# P101 A Complex case of MEN-1

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## INTRODUCTION:

Multiple Endocrine Neoplasia type 1 (MEN1) is an autosomal dominant hereditary cancer syndrome, caused by germ line and somatic mutations in the tumour suppressor MEN-1 gene (11q13). MEN-1 is characterized by tumours of the parathyroid (83–97%), pancreas (38–84%), and anterior pituitary (18–65%).

## METHODS:

Clinical, biochemical and radiological data of this patient diagnosed to have MEN-1 were analysed and the challenges in the management of these neuroendocrine tumours are discussed.

## CLINICAL PRESENATIONS:

A 45 year old gentleman presented with the following symptoms for 6 years duration

- Progressive enlargement of the hands ,feet and nose
- Decreased libido with erectile dysfunction
- Occipital headache
- Proximal muscle weakness & generalised body pain
- Pain in the right hip joint and difficulty in walking
- Lethargy and fatigue on arising from bed in the early morning and felt better with a cup of coffee
- Dyspepsia

No history of visual complaints / renal stone / fragility / fracture / flushing / GI bleed.

Investigations done at an other centre in -2007 showed an elevated serum prolactin levels with CT scan showing a pituitary tumour.

## ON EXAMINATION:

Coarse facies with acral enlargement (Figure 1), multiple collagenomas over the abdomen, neck and back (Figure 2). Acanthosis nigricans was present in the axilla and neck .

Blood pressure :110/70mmHg ; Pulse :90/min.

Visual fields and optic fundus examination were normal .

Testes volume (15 ml bilateral), SMR Tanner's stage 5.

| Biochemical | Value | Units | Normal range |
|---|---|---|---|
| Calcium Corrected | 10.8 | mg/dl | 8.3-10.4 |
| Phosphorus | 4.8 | mg/dl | 2.5-4.5 |
| iPTH | 880.6 | pg/ml | 8-74 |
| HbA1c | 5.7 | (%) | <5.7 |
| Testosterone | 151 | ng/dl | 270-1030 |
| LH | 5.01 | mIU/ml | 0.8 – 7.6 |
| FSH | 10 | mIU/ml | 0.7 – 11.1 |
| TSH | 3.45 | µIU/ml | 0.3 - 4.5 |
| T4 | 9.0 | mcg/dl | 4.5 - 12.5 |
| FT4 | 0.9 | ng/dl | 0.8 - 2.0 |
| HGH baseline | >40 | ng/ml | 0-5 |
| 1hour after OGTT | 36 | ng/ml | <2 |
| IGF-1 | 592 | ng/ml | 64-220 |
| 8am Cortisol | 7.25 | mcg/dl | 7-25 |
| Post Synacthen - cortisol | 12.2 | mcg/dl | ≥18 |
| On 72 hours fasting- | | | |
| • Plasma glucose | 45 | mg/dl | 70-100 |
| • Insulin | 15.9 | µIU/ml | <3 |
| • C peptide | 4.1 | pg/ml | <0.6 |
| Urine 5 HIAA | Negative | | |
| 24 hour metanephrine and nor metanephrine | Normal | mcg/day | <350<br><600 |
| Gastrin | 5150 | pg/ml | 0-90 |

## INVESTIGATIONS:

- Elevated - Calcium & iPTH- suggestive of PHPT
- Elevated Prolactin, GH & IGF-1 – suggestive of GH and Prolactin secreting tumours.
- Elevated C peptide & Insulin during hypoglycemia- suggestive of endogenous hyperinsulinemic hypo-glycemia along with elevated serum gastrin level- Insulinoma and Gastrinoma (PNETs)

## IMAGING:

- MRI of the Pituitary showed a Hardy's Grade-B/E 2.8x3.1x2.2 cm sellar mass with suprasellar and right parasellar extensions(Figure 3).
- MIBI Scan-Right inferior parathyroid adenoma.Figure-3)
- MRI of the abdomen revealed three T2 hyperintense pancreatic lesions (Figure 4,shown with the arrows)

## PET SCAN:

- An 18-fluro deoxy glucose positron emission computerized tomography(18-FDG PET CT) scan done to screen for other tumours /metastases showed thymic enlargement, bilateral adrenal adenomas, and also confirmed the other tumours described earlier. (Figure-5).

## METABOLIC HOMEOSTASIS:

- This subject had an interesting metabolic homeostasis due to multiple endocrine tumours secreting antagonistic hormones. GH and Insulin counter balanced the blood glucose and hence he did not have typical hypoglycaemic episodes. In addition, the opposing effects of PTH by GH through IGF-1 on the renal tubules maintained a normal serum phosphate level.

## TREATMENT-1:

- SEPT 2012: Underwent a 3 and 1/2 gland parathyroidectomy along with cervical thymectomy, following which the Calcium and iPTH normalised .
- Started on medical management for acromegaly, hyperprolactinemia and functioning pancreatic NETs with Octreotide LAR – 20mg intramuscular once a month, Cabergoline – 2mg twice a week, and Pantoprazole 80mg twice daily respectively.

**Histopathology** of parathyroidectomy tissues revealed multiple parathyroid adenomata and histopathology of thymic tissue was normal.

## TREATMENT-2:

- OCT 2013- Partial excision of the pituitary macroadenoma due to parasellar tumour extension, and financial constraints in continuing Octerotide LAR.
- Started on diazoxide therapy after the pituitary surgery for Insulinoma associated hypoglycemia.

