433 Teams

MEDICINE

17 Diabetic complications

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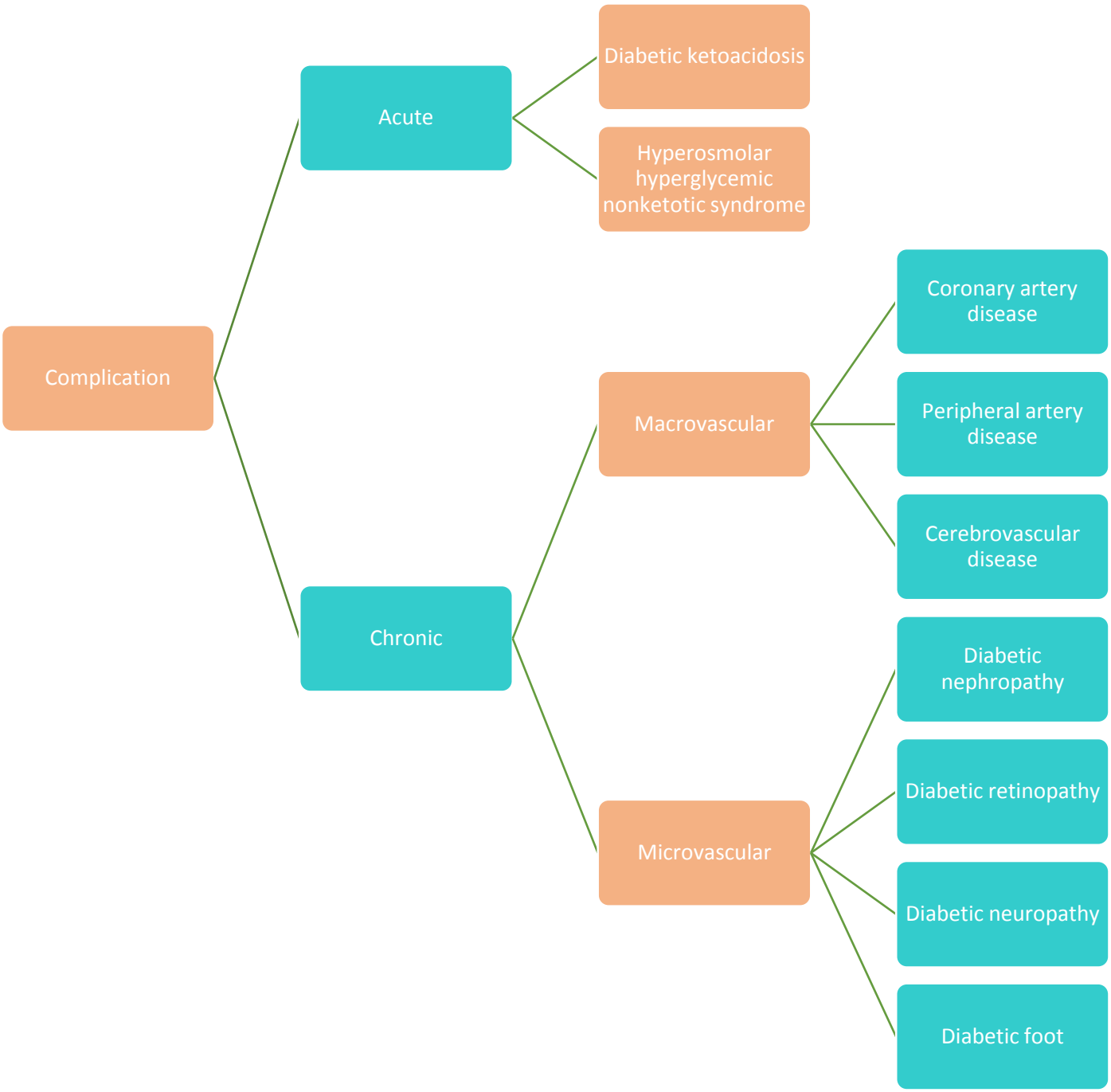
5. Define and Describe the Diabetic vasculopathy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Acute complications

