Case Report

Camurati-Engelmann Disease with Good Treatment Response to Losartan

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Abstract

Camurati–Engelmann disease (CED) or progressive diaphyseal dysplasia is a rare autosomal dominant inherited condition which belongs to the group of craniotubular hyperostosis. A 24-year-old man presented with insidious onset, progressive pain over both legs, and forearms for 3 years. He was born as the second child of a nonconsanguineous union by vaginal delivery at term without any complications. The clinical, radiological, and histopathological features were suggestive of CED. Transforming growth factor-β1 sequence analysis revealed a missense mutation (c.652C>T; p. Arg218Cys) confirming the diagnosis. He had a good response to treatment with Losartan. CED should be considered in the differential diagnosis of patients presenting with nonspecific limb pains and radiological features of skeletal dysplasia. Early recognition and diagnosis play a crucial role in management. This case discuss regarding the potential benefits of the drug losartan in the management of a rare bone disease for which the evidence from previous literature is scarce.

Keywords: *Camurati-Engelmann disease, losartan, steroids*

Introduction

Progressive bone pain in young adults can have various underlying causes, including osteomalacia, hyperparathyroidism, sclerosing bone disorders, primary bone tumors hematolymphatic malignancies, late-stage eosinophilic granuloma, and a variant of Langerhans cell histiocytosis. Camurati-Engelmann disease (CED) is a rare form of bone dysplasia characterized by hyperostosis and sclerosis of the diaphyses of the long bones and skull. In more than 90% of the patients, mutations in the transforming growth factor-beta-1 (TGF-β1) gene (19q13.1) are detected. Several medications, including corticosteroids, bisphosphonates, nonsteroidal anti-inflammatory drugs, and losartan have been used in the management of CED.

Case Report

A 24-year-old man presented with insidious onset, progressive pain over both legs, and forearms for 3 years. He was born as the second child of a nonconsanguineous union by vaginal delivery at term without any complications. There was no history of similar illness in the family. The developmental milestones were normal. On examination, vitals were stable, had marfanoid habitus, and rest of the systemic examination was unremarkable.

Hemoglobin was 14.8 g/dl, total leukocyte count 7100/ml, platelet count 2.5 lakhs/μL and erythrocyte sedimentation rate 17 mm in 1 h. Blood chemistries were normal. X-rays of the long bones and skull showed diffuse cortical thickening of diaphysis and epiphysis [Figure 1]. Computed tomography and magnetic resonance imaging of the right tibia showed diffuse cortical thickening and marrow edema [Figure 2]. A three-phase Tc^{99m}-methylene diphosphonate scan showed diffuse uptake throughout the skeleton [Figure 3]. Bone biopsy from tibia showed sclerotic bone with the markedly decreased trabecular volume of spongy bone, reduced marrow elements, and thin intertrabecular space [Figure 4]. With these clinical, radiological, and histopathological features the possibility of a sclerosing bone disorder, CED was considered. TGF-β1 sequence analysis revealed a missense mutation (c.652C>T; p. Arg218Cys) confirming the diagnosis. Genetic tests were not done for the other members of the family. He was started on oral methylprednisolone 16 mg daily which was tapered slowly and discontinued over a few months. He was initiated on losartan at a daily dose of 0.75 mg/kg

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which was continued. He had no side effects with losartan, including hypotension and electrolyte abnormalities. He reported a significant decrease in pain when followed up after 6 months. The family has been counseled that this is a genetic condition with autosomal dominant inheritance. Recurrence risk in future progeny of affected individuals is 50%. Additional family members can be tested for the mutation in a cost-effective way by targeted mutation analysis. Prenatal diagnosis was possible in at-risk pregnancies by fetal mutation analysis to enable informed reproductive decisions.

Discussion

CED or progressive diaphyseal dysplasia is a rare autosomal dominant inherited condition that causes characteristic anomalies in the skeleton. The average age of onset is about 13 years and almost always before 30 years.[1] The common clinical features include limb pain, dull bone pain, waddling gait, muscular weakness, and easy fatigability. Causes of bony leg pain in an adult include stress fractures, shin splints, osteomyelitis, fibrous dysplasia, osteoid osteoma, osteosarcoma, and other rarer causes such as adamantinoma, melorheostosis, hyperphosphatasia, histiocytosis, lymphoma, intramedullary sclerosis, endosteal hyperostosis, and sclerosteosis.[2]

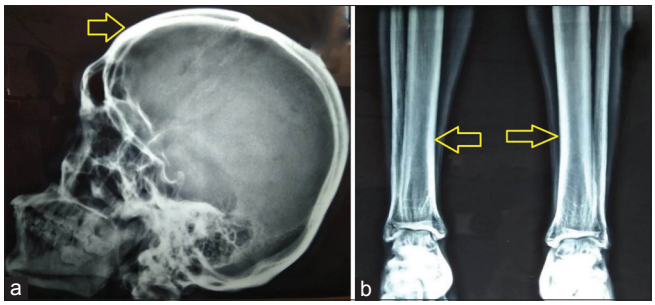

Figure 1: Radiograph of the skull (a) and both legs showing cortical thickening (b)

