted that exposure to 30-35 Gray leads to visual changes [3]. The median time interval to onset of retinopathy is 27 months but may range from few months to several years [4].

ESSENTIALS OF DIAGNOSIS

Photoreceptors are relatively preserved and resistant to the radiation effects. Therefore, the degree of visual loss depends on the severity of the occlusive vasculopathy and its sequelae.

Clinical Features: The earliest signs include capillary dilation and microaneurysm formation. Later in the course of the disease, a nonproliferative phase may develop. This phase is exudative. Hard exudates, intraretinal (superficial or deeper) and preretinal hemorrhages, telangiectasia, cotton wool spots and macular edema are frequently seen (Figs. **1** and **2**).

* **Corresponding author Veronica Kon Graversen:** Ophthalmology Department, University of North Carolina at Chapel Hill, NC, USA; Tel: (919)518-6361; Email: veronicakonjara@gmail.com

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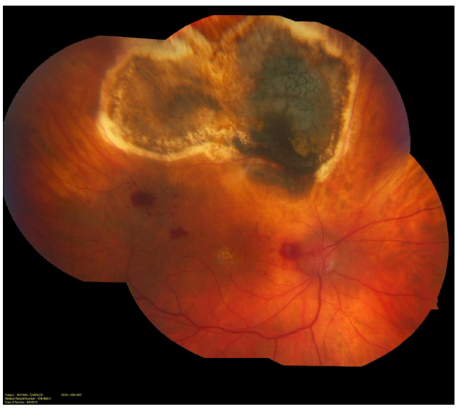

Fig. (1). Fundus photograph of a patient treated with ophthalmic plaque radiation for choroidal melanoma. The patient developed non-proliferative radiation retinopathy, showing retinal hemorrhages, hard exudates and telangiectasia.

Extensive retinal ischemia may lead to vascular occlusions, retinal neovascularization (Fig. **2**), vitreous hemorrhage, retinal detachment, and, in some cases, neovascular glaucoma. These late changes are recognized as the proliferative phase of the disease [1, 3].

Rarely, choroidal neovascular membranes (CNV), chorioretinal anastomosis and intravitreal polypoidal neovascularization have been reported [5 - 7].

Imaging. The diagnosis is mainly clinical; however, retinal diagnostic imaging provides valuable tools monitoring the progression of the disease and treatment response.

Optical coherence tomography: Ensures early recognition of macular changes. More severe and chronic cases may reveal outer retinal disruption [8].

Fluorescein angiography: Initial findings include varying degrees of capillary closure and dilation of microvasculature (Fig. **2**). The most affected areas are the peripapillary region and the macula [9].

Indocyanine green angiography: Detects areas of choriocapillaris perfusion defects [10].

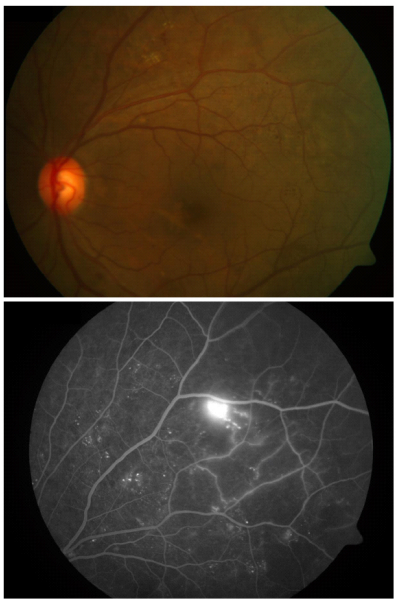

Fig. (2). Fundus photograph shows microaneurysms, hard exudates and and retinal hemorrhages. Fluorescein angiography reveals microaneurysms, capillary closure and retinal neovascularization.

DIFFERENTIAL DIAGNOSIS

1. Diabetic retinopathy.
2. Retinal vascular occlusions.
3. Occlusive retinopathy.
4. Retinal telangiectasia.
5. Human immunodeficiency virus retinopathy.
6. Hypertensive retinopathy.

MANAGEMENT

There are no specific treatment guidelines for radiation retinopathy. Macular ischemia is usually irreversible and is the most feared complication that results in blindness. Focal laser treatment can be applied to areas of macular edema [11]. In recent years, intravitreal or periocular steroids and anti-vascular endothelial growth factor (VEGF) therapies have been successfully used to treat center-involving macular edema [11 - 13]. Bevacizumab has been the most studied anti-VEGF in cases of radiation retinopathy. Nevertheless, similar outcomes have been reported with other anti-VEGF agents. Refractory cases may benefit from

CHAPTER 13

Ocular Ischemic Syndrome

Eleonora Lavaque*

Retina Department, Hospital Oftalmológico Santa Lucia, Buenos Aires, Argentina

Retina Department, Instituto Médico de Ojos, Buenos Aires, Argentina

Ocular ischemic syndrome (OIS) is caused by ocular hypoperfusion. Carotid stenosis superior to 70% or complete occlusion due to atherosclerosis is the common cause of this rare condition. In 80% of the cases, OIS is found unilaterally, on the same side of the carotid stenosis [1, 2]. Occasional causes of OIS secondary to ophthalmic artery obstruction include Takayasu disease or giant cell arteritis [3].

Described risk factors are: age between 50-80 years, male gender 2:1, and vascular diseases such as arterial hypertension (75%), diabetes (56%), coronary diseases, vascular stroke and hemodialysis [3 - 5].

ESSENTIALS OF DIAGNOSIS

Ninety percent of the patients present with a history of slowly progressive visual loss in the affected eye. Dull ischemic pain develops gradually and is relieved when the patient lies down [4, 5].

Anterior segment ischemic signs include iris or angle neovascularization, iridocyclitis with flare and cells in 20% of cases, cataract, iris atrophy, sluggish pupillary reaction to light [1]. Other less common signs of OIS are dilatation of conjunctival and episcleral vessels, corneal edema, and bullous keratopathy [4, 6].

Posterior segment signs are more frequent than anterior segment signs [4]. Posterior segment ischemic signs include narrow retinal arteries, perifoveal telangi-

* **Corresponding author Eleonora Lavaque:** Retina Department, Hospital Oftalmológico Santa Lucia, Buenos Aires, Argentina; Tel: 00-9-54-56458302; Fax: 00-54-11-48124494; E-mail: eblavaque@hotmail.com

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ectasia, dilated retinal veins, mid-peripheral retinal hemorrhages and micro-aneurysms. Neovascularization in the optic disc or retina and its complications (fibrovascular proliferation, cotton-wool spots, vitreous hemorrhage) may be present but are not frequent (Figs. **1-3**) [3, 4].

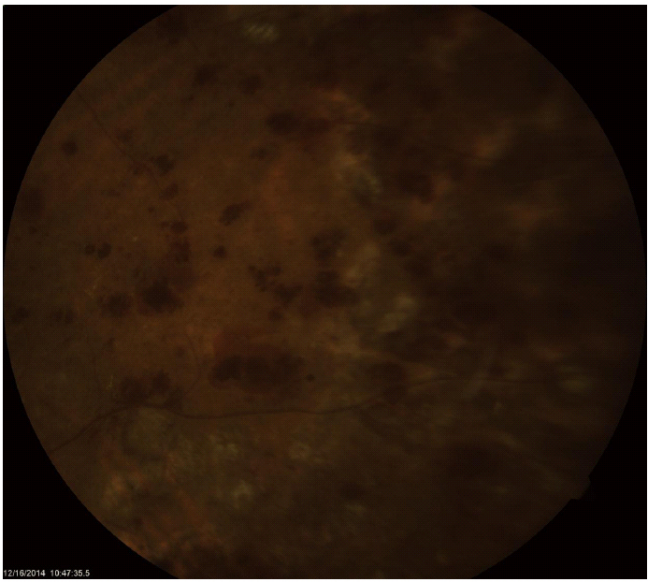

Fig. (1). Fundus photograph shows round circumscribed hemorrhages at the classical midperipherical location.

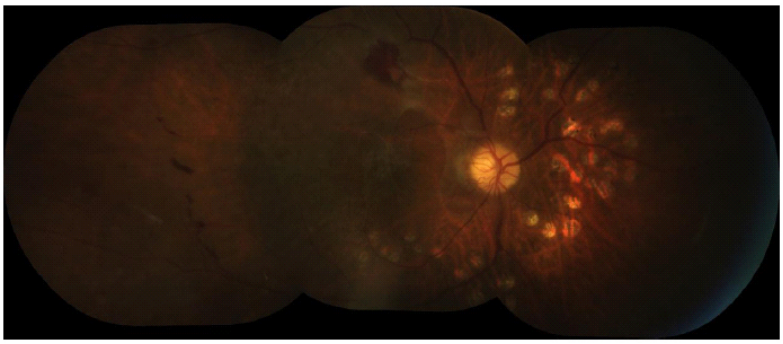

Fig. (2). 70-year-old Caucasian male patient. Medical background: diabetes, hypertension, coronary bypass, acute ischemic cerebral stroke, recent left carotid surgery, endarterectomy 2 months before, and indication for future right carotid endarterectomy because of 79% stenosis. Best-corrected visual acuity was 20/40 in the right eye, and hand motion in the left eye. Positive biomicroscopy: rubeosis iridis, hyphema in left eye. Intraocular pressure 15/60 mm hg. Fundus photograph of the right eye: preretinal hyaloid fibrosis, preretinal hemorrhage at an arteriovenous crossing. Ocular fundus findings in left eye: vitreous hemorrhage.

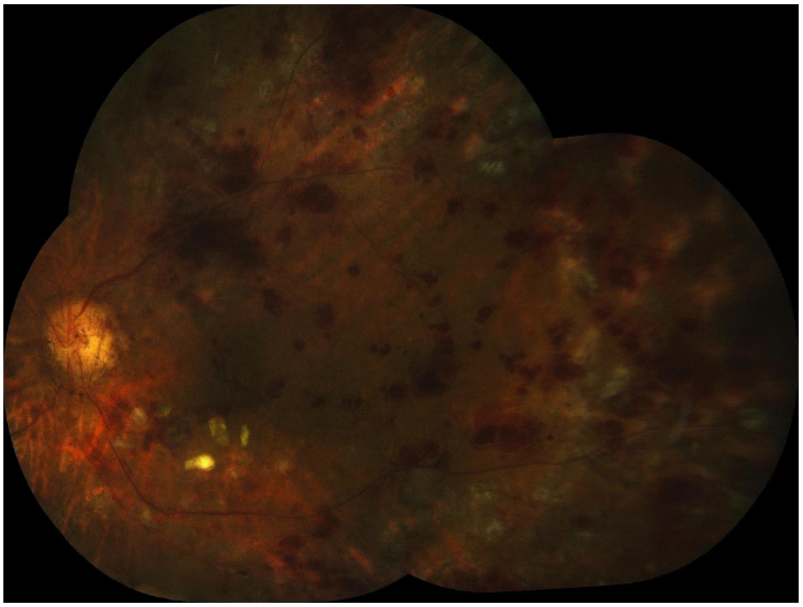

Fig. (3). Left eye of the same patient as Fig. (**2**), after vitrectomy and endophotocoagulation. Round hemorrhages and photocoagulation scars are present. After vitrectomy, visual acuity improved to 20/100, intraocular pressure improved to 26 mmHg with topical treatment.

A cherry-red spot, characteristic of macular ischemia, is seen in 12% of eyes, due to IOP exceeding the perfusion pressure or to a result of embolic occlusion of the central retinal artery [1, 4].

Eighty percent (80%) of OIS present with very characteristic retinal hemorrhages: they are round, located in the external retinal layers, and at the mid-periphery (Fig. **1**) [2, 3].

Intraocular pressure is usually normal or low. Although anterior segment neovascularization is frequent, elevated intraocular pressure is less common than expected due to flow restriction to the ciliary body. Normal-tension glaucoma can be present in eyes with normal ocular tension due to hypoperfusion to the optic disc [1, 2, 4].

In fluorescein angiography, 60% presents prolonged arm-to-choroid and arm-to-retina circulation time (Fig. **4**). The normal retinal filling time is approximately 5 seconds, but in the affected eye it may be 1 minute or longer [4].

CHAPTER 14

Dry Age-Related Macular Degeneration

Ana Domínguez Yates and **Virgil Alfaro***

Retina Consultants of Charleston, Charleston, South Carolina, USA

Age related macular degeneration (AMD) is a progressive and chronic disorder, characterized by the onset of degenerative changes in the macular area in people of 50 years of age or older [1]. Besides age, other risk factors are white race [2], smoking [3, 4] and female gender [5, 6]. Advanced AMD, is the leading cause of severe central vision loss in this age group, and geographic atrophy (GA) is responsible for 25% of cases. The Pathophysiologic mechanism still remains unclear but it is well known that the Retinal Pigment Epithelium (RPE) plays a key role [7]. Environmental and genetics factors can alter any given patient's susceptibility to the disease [8].

ESSENTIALS OF DIAGNOSIS

The changes in AMD involve the outer retina, RPE, Bruch's membrane and choriocapillaris [9]. Drusen are the hallmark features of AMD. They become visible on biomicroscopic fundus examination when their diameter exceeds 25 μm. They can be classified [10] by size as small (< 0-63 μm diameter), medium (64-124 μm diameter) or large (> 0-125 μm diameter) (Fig. **1**).

According to their appearance they can be classified as hard or soft. Hard or crystalline drusen (Fig. **2**) appear as small, round yellow-white spots with sharp borders. They correspond to accumulation or entrapment of hyaline material, lipids and mucopolysaccharides underneath RPE [11, 12]. Large areas of small hard drusen increase the risk of soft drusen and RPE atrophy at a relatively young age [13, 14]. Soft drusen are pale yellow-white spots, more than 63 μm in diame-

* **Corresponding author Virgil Alfaro:** Retina Consultants of Charleston, 3531 Mary Ader Ave # D, Charleston, SC 29414, Estados Unidos, USA; Tel: +1 843-763-4466; E-mail: virgil.alfaro@gmail.com

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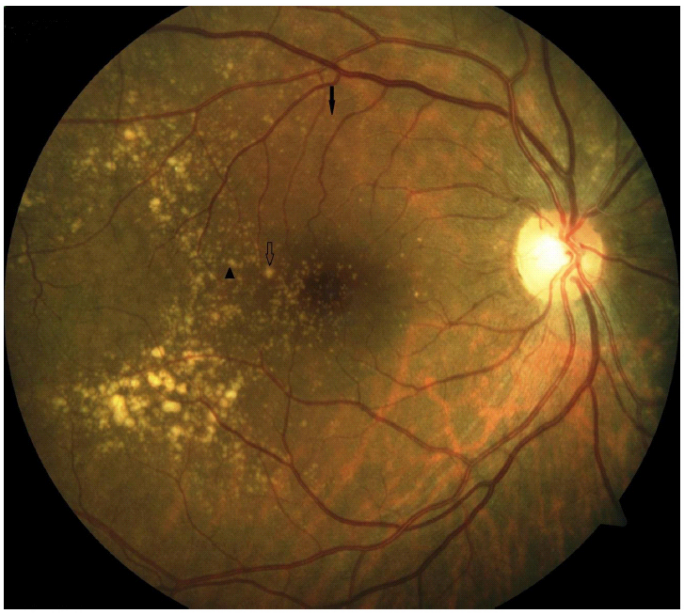

Fig. (1). 60-year-old patient with Dry AMD and visual acuity of 20/20 in both eyes. Small drusen (filled arrow); medium drusen, with a diameter equal or greater than one half of a large drusen (arrowhead); and large drusen, diameter greater than or equal to a large vein at the disc margin (unfilled arrow).

