Testicular mass in a resting cell

Q1: What does the ultrasound scan show?

The ultrasound scan shows bilateral hypoechoic intratesticular masses. The margins are well defined and the lesions are in close proximity to the rete testis (mediastinum testis).

Q2: Given the patient's history, what is the diagnosis?

The diagnosis is bilateral adrenal rest tumours or testicular tumours of adrenogenital syndrome.

Q3: Describe the pathophysiology of these lesions.

An adrenal cortical cell rest, an interstitial cell, and a pleuripotential cell have all been suggested as the origin of testicular masses in congenital adrenogenital syndrome. Embryologically the development of the adrenal gland and the genital ridge occurs in close proximity. Adrenal cell rests are therefore known to occur in the spermatic cord, testis, broad ligament, and the ovary. The normal pathway of synthesis of the steroids hormones is shown in fig 1. The commonest defect in adrenogenital syndrome or congenital adrenal hyperplasia is complete or partial deficiency of 21-hydroxylase followed by a deficiency of 11-β-hydroxylase. The enzyme 21-hydroxylase is crucial to the synthesis of both cortisol and aldosterone. A lack of this enzyme leads to excess synthesis of adrenal androgens and also stimulation of secretion of adrenocorticotrophic hormone (ACTH). This ACTH in turn acts on the adrenocortical cell rests leading to hyperplasia and formation of testicular masses in male patients. Hyperplasia of testicular adrenal rests is also known to occur in patients with Nelson's syndrome who have undergone adrenalectomy of the native glands.

Histologically the smaller lesions are located at the hilus in 86% as shown by Rutgers et al. The larger masses are more commonly situated in the testicular parenchyma. They tend to be well demarcated, unencapsulated brown masses separated into lobules by bands of fibrous tissue. Microscopically the most important differentiating feature from a Leydig cell tumour is the absence of renke crystals. Clinically adrenogenital syndrome exists in three forms—that is, prenatal virilisation with or without salt wasting, a late onset form, and an asymptomatic form. The testicular masses occur more commonly in the salt loosing form. They need not always be clinically palpable. These patients with congenital adrenal hyperplasia are prone to infertility secondary to impaired spermatogenesis and Leydig cell failure, both in the testicular masses group as well as in patients with no testicular masses. Treatment with hormone replacement (dexamethasone) is shown to reduce the size of these lesions as well as a reduction in the hardness of the testis. Compliance with treatment is shown to prevent their occurrence. A lack of decrease in size with compliance to treatment is also seen and can be secondary to extensive fibrosis or calcification in the lesions at diagnosis. However a study by Stikkelbroeck et al showed no significant correlation of the tumour size to the hormone replacement regimen or under treatment of these patients.

Q4: What is the role of imaging in the management of these lesions?

The presence of testicular tumours in congenital adrenal hyperplasia is well known but their diagnosis and management have always been a dilemma because of the inability to accurately diagnose the benign nature of the tumours. With advances in imaging techniques it is now possible to more accurately categorise the lesions, though the differential of a Leydig cell tumour will always need to be considered in the asymptomatic group with no hormonal dysfunction. Imaging plays a crucial part both in the diagnosis and follow up of these lesions. Ultrasound and magnetic resonance imaging (MRI) have equivalent sensitivity in detecting and assessing the size of the lesion.

These tumours tend to be bilateral, located closer to the hilum and can be intratubular or in the spermatic cord. On ultrasound they are usually hypoechoic but can be hyperchoic. Colour Doppler sonography can reveal a hypervascular or hypovascular nature and if hypervascular they have a characteristic spokewheel pattern. On T1 weighted MRI most are isointense (71%) but some can be hyperintense relative to the testicular tissue. After contrast they show enhancement. On T2 weighted MRI they are hypointense in relation to the testicular tissue (fig 2). Ultrasound and MRI are used in following up these lesions while the patient receives hormonal replacement as they are known to reduce in size with treatment. However they can be unresponsive to steroid treatment and may also gain autonomy. Imaging can prove useful in assessing unresponsiveness provided the patient is compliant to medication. In such circumstances resection of the tumour with testis sparing surgery is advocated in order to retain fertility. Post-operative MRI and ultrasound can be used for evidence of recurrent disease.

