Primary Hyperparathyroidism

Epidemiology: Incidence of the disease varies from 1 in 500 to 1 in 1000. Majority of the affected individuals are older women. It is one of the most common cause of hypercalcemia.

Pathophysiology: 1. Loss of the suppressive effect of extracellular Ca on PTH secretion; 2. Loss of normal sensitivity to Ca in parathyroid adenoma secondary to the reduction in the number of Ca-sensing receptors.

Diagnosis: A high or even inappropriately normal serum PTH in the presence of hypercalcemia confirms the diagnosis. Bone-density measurements at the hip and spine should be evaluated, regardless of age. There would be reduced DXA values at the femoral neck and relative preservation of the trochanter and lumbar spine. Differential diagnoses are thiazide or lithium carbonate use, benign familial hypercalcemia, etc.

Etiologies: Solitary adenoma (85%); Multi-gland hyperplasia (10%), either sporadic or in association with MEN type 1 or 2; Double adenoma (3%); Carcinoma (2%).

Clinical Presentation: 1. Electrolyte abnormalities including hypercalcemia, hypophosphatemia, elevated chloride level. 2. Nephrolithiasis is the most frequent complication, occurring in about 20% of the patients. 3. There may be diminished glomerular filtration rate. 4. Hypercalciuria (>300mg daily calcium excretion) is observed in up to 30% of patients. 5. Osteitis Fibrosa cystica has become most unusual even in elderly patients. 6. The condition is typically characterized by a preferential loss of cortical bone with a relative preservation of cancellous bone. Whether or not PTH-related bone loss is associated with an increased fracture risk remains unclear. 7. Some patients suffer from easy fatigability, a sense of weakness and mild cognitive impairment. 8. The association of PHPT with HTN has been well documented but not well understood. 9. While the circulating 1,25-dihydroxyvitamin D concentration may be elevated, levels of 25-hydroxyvitamin D tend to be low or in the lower range of normal in older individuals.

Surgery is recognized as the only definitive therapy for primary hyperparathyroidism. However, a large subgroup of older patients who are asymptomatic are unlikely to develop complications of the disease and may not need surgery. Parathyroidectomy is considered in patients who are asymptomatic or with complications. Guidelines are developed to target surgery on those who are asymptomatic and are most at risk of complications (Table one). Surgery is associated with 8.3% risk reduction in renal stone events. PHPT is associated with increased risk of acute MI up to 10 years prior to surgery, which decreases to a normal level after surgery.

Preoperative Localization: Ultrasound, CT, MRI and scintigraphy. Tm99 sestamibi scintigraphy is regarded as the most sensitive and most convenient to perform. Given limited specificity, confirmation with 2 approaches is recommended for accurate localization. However, in patients without prior neck surgery, there is no evidence that operative time is reduced or that the complication frequency decreased with preoperative imaging.
**Intraoperative Issues:** Local anesthesia is increasingly used in older patients. Intraoperative PTH assays indicate whether the patient has been cured or additional exploration is needed. Typically, serum PTH falls by 50% or more after the adenomas are removed (Figure one). Virtually all patients become normocalcemic.

**Postoperative period:** Serum calcium and PTH level normalize. Bone turnover decreases markedly over time. Bone density increases. But cortical bone loss in patients with PHPT is not readily reversible. Postoperative follow-up include serum calcium and PTH levels at 2 weeks, 6 months, and 12 months, DXA at 12 months.

**Surgical Complications:** Persistent hyperparathyroidism, recurrent hyperparathyroidism, postoperative hypoparathyroidism, recurrent laryngeal nerve palsy. Persistent hyperparathyroidism is usually the result of missing either an ectopic tumor or one of multiple abnormal glands. Recurrent hyperparathyroidism usually occurs in patients with familial disease.

**Medical Management:** Hydration, mobilization, moderate dietary calcium intake, avoidance of thiazide diuretics are recommended in treating asymptomatic PHPT and normocalcemic PHPT. The use of oral phosphate has been limited by its lack of efficacy, risk of metastatic calcification and gastrointestinal intolerance. Estrogen therapy reduces PTH-mediated bone resorption, but has little effect on serum levels of calcium and PTH. No data available on selective estrogen receptor modulators on serum calcium or PTH levels. Bisphosphonates like etidronate or clodronate do not result in sustained suppression of disease activity. Recent data support the use of the more potent bisphosphonates alendronate or risedronate. Both have shown short-term efficacy on surrogate markers, e.g. serum Ca and bone density. In older women, alendronate is well tolerated, reduces bone turnover, significantly improves bone density at the lumbar spine. Ca-sensing receptor agonists, calcemimetics may reduce PTH secretion directly via extracellular Ca-sensing receptors in parathyroid chief cells. Follow-up in patient who do not undergo surgery on serum calcium, urinary calcium excretion and creatinine clearance every 6 months, DXA every 12 months.

**Reference**