

Seeing the Signs: The Diabetic Eye

2 hours

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Description

Diabetic retinopathy is a leading cause of blindness and a well-known complication of diabetes. Diabetes has other influences and affects on the ocular system, and this presentation will utilize the latest in interactive technology to review the numerous ocular complications associated with diabetes. Current diabetes diagnosis, treatment and management will also be discussed.

Learning Objectives:

- Become familiar with the different classifications and characteristics within diabetes
- Understand the effects of diabetes on the orbital structures of the eye
- Identify the different classifications of diabetic retinopathy including signs and symptoms
- Learn the diagnostic criteria for DME and treatment
- Understand PDR signs and treatment

Outline

Case

48 YOF presents with acute loss of vision in her right eye and decreased vision in her left

- She was scheduled 2 weeks previously for an eye exam on a referral from her PCP but had fallen and was unable to make that appointment
- She reports that her vision in her right eye seems to be getting worse over the past several weeks.
- Was diagnosed with diabetes 1.5 years ago
- BS control has been erratic with range between between 6.7-13.3 (120-240)
- Last A1C: 9.1

Entrance Skills/Health Assessment

- VA: OD: finger count
 - OS: 6/12 (20/40)
- CVF: OD: unable to assess
 - OS: temporal hemianopsia
- Pupils: sluggish reactivity with a 2+ RAPD OD
- SLE: corneal arcus noted, no other significant findings
- IOP: 16, 16 mmHG OD, OS
- DFE: see photos
- Physical Presentation
- Upon entering the room I noted that her right hand was twitching

- I asked her how long that had been going on and she said about 2-3 weeks
- I asked her if she experienced headaches, to which she said she had bad headaches that even woke her up at night

Referral:

- Contacted her PCP who reported that she had examined the patient 3 weeks prior and had not noted any of these findings
- Referred the patient for an immediate MRI but wasn't able to be scheduled until the next day
- Imaging/Surgery Referral
- MRI revealed large mass in her brain
- Patient was diagnosed with a **Craniopharyngioma**
- She was referred for immediate surgery
- Neurosurgeon reported that she removed a tangerine sized Craniopharyngioma
- was the largest tumor she has ever removed

Craniopharyngioma

- slow-growing,
- epithelial-squamous origin,
- calcified cystic tumor
- arises from remnants of the craniopharyngeal duct
- Craniopharyngiomas have a benign histology but malignant behavior
 - they have a tendency to invade surrounding structures and recur after what was thought to be total resection
- No variance by sex or race is found
- Distribution by age is bimodal
 - peak incidence in children aged 5-14 years and older adults aged 65-74 years

Our Patient

- Patient had a complete resection of the tumor in addition to radiation therapy
- She developed several significant perioperative complications:
- Leakage of CSF which resulted in her having to have a shunt
- She subsequently developed an infection post surgically
- She is NLP in her right eye, but did regain 20/40 vision in her left eye
- Retains a temporal hemianopsia OS
- Diabetes control became erratic and was put on several hormone replacement medications

Pancreas Endocrine Function

The endocrine portion is arranged as discrete islets of Langerhans, which are composed of five different endocrine cell types (alpha, beta, delta, epsilon, and upsilon) secreting at least five hormones including glucagon, insulin, somatostatin, ghrelin, and pancreatic polypeptide, respectively.

Glucagon:

- works to raise the concentration of glucose and fatty acids in the bloodstream
- released when the concentration of insulin (and indirectly glucose) in the bloodstream falls too low

- causes the liver to convert stored glycogen into glucose, which is released into the bloodstream.

Insulin:

- regulates the metabolism of carbohydrates, fats and protein by promoting the absorption of carbohydrates, especially glucose from the blood into liver, fat and skeletal muscle cells.

