Pituitary tumors

- occur in 20–30% of patients
- These tumors can exhibit aggressive behavior and local invasiveness that makes them difficult to resect.

1 Prolactinomas are most common

Diagnosis:

- serum prolactin levels >200 g/L, with or without a pituitary mass evident by MRI.
- Values <200 g/L may be due to a prolactin-secreting neoplasm or to compression of the pituitary stalk by a different type of pituitary tumor.

2 Acromegaly due to excessive GH production is the second most common syndrome caused by pituitary tumors in MEN1.

3. Cushing's disease:

caused by ACTH-producing pituitary tumors or by ectopic production of ACTH or CRH by other components of MEN1 syndrome including islet cell or carcinoid tumors or adrenal adenomas.

Diagnosis:

pituitary Cushing's disease is generally best accomplished by a high-dose dexamethasone suppression test or by petrosal venous sinus sampling for ACTH after IV injection of CRH.

Adrenal adenomas /hyperplasia :

- occurs in about 37% of patients with MEN 1
- 50% are bilateral.
- They are generally benign and nonfunctional.
- In one series, one out of 12 patients developed a feminizing adrenal carcinoma.
- These adrenal lesions are pituitary independent

Tx of Pituitary Tumors

- Treatment of prolactinomas is with dopamine agonists (bromocriptine, cabergoline, or quinagolide) which usually returns the serum prolactin level to normal and prevents further tumor growth.
- Surgical resection of a prolactinoma not curative but may relieve mass effects.

- Octreotide reduces tumor mass in one-third of GH-secreting tumors and reduces GH and insulin-like growth factor I levels in >75% of patients.

- Pegvisomant, a GH antagonist, rapidly lowers insulin-like growth factor levels in patients with acromegaly .

- Radiation therapy in large or recurrent tumors.

Nonendocrine tumors

- Small facial angiofibromas
- subcutaneous lipomas .
- Collagenomas can present as firm dermal nodules.
- Malignant melanomas have been reported

MEN 2

- Sipple 1st described an association between thyroid cancer and pheochromocytoma in 1961.
- The thyroid cancer was discovered to be a medullary carcinoma in 1965.
- This familial constellation of pathology in conjunction with parathyroid hyperplasia was recognized as MEN 2 in 1968.

- Although pts with mucosal neuromas were identified at this time, the distinction between MEN 2A and MEN 2B was not made until 1975.

- MEN 2A pts do not have mucosal neuromas and marfanoid habitus found in MEN 2B pts.

- MEN 2A patients also have a less virulent form of medullary thyroid ca (MTC) than MEN 2B pts.

- MEN 2A pts may have parathyroid hyperplasia, which is rare in MEN 2B pts.

MEN 2A (Sipple's Syndrome)

- MEN 2A is a rare familial multiglandular syndrome that is inherited as an autosomal dominant trait.

- Pts have *ret* protooncogene (RET) mutation.

- Their first-degree relatives may have specific RET mutation.

Patients may present with:

1. **medullary thyroid carcinoma** (> 90%);

2. **hyperparathyroidism** (20–50%), due to hyperplasia or multiple adenomas in over 70% of cases;

3. **pheochromocytomas** (20–35%), which are often bilateral; or

4. **Hirschsprung's disease.**

Laboratory Studies

- Screening for medullary thyroid carcinoma is done with the pentagastrin stimulation test,
- Urinary catecholamines and metanephrines screen for pheochromocytomas.
- Serum calcium level and PTH levels screen for hyperparathyroidism.

Imaging Studies

- Perform CT scanning or MRI for imaging of the adrenals.
- If calcitonin levels are elevated at either baseline or with provocative testing, evaluate the chest and abdomen for metastatic disease.

Tx

- MTC : Total thyroidectomy has been recommended for pts as young as age 3 years for MEN 2A if they contain the genetic mutation.

- **Thyroid hormones**
- For supplemental therapy in hypothyroidism

Parathyroid disease

- Hyperparathyroidism usually manifests in patients older than 30 years.
- Histologically, consist of a chief-cell hyperplasia.
- If all parathyroid glands are enlarged, a subtotal parathyroidectomy is advocated, leaving an approximately 60-mg remnant.
- Cervical thymectomy because of the increased risk of supernumerary parathyroid glands.

- **Vitamin D supplements**

May increase serum calcium levels by improving calcium absorption.

Tx Pheochromocytoma

- Unilateral adrenalectomy avoids the risk of Addisonian crisis and improves the quality of life by not requiring replacement therapy.

- Some investigators have advocated bilateral adrenalectomy in all patients because of risk of malignancy (rare) and the operative complications from subsequent surgeries.

- **Mineralocorticoids**
- Partial replacement therapy for primary and secondary adrenocortical insufficiency

- **Corticosteroids**
- Cause profound and varied metabolic effects. Corticosteroids modify the body's immune response to diverse stimuli.

MEN 2B

- familial, autosomal dominant multiglandular syndrome that is caused by a mutation of the *ret* protooncogene (RET) on chromosome 10.

MEN 2B is characterized by;

1. mucosal neuromas (> 90%) with bumpy and enlarged lips and tongue,
2. Marfan-like habitus (75%),
3. adrenal pheochromocytomas (60%) that are rarely malignant and often bilateral,
4. medullary thyroid carcinoma (80%).
5. intestinal ganglioneuromas,
6. skeletal abnormalities (87%), and
7. delayed puberty (43%).

- Medullary thyroid carcinoma is aggressive and presents early in life. Therefore, infants having a parent with MEN 2B receive genetic screening; those carrying the RET mutation undergo a prophylactic total thyroidectomy by age 6 months.

Follow up

- Monitor pts for recurrence of medullary thyroid carcinoma with calcitonin, CEA, and +/- provocative calcitonin testing.
- Perform annual screening for hyperparathyroidism with serum calcium and PTH levels in MEN 2A patients.
- Obtain urinary catecholamine levels on an annual basis to assess for pheochromocytoma.
- Carefully monitor medication dosage and adverse effects

conclusion

- MEN is rare
- Inheritance is by autosomal dorminance
- effective management requires an understanding of endocrine neoplasia
- Early genetic testing help decisions for prophylactic surgeries for individuals at risk
- Early treatment of medullary thyroid carcinoma prevents death.
- Careful monitoring for pheochromocytomas can decrease the chance of hypertensive episodes