In the name of God

Hypercalcemia in infants and children

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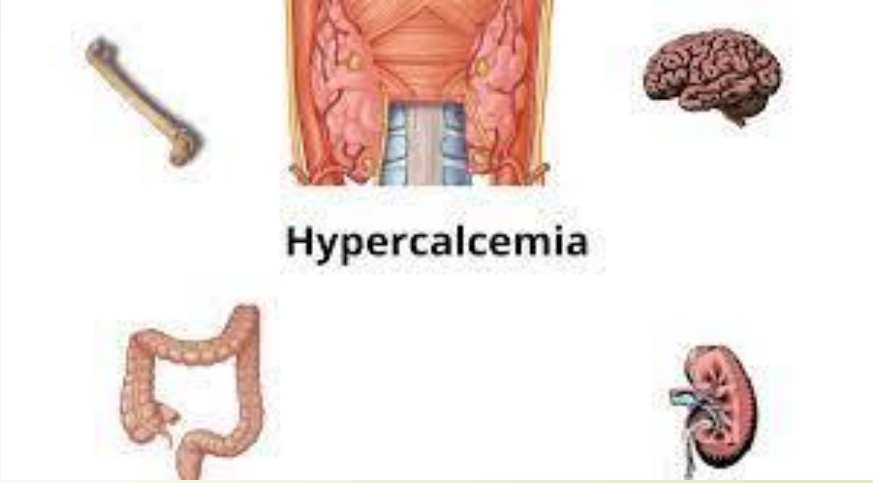
Etiology of hypercalcemia



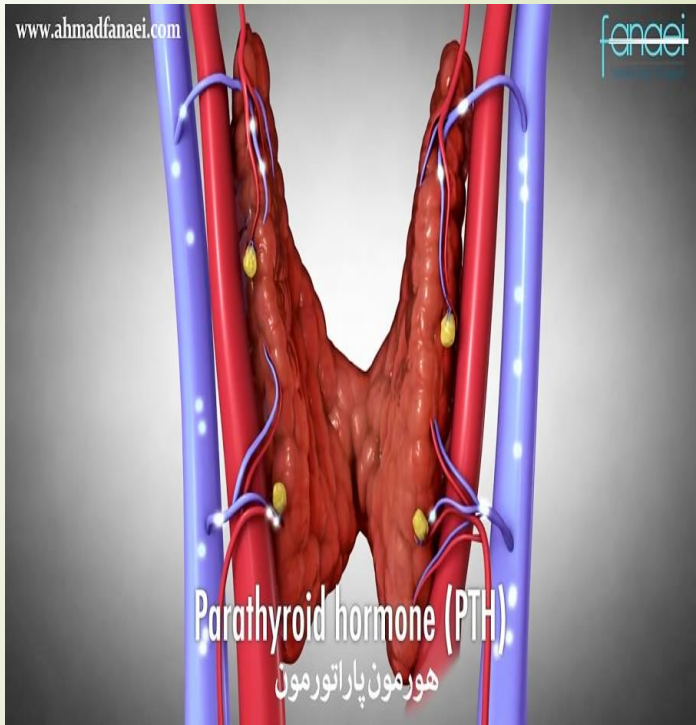
- **Hypercalcemia is a clinical problem**
- **Entry of calcium into the circulation > excretion of calcium into the urine or deposition in bone**
- **Accelerated bone resorption, excessive gastrointestinal absorption, or decreased renal excretion of calcium**
- **More than one mechanism may be involved.(Hyperparathyroidism , Hypervitaminosis D)**

Etiology of hypercalcemia

- Primary hyperparathyroidism
- Malignancy
- Greater than 90 percent of cases

Etiology of hypercalcemia

- Parathyroid mediated
- Non-parathyroid mediated



Parathyroid mediated

- Primary hyperparathyroidism (sporadic)
- Inherited variants
- Multiple endocrine neoplasia (MEN) syndromes
- Familial isolated hyperparathyroidism
- Hyperparathyroidism-jaw tumor syndrome
- Familial hypocalciuric hypercalcemia
- Tertiary hyperparathyroidism (renal failure)
- Maternal hypocalcemia