Glucagon/Insulin Control of Blood Sugar

Blood glucose levels

- In a normal person, the blood glucose concentration is narrowly controlled
- Fasting levels: 79-90 mg/dL (4.44-5.0 mmol/L)
- After meal: 120-140 mg/dL (6.67-7.78 mmol/L)
- Feedback systems for blood glucose rapidly return the blood glucose back to control levels within 2 hours

Important mechanisms for tight control:

- Liver function
- Glucagon & Insulin
- Blood Sugar
- Throughout a 24-hour period blood sugar typically maintained between 3.9-7.8 mmol/L (70-140 mg/dL)
- $[A1c (\%) \times 1.59] - 2.59 = \text{average Blood Glucose (in mmol/L)}$

Signs and Symptoms of Low Blood Sugar

Diagnostic tests for DM: A1C

- A1c- how much sugar is bound to hemoglobin in RBCs
- A1C shows the average level of blood glucose over the previous 3 months
- Other names: HbA1C, Glycated hemoglobin, glycosylated hemoglobin, glycohemoglobin
- New RBC starts with no glucose but it easily binds it. The more sugar in blood the more then binding and the higher A1c
- Normal: Less than 6.0%
- Pre-diabetes: 6.0-6.4%
- Diabetes: 6.5% or higher
- Goal is individualized, but commonly <7%

A1C Level and Future Risk of Diabetes

Diagnostic test for DM: Fasting Blood Sugar

- Fasting blood sugar can be assessed after 8 hours of fasting
- Less sensitive but quicker and easier
- Normal: 70-140 mg/dL (3.9-7.8 mmol/L)
- Impaired fasting glucose (IFG) :100-125 mg/dL (): ≥ 5.56 to 6.94 mmol/L)
- Diabetes: ≥ 126 mg/dL (7 mmol/L)
 - If confirmed by another test on a different day unless classic symptoms of DM are present

Diagnostic tests for DM: Oral Glucose Tolerance Test (OGTT)

Diagnostic test for DM: Random Plasma Glucose

- This test is typically done to confirm diabetes with severe diabetes symptoms
- Random plasma glucose is done at a time to get a “snapshot” of the glucose concentration in the bloodstream
 - it is often done in optometric offices if diabetes patients do not know what their blood sugar value or you have a suspicion a patient may have diabetes.
- Normal: 70-110 mg/dl (3.89-6.1 mmol/L)
- Diabetes: > 200 mg/dL (>11.1 mmol/L) and classic symptoms of diabetes

Diabetes Mellitus

- Diabetes mellitus is a syndrome of impaired carbohydrate, fat, and protein metabolism
- There are two main types of diabetes:
- Type 1 diabetes, or insulin-dependent diabetes mellitus (IDDM)
- occurs when the pancreas is unable to produce insulin.
- Type 2 diabetes, or non-insulin-dependent diabetes mellitus (NIDDM)
- occurs when the pancreas does not produce enough insulin or when the body does not effectively use the insulin that is produced.

Other Conditions

However there are other conditions that can result in altered blood sugar:

- Prediabetes refers to blood glucose levels that are higher than normal, but not yet high enough to be diagnosed as type 2 diabetes. Although not everyone with prediabetes will develop type 2 diabetes, many people will.
- Gestational Diabetes- type of diabetes that is first recognized or begins during pregnancy

Other causes:

- medication, neonatal diabetes, chemical-induced diabetes
- DM Type I is caused by autoimmune destruction of β cells in the pancreatic islets (95% of

Type 1 sometimes referred to as Type 1 A)

- Autoimmune targeting beta cells, the rest are not affected
- 3–5% of total cases of diabetes mellitus and usually presents in children
- Autoantibodies detected in 85-90% of DM Type 1
- 30% risk if 1 type of autoantibody in blood
- 70% 2 types
- 90% 3 types of autoantibodies in blood
- However, a small minority (5%) of these patients have no known etiology (idiopathic DM or Type 1 B)
- Most are of African or Asian ancestry
- No evidence of autoimmunity
- Strong family history
- Presenting Symptoms of DM I
- Clinical manifestations of DM I appear after gradual loss of β cells
 - Diabetes won't develop clinically until 80% loss in the beta cells

Polyuria:

- kidneys typically reabsorb the sugar in the blood but in DM can't keep up with the sugar in the blood so sugar is excreted in urine and this draws more water into urine
- Polydipsia: increased fluid movement via urination increases thirst
- Polyphagia: burn a lot of calories so they will eat a lot
- Weight loss: excessive burning of calories and excretion of sugar in urine
- Fatigue
- Diabetic ketoacidosis (start metabolizing fat), in 20-40% of children when they initially manifest with DM I

