An Atypical Presentation of Multiple Endocrine Neoplasia Type 1

Dr Sara Haboosh, Dr Adam Buckley, Dr Fatima Alkaabi, Dr Jeannie F Todd
Department of Endocrinology, Hammersmith Hospital, Imperial College NHS Trust, London

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.

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 diagnosed late 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