DIABETES MELLITUS: COMPLICATION

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COMPLICATION OF DIABETES

• Susceptibility to infections including tuberculosis, pneumonia, pyelonephritis, and mucocutaneous candidiasis

• Peripheral and autonomic neuropathy, manifesting as sensory loss, impotence, postural hypotension, constipation, and diarrhea.

• Vascular disorders (chiefly from microangiopathy in IDDM and from arteriosclerosis in NIDDM), including:
  – Retinopathy
  – Renal disease, notably glomerulosclerosis
  – Atherosclerosis, causing coronary artery disease, stroke, and gangrene of lower extremities.
Pathogenesis of Microangiopathy

- Long standing diabetes → hyperglycemia chronic
- Glycosylation of basement membrane proteins → leaky blood vessels.
- Thick and Leaky blood vessels.
- Narrow lumen.
- Ischemic organ damage.
Pathology of Diabetic complication

- **Islets.** Histologic changes in the islets range from complete hyalinization and fibrosis with occasional lymphocytic infiltration.

- **Small blood vessels.** Diabetic microangiopathy affect the small arteries and capillaries. The major early morphologic features are the disappearance of pericytes and a thickening of the basement membrane, visible in muscle, skin, retina, kidney, and other tissues.

- **Medium-sized and large blood vessels.** Lesions are especially common in the coronary, cerebral, mesenteric, renal, and femoral arteries.
Pathology of Diabetic complication

- **Kidneys.** The most characteristic lesion in nodular glomerulitis, with focal thickening of the capillary basement membrane and exudative accumulation of hyaline material.

- **Eyes.** In diabetic retinopathy, the microcirculation exhibits leaky microaneurysms, new formation of capillaries, and hemorrhage into the vitreous.
Pathogenesis of Complications
RENAL COMPLICATION

• There are a variety of complications involving the kidney.
• Both nodular and diffuse glomerulosclerosis can lead to chronic renal failure.
• Diabetics are prone to infections, particularly pyelonephritis.
• Both bacterial and fungal infections can occur.
Microangiopathy
Renal complications

Renal glomerulus demonstrating nodular glomerulosclerosis with diabetes mellitus
Renal complications

Renal glomerulus with nodular glomerulosclerosis along with hyaline arteriolosclerosis with diabetes mellitus, PAS stain
Renal complications

Kidney, acute pyelonephritis shown involving the medulla
Renal complications

Renal pelvis involved by an ascending urinary tract infection with Candida albicans, PAS stain.
Persons with diabetes mellitus, either type I or type II, have early and accelerated atherosclerosis.

- The most serious complications of this are atherosclerotic heart disease, cerebrovascular disease, and renal disease.
- The most common cause of death with diabetes mellitus is myocardial infarction.

Peripheral vascular disease is a particular problem with diabetes mellitus and is made worse through the development of diabetic neuropathy, leading to propensity for injury.
Angiopathy Atherosclerosis

Oclusive atherosclerosis
Atherosclerosis

Left anterior descending coronary artery sectioned along its length to reveal narrowing of the lumen, most pronounced in the proximal portion at the left, from advanced atherosclerosis, gross.
Atherosclerosis

Left anterior descending coronary artery section with a recent thrombus filling the lumen
Atherosclerosis

The interventricular septum has been sectioned to reveal a large recent myocardial infarction (about 4 to 7 days old) with a tan-yellow necrotic center surrounded by a zone of hyperemia.
Aortic atherosclerosis demonstrated in three aortas, from minimal at the bottom to severe at the top, gross.
Atherosclerosis

Foot with a previous healed transmetatarsal amputation demonstrating an ulcer in the region of the ankle, gross.
Atherosclerosis

Gangrenous necrosis and ulceration involving the lower extremity
Normal Retina
Diabetic retinopathy is shown here on funduscopic examination.
Proliferative diabetic retinopathy on funduscopic examination is shown here. This is a particularly serious complication in diabetics that can lead to blindness.
Cataracts of the crystalline lens with opacification, as shown here, are more frequent in persons with diabetes mellitus.
DIABETES AND NEUROPATHY

Prevalence of neuropathy in diabetes mellitus

- Disease onset: 7.5%
- 25 years after onset: 50%
- Overall: 30%
- Similar or slightly higher in NIDDM (Type 2) vs. IDDM (Type 1)
Neuropathy
Diabetes Mellitus - Mortality

- Myocardial infarction
- Renal failure
- Atherosclerosis heart disease
- Cerebrovascular accident (CVA)
- Infection
- Gangrene
- Hypoglycemia / Ketoacidosis
Neoplasms of the endocrine pancreas
General Concepts

• Islet cell tumors may be benign or malignant, functioning or nonfunctioning.

• Malignancy of islet cell tumors.
  – Islet cell tumors are considered benign if they are circumscribed or encapsulated and if no metastases are demonstrated.
  – Neoplasms without metastases but with infiltrative borders, mitoses, or vascular invasion are considered borderline lesions.
  – To diagnose an islet cell carcinoma, metastases to nodes or liver are needed.
Specific Tumors

• Benign, nonfunctional islet cell adenomas do not produce clinical problems and usually are found incidentally at autopsy.

• Insulinoma.
  – Beta cell origin.
  – Produce large quantities of insulin.
INSULINOMA

• About 90% of insulinomas are benign, 10% are malignant. Most insulinomas are solitary, but approximately 5% of patients have MEN type I.

• Endocrine or organoid pattern, with nests and cords of cells supported by fibrovascular stroma. Evidence of malignancy includes blood vessels and capsular invasion, numerous mitoses, and metastases to regional lymph nodes and the liver.

• In general, more slowly than adenocarcinomas of the pancreas, may have hepatic metastases. Typically, patients die because of the effect of the hypoglycemia produced by an unresectable tumor.
Insulinoma

This is an immunohistochemical stain for insulin in the islet cell adenoma. Thus, it is an insulinoma.
GASTRINOMA

- Are found in the pancreas.
- Cause the Zollinger-Ellison syndrome.
- The gastrin from the tumor leads to stimulation and hyperplasia of the gastric parietal cells, resulting in 10 to 20 times the normal amount of gastric acid being produced.
GASTRINOMA

Pathology.

- About 60% to 70% of gastrinomas are malignant;
- 30% are benign.
- 5% to 10% of patients have MEN type I
- Histologically, gastrinomas are similar to insulinomas in appearance and present the same difficulties in differentiating benign from malignant tumors.
VIPoma.

- Produce vasoactive intestinal polypeptide cause a syndrome known as pancreatic cholera.
- Also known as Verner-Morrison syndrome, or watery diarrhea, hypokalemia, and achlorhydria (WDHA) syndrome.
- Can be fatal → 80% of classified as malignant.
GLUCAGONOMA

• Alpha cell origin
• Clinical syndrome characterized by diabetes mellitus, necrotizing skin lesions, stomatitis, and anemia.
• Most of these tumors are malignant.
NONFUNCTIONAL ISLET CELL CARCINOMA

- No hormones make themselves known clinically by their malignant behavior, simulating adenocarcinomas.
- With obstruction jaundice, hepatic metastases, or a large mass in the abdomen.
- Histologically, an endocrine or organoid pattern may be seen in these tumors,
- 60% of nonfunction islet cell tumor are malignant.
NESIDIOBLASTOSIS

a condition usually found in newborn who present with uncontrollable hypoglycemia.
THANK YOU