Type 2 Diabetes

- DM II is caused by dysregulation of insulin release from β cells and insulin resistance in peripheral tissues
- Resistance to the actions of insulin in the peripheral tissues: fat, muscle, and liver
- Increased glucose production by the liver
- Defective insulin secretion, particularly in response to glucose stimulus
- DM II accounts for ~90-95% of DM
- Onset: 40-64 yo, average 54 yo
- >1/4 of adults age 65 and older have diabetes
- Type 2 is increasing in children and adolescents
- Prevalence: 9%
- Incidence rate parallels the rise of obesity
 - obesity is the most important environmental factor causing insulin resistance

Risk of developing DM II depends on genetics and health factors

- Increases with age
- Lack of physical activity
- Visceral obesity due to accumulation of fat in the omental and mesenteric regions correlates with insulin resistance. Subcutaneous abdominal fat seems to have less of an association with insulin insensitivity.
- Exercise is thought to affect the deposition of visceral fat
- History of gestational DM or delivering a baby weighing > 9 lbs
- Women with polycystic ovarian syndrome
- Genetics
- One parent: 40% risk
- Both parents: 70% risk
- Metabolic Syndrome

Diabetes Lab Testing

- A comprehensive metabolic panel is a blood test that measures sugar (glucose) level, electrolyte and fluid balance, kidney function, and liver function. The following lab tests are included in a comprehensive metabolic panel:
 - Albumin
 - Blood Urea Nitrogen (BUN)
 - Glomerular filtration rate (GFR)
 - Calcium
 - Potassium
 - Sodium
 - Alkaline Phosphatase (ALP)

- Carbon Dioxide (Bicarbonate)
- Chloride
- Creatinine
- Glucose

Total Bilirubin
 Total Protein
 Alanine Aminotransferase (ALT)
 Aspartate Aminotransferase (AST)

Kidney function

- Urinalysis can be used in conjunction with blood testing to help confirm systemic etiology of conditions

Urine Glucose

- Any glucose in the urine is abnormal

Urine Protein

- Proteinuria is an important indicator of renal disease

Urine Ketones

- Ketones are byproducts of body fat metabolism formed in the liver
- Ketonuria occurs in patients with diabetes

Kidney Function Tests:

- Serum Creatinine:
 - waste product that comes from the normal wear and tear on muscles of the body.
- Kidney impairment results in rise of creatinine level in the blood
- BUN (blood urea nitrogen):
 - If kidneys cannot filter wastes out of the blood due to disease or damage, then the level of urea in the blood will rise
- Glomerular filtration rate
 - rate of fluid filtered through the kidney
 - Reduced in chronic kidney disease/renal failure

Hypertension and Diabetes

- People with diabetes mellitus should be treated to attain systolic BP of <130 mHg and diastolic BP of <80 mHg (these target BP levels are the same as BP treatment thresholds).
- For people with CVD or CKD, including albuminuria, or with CV risk factors in addition to diabetes and hypertension, an ACE inhibitor or an ARB is recommended as initial therapy
- ACE inhibitors (e.g. lisinopril) may delay the progression of nephropathy and reduce the risks of cardiovascular events in hypertensive patients with diabetes mellitus type I and type II.
- For people with diabetes and hypertension not included in other recommendations in this section, appropriate choices include (in alphabetical order): ACE inhibitors, ARBs, dihydropyridine CCBs, and thiazide/thiazide-like diuretics

Liver Tests

- Liver tests (LTs) are blood tests used to reflect the presence of damage or inflammation.
- **alanine aminotransferase (ALT)** and aspartate **aminotransferase (AST)** are the most commonly used tests
- These enzymes normally found in the blood when liver cells are injured.
- The ALT is felt to be a more specific indicator of liver inflammation

- Cholesterol
- Cholesterol is an essential component of cell membranes
- Diabetes patients: LDL-cholesterol less than 2.0 mol/L
- **VLDL: Very low density lipoproteins**
 - VLDL particles mainly carry triglycerides to your tissues.
- **LDL: Low density lipoproteins**
 - Moves cholesterol from the liver to the body
 - High levels increase the risk of atherosclerosis
- **HDL: High density lipoproteins**
 - Moves cholesterol from the body to the liver
 - High levels thought to reduce the risk of atherosclerosis
 - **Known to have anti-thrombus and antioxidant properties**

