Multiple endocrine neoplasia type 1

Key facts

- Multiple endocrine neoplasia type 1 (MEN1) is an inherited condition that leads to growth of mainly benign (non-cancerous) tumours of the endocrine glands.
- MEN1 should be distinguished from MEN2 which is a separate genetic condition (see MEN2 factsheet).
- The features of MEN1 vary depending on the types of tumours that occur and the hormones they produce.
- The features of MEN1 usually present in adulthood and manifestation before teenage years is very rare.
- The most common presenting feature of MEN1 is hyperparathyroidism with raised calcium levels owing to growth of the parathyroid glands.
- MEN1 is an autosomal dominant condition caused by alterations in the *MEN1* gene.
- Individuals with an alteration in the *MEN1* gene should undergo regular surveillance to screen for MEN1-associated tumours and their hormonal effects.
- Early diagnosis, treatment and management improves outcome and quality of life for those affected.
- The prevalence of MEN1 has been estimated at 1 in 10,000 of the population.

Clinical features

- The features of MEN1 vary depending on the types of tumours that occur and the hormones they produce. The three most common tumours to occur in MEN1 are:

1. **Parathyroid tumours**
   - Onset of hyperparathyroidism is usually after the age of 20. Over 90% of patients with MEN1 will develop hyperparathyroidism by the age of 50.
   - Growths in the parathyroid gland result in hyperparathyroidism (raised PTH levels) and hypercalcaemia.
   - Hypercalcaemia can lead a wide range of symptoms including thirst, lethargy, aches and pains, muscle weakness and constipation.
   - If left untreated,the long term effects of hypercalcaemia can include osteoporosis and renal stones.
2. **Pancreatic neuroendocrine tumours**
   - May occur in up to 75% of MEN1 patients.
   - The symptoms will depend on the type of tumour and the hormones which are produced.
   - Gastronomas are the most common neuroendocrine tumours in MEN1, with excess gastric production leading to acid reflux, indigestion and gastric/duodenal ulcers.
   - Insulinomas producing excess insulin cause symptoms of hypoglycaemia.
   - About 10% of patients with MEN1 may experience more than one type of pancreatic tumour.
   - Some (pancreatic) neuroendocrine tumours have the potential to become malignant if left untreated and metastasise.
3. **Pituitary tumours (pituitary adenoma)**
   - Around 30% of MEN1 patients will develop a pituitary tumour.
   - The effect of the tumour will depend on which hormones are produced.

- Tumours may secrete prolactin (causing infertility issues), growth hormone (affecting the size of the jaw bone and hands and feet) and ACTH (causing the adrenal gland to overproduce cortisol).
- Some tumours can be non-functioning (do not produce hormones) and some may affect vision through compression of the optic nerve.

Diagnosis

A clinical diagnosis of MEN1 can be made when:

- a patient develops two or more MEN1 associated tumours; or
- a patient with a family history of MEN1 develops one MEN1 associated tumour.

Genetic basis

- MEN1 is caused by alterations in the *MEN1* gene, which are inherited in an autosomal dominant manner.
- An affected individual has one usual and one altered copy of the *MEN1* gene. Each time an affected person has a child they will pass on either the usual or the altered copy of the gene. Children of an affected individual therefore have a 1-in-2 (50%) chance of inheriting the gene alteration.
- A proportion of families with MEN1 will not have identifiable changes in the *MEN1* gene.

Clinical management

- Affected patients should be managed in a specialised endocrine clinic.
- Regular surveillance is needed to screen for MEN1 associated tumours and their hormonal effects.
- Screening may include a medical review for assessment of symptoms, biochemical screening to check the level of PTH /calcium and other hormones, imaging of the pituitary/pancreatic gland.
- Parathyroid tumours can be treated by surgical removal of the parathyroid glands. The tumours usually reoccur, so surgeons often remove 3 1/2 glands with implantation of the remaining portion.
- Treatment of pituitary tumours may require medical treatment or surgery, and in some cases radiotherapy.
- The treatment of pancreatic tumours will depend on the size, type number and location of the tumours.
- Proton pump inhibitors (inhibit stomach acid production) are used for medical treatment of gastrinomas.
- Treatment for insulinomas may involve surgical removal of a tumour (over 2cms) or partial/complete removal of the pancreas.
- Tumours may metastasise to the liver and may be treated by chemotherapy, newer targeted therapies (eg tyrosine kinase inhibitors) or radio ablation.
- Patients should be offered genetic counselling and testing of the *MEN1* gene.

Genetic testing

Indications for genetic testing and genetic counselling include:

- diagnostic testing in patients with two or more MEN1 associated tumours;
- consideration of testing in young patients (< 40) with isolated parathyroid hyperplasia;
- diagnostic testing in a symptomatic blood relative;
- predictive/presymptomatic testing for first degree relatives of an affected individual; and
- affected individuals who are considering prenatal diagnosis.

Genetic testing is available in the UK and usually provided through specialist clinics or regional genetic centres.

This information is intended for educational use and was current in March 2015. For clinical management, it is recommended that local guidelines and protocols are used.