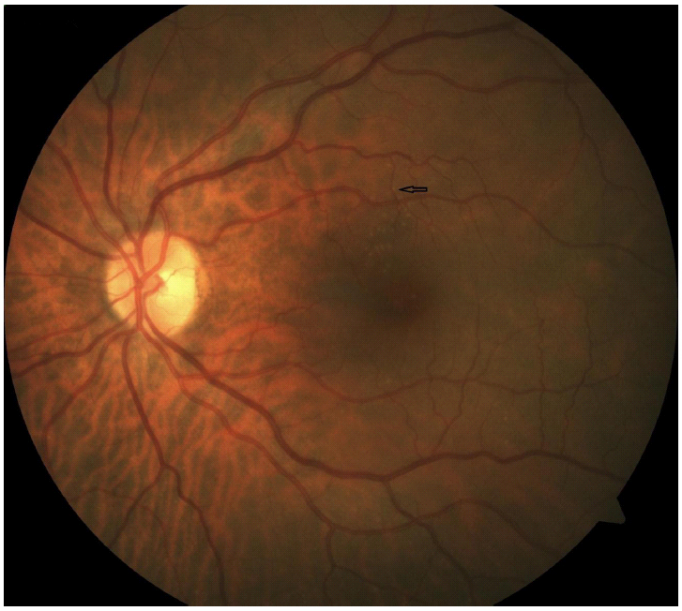

Fig. (2). Some small drusen in the superior macula in a 61-year-old patient. Hard drusen appear bright with sharp and very well defined borders (unfilled arrow).

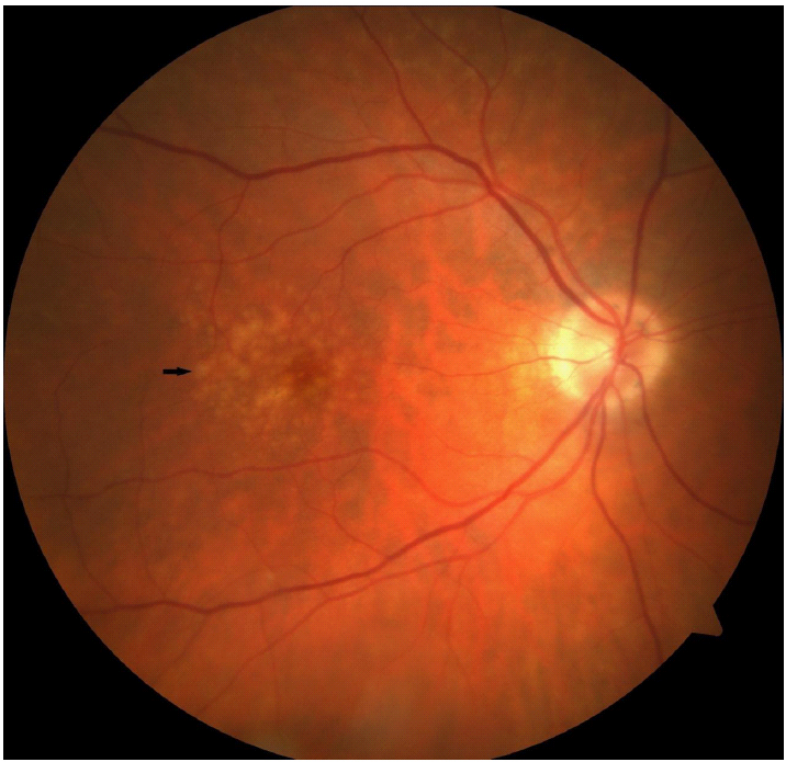

Fig. (3). Soft drusen in a 77-year-old patient. Big and pale yellow–white lesions ill-defined margins (arrow).

ter, with ill-defined boundaries, are preferentially located within the fovea (Fig. **3**). They are a result of RPE dysfunction and derive from basal linear deposits, between the RPE and the Bruch's membrane [11, 12]. Most of the molecular constituents of drusen reflex their complex pathogenesis: protein (immune response modulator; immunoglobulin and complement components; inflammation molecules), cellular components (RPE blebs, lipofuscin, and melanin, as well as choroidal dendritic cell), glycoconjugates, neutral lipids and zinc [15].

On Fluorescein angiography (FA), hard drusen appear as a bright early hyperfluorescence secondary to a window defects (Fig. **4 a-c**). On the other hand, soft drusen appear as progressively hyperfluorescent spots that persist in late phases due to staining (Figs. **5 a-d** and **6 a-c**).

CHAPTER 15

Wet Age-Related Macular Degeneration

Gerardo García-Aguirre[*, 1,2]

[1] *Retina Department, Asociaciós para Evitar la Ceguera en Mexico, Mexico City, Mexico*

[2] *Ophthalmology, Escuela de Medicina - Tec de Monterrey, Mexico City, Mexico*

Age-related macular degeneration (AMD) is one of the leading causes of legal blindness in patients over 60 years, especially in developed countries [1]. The prevalence of the disease varies according to ethnicity [2], and is more common in smokers [3, 4] and in women [5, 6]. The disease is classified in two stages, known as dry AMD (which is discussed in another chapter) which is characterized by the presence of drusen in the posterior pole, and wet AMD, in which the patient develops neovascularization that stems from the choroid, penetrates Bruch's membrane, and by leakage of fluid, hemorrhage and scarring, affecting the center of the macula.

ESSENTIALS OF DIAGNOSIS

When a choroidal neovascularization (CNV) develops, patients may complain of metamorphopsia and a central or paracentral relative scotoma.

Clinical examination usually reveals drusen, and the presence of intraretinal or subretinal fluid that causes thickening of the retina. Hemorrhage and hard exudates may also be observed (Figs. **1-6**).

[*] **Corresponding author Gerardo García Aguirre:** Retina Department, Asociaciós para Evitar la Ceguera en Mexico, Vicente García Torres 46, San Lucas Coyoacan, Mexico City 04030, Mexico; Tel: +52 (55) 10841400; E-mail: jerry_gar_md@yahoo.com

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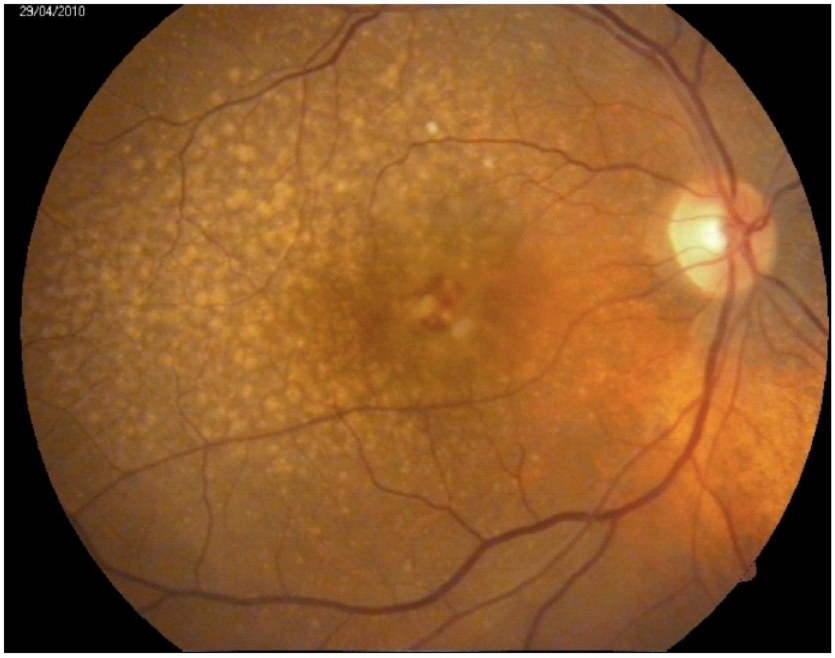

Fig. (1). Fundus photograph of the right eye with subfoveal CNV showing multiple soft and hard drusen in the macular area. A small subretinal hemorrhage may be observed nasal to the fovea.

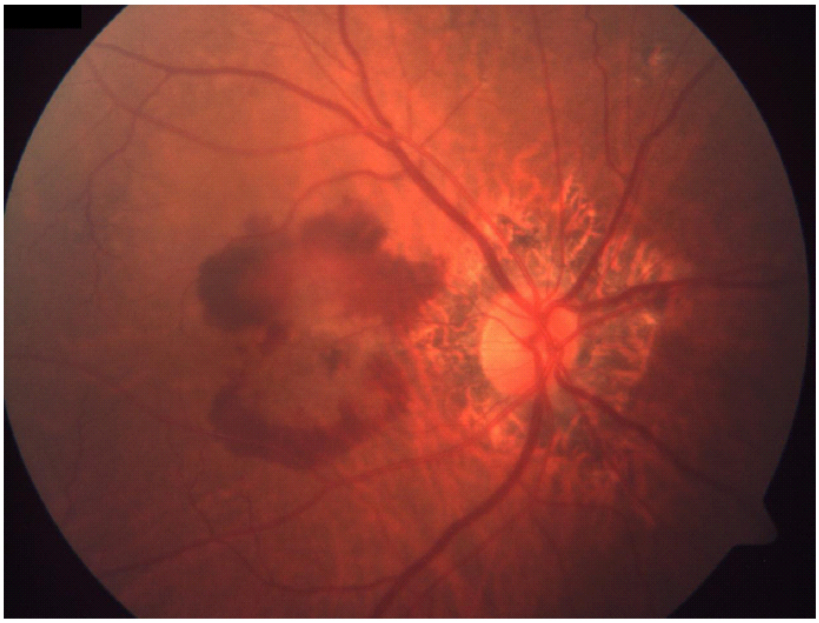

Fig. (2). Fundus photograph of the right eye with a subfoveal CNV and large submacular hemorrhage.

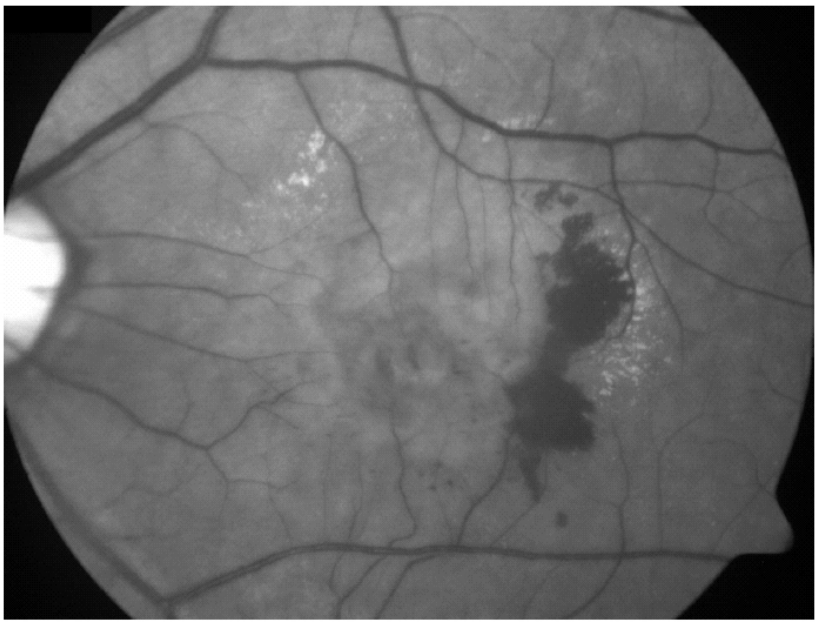

Fig. (3). Red-free fundus photograph of the left eye, showing a subfoveal CNV surrounded by hard exudates and submacular hemorrhage.

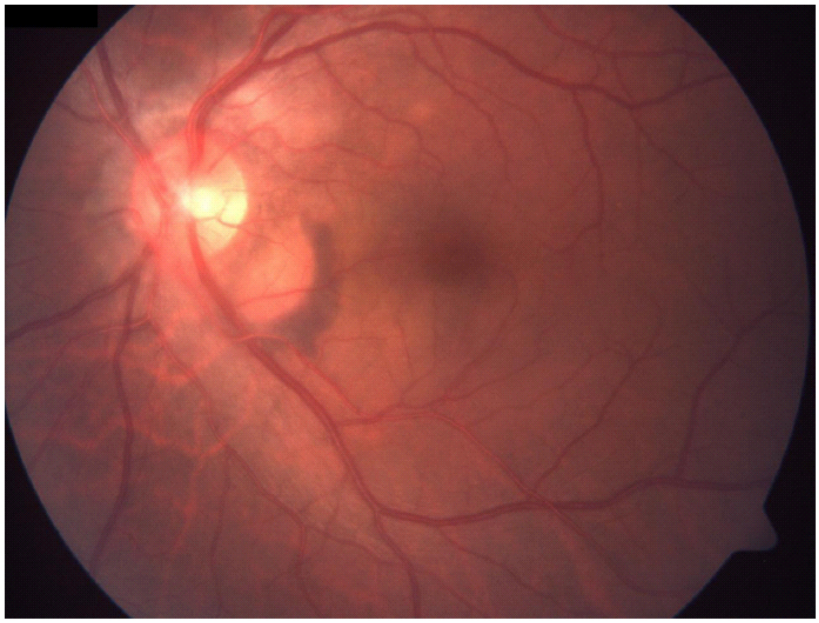

Fig. (4). Fundus photograph of the left eye displaying an extrafoveal CNV, just adjacent to the inferotemporal border of the optic nerve, with associated subretinal hemorrhage.

CHAPTER 16

Polypoidal Choroidal Vasculopathy

Jans Fromow Guerra*

Retina Department, Asociación para Evitar la Ceguera en México, IAP, México City, México

ESSENTIALS OF DIAGNOSIS

Polypoidal choroidal vasculopathy (PCV) is a retinal disorder involving the choroidal vasculature characterized by the presence of aneurysmal polypoidal dilations that commonly arise from a network of branching choroidal vessels, that was described in 1982 by Lawrence Yanuzzi. PCV usually shows a broad spectrum of manifestations both clinically and epidemiologically. For this reason, it has been widely debated whether to consider it a subtype of neovascular age-related macular degeneration (AMD) or a separate clinical entity. Some of the characteristics of PCV are shared by AMD but some others are radically different.

Epidemiology Essentials of PCV

- PCV predominantly occurs at a mean age of 68.4 years with a range of 21-93 years [1 - 3].
- PCV is more prevalent in non-Caucasians, such as Asians and African-Americans where it has been reported to be responsible up to 23-54.7% of wet AMD cases in these populations [4]. However, in Caucasians the prevalence of this disease has been reported in about 8-13% [5].
- PCV is more prevalent in females than in males in Caucasian (female 52% to 65%) populations and the opposite in Asians (men 63% to 78%) [2].