Recommendations for Management

- **A: A1c:** <7.0 for most non-pregnant adults
 - <8.0 for adults with limited life expectancy, history of hypoglycemia or advanced CVD
 - <6.5 for recent diagnosed or long-life expectancy
- **B: Blood Pressure:** <140/90 (USA) or 130/80 (Canada)
- **C: Cholesterol:** LDL-cholesterol less than 2.0 mol/L
- **D: Drugs:** to reduce CVD (e.g. statins, blood pressure, aspirin)
- **E: Exercise:** regular aerobic and resistance training proper nutrition and weight management
- **S: Smoking:** smoking cessation

Exercise and Diabetes

- As a prescription for exercise, aerobic exercise of mild to moderate intensity, including walking and jogging, 10–30 min a day, 3–5 days a week, is recommended.
- Resistance training of mild intensity with the use of light dumbbells and stretch cords should be combined in elderly individuals who have decreased muscle strength.
- An active lifestyle is essential in the management of diabetes, which is one of typical lifestyle-related diseases.

Clinical Indications

Lids

- Xanthelasmas reported to occur more frequently secondary to elevated serum lipid levels and may reflect poor diabetic control.
- Composed of foamy, lipid-laden xanthoma cells clustered around blood vessels and adnexal tissue within the superficial dermis
- Treatment includes surgical excision, CO2 ablation and topical trichloroacetic acid. Recurrence is common.

Cornea

- Patients with diabetes have decreased corneal sensitivity which is part of the peripheral neuropathy

- due to inactivation of the corneal nerves (trigeminal and their branches)
- higher risk of developing several corneal complications:
- superficial punctate keratitis,
- recurrent corneal erosions,
- persistent epithelial defects and
- corneal endothelial damage
- Evidence to demonstrate an abnormal basement membrane
- RCE,
- slow wound healing,
- neurotrophic ulceration and
- defective re-epithelialization
- Evidence to demonstrate an abnormal endothelium
- Thicker than normal cornea

Cornea-Poor Wound Healing

- Not normally a problem, but does pose a problem under stress situations
- Evidence to indicate that topical insulin can help improve healing and possible treatment for neurotrophic ulcers and persistent corneal defects

Cataract Surgery

- Diabetes patients develop cataracts earlier and require surgery sooner
- Better VA
- Be able to monitor for retinopathy
- Older cataract surgeries (prior to phaco) demonstrated an increase in diabetic retinopathy progression and the development of macular edema
- With newer phaco cataract surgery, less development/progressive of DR has been noted
- CME

Critical signs:

- Irregularity and blurring of the FLR
- Foveal thickening with or without small intraretinal cysts
- FA often shows early leakage and late macular staining
- Classically in a flower-petal or spoke-wheel pattern
- Note the central cyst of fluid on OCT
- Increased prevalence of CME in patients with diabetes
- CME that results in diabetes patients is often much more difficult to treat
- Recommend pre-treating patients with diabetes with topical NSAID and throughout post-op treatment

Vitreous

- Increased syneresis and liquefaction
- exhibit vitreous degeneration in a manner similar to that normally seen in older adults
- The vitreous provides the support framework for the development of neovascular complexes.

Clinical Considerations

- Patients experience a sudden painless decrease in vision, floaters, or haze after the hemorrhage.
- Small amounts of blood in the vitreous can take a patient to CF vision
- Complications include toxicity, proliferative vitreoretinopathy and glaucoma (“ghost cell glaucoma”)

Common Cause of Vitreous Hemorrhage

- Three most common causes include:
- Proliferative retinopathy
- E.g. diabetes, vascular occlusive (BRVO and CRVO), macroaneurysm and sickle cell
- untreated vitreous heme associated with PDR has a very poor visual prognosis
- PVD with/without retinal tear
- Apprx 3-14% of vitreous hemes
- Trauma
- 12-18% of vitreous hemes
- Major cause of vitreous hemes in patients under 40

Vitreous Hemorrhage (VH) and Vision Loss?

