

DIABETIC EYE DISEASE

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There are now 16 million people in the USA with DM, 7- 10 million have been diagnosed (about 5.1% of US adults > 20 years of age). Most of the undiagnosed have type 2 diabetes (noninsulin dependent DM), about 2.8% of the US population. It is the leading cause of end-stage renal disease, nontraumatic amputations, vascular disease, and the leading cause of blindness in the working population. One of the major reasons for unnecessary vision loss in DM is that only about 50% of diabetics receive timely eye exams. Diabetic retinopathy (DR) is the leading cause of blindness in ages 20 - 65 years, with 24,000 new cases of blindness every year. Type 2 DM is greater than 10 times more common than type 1 (insulin dependent DM). Type 1 develops at a rate of 30,000 new cases per year.

Protease inhibitors in the treatment of HIV can induce type 2 diabetes.

The primary diagnostic criteria for diabetes is defined as a fasting-glucose level of >126 mg/dL, confirmed on repeat readings. HbA1c is the gold standard for assessing the degree of control and are usually measured every 3 - 4 months. Normal range is 4% - 6%, with ideal control being under 7% and acceptable under 8%.

Patients over 12 years of age should have annual eye exams after 5 years of DM and immediately for patients over 30 years of age.

Nonmydriatic fundus photography with a 45 degree field will miss retinopathy beyond the arcades. New Panoramic 200 will image 200 degrees internally. Dilated 7 field photography is the current standard to detect and follow DR.

Study by William Mieler found that DR progressed in 35% of diabetics following PC IOL surgery (phaco), 50% in 2 months and the rest in 6 - 10 months. The most predictive presurgical conditions that lead to progression of the retinopathy were previous focal treatment of macular edema (5%) and preproliferative disease (27%). The duration of surgery and capsular ruptures were not found to be predictive.

Subconjunctival hemorrhage

Resolves in 1 - 2 weeks, unless there is a rebleed.

Patient reassurance.

Subcutaneous hemorrhage

Neuropathy of EOMs

Resolves in 3 - 6 months.

3rd nerve palsy show pupillary light reflex sparing.

Pseudo-Argyll Robinson pupil

Miotic, round, & light/near dissociation.

True AR pupil - Miotic, irregular, & light/near dissociation.

Cornea

Striae, recurrent epithelial erosions, pigment specks on endothelium.

Anterior chamber

Hyphema, hemolytic glaucoma, ghost cell glaucoma.

Iris

Neovascularization of the iris (NVI) or rubeosis iridis

Usually first seen at the pupillary margin but can initially be found in the angle.

Network of tiny blood vessels with a membrane demonstrating random growth patterns.

Very large vessels are called “fire hose.”

Ectropion uveae

Glaucoma

POAG - higher incidence than POAG in the general population.

Neovascular

Caused by neovascular membrane that covers the apex of the AC angle and contracts to close the angle (produces a false angle).

Very recalcitrant to treatment - filtration implants, ciliary body cryoablation, & direct ciliary body photocoagulation.

Rubeosis lentis

Rubeosis iridis that spreads onto the surface of the lens.

Nonproliferative diabetic retinopathy (background diabetic retinopathy - BDR).

Loss of mural cells (pericytes) and thickening of basement membrane.

Microaneurysm (25 - 50 um), patent or occluded.

Retinal hemorrhages

Superficial - flame-shaped or splinter-shaped in nerve fiber layer.

Dot & blot in middle layers.

Waxy exudates in middle layers

They are found in the middle to outer layers of the retina as seen on an OCT scan.

Exudative maculopathy.

Cotton-wool spots

Superficial infarctions of the ganglion cell and NFL.

Hemorrhagic maculopathy and resultant scarring

Diabetic macular edema (DME)

Serous maculopathy (clinically significant macular edema - CSME). DME is the is the major cause of moderate vision loss and legal blindness in persons with type 2 DM. DME can occur with any level of nonproliferative or proliferative DR. Approximately one-third of persons with CSME who are untreated will have a significant loss of central vision in 3 years.

Clear serous fluid accumulation that slightly elevates the superficial retina - often requires the use of a 60 D lens or better yet a Digital High Mag lens (mag & stereo) to detect its presence.

Sometimes there are tiny retinal bleeds or exudates in the thin elevated inner retina that seem to be floating just above the retina in the view.

Nonproliferative DR - preproliferative type

Capillary drop-out (closure) - very indicative of future neovascularization.

Intraretinal microabnormalities (IRMA) -shunting of blood thru preexisting vessels (resulting in vessel dilation) around areas of capillary drop-out, very indicative of future neovascularization.

Venous beading (segmental dilation) - very indicative of future neovascularization.

Venous tortuosity - omega and circle (donut) appearing vessels, etc.

Mild NPDR is considered when there is microaneurysms, hard exudates (lipoprotein deposits), small intraretinal hemorrhages, and retinal edema with a predilection for the macula.

Patients with more advanced NPDR (venous beading, IRMA, multiple CWS) should be watched for the development of PDR every 2 - 4 months. CWS on their own are poor predictors of progression of DR.

Proliferative diabetic retinopathy

Neovascularization of the disc (NVD) - on or within 1 DD.

Neovascularization elsewhere (NVE) - beyond 1 DD from the disc.

Neovascularization into the vitreous - neovascular frond "sea fan", either on the posterior vitreous face or into the vitreous gel.

Serous fluid leakage into the vitreous. Seen on an OCT scan.

Vitreous hemorrhage

Small or extensive.

Sx: slight or marked reduction in vision, red vision, red smoke, sudden onset of numerous floaters.

Signs: plume of red smoke, mild loss of retinal image to total loss of retinal image.