* **Corresponding author Jans Fromow Guerra:** Retina Department, Asociación para Evitar la Ceguera en México, IAP, Vicente García Torres, 46. San Lucas Coyoacán, México DF. México 04030; Tel: +52.55.10841400; Fax: +52.55.10841404; E-mail: fromow@me.com

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Clinical Essentials of PCV

- Localization: PCV can present in different regions: peripapillary, macular or extramacular. Prevalence of each one of these presentations varies according to different ethnic groups [6]. Different reports state that unilateral disease can be found in up to 79.4% to 91.8% of cases [6 - 8].
- Clinical appearance: Clinical examination will reveal orange-reddish colored vascular dilatations often associated to pigment epithelial detachments (PED), subretinal hemorrhage, hard exudates and drusen (Fig. **1**).

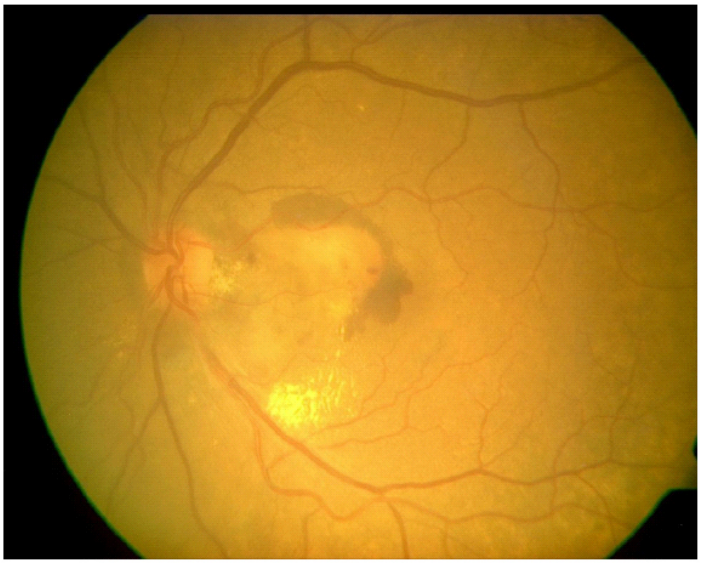

Fig. (1). Clinical appearance of peripapillary PCV.

- Angiographic & OCT Analysis (Figs. **2**-**6**): Indocyanine green angiography (ICGA) should be considered as the gold standard in PCV diagnosis since findings in FA can be easily mistaken for wet AMD especially in elderly patients with drusen and bilateral disease [8, 9]. ICGA will often reveal single or multiple polyps appearing as vascular aneurysmal dilatations arising from inner choroidal vessels often seen as a neovascular plaque or a so-called “branching vascular networks” (BVN). These findings are usually seen within the first 6 minutes after the injection of ICG [10]. However, PCV lesions may not be easily seen due to minor or extensive hemorrhage. A classification of PCV has been developed regarding the presence or absence of BVN determined by ICGA:

Type I PCV or "Polypoidal CNV" with an apparent BVN and type 2 PCV or "Typical PCV" with no or faint BVN. These 2 different PCV subtypes have distinct clinical course, treatment response and genetic background [11 - 13]. OCT shows important diagnostic characteristics (Figs. **2**, **3** and **6**). In most cases a sharp elevated PED is observed, that may be associated to a flat, shallower PED. Polypoidal lesions are usually attached to the back surface of the elevated PED. In type I PCV the flat shallower PED is associated with the BVN giving a "double layer sign" [14].

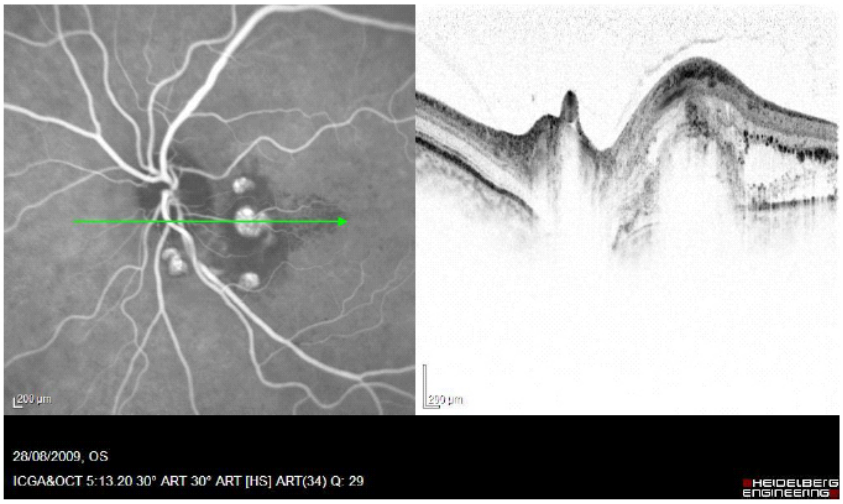

Fig. (2). ICGA and OCT appearance of peripapillary PCV of the same patient as Fig. (**1**).

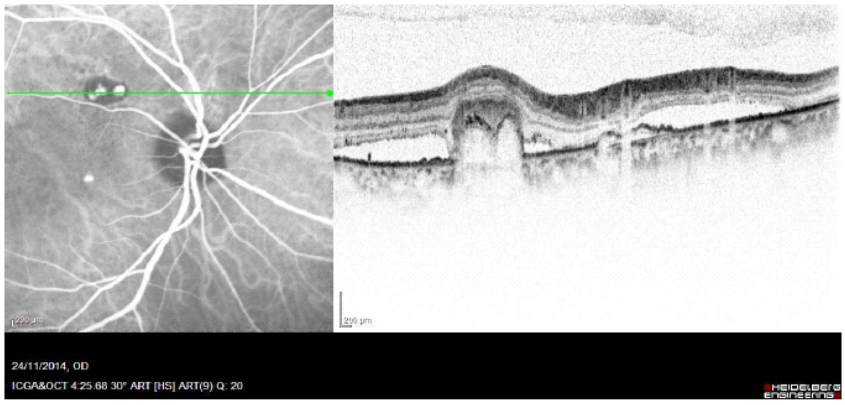

Fig. (3). Left: ICG-Macular Type 2 PCV with no or faint branching vascular network. Right. OCT image where an associated PED can be clearly observed.

CHAPTER 17

Retinal Angiomatous Proliferation (RAP)

Maximiliano Gordon[1,2,*] and **Guillermo Gordon**[†]

[1] *Centro de la Visión Gordon-Manavella, Rosario, Santa Fe, Argentina*

[2] *Retina Department, Ophthalmology Service, Hospital Provincial del Centenario, Rosario, Santa Fe, Argentina*

Retinal Angiomatous Proliferation (RAP), or type 3 neovascularization, is a different form of exudative age-related macular degeneration (AMD) [1]. Its main characteristic is an abnormal anastomosis between the choroidal and the retinal vessels. The pathogenesis of this entity remains controversial [2 - 4]. Yannuzzi *et al.* believe that the neovascular process originates within the neurosensory retina. In contrast, Gass proposed that the process begins with choroidal neovascularization (CNV) [1].

Gass' classification scheme is based on neovascularization relationship to the retinal pigment epithelium (RPE). Type 1 neovascularization describes new blood vessels growing under the RPE, while in Type 2 neovascularization these proliferate over the RPE. Freund has proposed modifying Gass' original classification by adding Type 3 neovascularization, which refers to a type of neovascularization with preference for the retina [1].

ESSENTIALS OF DIAGNOSIS

Symptoms are similar to those of AMD. However, patients with RAP tend to be older. The classical findings include retinal and preretinal hemorrhages, and pigment epithelial detachments, as well as small and multiple intraretinal blood [5].

[*] **Corresponding author Maximiliano Gordon:** Centro de la Visión Gordon - Manavella, Montevideo 763, CP 2000, Rosario - Santa Fe, Argentina; Tel/Fax: +54(341)4400239/4244850; E-mail: maximilianogordon19@gmail.com

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RAP classification distinguishes three vasogenic stages based on the nature and progression of the neovascularization process. Stage I involves capillary proliferation within the retina originating from the deep retinal plexus (intraretinal neovascularization [IRN]). Stage II is determined by IRN extending into the subretinal space (subretinal neovascularization [SRN]). Stage III describes progression to CNV, that can be clearly determined clinically or angiographically. This stage is sometimes characterized by a vascularized pigment epithelial detachment and retinal choroidal anastomosis (RCA) [6]. Stage-I RAP lesions manifest with intraretinal neovascularization with telangiectatic retinal capillaries and small angiomatous structures perfused by the retinal circulation. Stage-II RAP lesions extend beyond the photoreceptor layer into the subretinal space resulting in subretinal neovascularization. A serous PED is often seen. In stage-III RAP, it is presumed that an RCA is formed. Patients that are not treated for stage-III RAP lesions can develop large fibrotic scars [7]. In these cases, fluorescein angiography revealed poorly defined staining that simulates occult CNV (Figs. **1** and **3**).

Indocyanine green angiography (Fig. **3**) often helps make an accurate diagnosis. It revealed a focal area of hyperfluorescence corresponding to the neovascularization ("hot spot"). OCT may reveal intraretinal hyperreflectivity, corresponding to angiomatous proliferation associated with intraretinal or subretinal fluid (Figs. **2** and **4**) and/or RPE detachment [6]. Dilated fundus exam showed hemorrhages and lipid exudates in an area of occult CNV on the basis of fluorescein angiography and indocyanine green angiography (ICG) revealed the presence of a hot spot. These findings led to the diagnosis of RAP [6, 7].

DIFFERENTIAL DIAGNOSIS

Differential diagnosis should include other forms of CNV with ICG hot spots (occult CNV) and polypoidal choroidal vasculopathy (PCV). This latter disease presents with normally larger retinal hemorrhages and round reddish-orange macular lesions in the eye fundus. OCT is also a helpful tool in differentiating RAP, PCV, and occult membranes. In PCV, polyps appear in OCT as abrupt neurosensory detachment. Other differential diagnosis is macular telangiectasia.

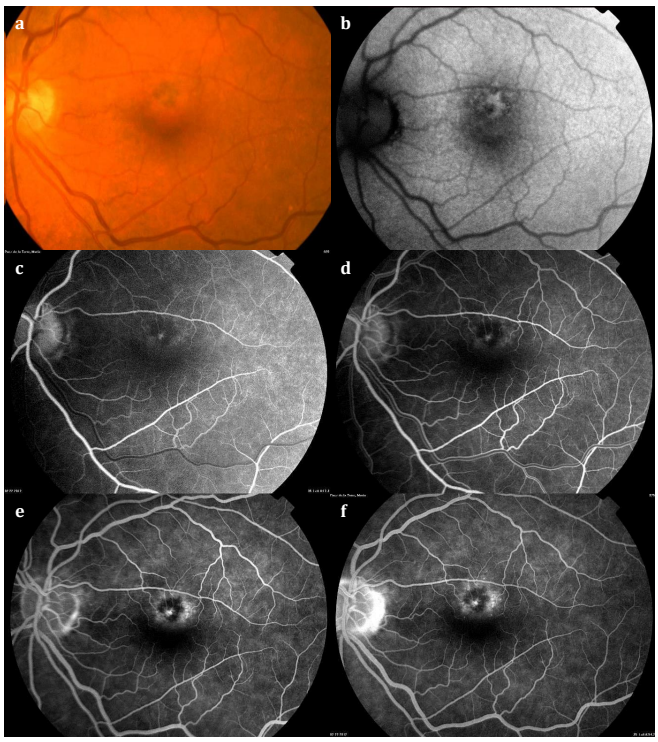

Fig. (1). A 73-year-old woman with retinal angiomatous proliferation. Fundus photograph and autofluorescence revealing perifoveal lesion (**a** and **b**). Fluorescein angiogram showing hyperfluorescence with diffuse leakage of dye (**c-f**) (Courtesy of Alejandro Lavaque, Argentina).

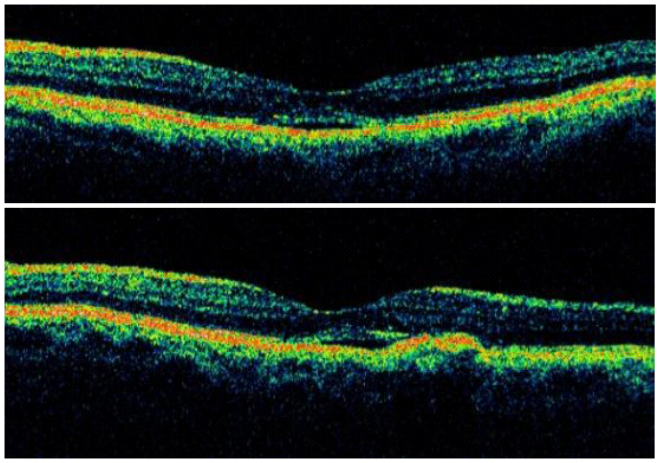

Fig. (2). OCT of the same patient shown in Fig. (**1**). OCT scans showing subretinal fluid and hyperreflective subretinal lesion (Courtesy of Alejandro Lavaque, Argentina).

CHAPTER 18

Choroidal Neovascular Membrane in Degenerative Myopia

Federico Furno Sola[1,2,*]

[1] *Ophthalmology Service, Sanatorio Mapaci, Rosario, Santa Fe, Argentina*

[2] *Grupo Laser Visión, Rosario, Santa Fe, Argentina*

ESSENTIALS OF DIAGNOSIS

Myopia is a common condition in many countries, particularly in East Asia, affecting approximately 40% of Chinese adults older than 40 years. The prevalence of myopia in developed countries is reported to be between 11% and 36%. The overall prevalence of pathologic myopia is approximately 1% to 4% in the general adult population although there is a wide geographical variation. The associated prevalence of visual impairment due to pathologic myopia is estimated to be 0.1% to 1.4%. The definition of pathologic myopia is not standardized, but is historically classified in clinical trial literature as a myopic refractive error greater than -6 diopters, or an axial length >26 mm, associated to degenerative changes involving the sclera, choroid and retina. Choroidal neovascularization secondary to pathological myopia is a common vision-threatening complication and often affects adults of working age, and develops in approximately 5% to 10% of patients with pathological myopia. The overall prevalence of choroidal neovascularization secondary to pathological myopia is therefore estimated to be approximately 0.04% to 0.05% in the general population [1, 2].

The chorioretinal lesions are viewed as a consequence of excessive axial elongation. It is believed that progressive distension of the posterior pole stretches the retina, choroid and sclera, as evidenced by the straightening of the temporal

* **Corresponding author Federico Furno Sola:** Grupo Laser Visión, Mariano Moreno 1397, Rosario – Santa Fe, Argentina; Tel: +54 (0341) 4472122; Email: furnosola@gmail.com

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retinal vessels, the appearance of peripapillary atrophy, and the thinning of the retina and choroid. Various changes may occur in the fundus of a patient with myopia, related to the presence of myopic conus, staphylomas, retinal pigment epithelium and choroid disturbances and atrophic areas (Figs. **1**-**3**). Lacquer cracks are linear or stellate; the lines are fine, irregular in caliber, yellowish-white, horizontally oriented, single and/or multiple. Lacquer cracks are ruptures of Bruch´s elastic lamina and carry a guarded visual prognosis because of their association with focal degenerative lesions and subretinal neovascularization along their course [1, 2].

It is generally accepted that the pigmented lesion described by Fuchs and the hemorrhagic lesion reported by Foerster represent different stages of the process of the development of CNV in myopia (Fig. **2**). Neovascularization has been identified to precede the development of Fuchs spots. The growth of choroidal new vessels induces a sudden painless reduction in vision usually associated with metamorphopsia. Biomicroscopically, it is observed as a light-gray, round or elliptic macular lesion (Fig. **3**). The lesion is usually discrete in size and located next to the fovea [1, 2].

