MULTIPLE ENDOCRINE NEOPLASIA TYPE 1 – PRESENTING WITH IMPOTENCE

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ABSTRACT

A 35-year old man presented with a 4-year history of impotence. His past history was significant for hypercalcaemia, bilateral pyelolithotomies for renal calculi and parathyroidectomy for hyperparathyroidism. He had an episode of haemetemesis and malaena a year before being seen here. Endocrine investigations revealed hyperprolactinemia, hypergastrinemia and increased basal acid output. Magnetic resonance imaging of the brain was indicative of a pituitary microadenoma. Computed tomographic scan of the abdomen revealed a bulky pancreas which was suggestive of a gastrin-secreting islet cell tumour. This case illustrates an unusual presentation of multiple endocrine neoplasia type 1 (MEN-1) with impotence and hyperprolactinemia. A short review of the literature was done.

Keywords: Impotence, prolactin microadenoma, MEN-1

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INTRODUCTION

The syndrome of multiple endocrine neoplasia type 1 (MEN-1) consists of tumours of the parathyroid, pituitary and pancreas. Patients with MEN-1 present for investigation in a variety of ways. The majority of patients present with symptoms related to hypercalcaemia and hyperparathyroidism. Islet cell tumours of the pancreas are involved in approximately 75% of the cases of MEN-1 (1).

In patients with pituitary tumours, one study reported that 45% of the tumours were functionless chromophobe adenomas, 30% were eosinophilic with associated acromegaly and 5% with Cushing's syndrome (1).

In the few patients who had prolactin-secreting adenomas as part of MEN-1, all of them were women and their presentation had invariably been secondary amenorrhoea (2-4). A literature survey showed no previous reports of male patients with hyperprolactinemia and MEN-1. We therefore describe in this case report a man who presented with impotence. Investigations demonstrated hyperprolactinemia secondary to a prolactin secreting adenoma in a setting of MEN-1.

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CASE REPORT

A 35-year old Indonesian Indian man with impotence for 4 years was referred to the authors' department for assessment of chronic renal failure and impotence in January 1989. Investigations revealed a hyperprolactinemia of 11690 mU/l (Normal 135-350mU/l).

On questioning it was determined that a right pyelolithotomy had been performed in 1977 in another hospital for renal calculi and in 1985 a left-sided pyelolithotomy was carried out for a similar reason. He was not investigated at that time.

In 1986, a subtotal parathyroidectomy was performed in India for hyperparathyroidism. No other details of the parathyroidectomy were available.

Specific questioning revealed a history of peptic ulcer disease in March 1988 when he had an episode of malaena and haemetemesis. A barium meal done in another centre confirmed the presence of a peptic ulcer. He was treated with antacids and cimetidine and was not followed up. Review of the family history was negative for endocrine problems.

On examination, he was an obese man in no distress. A surgical scar was seen over the neck. There were multiple cutaneous tags but no lipomas were detected. He was sightly pale. His blood pressure was 145/95 and the pulse rate was 90 per minute. The cardiovascular and respiratory systems were normal. Abdominal examination did not reveal any masses, there was no organomegaly. The testicles were normal in size and consistency. Examination of the central nervous system was unremarkable. The fundi and visual fields were normal.

Laboratory tests showed a hypochromic microcytic anaemia which was confirmed as beta-thalassaemia. The serum creatinine was 215 μmol/l and the blood urea nitrogen was 18 mmol/l. The total calcium was 2.3 mmol/l and the ionised calcium was 1.29 mmol/l. The mid-

molecule parathormone level was slightly raised at 150 pmol/l (Normal <95 pmol/l). The uric acid was 550 umol/l.

Gastroscopy revealed multiple erosions of the cap and second portion of the duodenum. A 0.6 cm ulcer was noted at the anterior aspect of the duodenum. Gastic fluid examination revealed a basic acid output/peak acid output ratio of 1:1 which is diagnostic of Zollinger-Ellison syndrome (5). The fasting serum gastrin level, while the patient was not taking anti H2 antagonists was 4170 mU/l (Normal <86 mU/l). Calcium infusion provoked greater than 25% elevation of gastrin level, which is diagnostic for Zollinger-Ellison syndrome (6). Computer-tomographic scan of the abdomen disclosed a bulky pancreas with no focal areas of abnormality.

