Clinical Case Report

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Camurati–Engelmann disease-a rare cause of tetany identified on bone scintigraphy

A case report

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Abstract

Rationale: Camurati–Engelmann disease (i.e., progressive diaphyseal dysplasia) is an extremely rare autosomal dominant bone disorder. The most common clinical manifestations were chronic skeletal pain, waddling gait, muscular weakness.

Patient Concerns: We described that a 27-year-old male with a 1-year history of intermittent tetany was referred for bone scintigraphy. The whole body bone scan images showed abnormal increased uptake of the tracer in the long bones of the upper and lower extremities as well as in the skull.

Diagnoses: Combined the family history, the findings of the images and the genetic study, the diagnosis of Camurati–Engelmann disease was confirmed.

Interventions and outcomes: The patient responded well to the treatment of calcium gluconate.

Lessons: Bone scintigraphy would be helpful in the diagnosis and assessing the severity of Camurati–Engelmann disease.

Abbreviations: CED = Camurati–Engelmann disease, TGF-β1 = transforming growth factor-β1, MDP = technetium-99m-methylene diphosphonate.

Keywords: bone scintigraphy, Camurati–Engelmann disease, case report, technetium-99m-methylene diphosphonate, tetany

1. Introduction

Tetany occurs when the concentration of calcium ions in extracellular fluids such as plasma falls below normal. Abnormally low extracellular calcium ion concentration can result from various etiologies, including hypoparathyroidism, vitamin D deficiency, alkalosis, acute pancreatitis, and the operation of thyroid.[1,2] Most of the tetany can be treated with calcium, vitamin D, and a controlled diet. We reported a case of 27-year-old Chinese man presented intermittent tetany; however, the clinical and biochemical manifestation could not identify the common cause of hypocalcaemic tetany. After the bone scintigraphy, the image revealed the possibility of Camurati–Engelmann disease, and the generic study confirmed this diagnosis. Previously, there was no report of Camurati–Engelmann disease (CED), as the cause of tetany.

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2. Case presentation

A 27-year-old male was hospitalized because of intermittent tetany. Past history taking did not reveal pre-existing disease. Physical examination disclosed the thickened upper and lower extremities. Laboratory tests revealed hypocalcemia (1.85 mmol/L, normal range: 2.1–2.62 mmol/L) and elevated levels of serum alkaline phosphatase (273 U/L, normal range: 15–130 U/L) in addition to normal levels of serum phosphorus, parathyroid hormone, rheumatoid factor, thyroid-stimulating hormone, and renal function. A detailed history taking revealed that the presence of thickened upper and lower extremities persisted since he was a child and several members of his family including his father and sister also suffered from the same symptoms. Bone scintigraphy was performed to evaluate the involved bones and provide effective signs for the diagnosis. The images were obtained using a 2-head gamma camera (INFINIA, GE, USA) with high resolution and low energy collimator, 256×256 matrix and 15 cm/min speed. After 2 hours of the intravenous administration of ^{99m}Tc-technetium-99m-methylene diphosphonate (MDP) with a dose of 740MBq, the planar whole body image was obtained (Fig. 1). The images revealed diffuse, symmetric intense uptake in the skull, and the long bones of upper and lower extremities. The tracer distribution in the other parts of the body was within normal limits. The x-ray of upper and lower extremities showed thickening diaphyseal cortical, sclerotic and narrowing medullary cavity, expanded diaphyseal segment in bilateral tibias, fibulas, ulnas, and radius (Fig. 2). These findings were consistent with the increased uptake observed on bone scintigraphy images. The genetic testing of the patient and his family members identically detected a mutation of heterozygous C-to-T transition at cDNA position +652, leading to an arginine to cysteine substitution at amino acid 218 (R218C) in exon 4 of the transforming growth factor-b1

