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Congenital Infantile Myofibromatosis: A Case Report and Review of Literature

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Abstract Congenital infantile myofibromatosis is a rare disorder with multiple fibromatous tumours in skin, bone, muscle, viscera and subcutaneous tissue presenting in early infancy. Multiple lytic bone lesions and vertebra involvement are also common, mimicking the clinical picture of metastatic tumours. However, it is a disease with variable prognosis depending on the type and extent of involvement. Spontaneous resolution occurs in most of the cases without visceral involvement. We report good outcome in a case of multicentric type of infantile myofibromatosis with no visceral involvement. Invasive investigations and aggressive intervention should be avoided in these cases.

Key words Clinical presentation; Congenital infantile myofibromatosis; Histology; Management; Radiological finding

Introduction

Congenital infantile myofibromatosis (IM) is a rare disorder with multiple fibromatous tumours in skin, bone, muscle, viscera and subcutaneous tissue. It usually presents in early childhood. Even though it is the commonest cause of fibrous tumour of infancy, only around 230 cases have been reported in the English literature by 1997.[1] Since the condition is not commonly known and its presentation may mimic malignant tumours, we present the clinical, histologic and radiographic findings of a baby girl presenting with multicentric type of IM with good outcome.

Case Report

A 10 weeks old girl presented with paucity of right lower limb movement for 2 days. There was no history of trauma or injury. The baby was born at full term with uneventful antenatal and postnatal courses. She was well all along. There was no parental consanguinity and the family history was unremarkable.

Physical examination showed a healthy baby with 2 bony nodules measuring 0.5 cm along the lambdoid sutures and a subcutaneous skin nodule measuring 0.3 cm by 0.3 cm over the right upper chest wall. There was paucity of movement and diminished deep tendon reflexes of the right lower limb. Her spine was normal with no gross spinal defect or scoliosis. She had normal anal tone and anal reflex. No bladder was palpable. There was hepatomegaly of 2 to 3 cm.

The liver parenchymal enzymes (alanine aminotransferase 51 U/L; aspartate aminotransferase 65 U/L), albumin adjusted calcium (2.72 mmol/L), phosphate (2.11 mmol/L) and lactate dehydrogenase (1059 U/L) were mildly raised. Erythrocyte sedimentation rate was slightly increased to 42 mm/hr. Complete blood picture, C-reactive protein and chest X-ray (CXR) were normal. Skeletal survey showed multiple lytic lesions in metaphyses of the humeri, radii, ulna, distal femora, tibia, fibula as well as bilateral talus and calcanei. Pathological fractures were noted over the distal tibia and fibula of the right lower limb (Figure 1). Skull X-ray showed multiple well-circumscribed punch out lesions and X-ray spine showed evidence of vertebral collapse. Urgent magnetic resonance imaging (MRI) of spine confirmed multiple vertebral collapse

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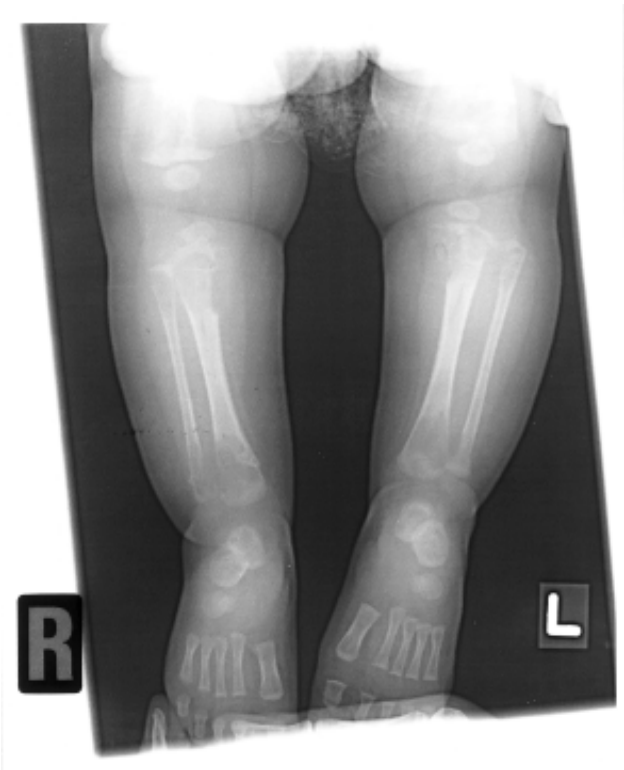

Figure 1 X-ray lower limbs showing multiple lytic lesions.