Vitreous scarring

Often the result of the toxic byproducts from the breakdown of hemoglobin. Whitish fibrosis in a small area or extensive scarring of most of the vitreous.

Retinal tears

Vitreous traction may result in operculated, flap (horseshoe), dialysis, & rarely a giant tear.

May be found in the posterior pole due to increased adhesion of the posterior vitreous cortex to the posterior retinal surface.

Retinal detachment

Rhegmatogenous resulting from tractional retinal tear. A rhegmatogenous RD associated with a tractional RD is a very difficult management problem, the success rate for a single procedure is around 60%. Tears may develop as a result of fibrotic tissue traction on the retinal surface and holes may develop as a result of atrophy of the retina and due to laser Tx.. Stable tractional RDs may not need to be treated, because of the complicated surgery to attain reattachment. Peripheral retinal breaks with a bullous RD require surgical intervention, scleral buckle and vitrectomy.

Tractional RD - no break & often seen in the posterior pole along the temporal arcades. Produced by fibrovascular proliferation with subsequent traction. In some cases there may be just a macular tractional detachment. Sometimes the progression of an extramacular tractional RD may produce tractional retinal folds thru the macula with resultant metamorphopsia and decrease in vision. Surgical success rate is variable but is reported to be around 80% for a single procedure; however, it is very dependent on the severity of the tractional RD.

Burned-out diabetic retinopathy

Treatment

Nearly 50% of patients that require laser Tx don't receive it due to socio-economic barriers to regular eye exams, geographic barriers to eye care, patient or doctor ignorance of need for regular eye exams.

Focal photocoagulation for treatment of macular edema - can reduce the risk of moderate vision loss by >50%, e.g. doubling of the visual angle down from 30% to 15% in ETDRS.

Pan retinal photocoagulation (PRP) for neovascularization - can reduce vision loss by >50% in high risk patients.

Patients with very severe NPDR should have PRP.

New treatment is the use of intraocular and periocular steroids. Kenalog (triamcinolone) triamcinolone acetonide, Retaane (anecortave acetate), and others) and antiVEGF intraocular injections. Macugen (pegatanib), Lucnetis (ranibizumab, Avastin (bevacizumab) are the most current antiVEGF drugs in use. Avastin is used in the treatment of colon cancer. The

upregulation of VEGF causes breakdown of the blood-retina barrier which leads to increased vascular permeability resulting in edema, stimulation of endothelial cell proliferation, neovascularization, growth mediator release, and leukocyte recruitment.

The Diabetic Control and Complications Trial

Precise control of blood glucose levels reduces long-term complications of diabetes in 50% of the patients. The study concluded that any improvement in HbA1c reduced the risk of complications. The study was of type 1 diabetics only but most believe that it also pertains of type 2.

The United Kingdom Prospective Diabetes Study (UKPDS) reflected HbA1c goals for patients with type 2 DM attained by the DDCT. New report in Lancet (1999;353:606-607,617-622) affirms benefit of tight control.

Diabetic Retinopathy Study

This study proved that PRP was effective in preventing severe visual loss in patients with high risk factors.

Early Treatment Diabetic Retinopathy Study (ETDRS)

ETDRS helped to elucidate the natural history of diabetic retinopathy. The baseline level of DR is a strong indicator of the risk of progression of sight-threatening eye disease. This study was to determine if early PRP would reduce the development of high risk characteristics in eyes with severe NPDR or DME. The study found after 7 years of follow up, that only 25% of treated patients developed high risk characteristics as compared to the group without treatment. However, the study found that early treatment of PPDR & PDR is the absence of high-risk characteristics was not indicated. Reasons: 25% of untreated patients never developed high-risk characteristics, after 7 years 4% of untreated eyes developed visual acuity or 5/200 or less as compared to 2.5% of the treated group (clinically & statistically insignificant), risk of developing complications due to PRP, e.g. macular edema, epiretinal membrane, etc. The study established criteria for classification and treatment of diabetic retinopathy that can prevent 98% of severe vision loss. Therefore, early detection and treatment can result in annual federal health savings of \$472.1 million. A savings of an additional \$624 million could be attained if all diabetics had annual eye exams for DR.

4-2-1 Rule

The most predictive findings of preproliferative retinopathy progressing to proliferative are: severity of hemorrhages, venous beading, and IRMA. The finding of hemorrhages in 4 peripheral quadrants, venous beading in 2 quadrants, or IRMA in 1 quadrant indicates severe NPDR which carries of a 50% chance of developing PDR in 1 year and a 70% chance in 3 years. Eyes with 2 or more of these findings are considered to have very severe NPDR and have a 75% chance of developing neovascularization in 1 year and 83% chance in 3 years. Eyes with very severe NPDR also have a 45% of developing high risk PDR in 1 year and 65% in 3 years.

Vitrectomy

Done to clear the scarred vitreous away in order to restore vision & prevent retinal detachments due to traction from fibrovascular tissue in the vitreous.

Diabetic Retinopathy Vitrectomy Study

Elucidated the most opportune time to perform vitrectomy in an effort to restore useful vision or to prevent further loss of vision. It also highlighted the potential complications of vitrectomy surgery. Vitrectomy for nonclearing vitreous hemorrhage is successful in 90% of cases. Eyes with severe fibrovascular proliferation require vitrectomy to remove the vitreous scaffolding and release vitreous traction.

Complications: vitreous hemorrhage, ghost cell glaucoma, neovascular glaucoma, rhegmatogenous RD.

Future Treatment

Beta-cell replacement therapy. Beta-cell transplantation and mechanical beta cells. In transplantations, 50% of transplants are working after 5 years and it frees the patient of insulin injections and hypoglycemic episodes.

Diabetic optic nerve neuropathy

Optic disc edema due to infarction of the nerve due to diabetic vascular ischemia.