Hyperparathyroidism

- Rare
- Hyperplasia
- Adenoma
- Multiple endocrine neoplasia (MEN) syndromes (1,2)
- Hyperparathyroidism-Jaw tumor
- Transient neonatal hyperparathyroidism

Neonatal severe hyperparathyroidism

- Rare disorder
- Symptoms shortly after birth, anorexia, irritability, lethargy, constipation, and failure to thrive
- Radiographs: subperiosteal bone resorption, osteoporosis, and pathologic fractures
- May be mild, resolving without treatment, or rapidly fatal course
- Histologically: parathyroid glands diffuse hyperplasia
- Affected siblings have been observed in some patients

Transient neonatal hyperparathyroidism

- Mothers with hypoparathyroidism (idiopathic or surgical) or with pseudohypoparathyroidism
- The maternal disorder had been undiagnosed or inadequately treated during pregnancy
- Chronic intrauterine exposure to hypocalcemia ,hyperplasia of the fetal parathyroid glands
- Manifestations involve the bones primarily, healing occurs 4 and 7 months

Familial hypocalciuric hypercalcemia

- AD
- Ca2+ -sensing receptor gene ,inactivating mutation
- 1 copy of this mutation exhibit autosomal dominant familial hypocalciuric hypercalcemia

Hyperparathyroidism–jaw tumor syndrome

- AD disorder
- Parathyroid adenomas and fibroosseous jaw tumors
- polycystic kidney disease, renal hamartomas, and Wilms tumor
- Affects adults primarily, it has been diagnosed as early as age 10 yr

Multiple endocrine neoplasia (MEN) syndromes

- MEN type I: AD disorder , hyperplasia or neoplasia of the endocrine pancreas (gastrin, insulin, pancreatic polypeptide, glucagon), anterior pituitary (prolactin), and the parathyroid glands

- Hyperparathyroidism is usually the presenting manifestation, rarely in children<18 yr of age, Genetic study

- MEN type II may also be associated with hyperparathyroidism

Non Parathyroid mediated

- Hypercalcemia of malignancy
- Increased calcitriol (activation of extrarenal 1alpha-hydroxylase)
- Vitamin D toxicity (exogenous, endogenous)
- Chronic granulomatous disorders
- Medications
- Sub cutaneous fat necrosis

Malignancy:

- Primary bone tumors
- Metastatic tumors with osteolysis
- Lymphoma, leukemia ,neuroblastoma,…….

- Dysgerminoma
- Pheochromocytoma

- Tumors secreting parathyroid hormone–related peptide, growth factors, cytokines, prostaglandins, osteoclast-activating factors

Medications:

- Hypervitaminosis D
- Thiazide diuretics
- Lithium
- Teriparatide
- Excessive vitamin A(prolonged ingestion >50,000 IU per day)
- Increased calcium intake
- Milk Alkali syndrome
- Antiestrogens
- Aminophylline
- Theophylline toxicity

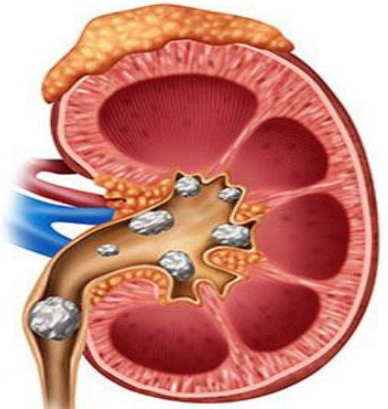
Other causes of hypercalcemia

- Hyperthyroidism
- Acromegaly
- Pheochromocytoma
- Adrenal insufficiency
- Immobilization
- Parenteral nutrition
- Milk-alkali syndrome
- Paget disease of bone, especially if the patient is at bed rest
- Congenital lactase deficiency
- Rhabdomyolysis and acute renal failure