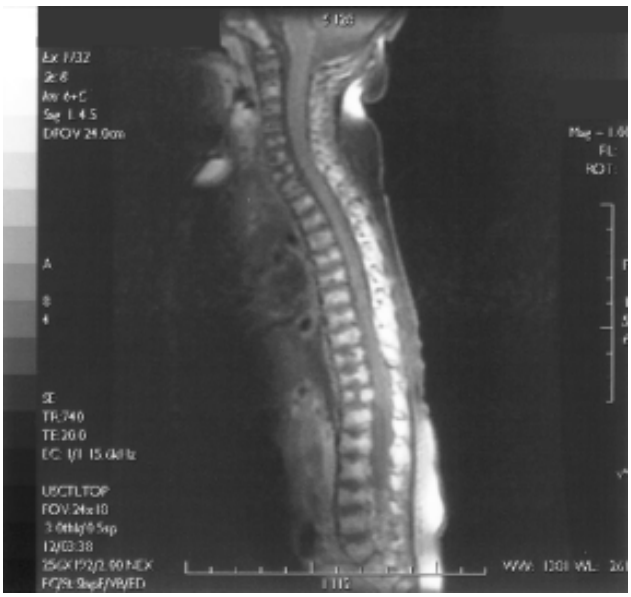

Figure 2 MRI spine showing multiple vertebral collapse.

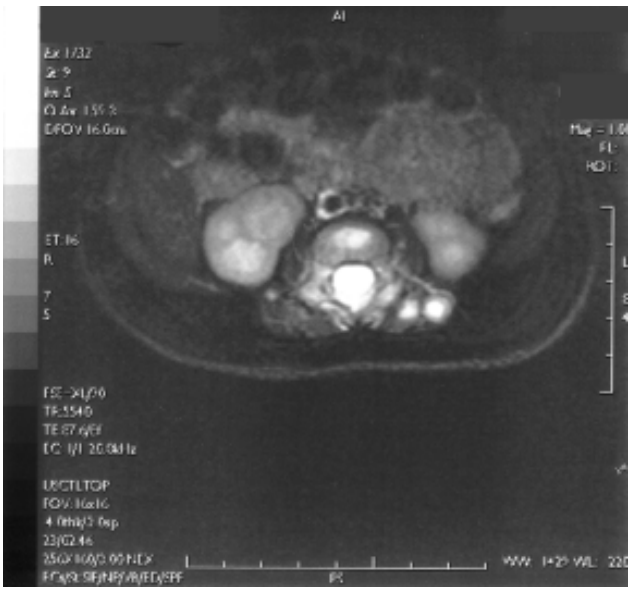

Figure 3 MRI spine showing ring enhancing lesions in the left erector spinae muscle.

involving C5, C7 and T8, T10-12 with no spinal cord or nerve root compression (Figure 2). Post-contrast images showed ring enhancing lesions in the left erector spinae muscle but no bony erosion in the adjacent vertebrae (Figure 3). The working diagnosis at that time included disseminated tuberculosis, leukaemia, Langerhan cell histiocytosis, soft tissue sarcoma with metastasis, neuroblastoma with metastasis and myofibromatosis. Bone marrow aspirate and trephine biopsy were normal, excluding histiocytosis and leukaemia. Urine for VMA and HVA was within normal range excluding neuroblastoma. Ultrasound guided (USG) biopsy of the left erector spinae muscle was performed and the smear and culture for AFB were negative. Histopathology report revealed plump spindle cells arranged in interlacing bundles, whorls and stellate arrangement. Some of the cells have eosinophilic cytoplasm. Most of the cells are strongly positive for actin and vimentin and negative for desmin. These features were compatible with myofibromatosis. Skin biopsy of the chest-wall nodule revealed features of myofibroma. Bone biopsy of the left tibial bone was also suggestive of myofibromatosis. USG brain and abdomen and echocardiogram were performed to look for visceral involvement. They were all normal.

In view of the absence of visceral involvement, the patient was treated conservatively and was regularly followed up in paediatrics and orthopaedics clinics. The bony nodules over the skull increased in size in the first half-year while new subcutaneous and bony nodules

developed during the first year of life. There was gradual regression in the second year of life. Neurological examination of the lower limbs was completely normal at 6 months of age. She had gross motor delay at 5 months of age and regular physiotherapy training was commenced with gradual improvement. Formal developmental assessment at 18 months of age showed normal development. Skeletal survey at one year of age, serial USG brain and abdomen at 6 months and 18 months were all normal. She had normal growth parameters at 25 months of age with head circumference and body weight in the 50th percentile and body height in the 25th percentile. Latest review by orthopaedic surgeon at 27 months of age showed no lower limb mal-alignment. Full range of movement was demonstrated in all joints of upper and lower limbs. X-ray of bilateral upper and lower limbs showed almost complete regression of lesion (Figure 4).

