

Diabetic retinopathy

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Abstract

This paper describes the importance of diabetic retinopathy in the loss of visual function. We exposed the most important risk factors, such as diabetes duration, poor metabolic control, pregnancy, puberty, hypertension, poor control of blood lipids, renal disease, and sleep apnea syndrome. We describe the pathogenesis of the disease, small retinal vessel microangiopathies which produce extravasation, edema and ischemia phenomena. We put special emphasis on the vascular endothelial growth factor (VEGF) and its pathogenic importance.

They are also described the main clinical symptoms as microaneurysms, intraretinal hemorrhages, hard and soft exudates, intraretinal microvascular abnormalities (IRMA), venous disorders, formation of new vessels and diabetic macular edema (the latter being the most common cause of vision loss).

Finally we describe the latest diagnostic techniques and eye treatment, with special emphasis on obesity surgery importance as more important preventive factor to eliminate the predisposing and precipitating disease symptoms.

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Key words: *Diabetic retinopathy. Metabolic surgery. VEGF.*

Introduction

Diabetic retinopathy is a retinal vasculitis caused by complications of diabetes mellitus. Ophthalmological changes that may occur are neovascularization and macular edema, the latter being the most frequent alteration. The incidence of diabetic retinopathy has

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RETINOPATIA DIABETICA

Resumen

En el presente trabajo se describe la importancia de la retinopatía diabética en la pérdida de función visual. Así como de los factores de riesgo más importantes, como la duración de la diabetes (tiempo de evolución), mal control metabólico, embarazo, pubertad, hipertensión arterial, mal control de lípidos en sangre, nefropatía, y síndrome de apnea del sueño. La patogenia de la enfermedad, como microangiopatías de pequeños vasos retinianos que produce extravasación, edema y fenómenos de isquemia. Se hace especial énfasis en el vascular endothelial Growth factor (VEGF) y su importancia patogénica.

También se describen los síntomas clínicos principales como microaneurismas, hemorragias intra retinianas, exudados duros y blandos, anomalías microvasculares intraretinianas (AMIR), arrosamiento venoso así como edema macular diabético (siendo esta última la más frecuente causa de pérdida de visión) y la formación de neovasos.

Finalmente se describen las técnicas más actuales de diagnóstico y tratamiento, haciendo especial énfasis en la importancia de la cirugía de la obesidad como factor preventivo más importante para eliminar los síntomas predisponentes y desencadenantes de la enfermedad.

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Palabras clave: *Retinopatía diabética. Cirugía metabólica. VEGF.*

increased very significantly to become the leading cause of visual impairment and blindness in adults over 20 years in industrialized countries.

Risk factors

Duration of diabetes

This is the most important factor. In type 1 diabetes with less than two years of evolution the incidence is 2% while diabetes with fifteen or more years of evolution, it reaches 98%. In type 2 diabetes treated with or without insulin, the incidence with 5 years of evolution

is 20% while with 15 years of evolution it reaches 80%. This apparent increased incidence of type 2 diabetes is due to the lack of an early diagnosis in asymptomatic patients. Diabetic retinopathy is very uncommon before puberty and rarely occurs 5 years before the beginning of diabetes.

Poor metabolic control

An early good glycemic control can prevent or delay the development of diabetic retinopathy. High levels of glycated hemoglobin is associated with a higher risk of severity.

Pregnancy

It is occasionally associated with rapid progression of diabetic retinopathy.

Puberty

The risk of diabetic retinopathy before puberty regardless of the duration of diabetes is very low and after age 13 increases the frequency and severity. Hormonal changes may be responsible for this.

High blood pressure

It has been one of the most researched systemic factors, known to be directly related to retinopathy although it is unclear whether hypertension is due to nephropathy and in this case, both would be diabetic complications.

Lipids

The relationship between high levels of lipids and retinopathy seems to be proved. High cholesterol levels are associated with elevated hard exudates levels. The severity of retinopathy is associated with high triglyceride levels.

Nephropathy

In multicentric studies the coincidence of nephropathy and diabetic retinopathy in both type 1 and type 2 diabetes was observed. Diabetic retinopathy may be the most common microvascular complication of diabetes, preceding nephropathy.

Sleep apnea syndrome

In diabetic patients suffering from this syndrome, diabetic retinopathy and macular edema can get worse.

Optimal control of all these risk factors can help to improve eye health of patients with diabetes.

Pathogenesis

Diabetic retinopathy is a microangiopathy affecting small retinal vessels, arterioles, capillaries and venules. The vascular lesion is the basis of the complications that are seen in the retina. Endothelial damage appears to be the leading cause of these lesions. This together with microvascular complications produce the clinical presentation of diabetic retinopathy.