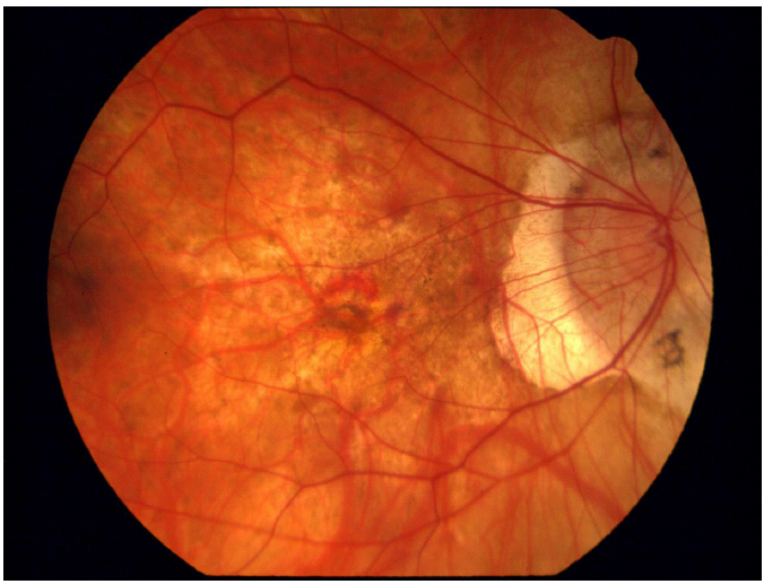

Fig. (1). Numerous areas of pigment epithelium atrophy and choriocapillaris extend to the macular region. A circular myopic crescent is visible.

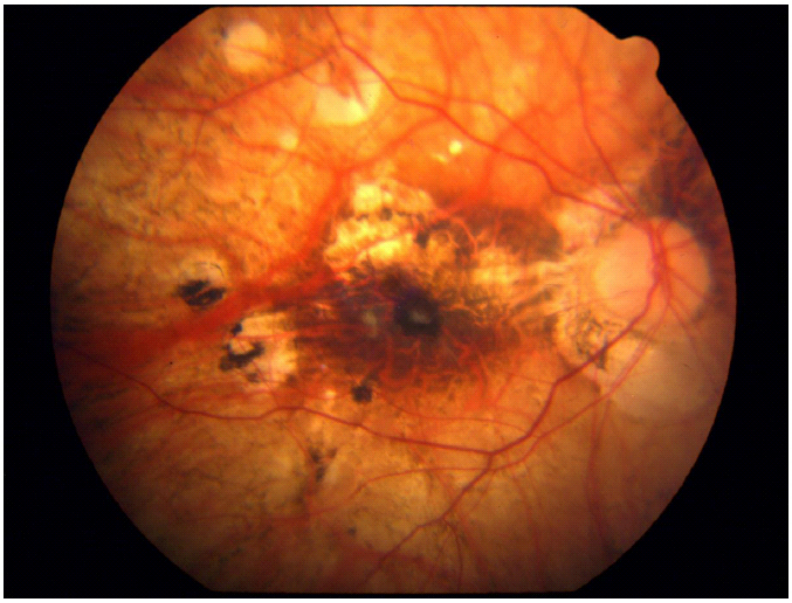

Fig. (2). Numerous areas of pigment epithelium and choriocapillaris atrophy extend into the macular region. A circular myopic crescent is visible. Hemorrhage occupies the center of the fovea.

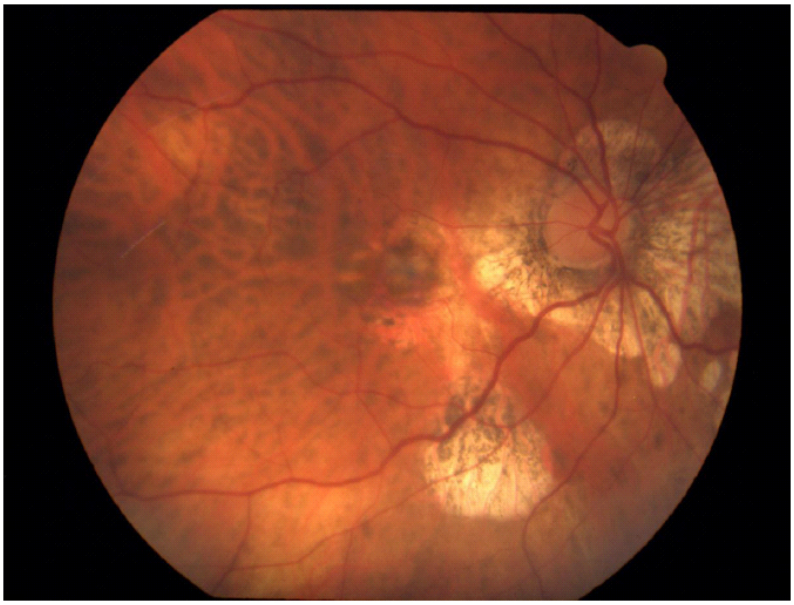

Fig. (3). Numerous areas of atrophy of the pigment epithelium and choriocapillaris extend to the macular region. A circular myopic crescent is visible. Choroidal new vessels with neovascular lesion and macular edema.

CHAPTER 19

Angioid Streaks

Michael Larsen[1,*], Mette K.G. Andersen[1], Naresh Mandava[2] and **Richard Hwang[3]**

[1] *Department of Ophthalmology, Glostrup Hospital and Faculty of Health Sciences, University of Copenhagen, Kobenhave Denmark*

[2] *Department of Ophthalmology, University of Colorado School of Medicine, Aurora, CO, USA*

[3] *Vitreoreitnal Disease and Surgery, Department of Ophthalmology, University of Colorado School of Medicine, Aurora, CO, USA*

Angioid streaks is the term used for a characteristic type of posterior segment lesion consisting of irregular and sometimes branching lines with a red or brownish appearance that extend from the rim of the optic disc to the periphery of the fundus (Figs. **1-4**, **8A, B**, **9A, B**) [1]. They were originally described by Doyne in 1889 [2]. The streaks are caused by breaks in the Bruch's membrane – retinal pigment epithelium (RPE) complex [1].

Angioid streaks can be seen in the presence of various extraocular conditions, most commonly pseudoxanthoma elasticum, a connective tissue disorder caused by defects in the *ABCC6* gene [3]. It gives rise to lax and dimpled skin, mainly on the flexor side of the neck, elbows and knees (Fig. **6**). The inheritance is mostly autosomal recessive, but autosomal dominant patterns can also be seen. The precise physiological function of ABCC6 is unknown, but it can be seen to be involved in transporting intracellular elements to the extracellular space. Defects in the ABCC6 protein lead to the accumulation of mineralized and fragmented

[*] **Corresponding author Michael Larsen:** Department of Ophthalmology, Glostrup Hospital and Faculty of Health Sciences, University of Copenhagen, Kobenhave, Denmark; Email: MICLAR01@regionh.dk

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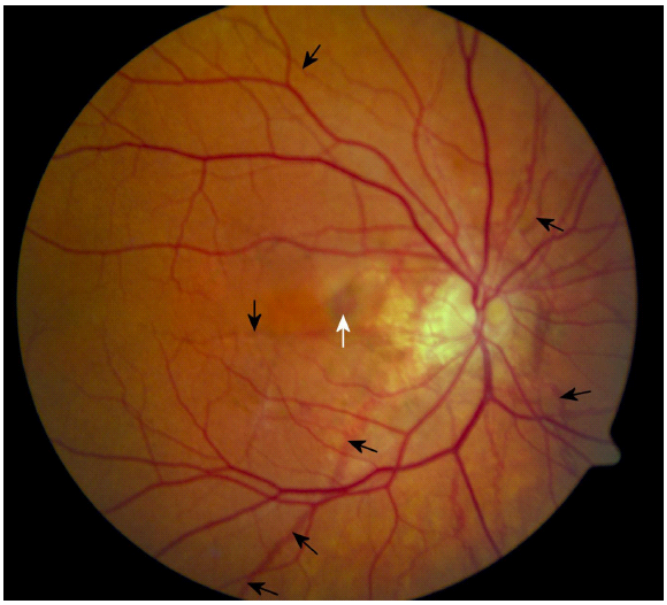

Fig. (1). Angioid streaks (black arrows) of the classic red type that resemble large choroidal blood vessels. The streaks are found behind the retinal blood vessels at the level of the retinal pigment epithelium. Red streaks stain early and prominently on fluorescein angiograms. Subfoveal choroidal neovascularization is also seen in this case (white arrow).

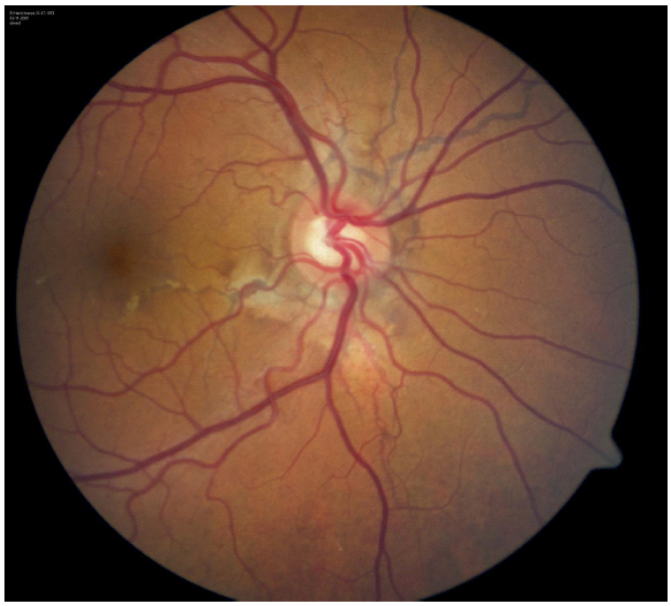

Fig. (2). Brownish and greyish pigmented angioid streaks temporal and superior of the optic disc in a patient with pseudoxanthoma elasticum. Note also subfoveal hemorrhage and choroidal neovascularization.

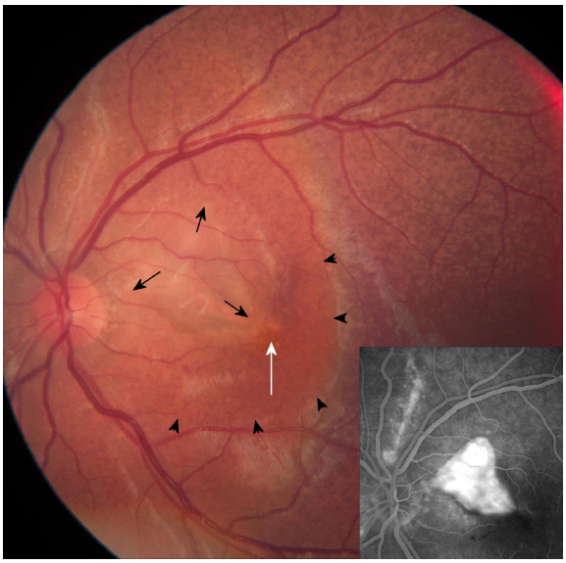

Fig. (3). Parafoveal classic subretinal neovascularization of choroidal origin (black arrows) in a patient with angioid steaks, one of which can be seen superior to the optic nerve head. Fluorescein angiography (lower right) shows prominent leakage, which explains the serous detachment of the neurosensory retina (black arrowheads). The upper right part of the color fundus photograph shows the spotted orange peel (peau d'orange) appearance of the diffuse outer retinal degeneration.

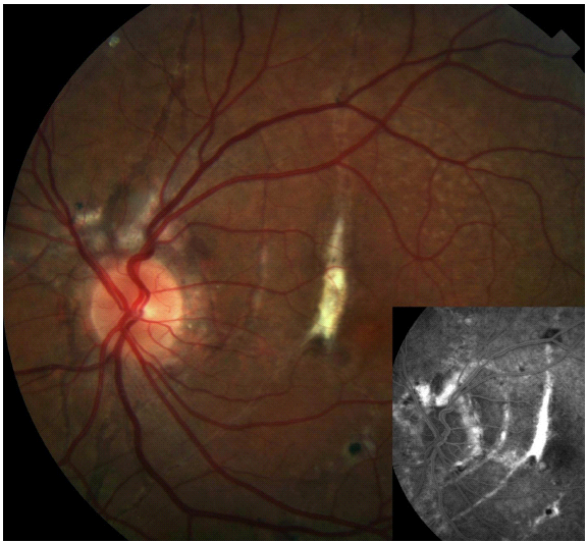

Fig. (4). Angioid streaks, a mixture of brownish streaks, pale atrophic areas, mainly around the margin of the optic disc, curved streaks concentric with the disc that are reminiscent of traumatic choroidal rupture lines and a small active choroidal neovascularization of approximately 250 μm diameter at the inferonasal margin of the fovea, emanating from the inferior tip of the large pale defect of the retinal pigment epithelium.

CHAPTER 20

Presumed Ocular Histoplasmosis Syndrome

Manuel Garza-León[1,*], Luz Elena Concha del Río[2] and **Miguel Pedroza Seres[3]**

[1] *Department of Medical Sciences, Division of Health Sciences, Universidad de Monterrey, Monterrey, Nuevo León, México*

[2] *Uveitis Department, Asociación para Evitar la Ceguera en México. I.A.P, Mexico*

[3] *Uveitis and Ocular Inmunology Department, Instituto de Oftalmología Conde de Valenciana, México, DF. Clínica de Retina, Guadalajara, J., Mexico*

Presumed ocular histoplasmosis syndrome (POHS) is an inflammatory eye disease that has been reported to be associated with systemic fungal infection by *Histoplasma capsulatum* [1]. It is restricted mainly to endemic countries and is mainly seen in the midwest of the United States and where *Histoplasma capsulatum* is endemic [2], although there have been reports of a similar disease from countries that are nonendemic zones for the microorganism [3].

ESSENTIALS OF DIAGNOSIS

POHS is a posterior uveitis, predominantly diagnosed clinically by the observation of characteristic fundus lesions in one or both eyes. The ocular triad of POHS consists in the presence of multiple atrophic choroidal spots (known as *histo spots*) (Fig. **1**), peripapillary atrophy (PPA) and maculopathy (Figs. **2**-**5**). Macular lesions are secondary to choroidal neovascularization (CNV) or atrophy and most of the time display a disciform pattern (Figs. **4**, **6**). Also, one of the key manifestations of POHS is the absence of inflammation in the vitreous. The disease occurs predominately in young adults and linear streaks are described in 5-16% of cases [3, 4]. Initially the disease occurs in one eye, being able to affect the second eye in 9-22% of cases [5, 6].