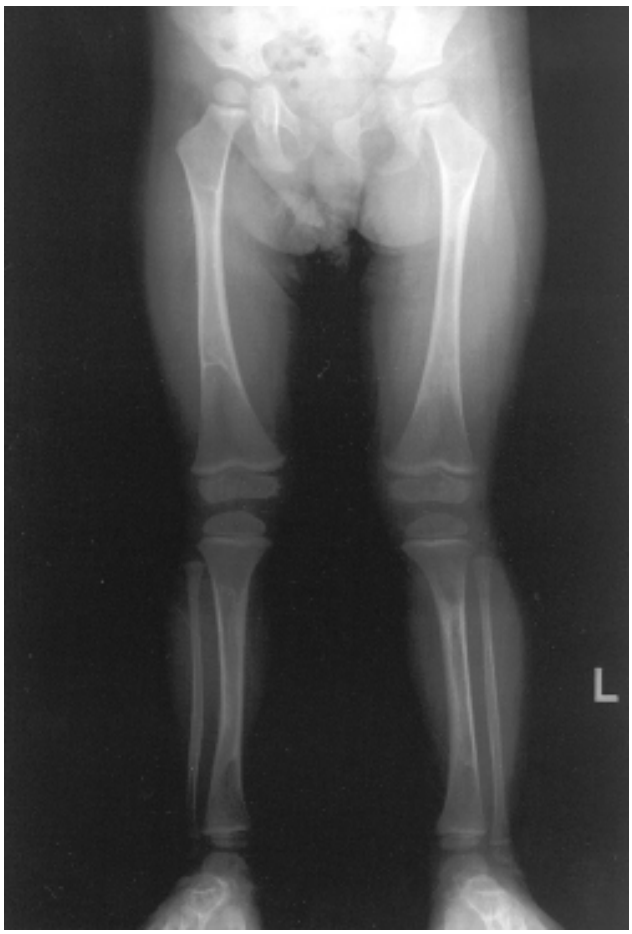

Figure 4 X-ray bilateral lower limbs showing almost regression of lesions.

Discussion

Classification

Infantile myofibromatosis was first described by Stout in 1954 as congenital generalised fibromatosis[2] and was renamed as infantile myofibromatosis by Chung and Enzinger in 1981[3] to emphasise the microscopic resemblance to smooth muscle tissue and frequent occurrence in both newborns and older infants. More than 230 cases had been reported by 1997.[1] Sixty percent of IM were noted at or shortly after birth and 88% occurred before 2 years of age.[3,4]

According to Wiswell, IM could be divided into 2 types – solitary and multicentric, with a further subdivision into the presence or absence of visceral involvement.[5] The solitary type that accounted for 50% of the cases, was defined by the presence of one nodule occurring most commonly in the skin, muscle, bone or subcutaneous tissue. There was a male preponderance of 1.7:1 in both types.[5] Our index case had multicentric type of IM without visceral involvement.

Clinical Presentations

The clinical manifestation depends upon the number and the location of the lesions. Any organ or tissue may be involved. The tumours can range in size from 0.5 to 7 cm and the lesions can vary in number from 1 to more than 100.[5] Around 20% of the solitary form appeared in older individuals.[3,5] According to Wiswell's review of 170 patients with IM, 53% of patients (90/170) presented with multiple lesions. Visceral involvement was more common in the multicentric type, occurring in 37% of those with multiple lesions.[5] A more recent review by Zeller et al of all reported cases up to 1997 showed a similar pattern.[1] The common sites of visceral involvement were the lung, heart, gastrointestinal tract, pancreas, and liver.[5] Lung involvement seemed to carry grave prognosis with mortality of 80%.[1,6] Bony lesions were quite commonly seen, occurring in 60% of the cases.[7] The common sites of bone involvement included the femur, tibia, rib, pelvis, spine (usually the vertebral body) and skull. Involvement of the central nervous system was extremely rare. However, there had been more recent reports on involvement of the spinal canal.[8,9] Our index patient had the typical clinical presentation of subcutaneous and bony nodules without visceral involvement. The paucity of movement of her right lower limb could be accounted for by the pathological fractures over the right distal tibia and fibular.

