Audit of Patients with Multiple Endocrine Neoplasia Type 1 in a Tertiary Referral Centre

CT Goudie*, SM Reddy*, S Curran, VER Parker, P Corrie, AS Shaw, NV Jamieson, RK Praseedom, EL Huget, A Jah, NR Carroll, JR Buscombe, S-Mi Park, HL Simpson *joint first authors

Institute of Metabolic Science
Cambridge University Hospitals NHS Foundation Trust
University of Cambridge Metabolic Research Laboratories

INTRODUCTION

Multiple endocrine neoplasia type 1 (MEN1) is characterised by parathyroid, pituitary and pancreatic tumours in association with neoplasia of intra-thoracic endocrine tissue, adrenal glands and cutaneous manifestations. We reviewed patients in our centre attending a dedicated MEN1 clinic, where detailed radiological and biochemical surveillance is undertaken (Thakker *et al*. 2012).

METHODS

Case notes and electronic records of patients attending a tertiary centre clinic for care of MEN1 were reviewed.

DEMOGRAPHICS

48 patients reviewed
- 100% Caucasian
- Mean age 49 years (range 14 – 89 years)
- 54% female, 46% male
- 3 deceased
  - 1 metastatic gastrinoma
  - 1 chest NET
  - 1 breast cancer
  - Mean age of death 56 years (range 45 – 75)

90% had confirmed MEN1 mutations
- 77% from families with more than one affected patient
- 38% detected through screening of family members
- 1 patient had novel MEN1 mutation Q554X

Prevalence in this catchment area is 1/20 000

In this cohort there were
- 42 primary hyperparathyroidism
- 32 pancreaticoduodenal NETs
- 13 pituitary tumours
- 10 adrenal masses
  - 3 bilateral
  - 1 functioning (resected)
- 2 thymic masses
  - 1 resected
  - 1 awaiting resection
- 1 multiple gastric carcinoid on SSA/surveillance
- 2 chest NETs surveillance
- 1 DIPNECH surveillance

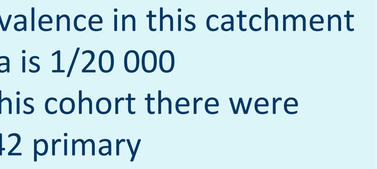


Fig1. Incidence of main MEN1 tumours in our cohort

PARATHYROID

88% developed primary hyperparathyroidism
- Mean age of diagnosis 40 years (14 - 82 years)
  - 55% of patients developed PHPT by 40 years

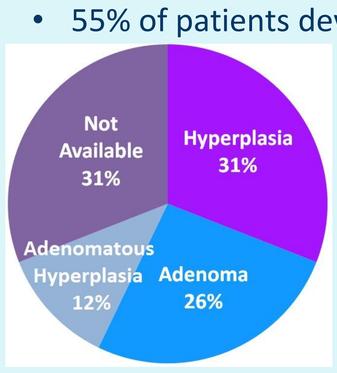


Fig2. Histological diagnoses

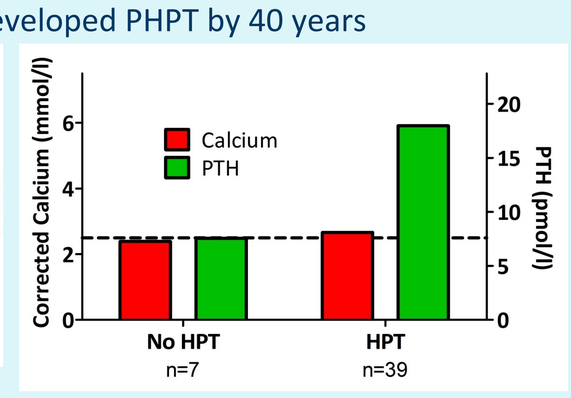


Fig3. Biochemical features of those with and without PHPT at diagnosis

- Complication rates
  - 33% renal stones
  - 17% osteoporosis (48% had a DEXA result available)
- 71% with PHPT who had an US parathyroid had an abnormal result
- 88% of those with PHPT who had a sestaMIBI had an abnormal result
- 76% were treated surgically
  - 5 patients had a repeat surgery
  - For 24%, reports were not available
- 2 patients were managed with cinacalcet for recurrent disease post-

