A novel mutation in the RUNX2 Gene; a rare cause of enlarged fontanel

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INTRODUCTION

Cleidocranial dysplasia(CCD) is a rare dominantly inherited bone disease that is characterized by delayed closure of fontanelles, presence of open skull sutures, hypoplastic or aplastic clavicles, supernumerary teeth, delayed eruption of permanent dentition, wide pubic symphysis, short stature and a variety of other skeletal changes. However, signs and symptoms can vary widely in severity, even within the same family. Heterozygous mutations in the Runt-related transcription factor 2 (RUNX2) gene, which encodes a transcription factor required for osteoblast differentiation are responsible for CCD.

OBJECTIVES

We present a child with enlarged anterior fontanel admitted with febrile seizure and diagnosed as CCD.

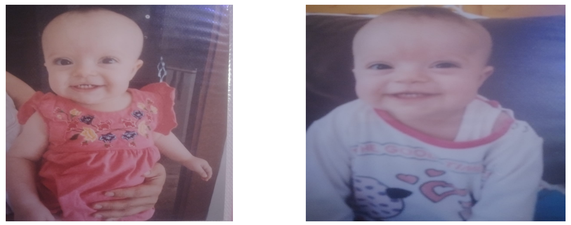

Figure 1. Frontal bossing and enlarged anteror fontanel

CASE

An 11-month-old female who is the second child of healthy parents was born after an uncomplicated pregnancy and an uneventful delivery and was admitted with a febrile seizure. Her parents are non-consanguineous, family history is unremarkable. Her motor skills and development were normal. Physical examination revealed a dome-shaped palate, frontal bossing and enlarged anterior fontanel (12x5cm) (figure 1). Initial laboratory evaluation including complete blood cell count, liver and renal function test, 25OH-vitamin D and thyroid function test were all normal. The electroencephalograph, brain magnetic resonance imaging, and Denver Development Screening Test also were normal. The whole body bone survey and three-dimensional computed tomography were normal except for widening of the sagittal suture and large anterior fontanel. Whole Exome Sequencing (WES) was performed to identify the etiopathogenesis in which a novel, in-silico pathogenic heterozygous c.471_472delGGinsAT (p.M157_A158delinsIS) mutation was detected in RUNX2 (NM_001024630.4) gene.

DISCUSSION

Cleidocranial dysplasia (CCD) which is a rare autosomal dominant disorder characterized by skeletal and dental abnormalities due to the disturbance in the ossification of the bones. Widening of cranial sutures, cranial ectasia, retention of deciduous teeth, delayed sprouting of permanent teeth, malformation of roots and tooth cysts with supernumerary teeth, clavicle hypoplasia or aplasia, and delayed closure of cranial sutures are the main features of the syndrome. The conical shape of a chest, small scapula, short stature, repeated respiratory tract and ear infection are the other symptoms of CCD. Cleidocranial dysplasia is caused by mutations in the RUNX2 gene which encodes the transcription factors required for differentiation and maturation of osteoblasts. The motor development of CCD patients may be slightly delayed but in most cases, mental development is normal. Although our patient did not have any dental or skeletal abnormalities, or recurrent respiratory or ear infections, she had frontal bossing and enlarged anterior fontanel. Since there was no reason to explain the cause of a large anterior fontanelle, WES was performed and a novel, insilico pathogenic heterozygousc 471_472delGGinsAT (p.M157_A158delinsIS) mutation was detected in RUNX2 () gene.

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CONCLUSION

Delayed closure and enlarged anterior fontanel are very common symptoms in developing countries due to undernutrition of 25 OH-vitamin D. However it should be kept in mind that CCD also can be present with similar findings. Herein we report a novel mutation in the RUNX2 gene.

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