- risk of severe visual loss without treatment for eyes with moderate or severe NVE increased from 6.9% to 29.7% in the presence of VH.
- the risk of severe visual loss in eyes with mild NVD increased from 10.5% to 25.6% in the presence of VH

Diabetic Retinopathy

- Almost 61% have some manifestation of diabetic eye disease
- Leading cause of new blindness in U.S. for 20-74 y.o.
- 12% of all new cases of blindness per year
- Risk of blindness about 25 X greater in DM
- Primarily due to diabetic retinopathy
- Early intervention lessens risk and severity of vision loss
- 50-65% have not had a DFE in the previous year
- **Risk Factors:**
 - **Duration of diabetes!**
 - Associated conditions
 - Poor glycemic control!
 - Dyslipidemia
 - Hypertension
 - Smoking
 - Pregnancy

Diabetic Macular Edema (DME)

- Also referred to as clinically significant macular edema (CSME)

- Consists of 3 clinical signs:
- Hard exudates with associated retinal thickening within 1/3rd DD of center of fovea
- Edema (retinal thickening) within 1/3rd DD of center of fovea
- Edema of 1 DD within 1 DD of center of fovea
- Treatment of CSME
 - Recommend all eyes with DME and reduced vision be treated (20/30 or worse)
 - Among eyes with CI-DME and good visual acuity (20/25 or better), there was no significant difference in vision loss at 2 years whether eyes were initially managed with aflibercept or with laser photocoagulation or observation and given aflibercept only if visual acuity worsened.
 - Observation without treatment unless visual acuity worsens maybe a reasonable strategy for CI-DME.

Standard of care: intravitreal anti-VEGF with focal laser photocoagulation if needed

- Afibercept (Eyelea®) 2 mg
- Ranibizumab (Lucentis®) 0.3 mg
- Bevacizumab (Avastin®) 1.25 mg (off-label)
- Intravitreal injections: Loading dose 1 inj/m then q 2 m
- VA compared to grid laser alone for at least 3 years
- Defer grid laser for 24 weeks → 50% don't need laser
- PDR
- Hallmark sign is any neovascularization: NVI, NVE or NVD
- Common patient presenting symptom is blurry vision secondary to vitreous heme
- Concern of tractional retinal detachment secondary to fibrotic proliferation
- Management is retinal consult for possible PRP, vitrectomy, and anti-VEGF injection.

High Risk PDR

- High risk PDR is characterized by the following:
- NVD > 1/4 to 1/3 disc area
- Any NVD with a pre-retinal or vitreous hemorrhage
- Moderate to severe NVE with a vitreous or pre-retinal hemorrhage
- Any NVI

Treatment of PDR

- Panretinal photocoagulation
- Laser absorbed by RPE
- 1200 to 2400 burns
- Placed in scatter pattern on retina to reduce NV (spare macula)
- Reduced risk of severe vision loss at 6 years by 50% in Diabetic Retinopathy Study
- Regression of NV occurs in 30 – 55% of eyes
- Follow q 2- 4 months

PRP complications

- Short term

- Pain during treatment
- Increased IOP
- Corneal abrasion
- Worsening of ME
- Vitreous heme
- Long term
 - Damage to uveal tract nerves
 - VA loss
 - Visual field loss
 - Retinal detachment
 - Subretinal neovascularization
 - Loss of dark adaptation (damage to the cones)
 - Cataract
 - accommodation
- Pan Retinal Photocoagulation

Lucentis for PDR

- Lucentis effectively treats PDR
- The Diabetic Retinopathy Clinical Research Network enrolled 305 participants with proliferative diabetic retinopathy in one or both eyes to randomly receive Lucentis or laser therapy.
- Laser group:
 - 50% required more than one treatment of laser
 - No improvement in VA
 - Significant loss of side vision and 28% developed DME
- Lucentis group:
 - Injection once a month for three months or until retina stabilized
 - No loss of side vision
 - Improvement of half of line of VA over two years and only 9% developed DME
 - Lucentis appears to be a safe alternative versus PRP for PDR
 - Patients will be followed for 5 years

Q&A / Discussion