Multiple bony swellings and joint stiffness

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An 18-year-old man walked into the out-patient department with complaints of spontaneous onset of pain and stiffness of neck and upper back for the last six years. On examination, multiple painless bony swellings were found over the nape of neck and dorsolumbar region. Similar bony swellings were also present over the left arm, forearm and both legs. Radiographic examination was done. X-rays of the neck and elbow are shown here.

Figure 1

Figure 2

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Questions

- 1 What are the findings on the X-rays?
- 2 What is the most probable diagnosis?
- 3 What abnormality may be present in the blood?

Answers

QUESTION 1

Ectopic bone formation in the soft tissue planes around cervical spine and elbow.

QUESTION 2

Myositis ossificans progressiva (fibrodysplasia ossificans progressiva).

QUESTION 3

Haematological parameters are normal. Eosinophilia may be present.^{1,2}

Discussion

Myositis ossificans progressiva (MOP) is a rare disorder characterised by progressive ectopic bone formation and skeletal malformation. It is inherited as an autosomal dominant trait and is four times more common in boys. Skeletal muscles, tendons, ligaments, fasciae and joint capsules are involved in the disease process. The pathological features are categorised into three stages: firstly oedema and round cell infiltration, secondly, degeneration of muscle fibres, formation of granulation tissue and osteoid tissue trabeculations, and thirdly, true ossification. The bone thus formed is not distinguishable clinically or histologically from true bone.³

The ectopic ossification starts in early childhood usually first affecting the neck or dorsal spine.⁴ A painful lump is first noticed with associated stiffness of the joint. Lumps gradually subside over the next few weeks and ectopic bone forms, resulting in irreversible limitation of movement. Sternocleidomastoid muscle is affected first and torticollis appears. Subsequently, the connective tissue of the paraspinal muscles, muscles of the limb girdles and mastication are involved. After the shoulder and spine, the jaw is the commonest site of involvement. Connective tissues of facial muscles, extra-ocular muscles, tongue, pharynx, oesophagus, sphincters, intestine, skin and abdomen (even after abdominal surgery)

are not involved. Ectopic ossification can be precipitated by trauma to muscles, biopsy of the lumps, intramuscular injections, careless venepuncture, and dental therapy. Excision of ectopic bone is followed by recurrence.⁵

Multiple skeletal abnormalities are commonly associated with MOP (box 1). Of these the abnormalities of the great toe and thumb are the most common. Extraskeletal manifestations include deafness and baldness.

The condition must be differentiated from torticollis, dermatomyositis, polymyositis haemorrhagica, calcinosis interstitialis ossificans, sarcoma, Klippel-Feil syndrome and diaphyseal aclasia.^{3,6} Diagnosis is based on clinical and radiological findings. Laboratory tests are normal⁷ and biopsy is contraindicated.

Management is difficult as various therapeutic regimes tested have caused no significant improvement. Surgical removal is not feasible because of recurrence of ectopic bone at the operative site.⁸ The modalities that have been tried are diathermy, repeated X-ray radiation, fibrinolysin, potassium iodide, vitamin E, parathyroidectomy and low calcium diet. Cortisone and adrenocorticotropin are effective only in the phase of active exacerbation of the disease. The most effective treatment has been intensive physiotherapy to increase the mobility of the unaffected muscles and promote a greater range of activity in the involved muscles.³

Ectopic (heterotopic) ossification (eg MOP, traumatic myositis ossificans) must be distinguished from heterotopic calcification in which calcium salts are deposited in tissues other than osteoid or enamel.