* **Corresponding author Manuel Garza-León:** Department of Medical Sciences, Division of Health Sciences, Universidad de Monterrey, Monterrey, Nuevo León, México; Tel: +52 8188824208; Fax: +52 81888242'8; E-mail: manuel@drgarza.mx

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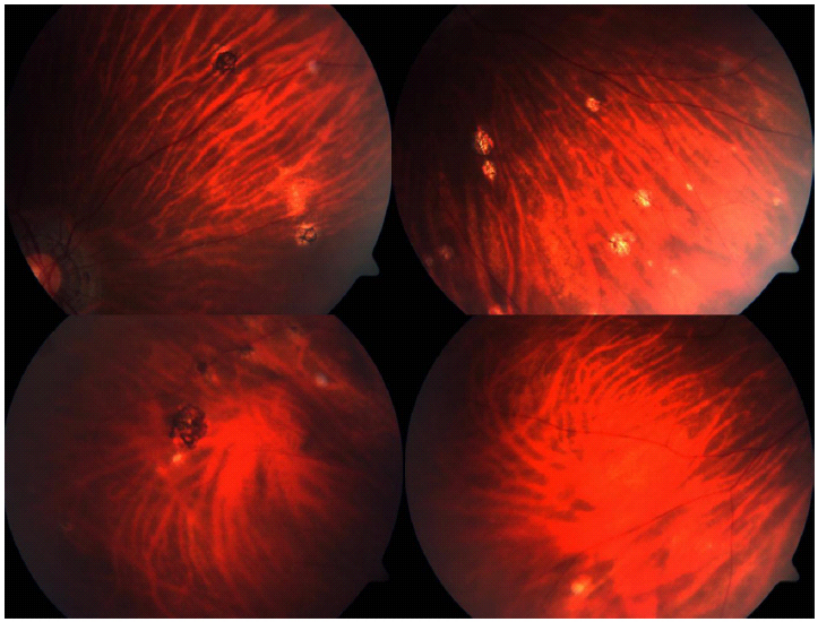

Fig. (1). Fundus photographs of a 62-year-old female. Visual acuity was 20/30 in the right eye and 20/25 in the left eye. The anterior segment had no inflammation, there were no vitreous cells. Several chorioretinal scars were observed in the posterior pole and periphery.

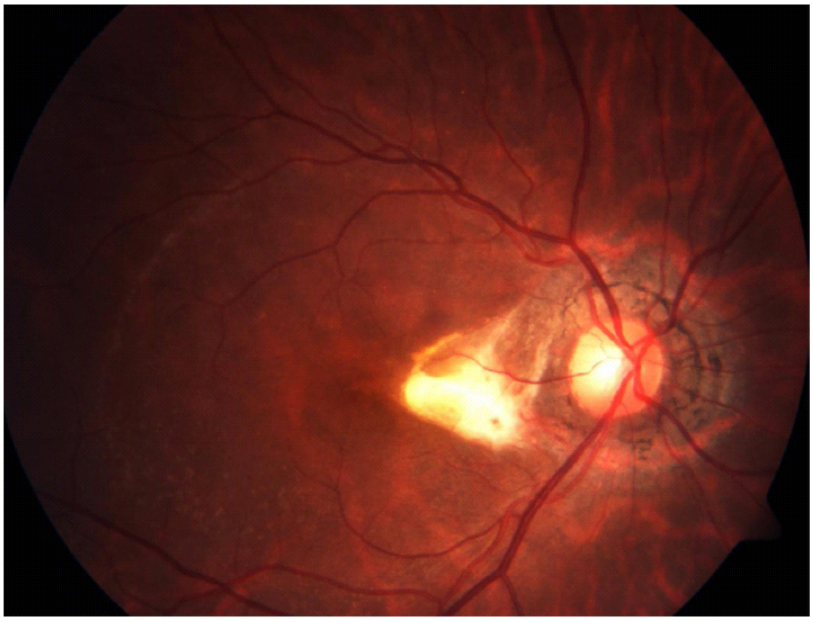

Fig. (2). Fundus photograph of the same patient as Fig. (**1**).

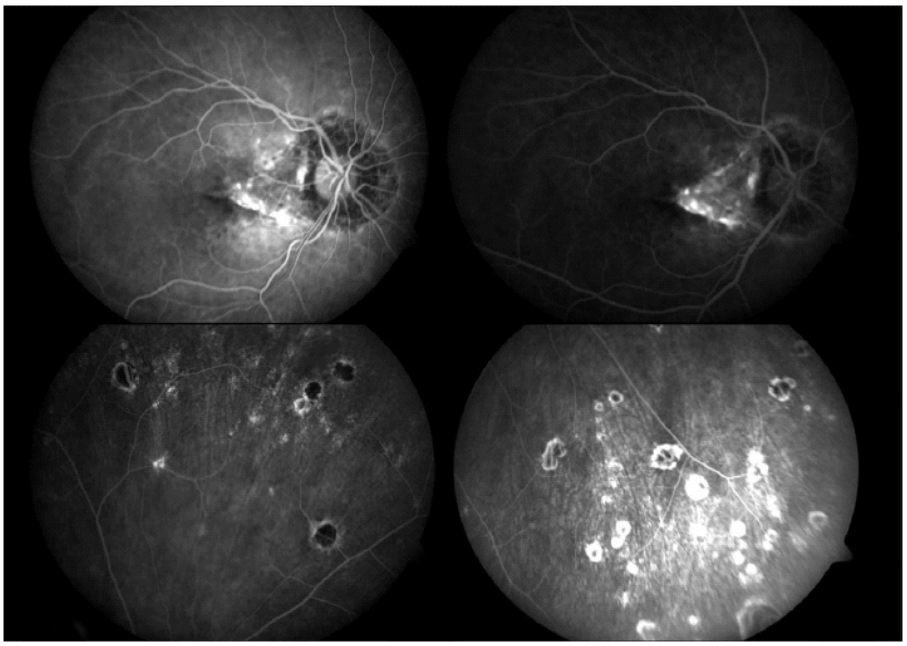

Fig. (3). Fluorescein angiogram of the same patient as Figs. (**1** and **2**). Dye accumulation due to a fibrous scar is observed adjacent to the optic nerve. Several histo spots may be observed in the periphery.

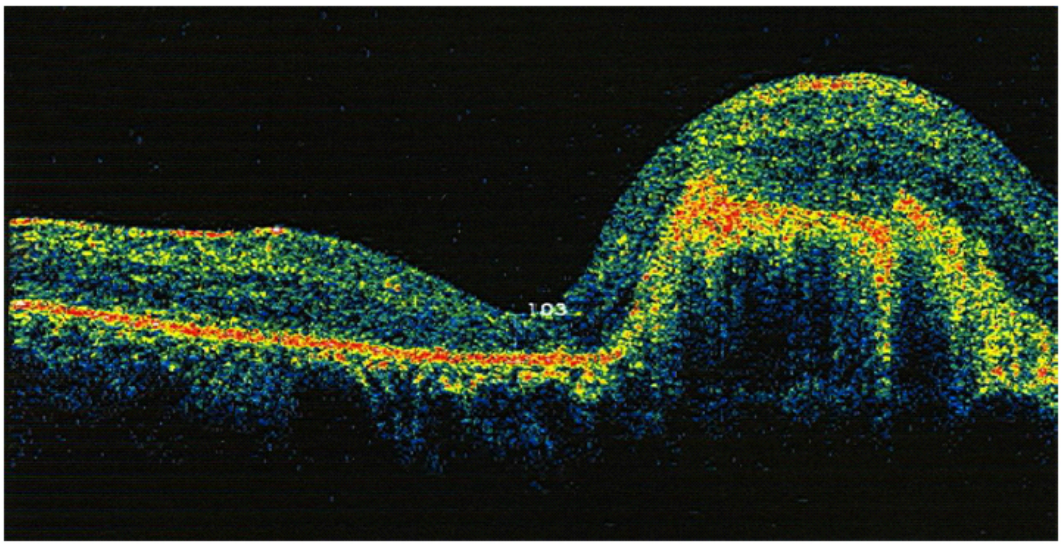

Fig. (4). OCT of the macula of the same eye as Figs. (**1-3**). A large area of subretinal fibrosis is observed.

CHAPTER 21

Epiretinal Membrane

Aristides J. Mendoza[1,2,*]

[1] *Retina Department, Centro Oftalmológico de Valencia (CEOVAL), Valencia, Venezuela*

[2] *Retina Department, OftalmoSalud, Arequipa, Peru*

The epiretinal membrane (ERM) represents the growth of avascular fibrotic tissue on the surface of the retina in the macular area, which causes loss of vision and distortion of images when it contracts [1].

ERMs can be caused by a variety of eye problems. They are classified as idiopathic when not linked to any other eye disease and usually appear after a posterior vitreous detachment as a result of the formation of retinal tears that release inflammatory cells and pigment epithelial cells deposited at the posterior pole. Secondary ERMs are associated with retinal detachment, intraocular inflammation, trauma and vascular diseases of the retina [2]. There are two types of ERMs that have different clinical presentations: simple and contractile. Simple ERMs are membranes with cellophane-like films on the internal limiting membrane (ILM) with little or no visual symptoms. In general, they are composed mainly of glial cells. On the contrary, tractional ERMs are thicker with contractile properties that cause wrinkling of the retina and are usually accompanied by decreased vision and metamorphopsia. They are composed of glial cells and contractile cells [3], and are also known as "macular puckers" (Fig. **1**).

Epiretinal membranes cause macular structural changes such as retinal folds, vascular leakage, macular thickening, cystoid macular edema, pseudohole formation, foveal ectopia, and foveal detachment by tractional forces on the retinal surface [4].

* **Corresponding author Aristides J. Mendoza:** Retina Department, OftalmoSalud, Arequipa, Av Mariscal Benavides No 307, Urb Selva Alegre, Arequipa, Peru; Tel: +51(054)287373; E-mail ampcff@hotmail.com

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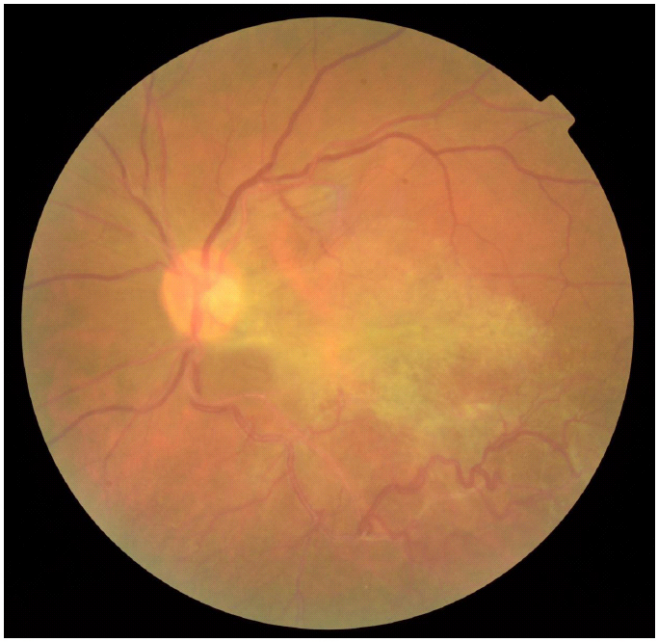

Fig. (1). Macular pucker secondary to BRVO (Courtesy of Mitzy E. Torres Soriano).

ESSENTIALS OF DIAGNOSIS

Epiretinal membranes typically affect otherwise healthy elderly individuals and are unilateral in approximately 90% of cases. Visual symptoms and decreased visual acuity will depend on the degree of distortion caused in the traction retinal membrane, which can generate a micro detachment of the posterior pole, as well as the presence or absence of macular or perimacular edema. Usually, thin epiretinal membranes don't cause many symptoms. However, in advanced cases, there is a reduction in vision, micropsia, metamorphopsia, Amsler grid distortion and, occasionally, monocular diplopia. Spontaneous separation of an epiretinal macular membrane, although uncommon, can occur [5, 6].

Slit lamp ophthalmoscopy: brightness or abnormal reflectivity in the macular region suggests the presence of an ERM (Fig. **2a**). More advanced ERMs can become opaque and thick, and may obscure underlying retinal features (Fig. **1**). ERMs cause changes in the retinal architecture with loss of foveal contour as a result of contraction.

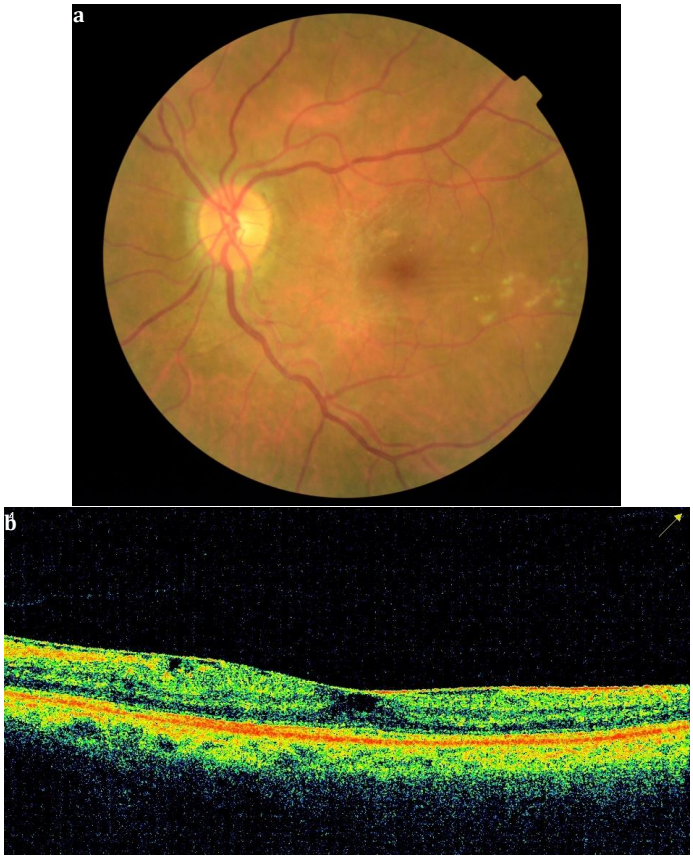

Fig. (2). (**a**) Fundus photograph that shows the typical clinical appearance of an ERM. The membrane adherent to the surface of the retina contracts and the retinal surface appears wrinkled. (**b**) OCT scan confirms ERM (Courtesy of Mitzy E. Torres Soriano).

In addition to visual acuity testing, the most common clinical tests involve fluorescein angiography and optic coherence tomography (OCT). Fluorescein angiography is moderately helpful, since it can show retinal vascular tortuosity, straightening, and leakage, as well as cystoid macular edema. OCT is the diagnostic method of choice, typically demonstrating a hyperreflective line in the surface of the retina that may be associated to retinal folding, increased macular thickness, cystoid macular edema, traction macular retinal detachment, and both lamellar or macular hole formation (Figs. **2b**, **3**-**6**). Amsler grid testing may help quantifying metamorphopsia in eyes with macular distortion [7]. Abnormal macular function has been shown using the electroretinogram [8, 9].

CHAPTER 22

Idiophatic Macular Hole

Luis M. Suarez-Tata[1,*], Moravia B. Suarez-Tata[1] and **Reinaldo García[1]**

[1] *Retina & Vitreous Service, Clínica Oftalmológica El Viñedo, Valencia, Venezuela*

Idiopathic macular hole (MH) is an acquired full thickness defect of the retina in the central macula. Macular holes were first described by Knapp in 1869 [1]. They typically occur in the sixth to eighth decade of life with a 3:1 predominance in women. The incidence of bilaterally is 5% to 10%. Tangential vitreoretinal traction (TVT) is the presumed cause of the MH.

ESSENTIALS OF DIAGNOSIS

Visual acuity, depending on the stage and severity of the MH, may be near normal or severely reduced to less than 20/400. Amsler grid will often reveal a central scotoma or metamorphopsia.