Final diagnosis

Bilateral adrenal rest tumours or testicular tumours of adrenogenital syndrome.

References


Figure 2 T2 weighted MRI scan of both testis showing isointense masses.

Learning points

- All testicular masses are not cancers.
- Patients with adrenogenital syndrome can develop testicular tumours in adrenal rest cells.
- Compliance to hormone replacement therapy is beneficial.
- Hormone replacement or testis sparing surgery are available options.
- Definitive diagnosis is difficult.
Pathological fracture in a pregnant woman

Q1: What is the differential diagnosis based on the history and the MRI (giant cell tumour, brown tumour, chondrosarcoma, secondaries in the bone)?

The differential diagnosis is giant cell tumour and brown tumour. A lytic lesion in a young woman with an associated pathological fracture and soft tissue mass raises several possibilities—for example, giant cell tumour, eosinophilic granuloma, brown tumour, or a primary bone tumour. Brown tumours are focal bone lesions caused by an increased osteoclastic activity and fibroblastic proliferation within primary hyperparathyroidism (PHP) or rarely secondary hyperparathyroidism. They are named after their typical brown haemorrhagic stroma with, also typical, giant cell formations. A brown tumour should always be ruled out in such a clinical situation by serum calcium concentration and parathyroid hormone assay. A preoperative biopsy is mandatory for the other lesions. A finding of giant cells on histopathology does not exclude a brown tumour. A giant cell tumour is characterised by the presence of multinucleated giant cells. Although the tumour is regarded as benign and has an indolent course, up to 50% of cases may recur locally. Typical giant cell tumours are radiologically easily distinguished from other bone tumours. Giant cell tumours are lytic, subarticular, eccentric, and often lack a sclerotic rim.

Q2: What other relevant blood investigations should be ordered in such patients (calcium, parathyroid hormone, alkaline phosphatase, acid phosphatase)?

Other relevant blood investigations are calcium and parathyroid hormone. The final histopathology report raised the suspicion of hyperparathyroidism. On testing the patient’s blood, the corrected calcium concentration was 3.2 mmol/L, with an increased concentration of parathyroid hormone of 314 ng/mL. Ultrasoundography of the neck revealed a parathyroid adenoma in the vicinity of the inferior pole of the right thyroid. The adenoma was successfully excised. In any such lytic lesion of the bone, the possibility of brown tumour should always be kept and blood calcium/parathyroid hormone assay should be mandatory to prevent surgical misadventure.

Discussion

In women of childbearing age the estimated incidence of PHP is eight per 100 000 population per year. Usually, pregnant women with PHP are asymptomatic or have minor complaints such as early fatigueability, constipation, thirst, or depression. These are common complaints that are usually attributed to pregnancy by patients. It is mandatory to correct PHP before childbirth to prevent postpartum hypercalcaemic crisis in the mother and hypocalcaemic crisis in the fetus. The hypercalcaemia can manifest itself in symptoms such as hyperemesis, pathological fractures, renal stones, pancreatitis, abortion, or fetal death. A hypercalcaemic crisis in the immediate postpartum period may be dangerous as the maternal efflux of calcium to the fetus is suddenly stopped. A neonate born to such a mother is at risk of tetany and convulsions within 3–14 days of the birth because of transient hypocalcaemia. Though PTH and calcitonin do not cross the placental barrier, calcium is actively transported across the placenta with the help of fett 1,25-dihydroxycholecalciferol. Maternal PHP results in high concentrations of serum calcium that acts to suppress the fetus’s PTH concentration. If this is not corrected beforehand, at birth the neonate is suddenly deprived of calcium and this is compounded by an inability to mobilise calcium from bone because of the high concentrations of calcitonin. This will result in acute neonatal hypocalcaemia causing tetany and convulsions by 2 weeks of age but can be delayed if the infant is breast fed. All neonates with tetany or seizures in first few weeks of life should have their mother's serum calcium concentrations checked to exclude PHP. Oral or parenteral calcium and magnesium are usually required for a short period only and it resolves within three to five months.