Basal prolactin level was very much increased at 11690 mU/l. The patient was not taking any drugs which may induce the secretion of prolactin. Magnetic resonance imaging of the brain reported an asymmetrical sella with an enlarged pituitary gland indicating a microadenoma. There was no suprasellar extension. Endocrine screening showed no abnormality in the ACTH-cortisol and TSH-thyroxine axis. The serum testosterone level was depressed at 1.4 nmol/l (Normal 9.0 - 33.0 nmol/l) and the FSH level was normal at 5.0 U/l (Normal 0.8 - 4.7 U/l).

Bromocriptine was initiated but was associated with untoward gastrointestinal complaints which necessitated its cessation. Surgery was offered but declined by the patient. He refused further invasive management and returned to Indonesia.

DISCUSSION

Our investigations demonstrated that this patient has MEN-1 with hyperparathyroidism, a gastrin-secreting islet cell tumour and a prolactin adenoma.

There is definite evidence of past hyperparathyroidism as illustrated by his past history of hypercalcaemia, nephrocalcinosis and bilateral renal calculi. The presence of normocalcaemia and mildly raised elevated parathormone level makes recurrent hyperparathyroidism unlikely. It had been shown that with familial MEN-1, the most helpful screening investigation is the measurement of serum calcium (7).

There is definite biochemical evidence of a gastrinoma as suggested by the basal acid output/peak acid output ratio of 1:1 (5). The calcium infusion test provoked a greater than 25% elevation in the serum gastrin which further confirmed the presence of a pancreatic islet-cell tumour (6). A calcium infusion test was performed because of the inavailability of secretin. The markedly raised gastrin levels were pathological, even in the setting of chronic renal failure (8) and could only be secondary to a gastrin secreting islet cell tumour. The presence of a generally bulky pancreas on computer-tomographic scanning of the abdomen in no way negates the diagnosis as it is well known that patients with MEN-1 have multiple and inoperable tumours (9,10). Computer-tomographic scanning was chosen as the tool for localisation as it is less invasive and is equally sensitive compared to selective angiography (11).

The unusual feature of this man is his presentation with impotence associated with hyperprolactinemia. Patients with renal failure have mildly raised prolactin levels which is felt to be due to increased secretion and decreased clearance (12, 13). The ingestion of drugs which induces the secretion of prolactin, such as metoclopramide and methyldopa, could further elevate prolactin levels but these were not taken by this patient. The disproportionate high level of prolactin compared to his renal failure, is secondary to a prolactin secreting pituitary tumour, as confirmed by magnetic resonance imaging of the brain.

Hyperprolactinemia had been incriminated for 8-11% of impotence in man (14,15). Among hyperprolactinemic men, impotence is a common symptom. Carter et al described impotence in 20 out of 22 men with raised prolactin levels (16). Both high prolactin and low testosterone levels play a role in the causation of impotence. The replacement of testosterone alone does not correct the impotence altogether and will require treatment for hyperprolactinemia.

Prolactin-secreting adenomas account for a quarter of patients with pituitary tumours without MEN-1. In MEN-1, one study showed that a third of pituitary adenomas is associated with acromegaly and a small 5 percent causes Cushing's Syndrome (1). It is rare for hyperprolactinemia to be associated with MEN-1 and to date all the patients reported had been females with secondary amenorrhoea (2-4).

In summary, this man has definite evidence of a prolactin-secreting islet tumour together with a past history of hyperparathyroidism. The presence of a prolactin-secreting pituitary tumour in a male with MEN-1 has, so far, not been reported.

Since the occurrence of endocrine tumours can occur at separate intervals, it is conceivable that impotent man with hyperprolactinemia may be manifesting a feature of MEN-1. As such a high index of suspicion is required in detecting an unusual presentation of this syndrome.

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