CASE STUDY JPAR 2022

Journal of Pharmaceutical Advanced Research

(An International Multidisciplinary Peer Review Open Access monthly Journal)

Available online at: www.jparonline.com

A Case Report on Camurati Engelmann Disease with Skeletal Dysplasia

Ponraj N*, Preethi R, Priya R, Renita Cresenciya J, Sajitha P, Sakthi Suvetha RV

Arulmigu Kalasalingam College of Pharmacy, Anand Nagar, KrishnanKovil, Virudhunagar District, Tamil Nadu, India.

Received: 02.08.2022 Revised: 12.08.2022 Accepted: 18.08.2022 Published: 31.08.2022

ABSTRACT:

A Camurati-Engelmann disease (CED) or progressive diaphyseal dysplasia is a rare autosomal dominant inherited condition worldwide. It belongs to the group of craniotubular hyperostosis. A 7-year-old male child presented with a complaint of Tiredness, and Fatigability for 1 Month and was diagnosed with severe anemia and admitted for blood transfusion. He was born as the third child of a nonconsanguineous union by vaginal delivery at term without any complications. The Child was admitted with the known Case of CED with Skeletal Dysplasia then the X-rays revealed the characteristic symmetrical thickening and sclerosis of the diaphyses of the appendicular skeleton and skull base, which is pathognomonic of Camurati- Engelmann's disease. This Case discusses regarding the management of the rare bone disease for which the evidence from previous literature is scarce.

Corresponding author

Mr. Ponraj N

Arulmigu Kalasalingam College of Pharmacy, Anand Nagar, KrishnanKovil,

Virudhunagar District, Tamil Nadu, India.

Tel: +91-8056710936

E. Mail ID: ponrajpvp812@gmail.com

Keywords: Camuratti engelmann disease, Diaphyseal dysplasia, Craniotubular hyeperostosis, Skeletal dysplasia.

INTRODUCTION:

CED is also regarded as generalized hyperostosis and endostosis, congenital more than one hyperostotic disease, sclerosing dysplasia, progressive diaphyseal dysplasia, and symmetric osteosclerosis, which is an uncommon genetic disorder. The gene-gene mutated in sufferers with CED encodes remodeling boom factor beta b1(TGF-b 1) (TGFB1; OMIM 190180) [1-3]. Mutations of this gene end result in expanded reworking and increased component activity, which performs an essential function in the bone redesigning process. The TGFB1 gene encodes a massive precursor polypeptide, which is post-translationally processed into an N-terminal peptide, recognized as "latency related peptide (LAP)," plus C-terminal matureTGF-b1. During

assembly, two TGF-b1 (Transforming growth factor beta b1) molecules accomplice with two LAPs (Latency associated peptides) to structure the "small latent complex" (SLC). During the secretory process, the SLC interacts covalently with the latent TGF-b1-binding proteins to shape the massive latent complicated (LLC-Large Latent Complex). Activators of TGF-b1 signalling act on LLCs to launch the mature increase element [4]. The eponym Camurati–Engelmann sickness is the most broadly widespread time period for this condition, even though lately the International Working Group on Constitutional Disease of Bone cautioned naming this circumstance diaphyseal dysplasia Camurati–Engelmann. It belongs to the team of intramembranous bone formation anomalies. CED is inherited as an autosomal dominant disorder and has variable penetrance. The gene accountable for CED has been recognized on chromosome 19q13 [5–7]. CED generally manifests in childhood, after tries at walking, though symptom onset has been described as early as three months and as late as the sixth decade [8]. Physical retardation is frequent and these adolescents usually begin taking walks at the age of three to four years, are pale, and are underweight. A usual weak point of skeletal muscle mass is frequently observed. Later in the route of the disease, their bodily circumstance normalizes, though they have a tendency to be taller than their peers. Symptoms typically begin with a stupid bone ache, which is intensified after bodily exercise. Severe ache is now not common. Anaemia, hepatosplenomegaly, and cranial nerve compression due to basilar cranium involvement are uncommon. Increased serum alkaline phosphatase tiers are common, and the erythrocyte sedimentation fee can be multiplied [9-11]. Primary imaging modalities consist of traditional radiography and, in some instances, CT, MRI, and bone scintigraphy. Classic radiological findings consist of each endosteal and subperiosteal cortical thickening affecting the diaphyses. These findings might also prolong the metaphyses however the epiphyses are typically spared. Typically, the lengthy bones, particularly femora and tibiae, are affected, however, skull, mandible, and vertebral involvement are additionally regularly found [12–16].