1. Diabetic ketoacidosis:

DKA is an acute, life-threatening medical emergency that can occur in both type I and type II diabetic patients (more common in type I)

Pathogenesis:

1. This is secondary to insulin deficiency and glucagons excess, both of which contribute to accelerated severe hyperglycemia and accelerated ketogenesis.
2. Severe hyperglycemia leads to an osmotic diuresis, which causes dehydration and volume depletion.
3. Consequences of DKA include hyperglycemia, ketonemia, metabolic acidosis, and volume depletion.

Precipitating factors:

1. Any type of stress or illness (e.g., infectious process, trauma, myocardial infarction, stroke, recent surgery, sepsis, GI bleeding)
2. Inadequate administration of insulin.

Clinical features:

- Nausea and vomiting
- Marked dehydration, orthostatic hypotension, tachycardia—volume depletion is always present.
- Abdominal pain (more common in children) that may mimic acute abdomen
- Fruity" (acetone) breath odor
- Kussmaul's respiration—rapid, deep breathing
- Polydipsia, polyuria, polyphagia, weakness
- Altered consciousness, drowsiness, and frank coma may occur if not treated.
- Symptoms usually occur rapidly, typically in less than 24 hours.

Diagnosis

Elevated blood glucose	Increased serum levels of acetoacetate, acetone and hydroxybutyrate.	Metabolic acidosis	Increased anion gap

Management

1. Insulin 2. Fluid 3 Electrolyte replacement

Notes

The main problem is in hyperglycemia , especially the diabetic ketoacidosis , it is an emergency the P^H decreases below 7 an usually the patient is having a precipitating factor (e.g. not taking enough insulin or having severe infection.)

Treatment: Admitted to ICU, IV fluids, insulin.

2. Hyperosmolar hyperglycemic nonketotic syndrome:

- A state of severe hyperglycemia, hyperosmolarity, and dehydration
- It is typically seen in elderly type II diabetic patients.

Pathogenesis:

1. Low insulin levels lead to hyperglycemia. Severe hyperglycemia causes an osmotic diuresis, leading to dehydration.
2. Ketogenesis is minimal because a small amount of insulin is released to blunt counterregulatory hormone release (glucagons).
3. Ketosis and acidosis are typically absent or minimal.
4. Severe dehydration is due to continued hyperglycemic (osmotic) diuresis. The patient's inability to drink enough fluids (either due to lack of access in elderly/bedridden patients or to inadequate thirst drive) to keep up with urinary fluid losses exacerbates the condition.
5. Precipitating events are similar to those of DKA.

Clinical features:

Thirst, polyuria	Signs of extreme dehydration and volume depletion—hypotension, tachycardia	CNS findings and focal neurologic signs are common (e.g., seizures)—secondary to hyperosmolarity.	Lethargy and confusion may develop, leading to convulsions and coma.

Diagnosis

1. Elevated blood glucose (> 700 mg/dl)
2. Extremely high serum osmolality
3. High BUN (prerenal azotemia)
4. Mild metabolic acidosis without ketosis

Management

1. High volume fluid
2. Electrolyte replacement
3. Insulin

Notes

Hyperosmolar means that the blood sugar is very high. It may rise to 600 or even 1000. The normal blood volume is 6 liters but when the patient has hyperosmolar, his blood reaches to 2 liters only more than two-thirds is gone (severe hypovolemia). So these patients' blood becomes very elastic and viscous they have myocardial infarction, stroke.

Hypovolemic shock, which is an acute emergency, they must be admitted to the ICU. The mortality in this case is more than 50%.