- Williams-Beuren syndrome(excessive production of 25(OH)D and 1,25(OH)2D)
- Mucolipidosis type II
- Distal renal tubular acidosis
- IMAGe syndrome
- Post bone marrow transplantation for osteopetrosis
- Severe congenital hypothyroidism
- McCune-Albright syndrome
- Jansen metaphyseal dysplasia

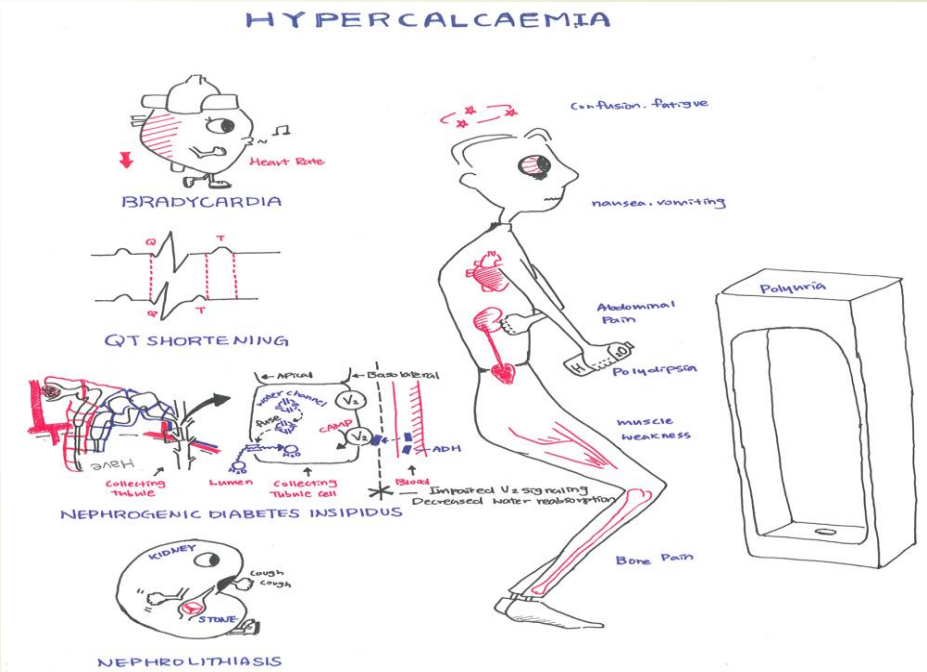
Clinical manifestations of hypercalcemia

- FTT, Headache, Abdominal pain, Fever……
- Renal
- Polyuria, Polydipsia, Nephrolithiasis, Nephrocalcinosis, Distal renal tubular acidosis, Nephrogenic diabetes insipidus, Acute and chronic renal insufficiency
- Gastrointestinal
- Anorexia, nausea, vomiting, Constipation, Pancreatitis, Peptic ulcer disease



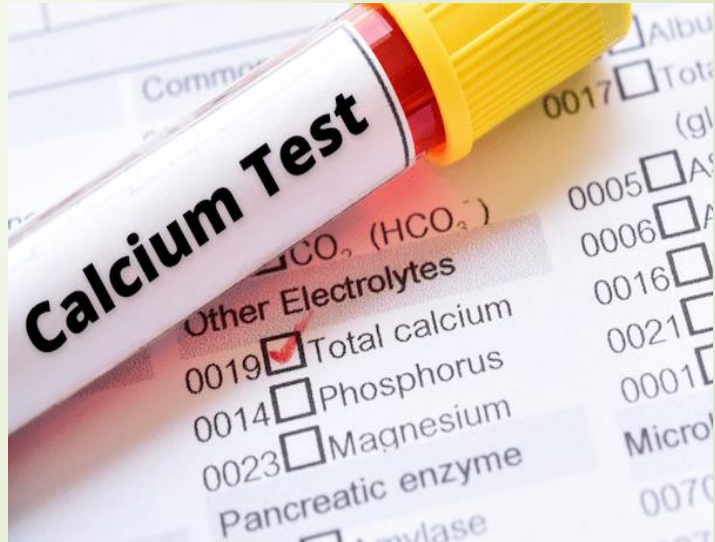
Clinical manifestations of hypercalcemia