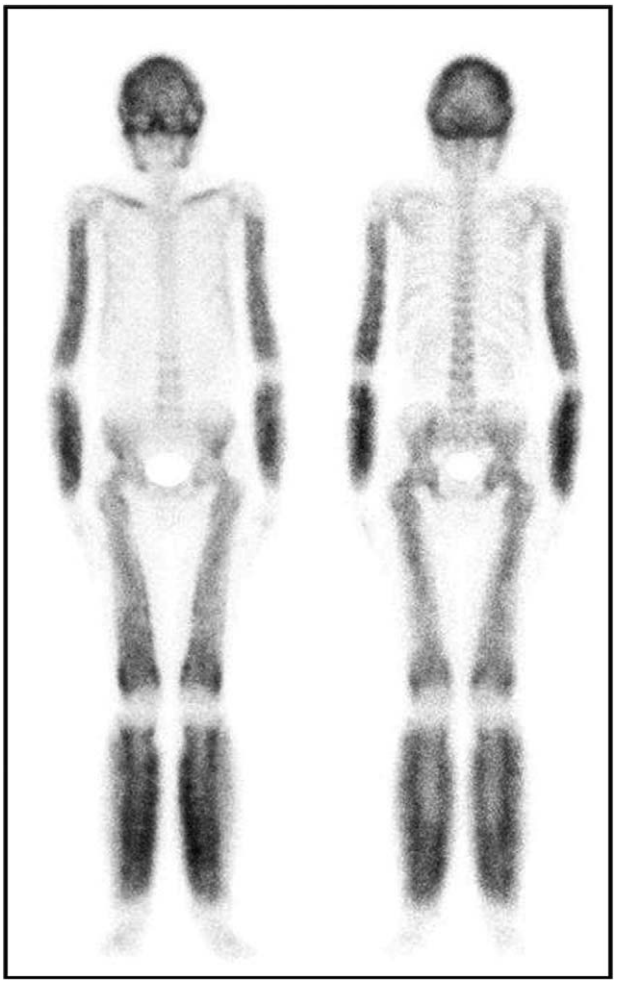

Figure 1. Whole body bone scan revealed diffuse, symmetric intense uptake in the skull, and the long bones of upper and lower extremities.

(TGF-β1) gene (Fig. 3). This mutation had been previously reported in CED patients. Combined the family history, the findings of the images and the genetic study, the diagnosis of Camurati–Engelmann disease was made. The patient responded well to the treatment of calcium gluconate.

The patient written informed consent was waived due to the retrospective nature of the presented case. Patient information was anonymized and deidentified.

3. Discussion

Camurati–Engelmann disease (Mendelian Inheritance in Man 131300), also known as progressive diaphyseal dysplasia, is a rare skeletal disease and characterized as sclerosing bone dysplasia inherited in an autosomal dominant manner. Only 45 families and approximately 170 cases have been described worldwide in the literature. The clinical spectrum of CED is variable, and the most common symptoms are pain, waddling gait, and muscular weakness.[3–6] The noncommon symptoms including reduced muscle mass, exophthalmus, facial paralysis, hearing difficulty, and loss of vision could also be observed accidently. However, the intermittent tetany, as the main symptom at the time of initial presentation, was extremely rare. It was reported that the mutations in the gene encoding for TGF-β1 were responsible for CED.[7–13] With the presence of mutation in the TGF-β1 gene, the effect of bone deposition by osteoblasts was inhibited and the effect of bone resorption by osteoclasts was enhanced. Therefore, the hypocalcemia could be associated with the abnormal bone metabolism, which might explain the intermittent tetany.

Before the widely application of genetic testing, the diagnosis of CED was mainly established by the combination of family history, clinical examination, and imaging findings. The genetic study established the close relation between the mutations in the gene encoding for TGF-β1 and CED, which helped the diagnosis of CED more accurately and easily. However, the imaging findings are also essential for providing diagnostic evidences. Because of the advantage of evaluating the involvement of the