Slit-lamp biomicroscopic examination usually shows a round retinal defect that involves the fovea. Several diagnostic maneuvers may be used to find out if the lesion observed in examination is indeed a full-thickness defect (*vs.* a macular *pseudo* hole). If a tall, narrow beam is focused on the lesion, the patient may perceive a break or dent in the beam (the so-called "Watzke-Allen test). This also may be tested using the aiming beam of a retinal laser photocoagulator.

The gold-standard diagnostic tool is optic coherence tomography (OCT), due to the fact that it is non-invasive, has a very high resolution, allows careful evaluation of retinal structures and the vitreomacular interface.

[*] **Corresponding author Luis M. Suarez Tata:** Clínica Oftalmológica El Viñedo, Valencia, Venezuela; Tel/Fax: +58 (412) 3474188; E-mail: luismiguelsuarez@gmail.com

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It also enables quantitative information such as minimum hole diameter, base diameter and retinal edge thickness [2].

Fluorescein angiography may also be used but has fallen into disuse, since findings are vague (a window defect corresponding to loss of xanthophyll pigment), and compared to OCT has very little sensitivity and specificity.

Classification

Gass described different stages of development of MH (Table **1**) [3, 4]. Nowadays, with OCT and the identification of vitreomacular traction and its relationship with MH, the International Vitreomacular Traction Study Group has proposed a new classification based on OCT findings and the status of the vitreomacular interface (Tables **2**-**4**) [5].

Table 1. Stage of development of idiopathic macular hole.

Normal	Layer of vitreous cortex lying on internal limiting membrane of retina (Figs. **1** and **2**)
Stage 1A:	Early contraction of outer part of vitreous cortex with foveolar detachment (Fig. **3**)
Stage 1B:	Occult hole. Dehiscense of the retinal photoreceptor layer at the umbo with centrifugal retraction of the retinal receptors. Further vitreous contraction and condensation of the prefoveal vitreous cortex with foveal detachment (Figs. **3**-**5**)
Stage 2:	Small perifoveal dehiscense. Small (< 400 μm) (Figs. **6** and **7**)
Stage 3:	Larger central full-thickness hole usually accompanied by a rim of retina elevation (>400 μm) (Figs. **8** and **9**). The posterior cortical vitreous remains attached. There may be a small operculum overlying the macular hole.
Stage 4:	Macular hole has an associated complete posterior vitreous detachment. These holes are usually large (> 400 μm) (Figs. **10**-**13**)

Based on Gass JD [3, 4].

DIFFERENTIAL DIAGNOSIS

There are several diseases that may resemble MH clinically but have distinct appearances on OCT. Macular pseudohole is an epiretinal membrane that spares the center of the fovea, causing its borders to elevate, clinically resembling a MH. The Watzke-Allen test is negative, and on OCT, the outer retinal layers are spared (Figs. **12**-**14**). Lamellar macular hole is also usually associated to an epiretinal membrane, and on OCT shows an irregular foveal contour with schisis of the

retinal layers in the parafovea, and a preserved photoreceptor layer (Figs. **14-19**). Vitreomacular traction syndrome has also to be considered, and actually is believed to play an important role in the pathophysiology of MH. Other differential diagnoses include macular telangiectasia and solar retinopathy [6, 7].

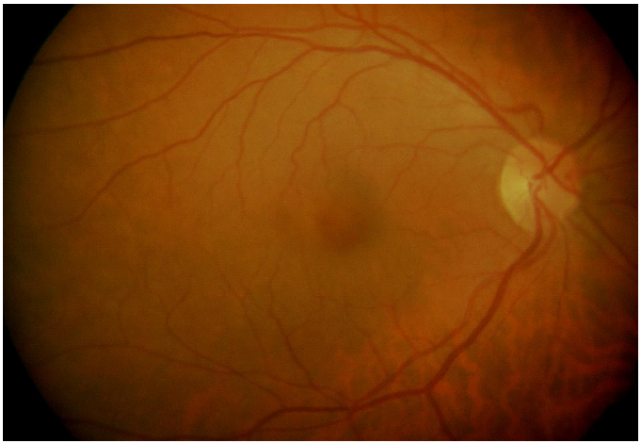

Fig. (1). Fundus photograph showing a normal macula.

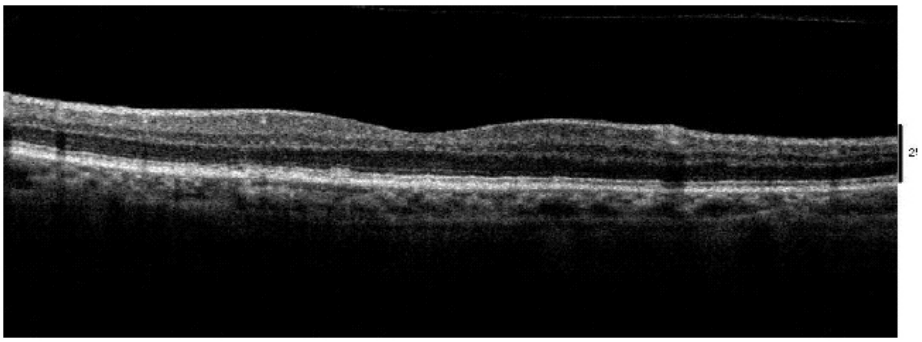

Fig. (2). Optical coherence tomography (OCT) image of a normal macula.

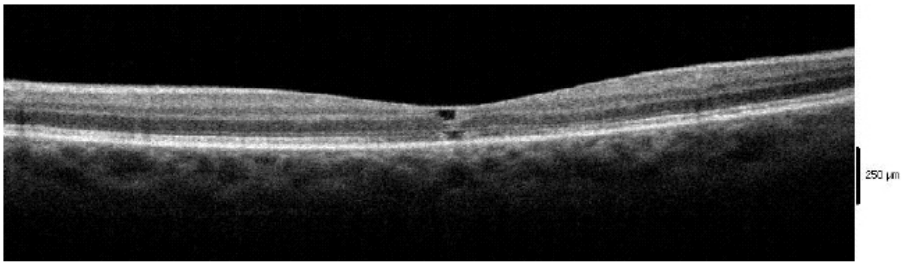

Fig. (3). OCT image of a macular hole stage 1-A, showing hyporeflective spaces in the inner and outer retina.

CHAPTER 23

Macular Pseudo-hole

Jose A. Roca[1,*], Hugo Luglio[2] and **Daniela Roca[1]**

[1] *Ophthalmology Department, Clínica Ricardo Palma, Lima-Peru, Peru*

[2] *Macula D&T, Lima-Peru, Peru*

ESSENTIALS OF DIAGNOSIS

The term "macular pseudo-hole" (MPH) was coined by Allen and Gass in 1976 [1] to describe any foveal lesion that has a biomicroscopic appearance of a full-thickness macular hole (FTMH), but is not. It is usually formed by a centrifugal contraction of an epiretinal tissue (epiretinal membrane) that surrounds but does not cover the foveolar area, making the borders have a more vertical appearance [2].

The patient usually has no complaints, and the visual acuity is normal or nearly normal, ranging from 20/15 to 20/100 (median 20/25) [3]. Because of the good surgical results of true macular holes, it is important to differentiate between a true macular hole and a macular pseudo-hole. The appearance of a true macular hole is different, usually very round, with a halo of marginal detachment surrounding the hole, tiny yellow deposits in its base (within the hole), a translucent operculum in front of some holes, and a zone of hyperfluorescence corresponding to the size of the hole during the early stages of angiography. These characteristics are not seen in a macular pseudo-hole.

Biomicroscopy of a patient with a macular pseudo-hole usually reveals crinkling of the inner retinal surface surrounding the hole in the epiretinal membrane and a punched-out appearance in the area of the hole (Fig. **1**) [4]. As the slit beam is

Correspondence: **Corresponding author Jose A. Roca:** Ophthalmology Department, Clínica Ricardo Palma, Torre B, piso 10, San Isidro, Lima-Peru; Tel: +51 (1) 2242224; E-mail: jaroca62@gmail.com

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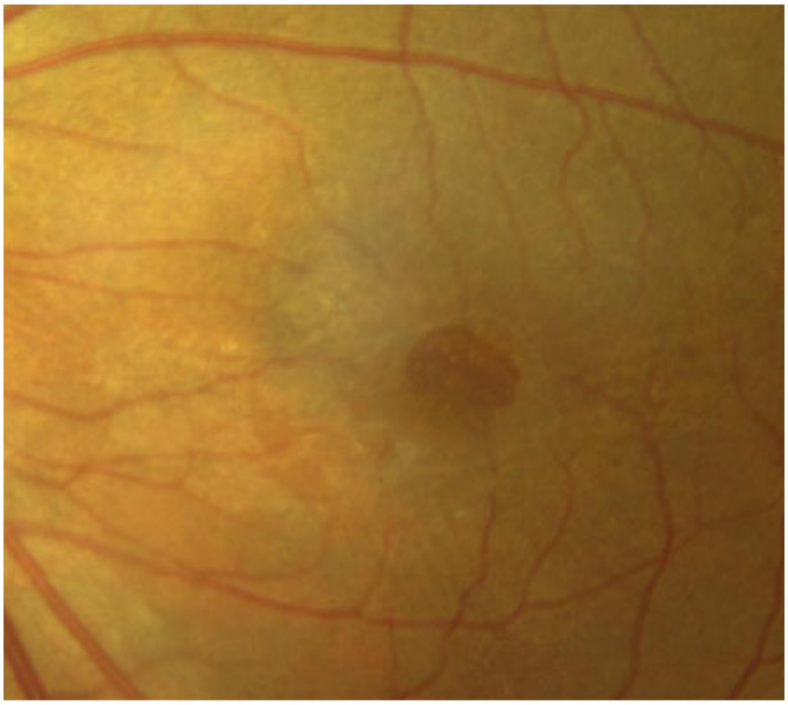

Fig. (1). Fundus photograph of the left eye, showing a macular pseudohole with an epiretinal membrane.

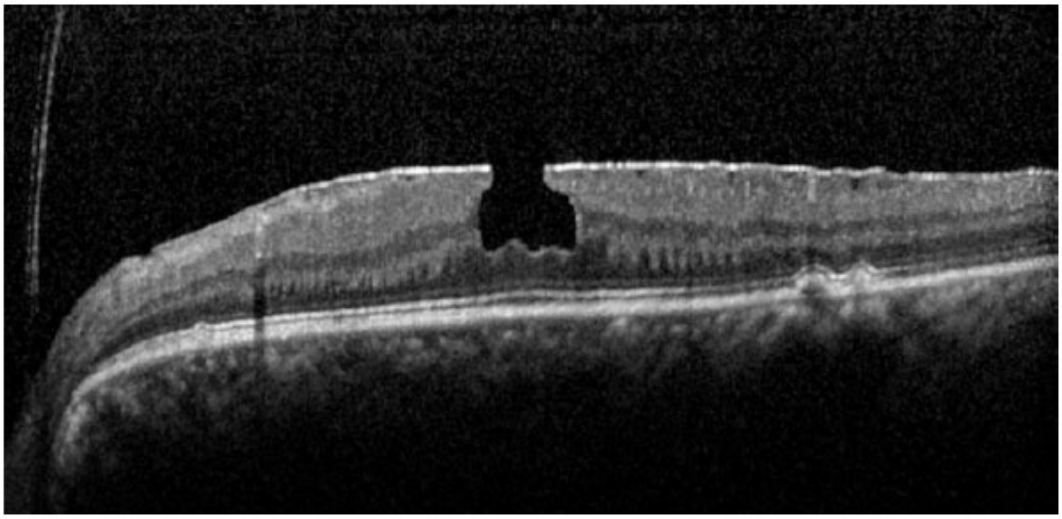

Fig. (2). OCT of the same patient of Fig. (**1**), showing a macular pseudo-hole with an epiretinal membrane with a U form fovea and preserved outer retinal layers.

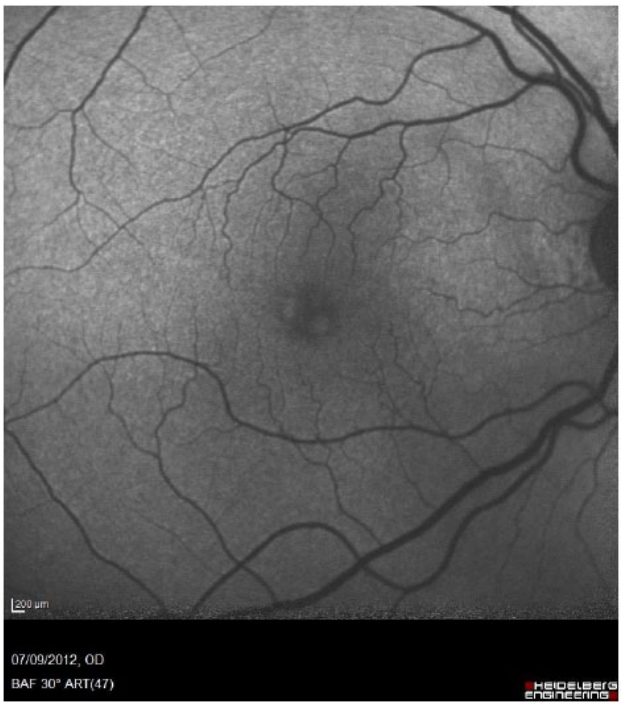

Fig. (3). Autofluorescence of a macular pseudo-hole.

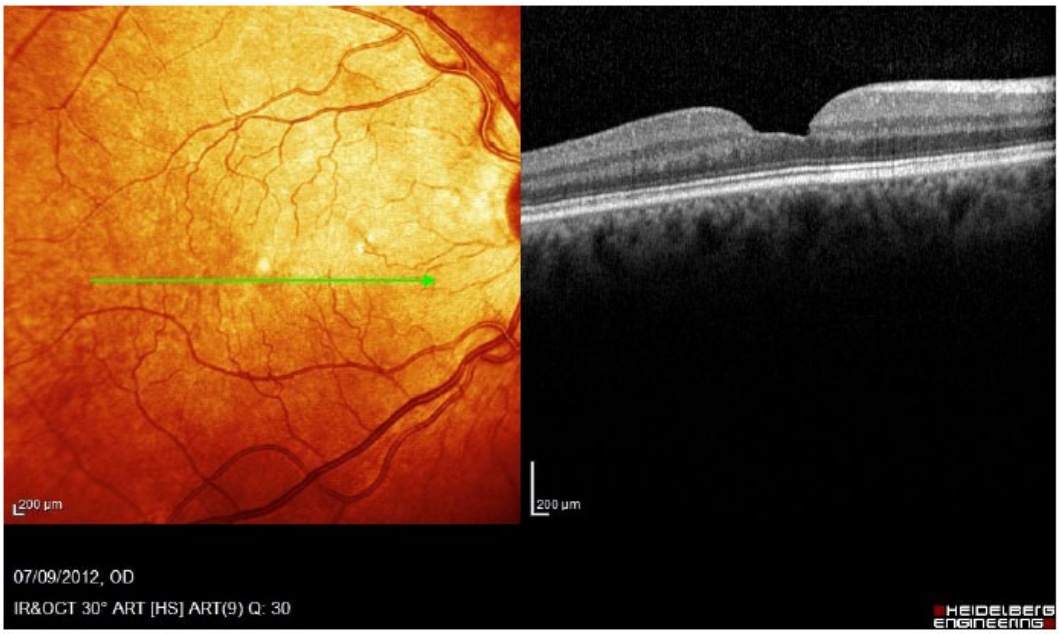

Fig. (4). OCT image of a macular pseudohole showing slight distortion of the foveal contour.