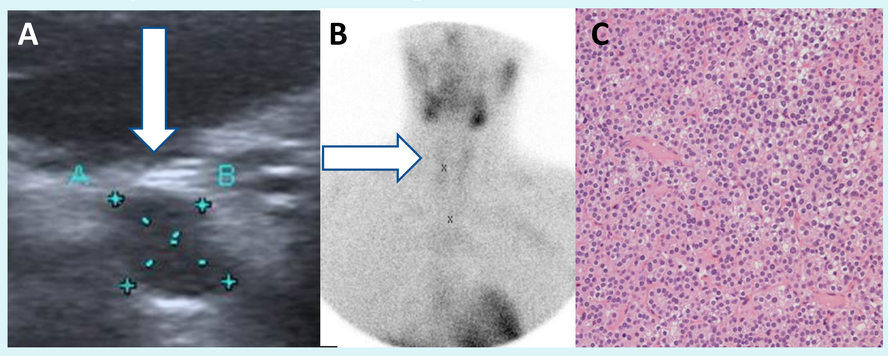


Fig4. 18 year old male with MEN1
A) US
B) SestaMIBI
C) Hyperplastic parathyroid histology

PANCREATICODUODENAL NETs

67% developed neuroendocrine tumors

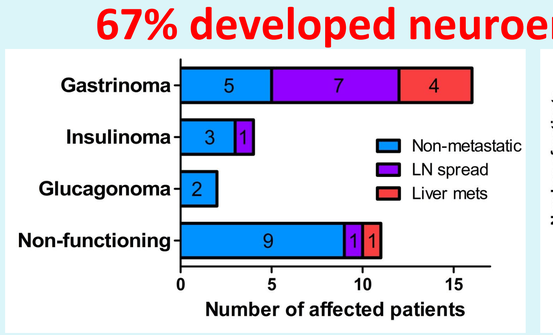


Fig5. Frequency of PNET subtypes, illustrating numbers of metastatic and non-metastatic disease

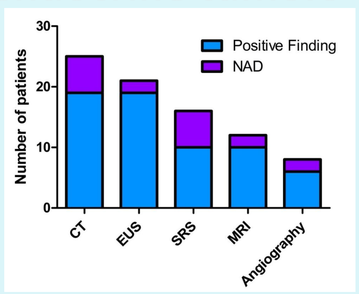


Fig6. Positive findings on surveillance imaging

- Mean age of diagnosis 43 years (16 – 72 years)

Fig7. Gut hormone profiles at diagnosis

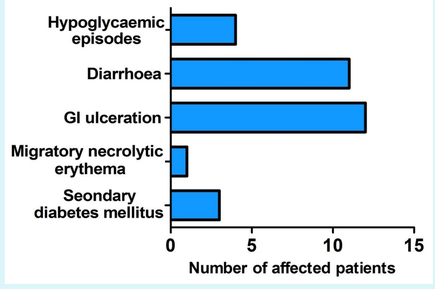


Fig8. Clinical features prior to surgery

Mean size of tumour was 1.5cm

Insulinomas (n=4)
- Mean age of diagnosis 25 years (16 – 34 years)
- Glucose mean level 2.4mmol/l (range 1.7 – 3.5)
- Insulin mean level 57pmol/l (range 32 – 101)
- Proinsulin mean level 18pmol/l (range 15 – 20)
- 100% underwent surgery, with 100% currently in remission

Gastrinomas (n=16)
- Mean age of diagnosis 46 years (19 – 72 years)
- Gastrin mean level 339pmol/l (range 9 – 2483)
- 5 patients underwent surgery due to enlargement or worsening symptoms (2 Whipple's procedures, 2 total pancreatectomies, 1 distal pancreatectomy)
- 3 patients who underwent surgery were found to have positive lymph node metastases on histology
- PPIs were given to 73% of patients with gastrinomas

Glucagonoma and non-functioning PNETs have been managed with surveillance only

Somatostatin analogues given to 4 patients

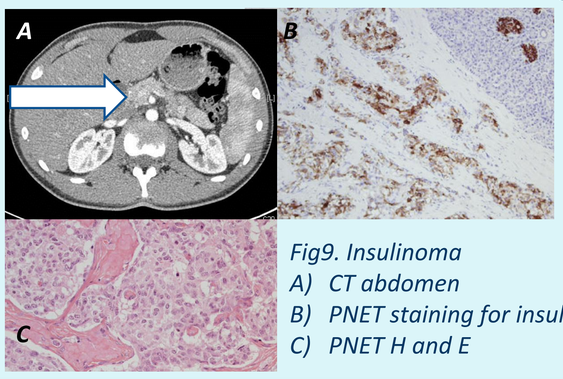


Fig9. Insulinoma
A) CT abdomen
B) PNET staining for insulin
C) PNET H and E

Fig10. Imaging of patient with MEN1 and gastrinoma
A) Octreotide scan
B) Endoscopic US of pancreas
C) CT abdomen