It usually have precipitating factors: overuse of the diabetics

Chronic complications:

1. Macrovascular complications:

- Coronary artery disease (CAD)
  - Risk of CAD is two to four times greater in diabetic than in no diabetic persons.
  - Most common cause of death in diabetic patients
  - Silent myocardial infarctions are common.
- Peripheral artery disease - in up to 60% of diabetic patients
- Cerebrovascular disease (stroke)

2. Microvascular complications:

- Diabetic nephropathy
- Diabetic retinopathy
- Diabetic neuropathy
- Diabetic foot

The risk of coronary events is greatly reduced if the patient can eliminate or reduce other major cardiovascular risk factors (smoking, HTN, hyperlipidemia,Obesity).

Macrovascular complications:

- The main problem is accelerated atherosclerosis, which puts patients at increased risk of stroke, MI, and CHF.
- The accelerated atherosclerosis in diabetics is the reason the target BP is lower in diabetics (130/80) than in general population (140/90), and the reason the target LDL is lower in diabetics is less than 100 mg/dL.
- The cause of accelerated atherosclerosis is not known, although glycation of lipoproteins and increased platelet adhesiveness/aggregation are thought to be two potential causes. In addition, the process of fibrinolysis may be impaired in diabetic patients.

Management

1. For every 1% reduction in Hemoglobin A1c, there is a 14% reduction in the risk of MI.
2. For every 10 points reduction in blood pressure, there is an additional 12% reduction in risk of MI.
3. Coronary artery bypass should be performed in a diabetic patient even if there is only two vessel coronary disease.
4. Statin should be considered for every patient with LDL >100 mg/dl.

Microvascular complications:

- **Diabetic Nephropathy:**
  - Most important cause of end-stage renal disease (ESRD)

Pathologic types:

1. Nodular glomerular sclerosis (Kimmelstiel–Wilson syndrome) - hyaline deposition in one area of glomerulus—pathognomonic for DM.
2. Diffuse glomerular sclerosis—hyaline deposition is global—also occurs in HTN
3. Isolated glomerular basement membrane thickening.

Microalbuminuria/proteinuria:

1) If microalbuminuria is present, strict glycemic control is critical (has been shown to limit progression from microalbuminuria to clinical proteinuria).

2) Without effective treatment, the albuminuria gradually worsens - HTN usually develops during the transition between microalbuminuria and progressive proteinuria.

- Persistent HTN and proteinuria cause a decrease in glomerular filtration rate (GFR), leading to renal insufficiency and eventually ESRD.

3) HTN increases the risk of progression of diabetic nephropathy to ESRD. Control BP aggressively.

4) Initiate ACE inhibitors or ARB immediately. These agents are proven to decrease the rate of progression of nephropathy.

5) Microalbuminuria is the screening test! If you wait for the dipstick to be positive for protein, you have waited too long. Remember that microalbuminuria means levels of albumin are between 30 and 300 mg per 24 hours. But the dipstick for urine becomes trace positive at 300 mg of protein per 24 hours.

6) It usually takes 1 to 5 years for microalbuminuria to advance to full-blown proteinuria. However, with proper treatment (i.e., using ACE inhibitors to control BP) this can be prolonged.

7) Once diabetic nephropathy has progressed to the stage of proteinuria or early renal failure, glycemic control does not significantly influence its course. ACE inhibitors and dietary restriction of protein are recommended.

Management:

Notes

The most The diabetes does not affect the hydrostatic pressure but affects the oncotic pressure. Therefore, when the patient first gets diabetes he will develop High GFR due to hyperglycemia so the filtration barrier molecule will leak the smallest protein in the protein, which is the albumin, which will cause microalbuminuria (leaking of microprotein). So these protein precipitates in bowman's capsule , so it transforms from normal glomerulus to sclerotic (fibrous) glomerulus, so it doesn't function and the patient may have renal failure.
In proteinuria, the GFR decreases and is indicative of nephrotic syndrome development. (More than 3 g) When a diabetic patient develops nephrotic syndrome, he will be on dialysis in 5-7 years. Can be prevented by screening the microalbuminuria (the phase before proteinuria) so they take ACEI, stop smoking, diet, control the glucose

- **Diabetic Retinopathy:**
  - **Background (nonproliferative) retinopathy accounts for the majority of cases.**

- Funduscopic examination shows hemorrhages, exudates, microaneurysms, and venous dilatation.
- These patients are usually asymptomatic unless retinal edema or ischemia involves the central macula.
- Edema of the macula is the leading cause of visual loss in diabetic patients.
- HTN and fluid retention exacerbate this condition.