CHAPTER 24

Vitreomacular Traction

Mitzy E. Torres Soriano[1,2,3,*] and **Maximiliano Gordon**[2,3]

[1] *Unidad Oftalmológica "Dr. Torres López", Centro Médico Cagua, Cagua, Venezuela*

[2] *Retina Department, Ophthalmology Service, Hospital Provincial del Centenario, Rosario, Santa Fe, Argentina*

[3] *Centro de la Visión Gordon-Manavella, Rosario, Argentina*

Vitreomacular Traction Syndrome (VMT) occurs as a result of incomplete posterior vitreous detachment, resulting in persistent vitreous traction on the posterior retina [1].

The prevalence of VMT syndrome is 22.5 per 100,000 population. The annual incidence is 0.6 per 100,000 population. The prevalence and incidence of VMT associated with diabetic retinopathy, diabetic macular edema, age-related macular degeneration, and other macular diseases (concurrent VMT) are much higher [2].

ESSENTIALS OF DIAGNOSIS

Patients may be asymptomatic or present the following symptoms: decreased visual acuity, metamorphopsia, photopsia, and micropsia [1]. Symptoms usually progress gradually [3].

Optical coherence tomography (OCT) allows visualization of the vitreomacular interface and confirms vitreomacular adhesion or traction. Intraretinal cystic changes and foveal detachment can be seen.

Recently, OCT-based anatomic definitions and classifications have been proposed by the International Vitreomacular Traction Study (IVTS) Group to define these entities (Table **1**) [4].

* **Corresponding author Mitzy E. Torres Soriano:** Centro de la Visión Gordon - Manavella, Montevideo 763, CP 2000, Rosario - Santa Fe, Argentina; Tel: +54 (0341) 4400239; E-mail: mitzytorres@yahoo.com

Table 1. IVTS classification system for vitreomacular adhesion and vitreomacular traction.

Vitreomacular Adhesion (VMA): Evidence of perifoveal vitreous cortex detachment from the retinal surface. Macular attachment of the vitreous cortex within a 3-mm radius of the fovea. No detectable change in foveal contour or underlying retinal tissues.	**Classification** ***By size of attachment area:*** Focal <1500 µm (Fig. **1**) Broad >1500 µm, parallel to RPE and may include areas of dehiscence ***(By presence of concurrent retinal conditions:)*** Isolated Concurrent
Vitreomacular Traction (VMT): Evidence of perifoveal vitreous cortex detachment from the retinal surface. Macular attachment of the vitreous cortex within a 3-mm radius of the fovea Association of attachment with distortion of the foveal surface, intraretinal structural changes, and/or elevation of the fovea above the RPE, but no full-thickness interruption of all retinal layers.	**Classification** ***By size of attachment area:*** Focal <1500 µm (Figs. **2**, **3** and **5**) Broad >1500 µm, parallel to RPE and may include areas of dehiscence (Fig. **4**) ***By presence of concurrent retinal conditions:*** Isolated Concurrent

Based on International Vitreomacular Traction Study Classification.

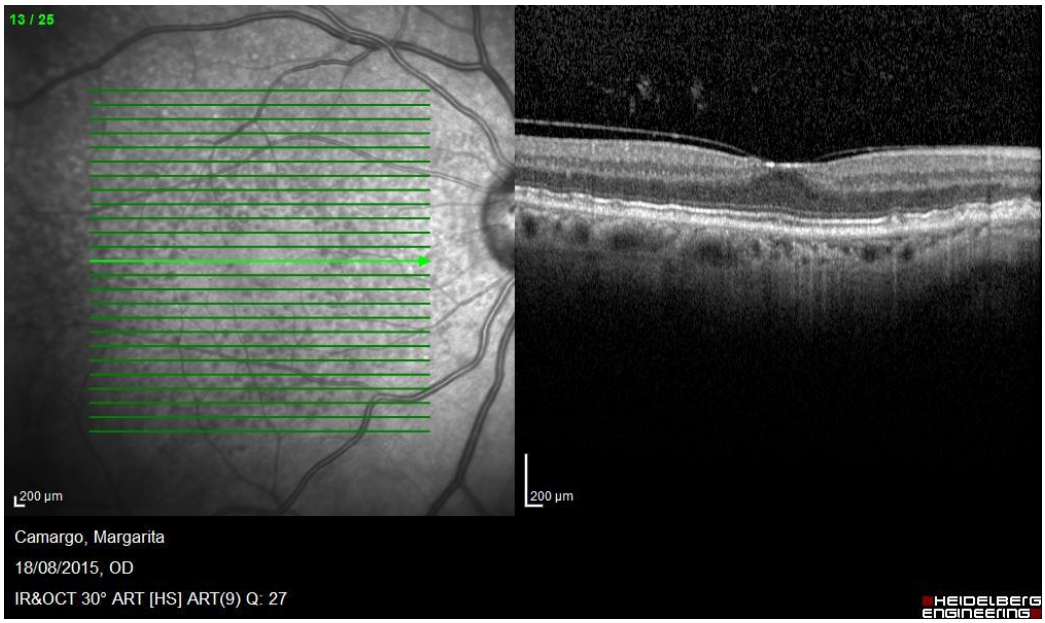

Fig. (1). Focal vitreomacular adhesion: partial vitreous detachment.

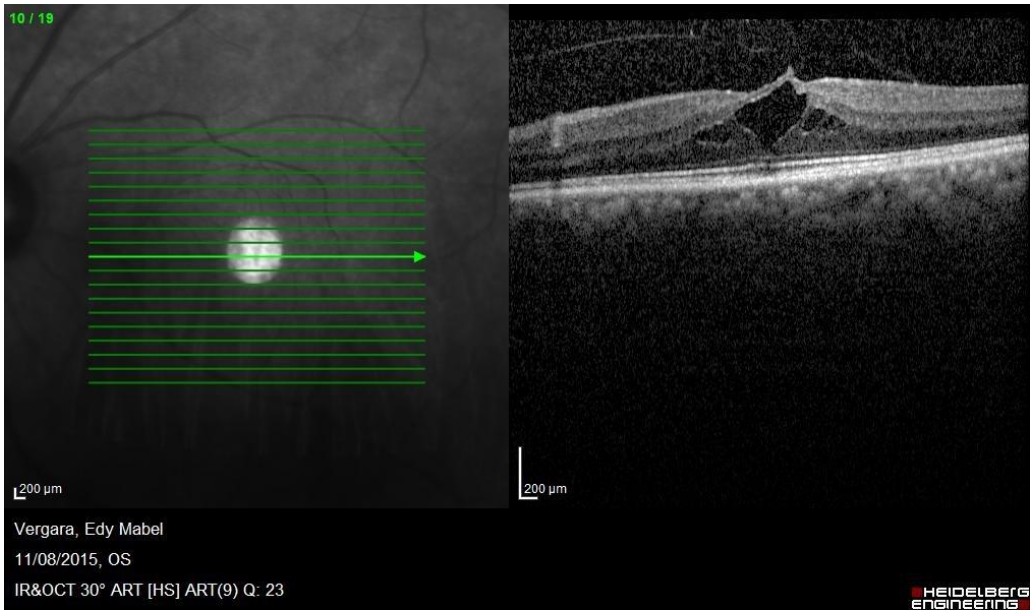

Fig. (2). Focal vitreomacular traction causing distortion of the foveal contour and separation of retinal layers.

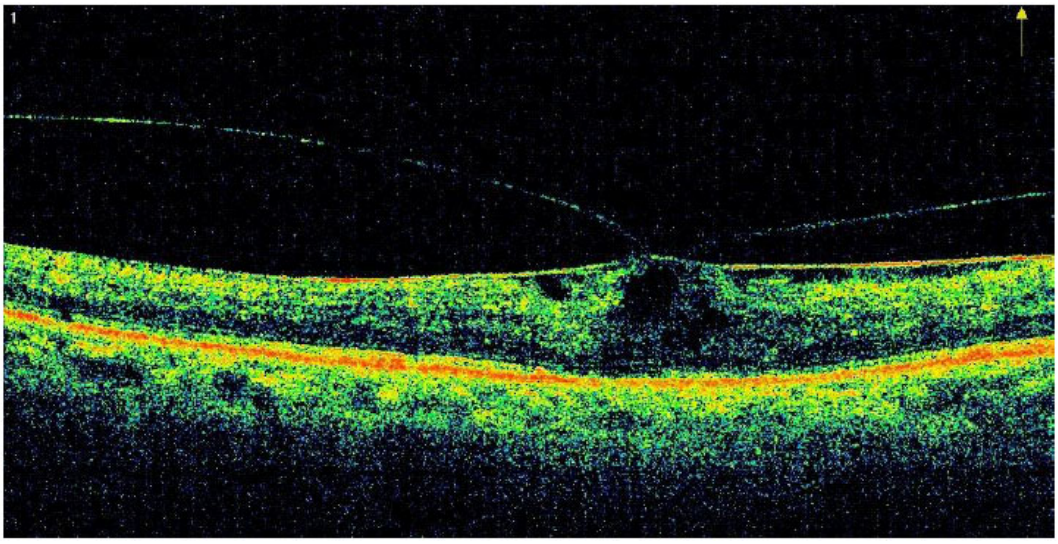

Fig. (3). Focal vitreomacular traction in V pattern, epiretinal membrane and significant distortion of the retinal architecture.

CHAPTER 25

Pseudophakic Cystoid Macular Edema

Andrés Bastien*

Universidad de Buenos Aires-Universidad del Salvador, Retina and Vitreous, Argentina

ESSENTIALS OF DIAGNOSIS

Pseudophakic cystoid macular edema (CME) was first described in 1953 by A. Ray Irvine, Jr., in patients with unexplained visual loss following intracapsular cataract surgery [1]. The cause of the visual loss was identified by Gass and Norton as marked macular edema with a classic perifoveal petalloid pattern of staining and late leakage from the optic nerve on intravenous fluorescein angiography (Figs. **1 - 3**) (FA) [2]. The incidence of angiographic CME has decreased with the transition from intracapsular cataract extraction (60%) to extracapsular cataract surgery (20%) and with small-incision phacoemulsification [3, 4]; 20-30% of patients undergoing phacoemulsification have CME on FA [5, 6] and optical coherence tomography (OCT) (Figs. **4** and **5**) suggests that it may be found in up to 40% of patients [7]. The majority of patients do not experience visual changes [6, 8]. The incidence is lower with current surgical techniques (0.1% to 2.35%) [9, 10].

Most patients with CME have spontaneous resolution of the edema within 3-4 months [11] One year after surgery, a small minority of patients (<1%) in the absence of treatment may still have decreased visual acuity from CME [12].

Pathogenesis

Various factors and many presumed mechanisms may be involved in the pathogenesis of CME, including the release of mediators of inflammation such as

* **Corresponding author Andrés Bastien:** Universidad de Buenos Aires-Universidad del Salvador, Retina and Vitreous, Argentina; Tel/Fax: 00541148114482; E-mail: andresbastien@aol.com

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prostaglandins, light toxicity, and mechanical irritation [13 - 15]. Inflammatory mediators disrupt the blood-aqueous barrier (BAB) and blood-retinal barrier (BRB), leading to increased vascular permeability resulting in macular edema. Breakdown of the BAB and BRB may be associated with diabetes, glaucoma, and uveitis [16]. Surgical complication of the anterior segment may lead to the release of arachidonic acid from cell membranes, with production of either leukotrienes *via* the lipooxygenase pathway or prostaglandins *via* the cyclooxygenase pathway [13, 14]. These inflammatory biomarkers result in increased retinal vessel permeability and the development of edema. Contraction of the posterior hyaloid as a result of inflammation may lead to mechanical traction onto the perifoveal retinal capillaries and result in CME [15].

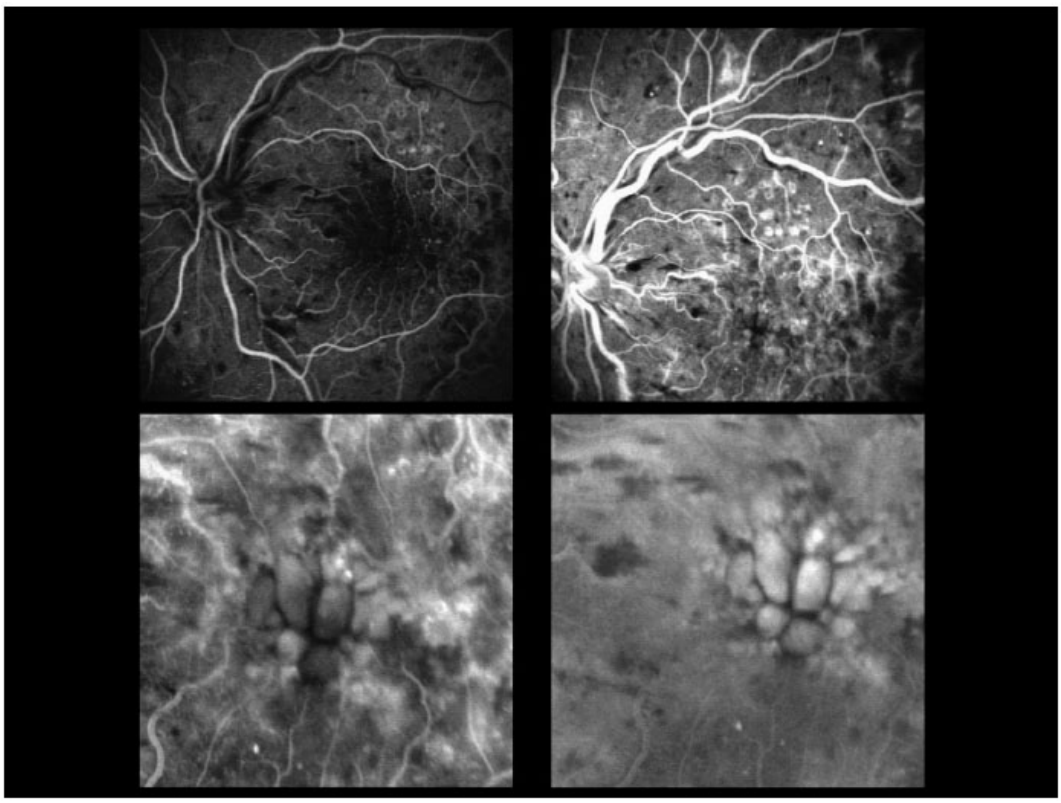

Fig. (1). Fluorescein angiography. Perifoveal petalloid staining.