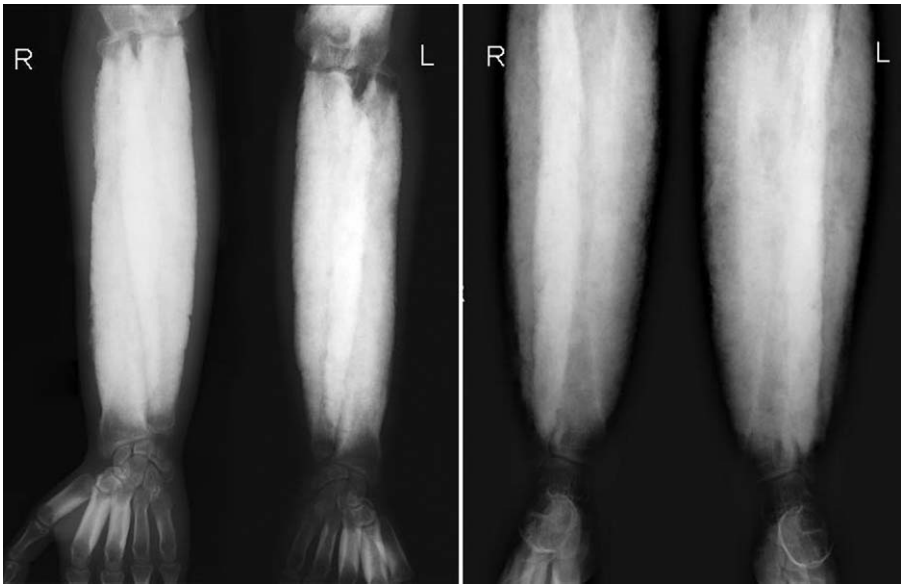

Figure 2. The x-ray of upper and lower extremities showed thickening diaphyseal cortical, sclerotic and narrowing medullary cavity, expanded diaphyseal segment in bilateral tibias, fibulas, ulnas, and radius.

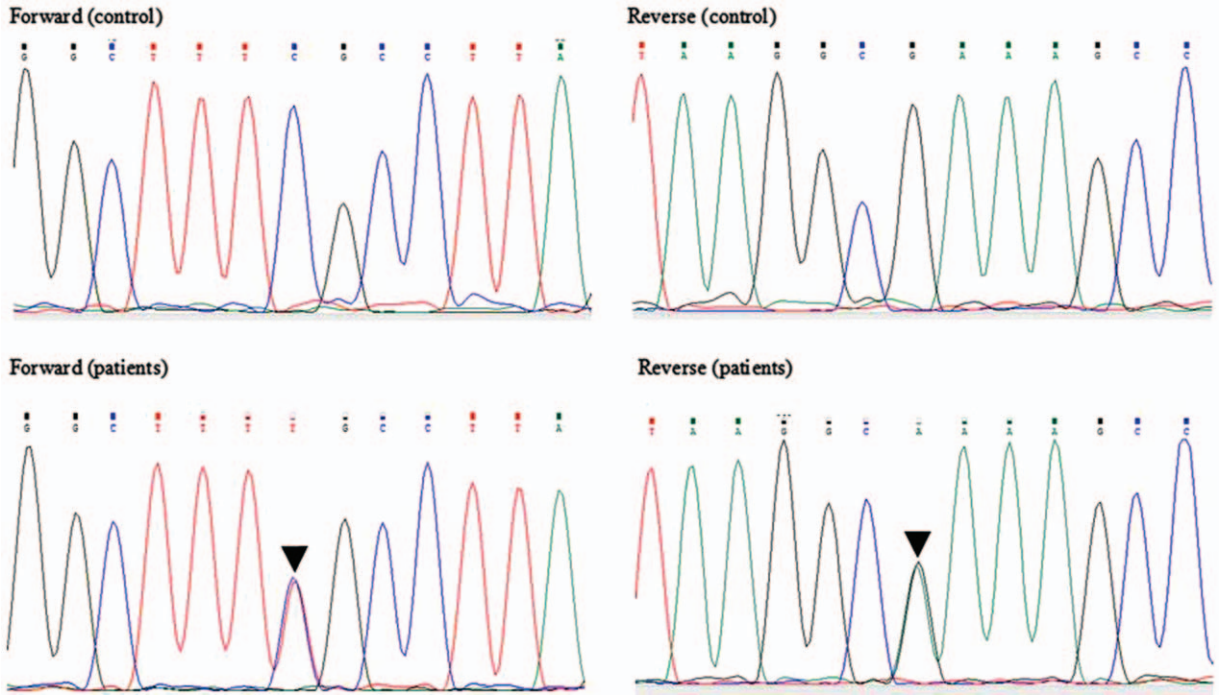

Figure 3. The genetic study detected a mutation of heterozygous C-to-T transition at cDNA position +652 (arrows) in the patients and his family members. (The control means the gene of healthy person.).

whole skeleton, the bone scintigraphy was widely used to help evaluate the severity of CED. Furthermore, the bone scintigraphy could also be used to help assess treatment effects and early diagnosis with the advantage of more sensitivity than x-ray.[14–16]

The low incidence of CED, absence of characteristic clinical symptom, and yet poor recognition may contribute to lack of suspicion among clinicians. Fortunately, in the current case, the bone scintigraphy identified the abnormalities and provided some important evidence for the diagnosis of CED. The present study highlighted the clinical significance of bone scintigraphy in the diagnosis of this rare and poorly recognized genetic bone disorder, a rare cause of tetany.

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