- Musculoskeletal
- Muscle weakness, Bone pain. Osteopenia/osteoporosis, Pathologic fracture, Genuvalgus
- Neurologic
- Decreased concentration, Confusion,Fatigue,Stupor, coma, Convulsion,Irritability
- Cardiovascular
- Shortening of the QT interval, Bradycardia,Hypertension



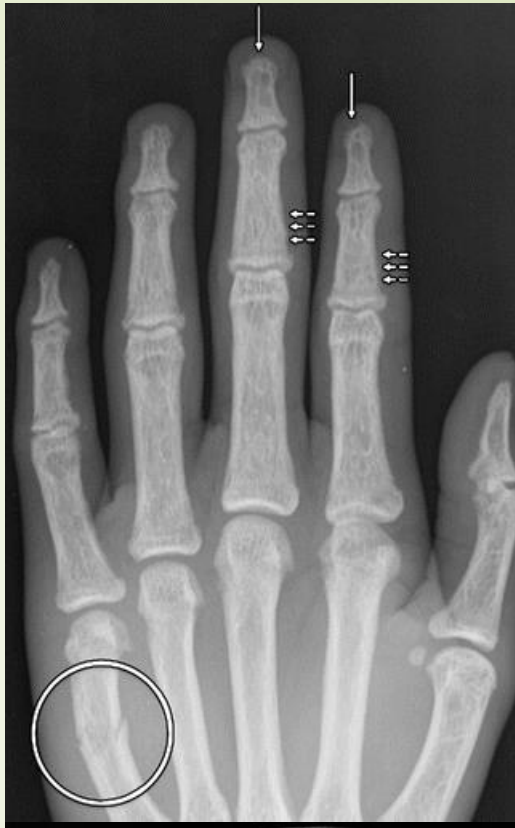
Hyperparathyroidism laboratory findings

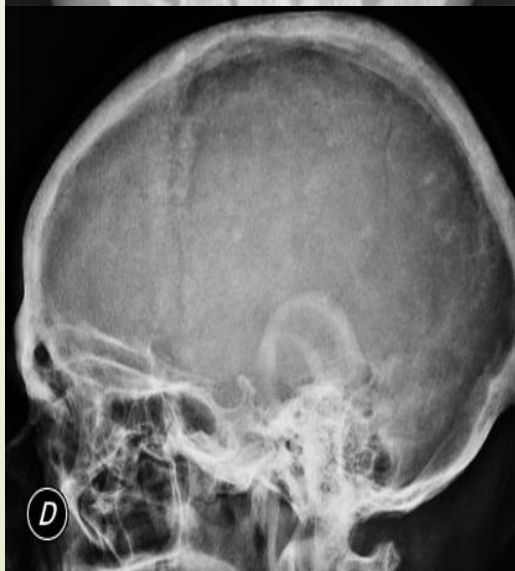
- Serum calcium level is elevated و adenomas levels >12 mg/dL hyperplasia; 15 to 20 mg/dL ,ionized calcium levels increased
- Serum phosphorus level < 3 mg/dL or less, serum magnesium is low
- Urine low SG
- Bun, uric acid may be elevated
- Adenomas with skeletal involvement, Alk Ph elevated, in hyperplasia normal
- Intact PTH elevated, especially in relation to the level of calcium
- Calcitonin levels are normal
- Parathyroid crisis



Radiographic findings

- Resorption of subperiosteal bone, margins of the phalanges of the hands
- Skull, gross trabeculation or a granular appearance ,absent lamina dura
- Cysts, fractures, deformities
- 10% of patients radiographic signs of rickets
- Radiographs of the abdomen renal calculi or nephrocalcinosis



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