An Atypical Presentation of Multiple Endocrine Neoplasia Type 1

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Introduction

- Multiple Endocrine Neoplasia Type 1 (MEN-1) is an autosomal dominant condition which predisposes individuals to tumours of the parathyroid, pituitary and pancreas. The penetrance of MEN-1 is nearly 100% by 50 years of age
- Hyperparathyroidism in MEN- 1 typically presents in the second to fourth decade of life, approximately two decades earlier than sporadic primary hyperparathyroidism
- In contrast to sporadic primary hyperparathyroidism, where single gland disease is typical (85% of cases) , MEN-1 typically affects multiple parathyroid glands
- We describe an unusually late presentation in a gentleman with asymptomatic hypercalcaemia and a family history of hyperparathyroidism who was diagnosed with a novel pathogenic variant of MEN-1

Case Report

- A 64 year old man presented to the Endocrinology clinic for investigation of mild hypercalcaemia (2.68 mmol/L) incidentally discovered during pre-operative workup for elective removal of a testicular cyst. He had no family history of renal stones. His younger brother had undergone a parathyroidectomy at the age of 60. His father died in a road traffic accident aged 54. His mother was 84 and had no history of endocrine disease.
- Baseline blood results are shown in Table 1. The calculated urine calcium:creatinine ratio was 0.027, excluding Familial Hypocalciuric Hypercalcaemia. Bone Densitometry scan revealed osteopaenia of his non-dominant radius. Ultrasound examination of the renal tract was unremarkable. A single left superior parathyroid adenoma was identified on ultrasound (Figure 1), concordant with an area of increased uptake and delayed washout seen on Sestamibi SPECT CT (Figure 2).
- Further discussion revealed that his brother's hypercalcaemia resolved only after resection of multiple parathyroid glands. A gut hormone profile demonstrated elevation in Chromogranin B and Pancreatic Polypeptide (Table 2).
- Imaging of the pancreas with MRI, Endoscopic Ultrasound and Gallium DOTATATE PET CT (Figures 2 and 3) confirmed the presence of multiple lesions with features characteristic of neuroendocrine tumours. MRI of the pituitary was unremarkable.

Table 1 Relevant baseline blood tests

Adj Ca (2.20-2.60)	**2.68 mmol/L**
Inorg PO4 (0.8-1.50)	0.92 mmol/L
PTH (1.6-7.2)	**13.8 pmol/L**
Prolactin (60-300)	73 milliunit/L
Vitamin D (70-150)	75 nmol/L

Fig 1. Ultrasound Parathyroid

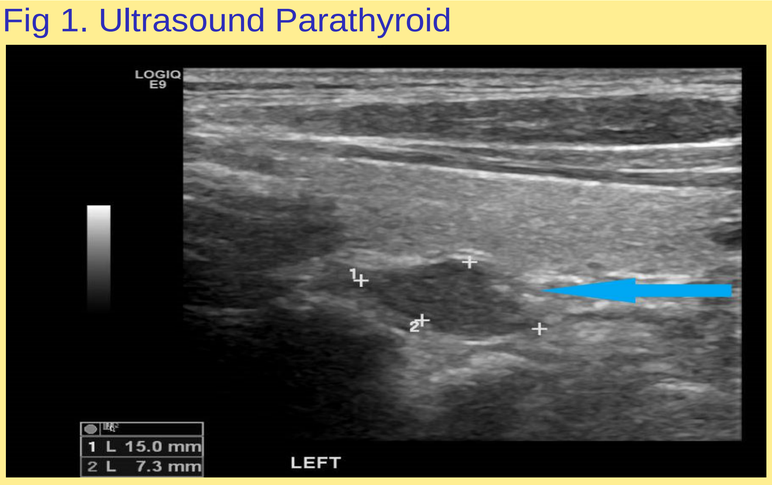

Fig 2 :Parathyroid Sestamibi SPECT CT

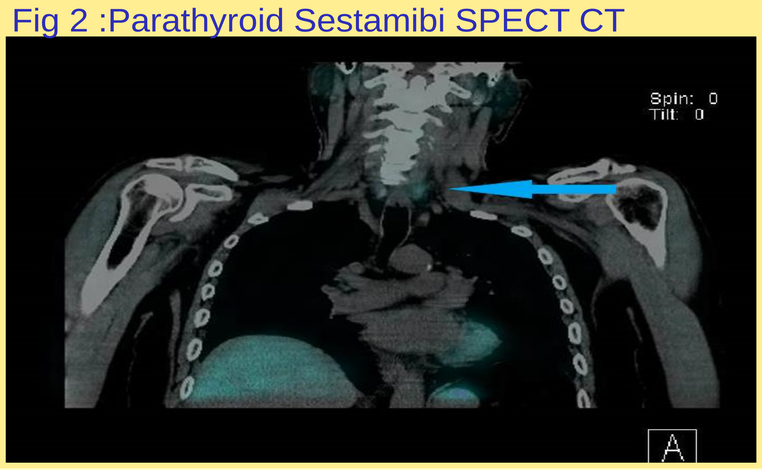

Fig 3 : Ga68 DOTATATE PET CT (fused)