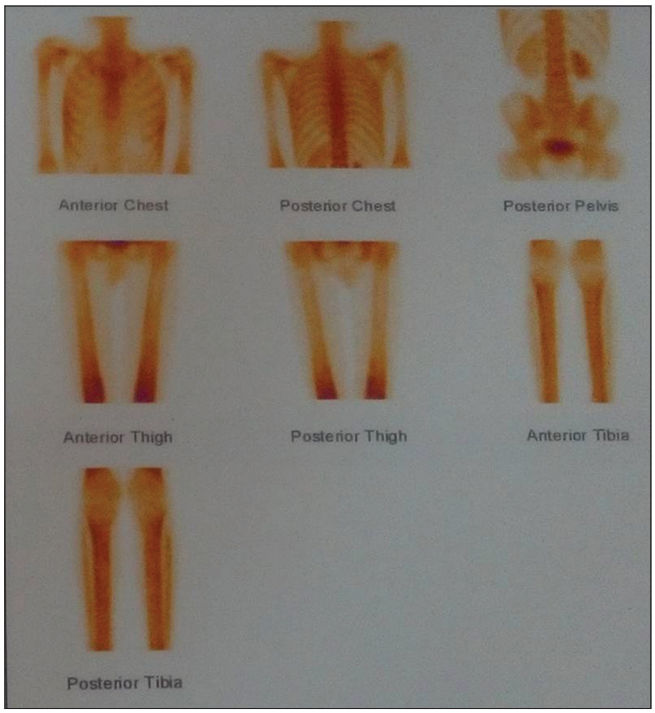

Figure 3: Tc^{99m}-methylene diphosphonate scan showing diffuse uptake throughout the skeleton

Bone dysplasia which can closely mimic CED is Ribbing disease. The distinction between Ribbing disease and CED is difficult even though several differences are pointed out in the literature. CED presents during childhood, whereas Ribbing disease is usually seen after puberty. The pattern of involvement of bones in CED is bilaterally symmetrical, whereas Ribbing disease is either unilateral or asymmetrically bilateral. CED affects the diaphysis of long bones and bones formed by intramembranous ossifications; hence, the skull is involved almost as frequently as the long bones.[3] Ribbing disease has been reported only in the long bones. Several authors have thus concluded that CED and Ribbing disease may represent phenotypic variations of the same disorder.[4]

The evidence regarding the effectiveness of various drugs used for managing CED is based on a number of case reports. Several medications, including corticosteroids, biphosphonates, nonsteroidal anti-inflammatory drugs, and losartan, were tried in patients with variable results. Improvement in symptoms significantly among

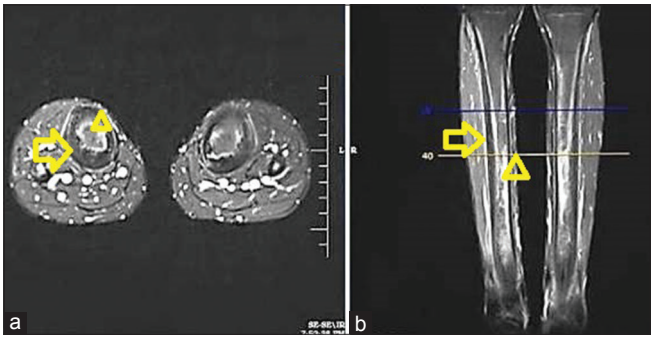

Figure 2: Short tau inversion recovery axial (a) and coronal (b) images showing cortical thickening (arrows) with bone marrow edema in the diaphysis of both tibias (arrow heads)

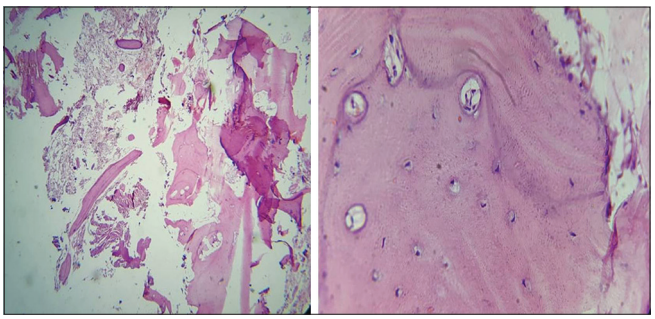

Figure 4: Bone biopsy from tibia showing sclerotic bone with markedly decreased trabecular volume of spongy bone, reduced marrow elements and thin inter trabecular space

a prepubertal girl aged 9 years and a boy aged 13 years with losartan was previously reported.[5,6] Losartan, an angiotensin II Type 1 receptor antagonist, has been found to down regulate the expression of TGF-β Type 1 and 2 receptors. Clinical trials with losartan have shown a benefit in Marfan syndrome, while trials are underway for Duchenne muscular dystrophy and other myopathies associated with TGF-β1 signaling.

CED should be considered in the differential diagnosis of patients presenting with nonspecific limb pains and radiological features of skeletal dysplasia. Early recognition and diagnosis play a crucial role in management. This case discusses regarding the potential benefits of the drug losartan in the management of a rare bone disease for which the evidence from previous literature is scarce.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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