CASE REPORT:

A 7 years old Male child initially presented with a complaint of Tiredness and fatigability for 1 month and a known case of CED with Skeletal dysplasia was confirmed at Government Rajaji Hospital, Madurai and He had Severe anaemic signs were observed. He was born as the Third child of a non-consanguineous union by vaginal delivery at term without any complications. There was no history of similar illnesses in the family. The developmental milestones were normal. On examination, their Vitals are stable, the boy was thin. His long bones were irregular to palpation, and he experienced exquisite tenderness over his limbs. X-rays showed (Fig 1) cortical thickening of the diaphysis of long bones, with sclerosis of the base of the skull. All clinical features were consistent with a diagnosis of CED. Hemoglobin was 8.2 g/dL, total count 5900 cells, platelet count 60,000 µL, Differential count (Polymorphs count 33, lymphocyte count 62, and Monocyte count 5 %). X-rays of the long bones and skull showed diffuse cortical thickening of diaphysis and epiphysis. Genetic tests were not done for the other members of the family He was started on Tablet Calcium 200 mg, Tablet Ferrous Sulfate 10 mg and Tablet B. Complex 15 mg once daily and PRBC transfusion was done.

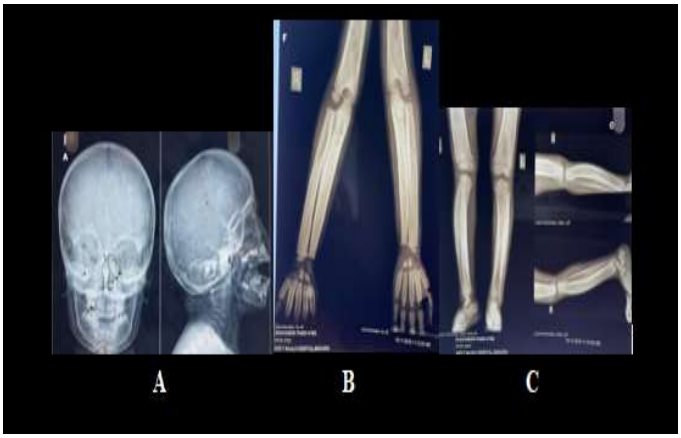

Fig 1. The radiographical report X-ray images showing features of Camurati-Engelmann disease in the patient at presentation (A) Frontal radiograph of the skull shows sclerosis and cortical calvaria and the Lateral radiograph of the skull shows sclerosis and thickening of the skull base and mandible, (B), the x-ray of the right-hand shows the sclerotic changes in the diaphyses, Similar changes were observed in the left hand, (C) Thickening and irregularity of endosteal and periosteal sides of diaphyses of all long bones of Tibia, fibula, and femur.

DISCUSSION:

A CED or modern diaphyseal dysplasia is an uncommon autosomal dominant inherited situation that motives attribute to anomalies in the skeleton. The common age of onset is about thirteen years and nearly continually earlier than 30 years [17]. The frequent scientific facets consist of limb pain, stupid bone pain, waddling gait,

muscular weakness, and effortless fatigability. Causes of bony leg ache in a person encompass stress fractures, shin splints, osteomyelitis, fibrous dysplasia, osteoid osteoma, osteosarcoma, and different rarer reasons such as adamantinoma, melorheostosis, hyperphosphatasia, histiocytosis, lymphoma, intramedullary sclerosis, endosteal hyperostosis, and sclerosteosis [18]. Bone dysplasia which can carefully mimic CED is a Ribbing disease.

The difference between Ribbing ailment and CED is challenging even though countless variations are pointed out in the literature. CED provides in the course of childhood, whereas Ribbing disorder is generally viewed after puberty. The sample of involvement of bones in CED is bilaterally symmetrical, whereas Ribbing ailment is both unilateral or asymmetrically bilateral. CED influences the diaphysis of lengthy bones and bones fashioned by means of intramembranous ossifications; hence, the cranium is concerned nearly as regularly as the lengthy bones [19]. Ribbing ailment has been said solely in the long bones. Several authors have as a consequence concluded that CED and Ribbing sickness may additionally symbolize phenotypic variants of the identical disorder [20]. The proof concerning the effectiveness of a number of pills used for managing CED is primarily based on a number of case reports. Several medications, together with corticosteroids, biphosphonates, nonsteroidal anti-inflammatory drugs, and losartan, have been tried in sufferers with variable results.

Improvement in signs and symptoms appreciably amongst a prepubertal woman aged 9 years and a boy aged thirteen years with losartan was once in the past reported [21]. Losartan, an angiotensin II Type 1 receptor antagonist, has been determined to down-adjust the expression of TGF-β Type 1 and two receptors. Clinical trials with losartan have proven a gain in Marfan syndrome, whilst trials are underway for Duchenne muscular dystrophy and different myopathies associated with TGF-β1 signalling.

CONCLUSION:

CED has to be regarded in the differential analysis of sufferers offering nonspecific limb pains and radiological points of skeletal dysplasia. Early focus and analysis play a quintessential position in management. This case discusses related to the possible advantages of the drug losartan in the administration of an uncommon bone disorder for which the proof from preceding literature is scarce.

ACKNOWLEDGEMENT:

The authors wish to thank the authority of Arulmigu Kalasalingam College of Pharmacy, Anand Nagar, to carry out this case study.