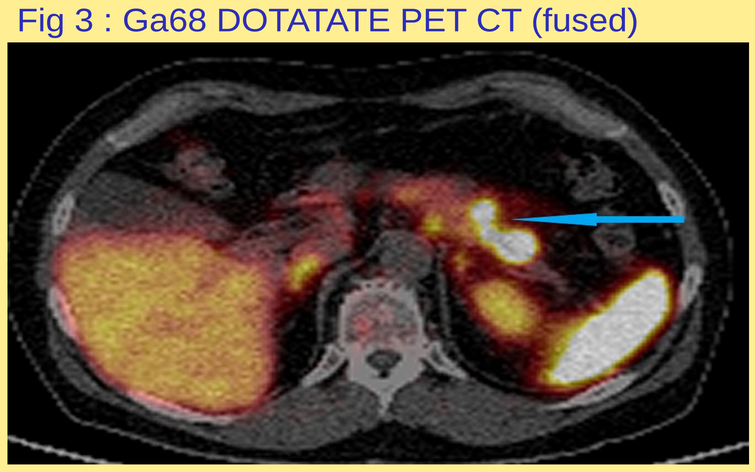

Fig 4 : Ga68 DOTATATE PET

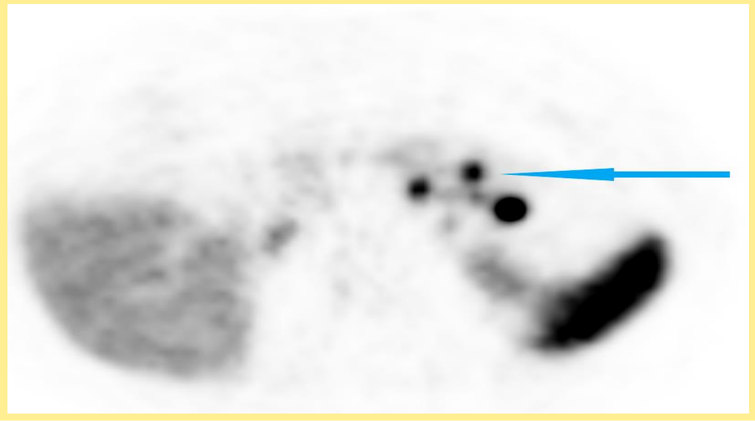

Table 2 Gut Hormones

Chromogranin A (0-60)	19 pmol/L
Chromogranin B (0-150)	**233 pmol/L**
Pancreatic Polypeptide (0-300)	**575 pmol/L**
Gastrin (0-40)	10 pmol/L
Glucagon (0-50)	37 pmol/L
Somatostatin (0-150)	<10 pmol/L
VIP (0-30)	<4 pmol/L

Further Investigations

- Genetic analysis identified a novel pathogenic *MEN1* missense variant, p.(Ile360Phe) (c.1078A>T) which lies in helix 16 of menin, a structurally important region of the protein which forms part of the wall of the JunD binding pocket. JunD, in the absence of menin, switches from a growth suppressor to a growth promoter.
- The patient's brother , his only sibling, was subsequently tested and found to have the same mutation. He has been referred to the Endocrinology clinic for MEN-1 work-up
- Neither the patient nor his brother have children

Discussion and Conclusion

- Primary Hyperparathyroidism is the most common endocrinopathy in MEN-1, reaching nearly 100% penetrance by age 50
- A literature search identified one report of MEN-1 diagnosed in the seventh decade. However, the seemingly unaffected patient was screened as a result of a known MEN-1 mutation in her younger family members.
- In contrast, our patient was the index case diagnosed atypically in older age with a novel pathogenic MEN-1 variant
- This case demonstrates that older age at presentation and concordant localisation to a single parathyroid gland on imaging does not preclude the diagnosis of MEN-1

References

1. Thakker RV, Newey PJ, Walls GV, Bilezikian J, Dralle H, Ebeling PR, Melmed S, Sakurai A, Tonelli F, Brandi ML, Endocrine Society Clinical practice guidelines for multiple endocrine neoplasia type 1 (MEN1) J Clin Endocrinal Metab. 2012;97(9):2990. Epub 2012 Jun 20

2. Late onset asymptomatic pancreatic neuroendocrine tumour- A case report for the phenotypic expansion of MEN Kaiwar C, Macklin SK, Gass JM, Jackson J, Klee EW, Hines SL, Stauffer JA, Atwal PS. Hereditary Cancer in Clinical Practice 2017 15:10 Pub 21st July 2017

3 Guidelines for diagnosis and therapy of MEN type 1 and type 2 Brandi ML, Gagel RF, Angeli A, Bilezikian JP, Beck-Peccoz P, Bordi C, Conte-Devolx B, Falchetti A, Gheri RG, Libroia A, Lips CJ, Lombardi G, Mannelli M, Pacini F, Ponder BA, Raue F, Skogseid B, Tamburrano G, Thakker RV, Thompson NW, Tomassetti P, Tonelli F, Wells SA Jr, Marx SJ. J Clin Endocrinol Metab. 2001 Dec;86(12):5658-71

BES2018 7--CC

Neuroendocrinology and pituitary

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Poster presented at: SfE BES 2018 19-21 November GLASGOW

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