Etiology

The etiology of IM is so far unknown. Some authors proposed that it might be due to fetal stimulation by estrogenic hormone, due to proliferation of lesions similar to myofibromatosis in guinea pigs after administration of the hormone.[10] More recently, very high urinary basic fibroblast growth factor levels were observed in an infant with multicentric IM with visceral involvement, suggesting that abnormal angiogenic stimulation originating in the pericytes might result in myofibroblastic proliferation and myofibromatosis.[11] Although most cases seemed to be sporadic, several families with IM in more than 1 family member had been reported.[12-16] There were consanguinity in 3 families[13,14,16] favouring autosomal recessive mode of inheritance; while reports of IM in half-siblings and successive generations[12] supported an autosomal dominant inheritance. There was no genetic loci identified yet but one recent report revealed a pseudodiploid karyotype with an interstitial deletion of the long arm of chromosome 6, del(6)(q12q15) as the sole anomaly.[17]

Diagnosis

Radiological Investigations

Radiological investigations are not always helpful in confirming the diagnosis but are very important in assessing the extent of disease and in monitoring the clinical course. Common findings of bone lesions on plain X-ray include well-defined lytic lesions with or without sclerotic borders. The metaphysis is usually involved for lesions in tubular bones with pathological fracture as an associated finding.[7] The lesions have variable appearance on computed tomography (CT) or MRI scans. CT scans show a low density region on a precontrast scan, with homogeneous enhancement after iodine injection.[18] MRI features are nonspecific including low signal on T-1 weighted images[14,19] and high-density foci[19,20] on T-2 weighted images.

Our index patient had the characteristic X-ray findings of multiple lytic lesions in metaphysis of long bones and pathological fractures. The diminished deep tendon reflexes in the right lower limb at presentation could not be accounted for by the absence of spinal cord or nerve root compression in her MRI spine. However, the deep tendon reflexes of the right lower limb normalised on follow up.

Histology

Making the definitive diagnosis usually depends on histology from adequate tissue samplings. Macroscopically, the nodule is usually well encapsulated and circumscribed. Microscopically, each nodule has a central and peripheral zone. The peripheral area consists of spindle cells with eosinophilic cytoplasm and ovoid nuclei arranged in well-demarcated short bundles and fascicles resembling smooth muscle. The central portion consists of less differentiated rounder cells with pale cytoplasm and basophilic, small round nuclei, often arranges in a haemangiopericytoma-like pattern.[3,12] The intermediate cellular differentiation is indicated by its specific immunocytochemical staining. It usually stains positive for vimentin (indicating mesenchymatous differentiation and fibroblast nature) and actin, but negative for desmin (smooth muscle marker) and S-100 protein. Our index patient also had this typical histological finding and immunocytochemical staining.

Prognosis

The usual clinical course of the solitary form is initial rapid growth followed by spontaneous regression within the first 2 years. The recurrence rate of solitary lesion after excision was reported to be 7-10%.[3,5] In multicentric form without visceral involvement, the prognosis is also excellent with expected spontaneous regression of nodules in one to two years or not recurring after surgical excision.[3,5] Spontaneous regression was observed in around 30-60% of patients with multicentric disease, though initial increase in size and number might occur.[5] The mortality rate was zero in the solitary group and 1.3% in the multicentric group without visceral involvement.[1]

Visceral lesions are associated with significant morbidity and mortality, and deaths usually result from complications of the visceral involvement. The mortality rate in multicentric form with visceral involvement was as high as 76%.[1,5] Thirty-three percent of such infants died in the first four months of life from vital organ dysfunction, failure to thrive or infection. More recent studies showed that unfavorable prognosis was more related to the extent and location of visceral lesions, rather than to their presence alone.[21] Moore recently proposed that disease regression could be predicted by MRI findings of a collapsed rim of low intensity around a central focal area of very intense signal on T2-weighted images.[20]

Management

No established management protocol exists. Conservative management is usually adopted for those without visceral involvement and complications. Periodic clinical and radiological re-evaluation with chest X-ray, skeletal survey, ultrasonogram, CT scans, contrast study of the gastrointestinal tract and echocardiogram is warranted

until the condition is stable. This is the management strategy we had adopted for our patient. Surgical excision is reserved for lesions that adversely affect vital function. In aggressive cases, there was limited experience of success with radiation therapy, different combination of chemotherapy,[3,5,22,23] steroid injection[3,5,24] and alpha interferon.[25] Evaluation of the efficacy of these regimens is difficult owing to the small numbers involved and the tendency for spontaneous regression.

Conclusion

Though a rare disorder, IM must be considered when evaluating children who present with either multiple lytic bone lesion or solitary/multiple tumours in the soft tissues, particularly during the neonatal or infancy period. Spontaneous resolution occurs in most of the cases without visceral involvement. Invasive investigations like tissue biopsy and aggressive intervention should be avoided in these cases.

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