REFERENCES:

1. Dannenmaier B, Weber B. Observations on the Camurati–Engelmann syndrome. Rofo, 1989; 151(2): 175-178.
2. Greenfield GB. Radiology of bone diseases. 4th ed. Philadelphia: Lippincott; 1986.
3. Vanhoenacker FM, De Beuckeleer LH, Van Hul W, *et al*. Sclerosing bone dysplasias: genetic and radio clinical features. Eur Radiol, 2000; 10: 1423–1433.
4. Janssens K, Gershoni-Baruch R, Van Hul E, *et al*. Localisation of the gene causing diaphyseal dysplasia Camurati–Engelmann toc hromosome 19q13. J Med Genet, 2000; 37: 245-249.
5. Janssens K, Vanhoenacker F, Bonduelle M, *et al*. Camurati–Engelmann disease: review of the clinical, radiological, and molecular data of 24 families and implications for diagnosis and treatment. J Med Genet, 2006; 43: 1-11.
6. Ramanan AV, Hall MJ, Baildam EM, Mughal Z. Camurati–Engelmann disease- a case report and literature review. Rheumatol, 2005; 44: 1069-1072.
7. Simsek S, Janssens K, Kwee MI, Van Hul W, Veenstra J,Netelenbos JC. Camurati–Engelmann disease (progressive diaphysealdysplasia) in a Moroccan family. Osteoporos Int, 2005; 16: 1167-1170.
8. Hundley JD, Wilson FC. Progressive diaphyseal dysplasia: a review of the literature and report of seven cases in one family. J Bone Joint Surgery (Am), 1973; 55: 461-474.
9. Mastragelopulos N, Bahr R, Pfister U. Camurati–Engelmanndisease (progressive diaphyseal dysplasia). Differential diagnostic problems. Unfallchirurgie, 1989; 15(2): 104-107.
10. McCarthy EF, Sack GH. Hyperphosphatasia with massive osteoectasia: a 45-year follow-up. Skeletal Radiol, 2007; 36: S2-S6.
11. Nishimura G, Nidhimura H, Tanaka Y, *et al*. Camurati–Engelmanndisease type II: Progressive diaphyseal dysplasia with striations of the bones. Am J Med Genet, 2002; 107: 5-11.
12. Saraiva JM. Progressive diaphyseal dysplasia: a three-generation family with markedly variable expressivity. Am J Med Genet, 1997; 71(3): 348-352.
13. Kaftori JK, Kleinhaus U, Naveh Y. Progressive Diaphysealdysplasia (Camurati–Engelmann): radiographic follow-up and CT findings. Radiol, 1987; 164: 777–782.

14. Shier CK, Krasicky GA, Ellis BI, Kottamasu SR. Ribbing's disease: radiographic-scintigraphic correlation and comparative analysis with Engelmann's disease. J Nucl Med, 1987; 28: 244-248.
15. Clybouw C, Desmyttere S, Bonduelle M, Piepsz A. Camurati–Engelmann disease: contribution of bone scintigraphy to genetic counselling. Genet Couns, 1994; 5: 195-198.
16. Janssens K, Vanhoenacker F, Bonduelle M, Verbruggen L, Van Maldergem L, Ralston S, *et al*. Camurati-Engelmann disease: Review of the clinical, radiological, and molecular data of 24 families and implications for diagnosis and treatment. J Med Genet, 2006; 43: 1-11.
17. Mukkada PJ, Franklin T, Rajeswaran R, Joseph S. Ribbing disease. Indian J Radiol Imaging, 2010; 20: 47-49.
18. Byanyima RK, Nabawesi JB. Camurati-Engelmann's disease: A case report. Afr Health Sci, 2002; 2: 118-120.
19. Damle NA, Patnecha M, Kumar P, Gadodia A, Subbarao K, Bal C. Ribbing disease: uncommon cause of a common symptom. Indian J Nucl Med, 2011; 26: 36-39.
20. Simsek-Kiper PO, Dikoglu E, Campos-Xavier B, Utine GE, Bonafe L, Unger S, *et al*. Positive effects of an angiotensin II type 1 receptor antagonist in Camurati-Engelmann disease: A single case observation. Am J Med Genet A. 2014; 164A: 2667-26671.
21. Ayyavoo A, Derraik JG, Cutfield WS, Hofman PL. Elimination of pain and improvement of exercise capacity in Camurati-Engelmann disease with losartan. J Clin Endocrinol Metab, 2014; 99: 3978-3982.

Conflict of Interest: None
Source of Funding: Nil
Paper Citation: Ponraj N*, Preethi R, Priya R, Renita Cresenciya J, Sajitha P, Sakthi Suvetha RV. A Case Report on Camurati Engelmann Disease with Skeletal Dysplasia. J Pharm Adv Res, 2022; 5(8): 1607-1610.