  - **Proliferative retinopathy:**
    1. Key characteristics are new vessel formation (neovascularization) and scarring.
    2. Two serious complications are vitreal hemorrhage and retinal detachment.
    3. Can lead to blindness. Laser photocoagulation is the treatment.

Notes

The most active cell in the body is the rods and conns in the retina. These cells are insulin dependent. In diabetic patient, they develop retinal inertia there is blood and glucose but no insulin to enter the glucose to the cells so the rods and conns sense that there is no glucose so they give a false signal. So in the retina forms new vessels develop (proliferative retinopathy) these are very fragile and can bleed easily and cause vitreous hemorrhage that lead to clot and fibrosis and then retinal detachment.

So, it started with insulinopenia (relative inertia) and ended with new vascularization and bleeding then complete structure damage.

- **Diabetic neuropathy:**

1. **Peripheral neuropathy (distal symmetric neuropathy)**

- Usually affects sensory nerves in a "stocking/glove pattern"—Usually begins in feet, later involves hands (longest nerves affected first). Numbness and paresthesias are common.
- Loss of sensation leads to the following: ulcer formation (patients do not shift their weight) with subsequent ischemia of pressure point areas; Charcot's joints.
- Painful diabetic neuropathy—hypersensitivity to light touch; severe "burning" pain (especially at night) that can be difficult to tolerate. Treatment is with gabapentin, tricyclic antidepressants or pregabalin.

2. **CN complications - (secondary to nerve infarction)**

- Most often involves CN III, but may also involve CN VI and IV
- Diabetic third nerve palsy: eye pain, diplopia, ptosis, inability to adduct the eye; pupils are spared

3. **Mononeuropathies – Secondary to nerve infarction**

- Median nerve neuropathy, ulnar neuropathy, common peroneal neuropathy
- Diabetic lumbosacral plexopathy—severe, deep pain in the thigh; atrophy and weakness in thigh and hip muscles; recovery takes weeks to months.
- Diabetic truncal neuropathy—pain in distribution of one of the intercostal nerves.

4. Autonomic neuropathy

- Impotence in men (most common presentation)
- Neurogenic bladder—retention, incontinence
- Gastroparesis—chronic nausea and vomiting, early satiety
- Constipation and diarrhea (alternating)
- Postural hypotension

Gastroparesis:

After several years, DM decreases the ability of the gut to sense the stretch of the walls of the bowel. Stretch is the main stimulant to gastric motility. Gastroparesis is an immobility of the bowels that leads to bloating, constipation, early satiety, vomiting, and abdominal discomfort. Treatment is with metoclopromide and erythromycin, which increase gastric motility.

Management

- For peripheral neuropathy, Anelgiscs, Gabapentin, Pregablain, Amitriptyline and Carbamazepine.
- Gabapentin, Pregablain are the best.
- For Gastroparesis, metoclopramide or erythromycin.

Notes

The neural cells don't rely on insulin to get glucose, they get it directly (independently). In diabetes, it supposed that they don't have problem, but the problem comes from Schwann cells.

Schwann cells are relying on insulin completely, so in hyperglycemia when insulin is not sufficient. It get the energy from other means which is Sorbitol pathway. When sorbitol accumulates in Schwann cells, the fluids shift from outside to Schwann cells and swell up. That's why the patient feels paresthesia because of compression to the axon. With long-standing of diabetes and carelessly from the patient, the axon will be cut and then he won't feel any pain

Diabetic foot:

- Caused by a combination of artery disease (ischemia) and nerve disease (neuropathy) can lead to ulcers/infections and may require amputation.
- With neuropathy, the patient does not feel pain, so repetitive injuries go unnoticed and ultimately lead to nonhealing..
- In addition, neuropathy may mask symptoms of PVD (claudication/rest pain). Also, calcific medial arterial disease is common and can cause erroneously high BP readings in lower extremities.