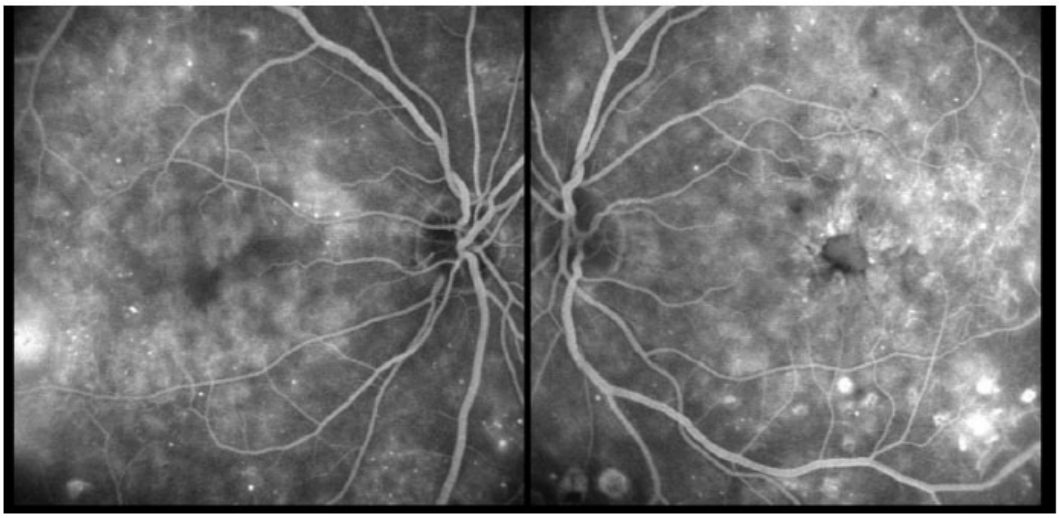

Fig. (2). Fluorescein angiography. Perifoveal petalloid staining.

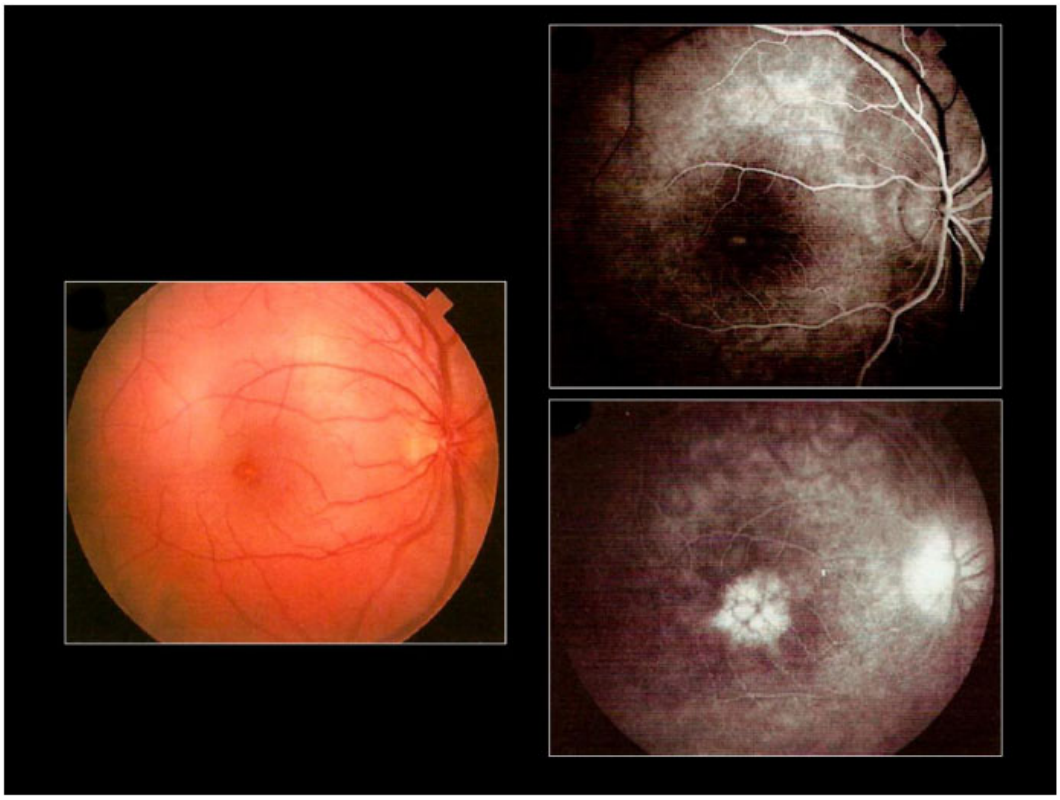

Fig. (3). Fluorescein angiography with macular late leakage.

CHAPTER 26

Central Serous Chorioretinopathy

Daniel D. Kim[1], Paul Baciu[1] and **Michael D. Ober[1,2,*]**

[1] *Department of Ophthalmology, Henry Ford Health Systems, Detroit, MI, USA*

[2] *Retina Consultants of Michigan, Southfield, MI, USA*

ESSENTIALS OF DIAGNOSIS

Central serous chorioretinopathy (CSC) is an idiopathic disorder characterized by serous detachment of the neurosensory retina. It has an incidence of roughly 6/100,000 individuals [1 - 3]. Affected patients are usually young to middle age adults (ages 25-45), male (5-10:1 male:female ratio), and of "Type A" personality [4 - 6]. The symptoms present unilaterally (60-90% of the time) and patients often complain of blurred central vision and metamorphopsia with a hyperopic shift [1 - 3, 5, 7]. A history of recent psychosocial stressors, or steroid use is often present. Disorders causing elevated levels of catecholamines are known to predispose. Furthermore, pregnancy, phosphodiesterase inhibitors, and illicit drug use have also less commonly been associated with onset of symptoms [2, 3, 6, 8].

Despite decades of study, the precise etiology and pathophysiology remain elusive. Much has been learned, however, through multimodal imaging studies that often yield pathognomonic findings (Fig. **1**). Fluorescein angiography (FA) in acute cases reveals a focal leak at the level of the retinal pigment epithelium (RPE) appearing as an expanding hyperfluorescent dot (30% have more than one) sometimes elevating into a smokestack appearance in 10-20% (Figs. **2** and **3**). Ultimately, the subretinal fluid pocket can extend inferiorly due to gravity creating descending atrophic tracts, which are best seen with fundus autofluorescence (FAF) [2, 3, 6, 8]. Chronic cases reveal multiple leaks in close

* **Corresponding author Michael D. Ober:** Retina Consultants of Michigan, 29201 Telegraph Road, Suite 606, Southfield, MI 48034, USA; Tel: (248) 356-6473; Fax: (248) 356-6473; E-mail: obermike@gmail.com

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proximity with mottled hyper and hypofluorescence of the RPE corresponding to "sick RPE syndrome" [9, 10]. Indocyanine green angiography (ICGA) demonstrates hyperfluorescence in mid-frames (not present early or late) often described as choroidal hyperpermeability (Fig. **4**) [2, 3, 6, 8, 11, 12].

As OCT technology has improved, it has become critical for diagnosis. Findings include subretinal fluid, RPE detachments, and retinal atrophy. Less common features include cystoid macular edema or cystoid macular degeneration, which is differentiated by lack of corresponding FA leakage and poor visual potential [2, 5, 8]. While relatively new, visualization of the choroid using enhanced-depth imaging shows marked thickening of the choroid in CSC (Fig. **5**), most prominent in zones of choroidal permeability with active angiographic leakage [8, 13].

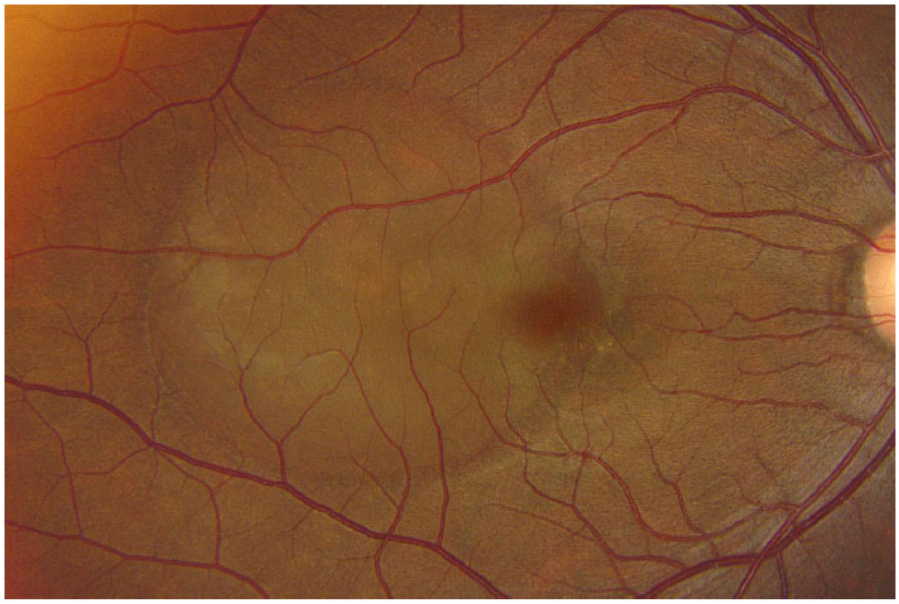

Fig. (1). CSC Fundus photo showing subretinal fluid causing serous retinal detachment (Photo Credit: Henry Ford Ophthalmic Photography).

Fundus autofluorescence is being used more frequently to image patients with CSC. Over time, a neurosensory detachment leads to an accumulation of lipofuscin from shed photoreceptor outer segments yielding patches of speckled hyperautofluorescence that can become more prominent when subretinal fluid first resolves. Over time, these areas become hypoautofluorescent as noted around

old leaks and chronic descending atrophic tracts [2, 8, 14]. Other diagnostic modalities include multifocal ERG, which shows broad retinal functional disturbances, and abnormal visual field testing, especially on microperimetry, indicating that central visual acuity underestimates the amount of visual impairment [8, 15].

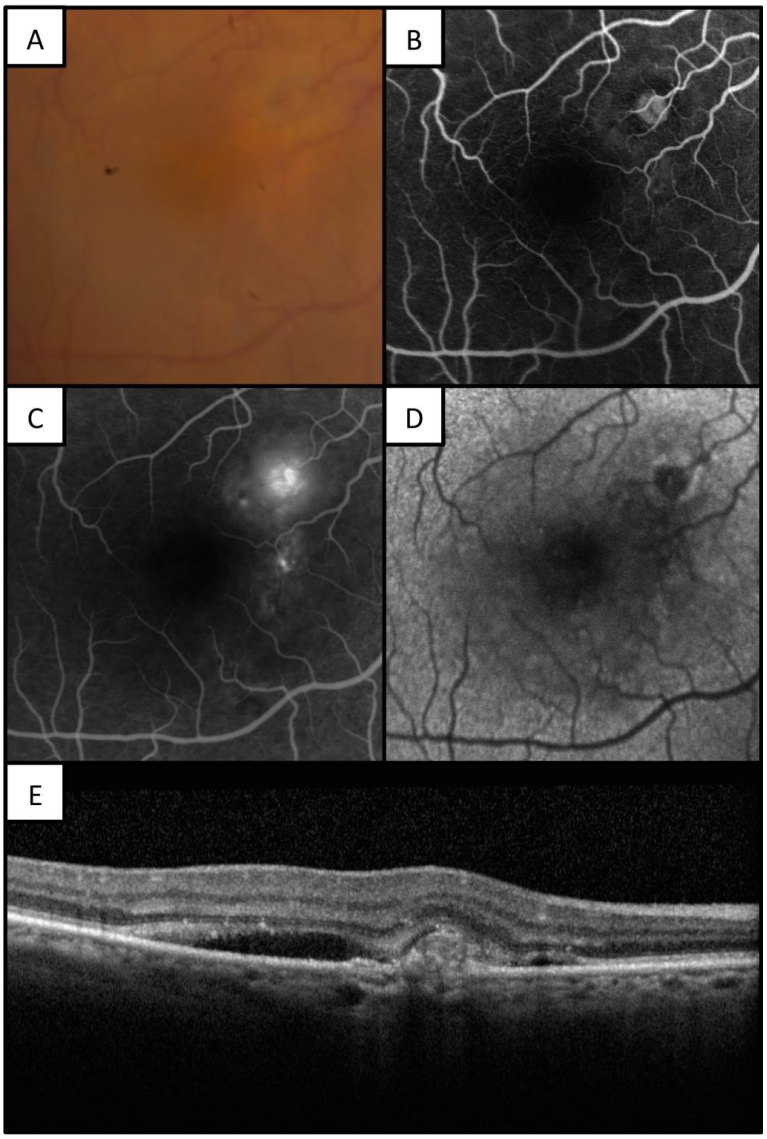

Fig. (2). RPE blowout as imaged by fundus photography (**A**), early (**B**) and late (**C**) fluorescein angiography, autofluorescence (**D**) and OCT (**E**) (Photo Credit: Lorrene Santiego).

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Mitzy E. Torres Soriano

Dr. Mitzy E. Torres Soriano graduated with honors in medicine at the University of Carabobo, Maracay, Venezuela in 2001. Then in 2003 she began her postgraduate studies in Ophthalmology in Hospital Miguel Pérez Carreño (Caracas, Venezuela) where she also served as Chief Resident, and completed them in 2005. From 2006 to 2008, she did a fellowship in Retina and Vitreous in Asociación para evitar la Ceguera. Hospital Dr. Luis Sánchez Bulnes, in Mexico. She dedicates her clinical practice to the medical and surgical treatment of retinal and vitreous diseases.

She has taken many courses and attended numerous congresses on ophthalmology, and has also written various articles and book chapters. She provides review services to several science international journals about ophthalmology and contributes in retinal clinical research.

Gerardo García-Aguirre

Dr. Gerardo García-Aguirre graduated magna cum laude, obtaining his medical degree at the School of Medicine, Tecnológico de Monterrey, in Monterrey, Mexico in 2002, and his residency in Ophthalmology and Retina fellowship at Asociación para Evitar la Ceguera en México, in Mexico City. In 2008 he became an attending physician at the same hospital. He is author or coauthor of over 30 papers, 15 book chapters and one book in the field of ophthalmology.

Maximiliano Gordon

Dr. Maximiliano Gordon graduated in medicine from Universidad Nacional de Rosario, Rosario, Argentina, in 1999. He did an ophthalmology residency at Centro de la Vision, located in Rosario, between 2000 and 2002, and a fellowship in Retina and Vitreous at the Asociación para Evitar la Ceguera, at Hospital Luis Sanchez Bulnes, located in Mexico City, Mexico, between 2006 and 2008.

With more than 10 years of experience in clinical and surgical management of diseases of the retina and vitreous, he currently works as a retina specialist in Centro de la Vision Gordon-Manavella and as instructor in the residency program of the Retina department of Hospital Provincial del Centenario, in Rosario.

Veronica Kon Graversen

Dr. Veronica Kon Graversen attended Catholic University of Santiago de Guayaquil, School of Medicine where she graduated Summa Cum Laude. She was then accepted into one of the most prestigious ophthalmology training programs in Latin America at the Ophthalmology Institute Conde de Valenciana in Mexico city. She then completed a two-year Retina and Vitreous surgical fellowship at the Association to Prevent Blindness in Mexico (APEC), Luis Sanchez Bulnes Hospital, under the preceptorship of Hugo Quiroz Mercado.

Dr. Kon Graversen completed a second ophthalmology residency program at the University of North Carolina at Chapel Hill, where she also served as Chief Resident. She is eligible to be board certified in Ophthalmology. She has published numerous articles in peer-reviewed journals and has lectured at multiple international meetings. She recently moved to Denmark with her husband and is affiliated with Glostrup Hospital.