Final diagnosis

Hyperparathyroidism.

References


A man with abdominal pain

Q1: What does the chest radiograph show (fig 2 in questions, p 741)?

The chest radiograph shows a homogenous round opacity in the left upper zone with erosions of the second, third, and fourth ribs.

Q2: What are the findings on computed tomography of the chest (fig 2 in questions, p 741)?

Chest computed tomography reveals erosion of the second, third, and fourth ribs with soft tissue mass in the extrapleural space. In addition there is erosion of thoracic vertebrae. Differential diagnosis includes secondaries in the rib and tuberculosis of the rib with an abscess in the extrapleural space.

Q3: What are the findings on computed tomography of the abdomen (fig 3 in questions, p 741)?

Abdominal computed tomography shows erosion of the lumbar vertebrae, with bilateral thick walled cysts suggesting a bilateral posas abscesses. Aspiration of the abdominal cyst revealed turbid straw coloured fluid with a protein content of 76 g/L. Staining for acid fast bacilli was negative and cytology showed few lymphocytes in an eosinophilic background. At thoracotomy, a tumorous mass (fig 1 below) measuring 10 × 10 cm was seen adherent to the second, third, and fourth ribs on the left side with mass effect on the upper lobe of the lung. Cut section was fleshy. Histology confirmed a tuberculous granulomatous lesion; acid fast bacilli were identified.

The patient was started on isoniazid, rifampicin, ethambutol, and pyrazinamide. There was significant improvement in the general condition within one month of initiation of treatment, with spontaneous regression of the cystic swelling of the abdomen.

Discussion

Bone and joint tuberculosis is a common form of extrapulmonary tuberculosis and takes fourth place among all sites. In spinal tuberculosis, thoracic and lumbar spine are the most frequent locations. Rib tuberculosis is an uncommon form of osteoarticular tuberculosis and constitutes 5% of all cases of bone and joint tuberculosis. The case reported has tuberculosis involving the rib and lumbar vertebrae with bilateral posas abscesses. Skeletal tuberculosis may occur as a progressive primary infection particularly in children or as reactivation of a quiescent primary focus after immunosuppression. It is the foremost inflammatory process affecting the ribs. In the thoracic region, the lung may be invaded through adhesions of pleura. In the lumbar region, cold abscess can collect beneath the posas fascia, iliac muscle and this can extend to inguinal region beyond the inguinal ligament. The onset of musculoskeletal tuberculosis is usually insidious and local pain is the most common and earliest symptom followed by impairment of function and swelling. A
painless cold abscess may be the only presentation, as was seen in the present case. A single site of tuberculous involvement is the rule; multiple locations are rare and it is common in the immunocompromised state. The combination of rib destruction and an extrapleural rib soft tissue opacity makes tuberculosis a highly likely diagnosis. The rib erosion and the soft tissue mass closely simulates secondaries of the rib. In a report by Adil et al, two of their four patients had a pseudotumorous lesion.

Computed tomography of the chest is useful in diagnosis of osseous tuberculosis. Bone sclerosis, associated soft tissue abscess, osteolytic lesion, and a sequestrum suggests chest wall tuberculosis. In summary, while evaluating a patient with a destructive spinal lesion, there should be a heightened index of suspicion for spinal tuberculosis. Rib tuberculosis can present as a pseudotumorous lesion.

Final diagnosis
Multiple osseous tuberculosis.

Reference

Warwick University Short Course
16–17 March 2005: An Introduction to Immunology. For further information contact: Dr Steve Hicks, Department of Biological Sciences, University of Warwick, Coventry CV4 7AL, UK. Tel: +44 (0)24 76 523540; fax: +44 (0)24 76 523701; email: s.j.hicks@warwick.ac.uk (web: http://template.bio.warwick.ac.uk/shortcourses/05immleaf.pdf).
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