- **Increased susceptibility to infection:**

- This results from impaired WBC function, reduced blood supply, and neuropathy. Wound healing is impaired in diabetic patients, and this can be problematic postoperatively.
- Diabetic patients are at increased risk for the following infections: cellulitis, candidiasis, pneumonia, osteomyelitis, and polymicrobial foot ulcers.
- Infections of ischemic foot ulcers may lead to osteomyelitis and may require amputation.

These researches were recommended by the doctor

UK Prospective Diabetes Study:

https://www.dtu.ox.ac.uk/UKPDS/

DCCT and EDIC:
http://www.niddk.nih.gov/about-niddk/research-areas/diabetes/dcct-edic-diabetes-control-complications-trial-follow-up-study/Documents/DCCT-EDIC_508.pdf

MCQs

A 50-year-old obese woman has long-standing type 2 diabetes mellitus inadequately controlled on metformin and pioglitazone. Insulin glargine (15 units subcutaneously at bedtime) has recently been started because of a hemoglobin A1C level of 8.4. Over the weekend, she develops nausea, vomiting, and diarrhea after exposure to family members with a similar illness. Afraid of hypoglycemia, the patient omits the insulin for 3 nights. Over the next 24 hours, she develops lethargy and is brought to the emergency room. On examination, she is afebrile and unresponsive to verbal command. Blood pressure is 84/52. Skin turgor is poor and mucous membranes dry. Neurological examination is nonfocal; she does not have neck rigidity.

Laboratory results are as follows:
Na: 126 mEq/L K: 4.0 mEq/L Cl: 95 mEq/L HCO3: 22 mEq/L
Glucose: 1100 mg/dL BUN: 84 mg/dL Creatinine: 3.0 mg/dL
Which of the following is the most likely cause of this patient's coma?

a. Diabetic ketoacidosis
b. Hyperosmolar coma
c. Syndrome of inappropriate ADH secretion d. Drug-induced hyponatremia
e. Bacterial meningitis

The answer is b. (Fauci, p 2285; Gardner, pp 875-881.) This woman with poorly controlled diabetes has developed hyperglycemia and lethargy during an episode suggestive of viral gastroenteritis. Her presentation is most consistent with hyperosmolar nonketotic coma. This condition typically occurs in type 2 diabetics who become volume depleted and develop renal insufficiency. Glucose is no longer able to spill out into the urine, the blood glucose skyrockets, and severe hypertonicity leads to brain dysfunction and coma. Serum osmolarity is calculated by the formula:

This patient's serum osmolality is as follows:
Thus, the serum osmolarity is greater than 350 mOsm/L. Although the serum sodium is usually the main determinant of osmolarity, extreme hyperglycemia contributes significantly to this patient's hypertonicity. Osmotically active particles in the extracellular fluid space pull water out of the intracellular space. This causes cellular dehydration in the brain and consequently the patient's CNS changes. Diabetic ketoacidosis would be associated with a much lower serum bicarbonate level and with an elevated anion gap. This patient's anion gap is 9 mEq/L (126 − [95 + 22]), which is well within the normal range. This patient's hyponatremia is minimal and is related to the osmotic effects of hyper- glycemia. Patients with SIADH have an inappropriate production of ADH, leading to water retention and consequent hypotonicity (not hypertonicity, as in this case). The diagnosis of SIADH or drug-induced hyponatremia cannot be made in the setting of severe hypovolemia. Although the oral hypoglycemic chlorpropamide can cause drug-induced hyponatremia, this patient was not taking a sulfonylurea. Although meningitis can be associated with hyponatremia, this patient's hypertonicity and lack of meningeal signs point toward hyperosmolar nonketotic coma as the cause of her illness.

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