**Histopathology** of pituitary tumor showed immunopositive for prolactin and growth hormone.

## TREATMENT-3:

- AUG 2014- Distal pancreatectomy with enucleation of PNETs in the head and uncinate process of pancreas, excision of duodenal(D2) submucosal tumours along with omental lymph node dissection.

**Histopathology** showed tumour cells arranged in thick trabeculae and pseudoglandular structures with immuno-histochemistry showing a diffuse cytoplasmic positivity for synaptophysin, pan cytokeratin and chromogranin, and a MIB-1 index of 2-3%, confirming multiple NETs in the pancreas and duodenum. One fifth of omental lymph nodes had metastatic tumour deposits.

- ➢ Post-operatively he developed diabetes mellitus and glycaemic control was achieved with basal bolus insulin regimen.
- ➢ Following resection of the NETs, serum gastrin, growth hormone and IGF-1 levels declined suggestive of GHRH secreting PNETs.

## LAST FOLLOW-UP –FEB 2015:

- Blood glucose level are well control with basal bolus insulin regimen.
- Cabergoline was continued for persistent hyperprolactinemia.

**Figure-1**

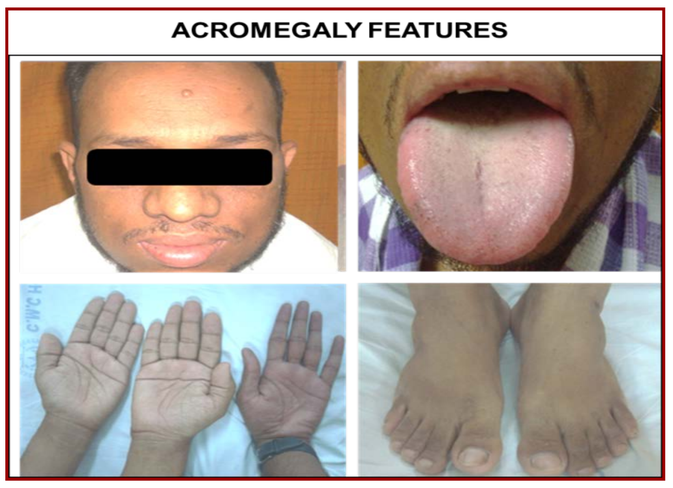



**Figure-2**

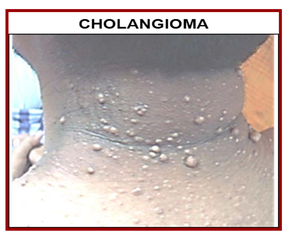



**Figure-3**

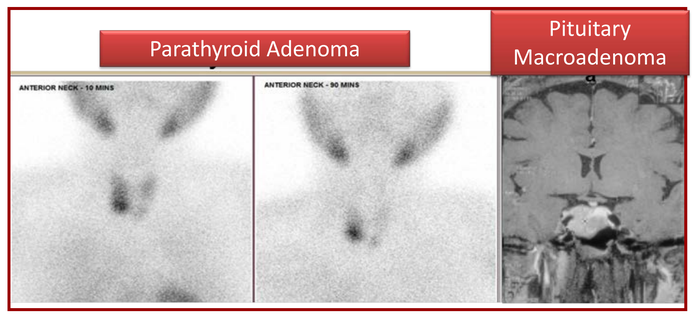



**Figure-4**

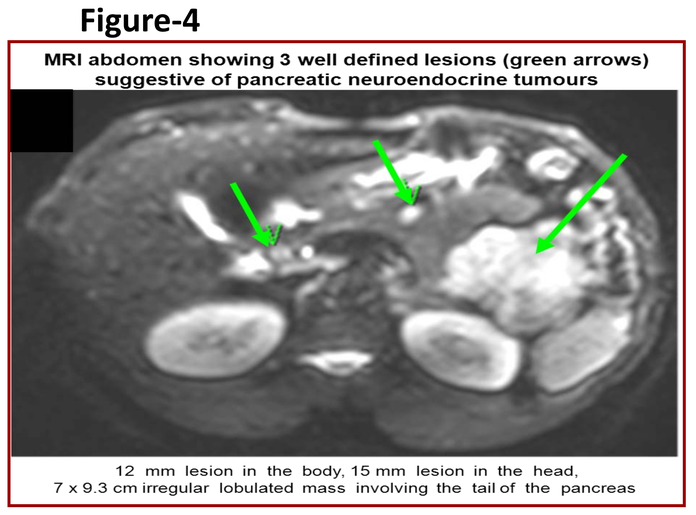
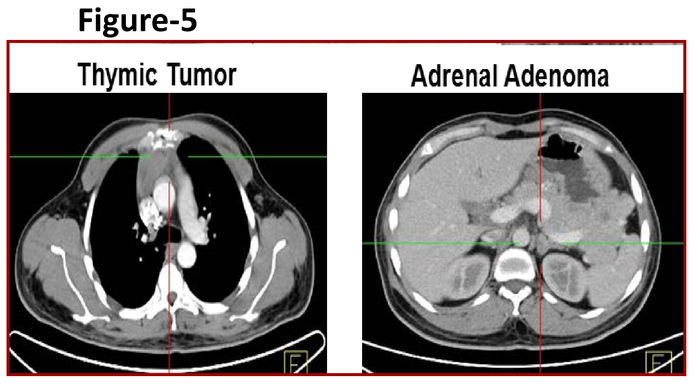



**Figure-5**




## CONCLUSION:

- The present case of MEN-1 highlights the challenges in the management; Necessitating a multidisciplinary team approach in view of multicentric tumours and also risk of recurrences.

## REFERENCES:

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