How can maintained hyperglycemia linked to predisposing factors produce endothelial damage, consequent obstructive phenomena and extravasation of diabetic retinopathy?

Biochemical changes (increased sorbitol and glucose metabolism final products) hematologic changes (hypercoagulability), anatomical changes (thickening of the basal membrane and pericyte loss) physiological changes (reduced blood supply) and blood-retinal barrier breakdown.

Consequences

Increased permeability of vessels losing plasma proteins and lipids leading to retinal edema and hard exudates. Phenomena of microthrombosis with retinal microinfarcts that produce Cotton wool spots (soft exudates) synonymous with hypoxia and ischemia. Hypoxia produces an effect for releasing angiogenic factors and new vessel formation in retina and iris (rubeosis iridis) The extravasated liquid produces edema especially in macular area.

In these circumstances vascular endothelial growth factor (VEGF) is synthesized in several retinal cells (not only endothelium) and in case of hypoxia it increases 30 times its production. This is important because of two mechanisms:

- It stimulates neovessels formation.
- It stimulates vascular permeability and edema. In consequence, all retinal cells (vessels, glia and neurons) become altered and lead to visual deficits.

Clinical presentation

Nonproliferative diabetic retinopathy

It is characterized by the appearance of:

a) *Microaneurysms*. The earliest sign is the appearance of red spots. These are saccular dilations due to hyperpermeability. They can decrease, disappear and reappear in other locations. Microaneurysms are a sign of severity and progression of the disease.

b) *Intraretinal hemorrhages*. Are due to blood extravasation and can be deep or superficial (flame-shaped). It can disappear and reappear. It indicates severity.

c) *Hard exudates*. These are deposits of lipids with a predilection for the macular region. In ophthalmoscopy are seen as small white to yellow deposits. It indicates severe cystoid macular edema.

d) *Soft exudates or cotton wool spots*. These are the result of arteriolar occlusion and microinfarcts, seen as dark areas in angiography. It increases with disease progression.

e) *Intraretinal microvascular abnormalities (IRMA)*. These are large areas of non-perfusion and ischemia indicating severity and disease progression.

f) *Rosary-like abnormality of retinal veins*. It is the most important vascular change. It is characterized by irregular, segmented beading of the retinal veins. It indicates a high probability of progression to proliferative diabetic retinopathy.

Proliferative diabetic retinopathy

a) *Neovessels*. It appears as a response to ischemia -in optical disk or periphery and in AGF it shows intense fluorescence.

b) *Fibrous proliferation*.

c) *Preretinal or subhyaloid Bleeding*.

d) *Recurrent hemovitreal*.

e) *Fractional retinal detachment*.

f) *Late stages*. Rubeosis iridis, neovascular glaucoma and phthisis bulbi.

g) *Macular edema*. It is the most frequent cause of vision loss in diabetes. It is due to the output of plasma components that produce a macular thickness and this fluid can not be compensated by the saturated external blood-retinal barrier.

Diagnosis

1. Clinical diagnosis ophthalmoscopy.
2. Angiography.
3. Optical Coherence Tomography (OCT).

Treatment

1. *Medical*. Good glycemic control, avoid risk factors, control of hypertension, hyperlipidemia and obesity. Kidney function control. Prevent sleep apnea syndrome as well as a good glycemic control in pregnancy.

2. *Laser photocoagulation*. It is one of the most important advances in Ophthalmology. Argon laser is used to burn tissue and replace it by a glial scar (which consumes little oxygen) Capillaries disappear and neovascular proliferative factors are eliminated. It is

usually done in all retinal extension (panphotocoagulation).

How do we treat proliferative changes in the macula? Using intravitreal treatments.

a) Antiangiogenic drugs or antiVEFG, Ranibizumab (Lucentis), Bevacuzumab (avastin) compassionate use.

b) Intravitreal corticoids (for macular edema) Ozurdex. It is an intravitreal implant of dexamethasone prolonged release (3 months) with low impact of intraocular pressure. Triamcinolone

c) Surgery: Vitrectomy.

Conclusions

Diabetic retinopathy is a complication of diabetes mellitus. There are 5-year latency between symptom onset and diagnosis which should serve to treat all the predisposing factors, where bariatric surgery plays an important role in preventing progression.

Retinal hypoxia-ischemia is the key factor in the evolution of the disease. It requires a good control of the underlying disease.

Angiography plays a very important role regarding both diagnosis and treatment.

It is mandatory to treat neovascularization and areas of ischemia with argon laser photocoagulation. Anti-VEGF treatment plays a relevant role in the treatment of diabetic retinopathy.

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