MOP: skeletal manifestations

Foot

- microdactyly or adactyly of great toe
- hallux valgus
- hallux rigidus
- variable reduction defects of all toes

Hand

- short first metacarpal
- short fifth finger
- fifth finger clinodactyly
- short broad metacarpals

Others

- abnormal cervical vertebra
- short broad femoral neck
- exostosis, especially of proximal tibia
- kyphosis
- scoliosis
- ectopic ossification

Causes of dystrophic calcification

In dead tissues

- old healed lesions of tuberculosis, histoplasmosis, coccidioidomycosis
- dead parasites: *Trichinella spiralis*, hydatid cyst, schistosoma ova, cysticercosis, dead foetus (Lithopaendion)
- fat necrosis: acute pancreatitis, traumatic lesion of breast
- thrombi: phlebotitis
- haematoma: traumatic subdural haematoma or myositis ossificans

In degenerate tissues

- scars
- chronic inflammatory granulation tissue: rheumatic heart disease, infective carditis, constrictive pericarditis, ankylosing spondylitis
- atheroma in aorta and coronary vessels
- Monckeberg's sclerosis
- senile tissue: costal cartilages, pineal gland dura mater, supraspinatus tendon
- degenerate tumours: large uterine fibroids, psammoma bodies of meningiomas, cystadenoma, cystadenocarcinoma, carcinoma of ovary, breast cancer
- sundry lesions: pulmonary alveolar microlithiasis, corpora amylacea in prostate, calcinosis universalis in systemic sclerosis of dermatomyositis, CREST syndrome, scleroderma, tumoural calcinosis, idiopathic calcinosis of scrotum, gout and pseudogout, fluorosis

Box 1

Box 2

Causes of metastatic calcification

- hyperparathyroidism*: hyperplasia, neoplasia
- increased calcium absorption from bowel: hypervitaminosis D, compulsive milk intake, sarcoidosis, idiopathic hypercalcaemia of infants
- hypophosphatasia
- destructive bone lesion*: cancer metastasis, lymphoma, multiple myeloma, leukaemia
- solid tumours without bone metastasis (paraneoplastic syndrome): squamous cell carcinoma of lung, head and neck
- hypoparathyroidism: basal ganglia calcified
- renal tubular acidosis: only nephrocalcinosis
- lithium, thiazide, spironolactone
- prolonged immobilisation, Paget's disease

*most common causes

Box 3

Two varieties of heterotopic calcification have been described.⁹

- dystrophic: calcium salts are deposited in dead or degenerate tissues with normal calcium and phosphorus levels. The causes are described in box 2.
- metastatic: calcium salts are precipitated in normal tissues due to disturbance in calcium and phosphorus metabolism, usually hypercalcaemia. The causes are described in box 3.

In dystrophic calcification, investigations are normal and treatment is symptomatic. In metastatic calcification, a series of investigations can help in diagnosing the aetiology

including serum calcium, phosphorus and alkaline phosphatase, complete blood counts with erythrocyte sedimentation rate, serum parathyroid hormone, urine calcium and hydroxyproline, plasma 25 (OH) vitamin D and 1,25 (OH)₂ vitamin D, serum electrophoresis, neck ultrasonography, skeletal survey, computed tomography scan, bone scan and bone biopsy.¹⁰ Treatment of the underlying aetiology can bring the calcium levels back to normal. The various drugs found to be useful are mithramycin, glucocorticoids, calcitonin, bisphosphonates, phosphate, gallium nitrate and WR2721.^{11,12} If the hypercalcaemia in sarcoidosis fails to respond or side-effects develop then chloroquine, hydroxychloroquine and ketocanazole can be used.¹³ Paclitaxel, a novel anticancer drug, has been shown to cause prompt resolution of hypercalcaemia mediated by parathyroid hormone-related protein which had previously proven to be refractory to both multiple conventional antihypercalcaemic agents and anthracycline-containing chemotherapy combinations. However, definite guidelines are still required for its use as an antihypercalcaemic agent.¹⁴ Various nonspecific measures like rehydration, furosemide, dialysis and mobilisation of the patient also help.¹¹

Final diagnosis

Myositis ossificans progressiva

Keywords: ossification, calcification, myositis ossificans progressiva, hypercalcaemia

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