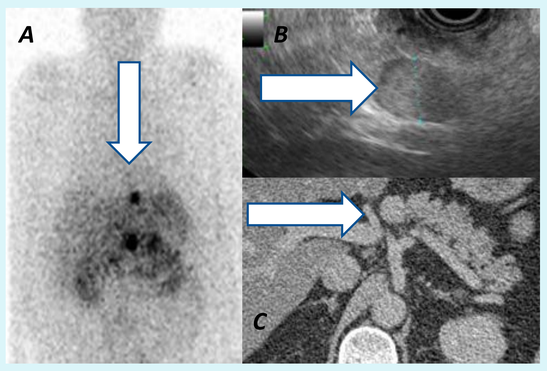
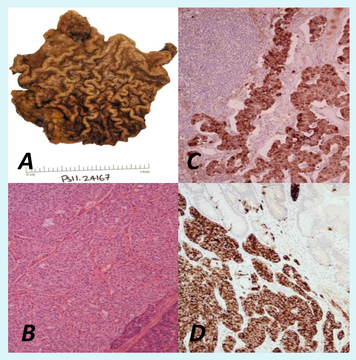


Fig11. Pathology of patient with MEN 1 and gastrinoma
A) Macroscopic image of stomach showing increased rugae
B) PNET H and E
C) PNET staining for gastrin
D) Lymph node staining for CgA



PITUITARY

27% developed pituitary adenomas
- Mean age at diagnosis 48 years (23 – 60 years)

Tumour Type	N (%)	Mean Age at Diagnosis (range)
Prolactinoma	6 (46%) 5 Macro; 1 Micro	31 years (23 - 60)
Corticotroph	2 (15%)	57 years (54 - 59)
Non Functioning	5 (39%)	54 years (46 - 60)

- 73% with pituitary adenomas had a lesion on MRI pituitary
- 3 patients underwent curative trans-sphenoidal surgery
- 5 patients were managed with dopamine agonist therapy alone
- 5 patients have been managed with surveillance only

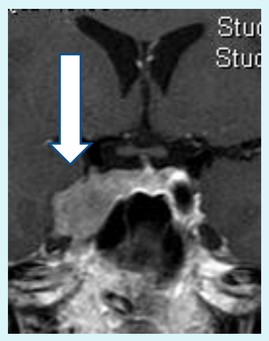


Fig12. MRI pituitary demonstrating macroprolactinoma

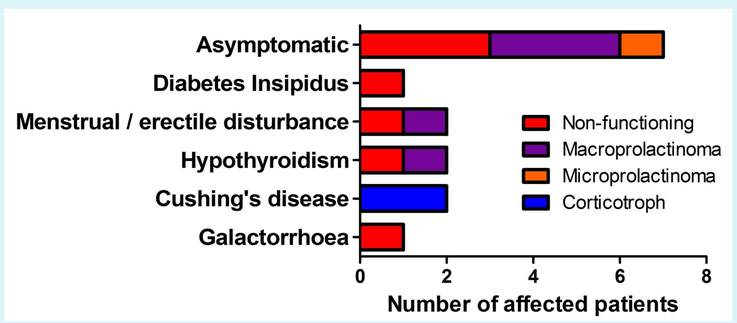


Fig13. Clinical features prior to surgery
- *1 patient had both diabetes insipidus and hypothyroidism*

DISCUSSION

The characteristics of MEN1 patients presenting to our service is consistent with previous reports (Pieterman *et al*. 2011).

Five patients have undergone pancreatic surgery, one of whom died 10 years after surgery. Two patients had previously unidentified lymph nodes discovered at surgery – it remains uncertain whether these patients will remain disease free. Optimal management of such patients remains unclear. NETs in MEN1 may often behave in an indolent manner and conservative management is often appropriate. Systemic therapies with conventional chemotherapy and newer biological agents are available but efficacy in this context is yet to be seen.

The wide-ranging manifestations of MEN1 emphasise the need for specialist review with a multidisciplinary team approach to achieve optimum outcomes.

REFERENCES

1. Thakker, RV *et al*. "Clinical Practice Guidelines for Multiple Endocrine Neoplasia Type 1 (MEN1) ". *J Clin Endocrinol Metab* 97: 2990 –3011, 2012.

2. Pieterman, CRC *et al*. "Care for patients with multiple endocrine neoplasia type 1: the current evidence base". *Familial Cancer* 10:157–171, 2011.