

Case report

Case Report of Chondrodysplasia Punctata: A Rare Complication of Hyperemesis Gravidarum

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Abstract

Chondrodysplasia punctata is a very rare congenital disorder characterized by abnormal calcification within growing cartilage at the ends of the long bones affecting their growth. It has seen in inherited and acquired disorders. Acquired cases may be seen in infants of mothers with deranged vitamin K metabolism during pregnancy as in severe hyperemesis gravidarum. We report 2.5 years girl with features of chondrodysplasia punctata in whom maternal prenatal pregnancy history was remarkable of hyperemesis gravidarum. According to my information, this is the first recorded case in holy Karbala governorate.

Keywords: Chondrodysplasia punctata, hyperemesis gravidarum, vitamin K deficiency embryopathy.

Introduction

Chondrodysplasia punctata (CDP) is a very rare congenital disorder characterized by punctate or dot-like calcium deposits within growing cartilage at the ends of the long bones affecting their growth⁽¹⁻⁶⁾.

Clinically, the most prominent features of patients with CDP are short stature, growth abnormality and usually associated with characteristic facial appearance, (Binder phenotype) particularly a short flat nose, depressed nasal bridge and frontal bossing⁽⁷⁾.

Radiologically, it appears as stipples (punctuates) around the ends of bones and in cartilage.⁽²⁾

Etiologically, CDP is heterogeneous group of wide variety of disorders involving many inherited cases of CDP usually caused by mutations of this gene and thus responsible for the different clinical phenotypes inherited and acquired diseases. Inherited cases of CDP usually caused by mutations of this gene and thus responsible for the different clinical phenotypes⁽⁷⁾. Acquired

conditions during pregnancy include maternal illnesses involving disruption of the vitamin K metabolism^(4, 7, 8). There are reported rare cases of CDP associated with hyperemesis gravidarum HG^(4, 9-11). HG is a severe form of nausea and vomiting of pregnancy associated with weight loss greater than 5% of pre-pregnancy weight⁽¹¹⁾.

We report 2.5 years girl presented with features of CDP in whom maternal prenatal history was remarkable of HG. According to my information, this is the first recorded case in holy Karbala governorate.

Case Report

Girl, 2.5 years old, presented with inability to stand and walk. On examination the girl had short stature and bony bowings in both forearms and legs. Facial features showed mild depressed nasal root, prominent forehead, widely set eyes (Fig. 1). Her hair is coarse, lusterless and sparse. The spines look normal, no kyphosis or scoliosis. The patient can speak only simple words.

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Figure 1. Photograph demonstrating depressed nasal bridge, widely placed eyes and sparse hair



Figure 2. Radiograph demonstrating stippled epiphysis in proximal and distal femoral and tibial epiphysis.

Her medical history revealed dermatological consultations for scaly scalp and ichthyotic skin in the first months of life. No history of respiratory tract infections, seizures and congenital cataracts.

Radiograph of long bones revealed multiple discrete punctate calcifications in the epiphyses and metaphyseal dysplasia which compatible with typical signs of (CDP) (Fig. 2). The spine (bilateral paraspinally and overlying vertebral body midportion) and the pelvis also showed multiple discrete punctate calcifications

Blood investigations revealed alkaline phosphatase 132 U/L, Serum Ca⁺ 10.33 mg/dl, Serum K 4.5, Serum Na 140 mg/dl, Serum Cl. 103, Serum phosphorous -7.1 mg/dl, B.U. 26 mg/dl, T4 149.6 mmol/L (66-181) T3 4.16 mmol/L (1.2-3.1).

Echo showed no heart defects.

She was born vaginally from a healthy 20 years-old mother and 22 years old father. The mother suffered from attacks of severe vomiting during pregnancy and subsequently required oral anti-emetics and intravenous hydration for three-four times. An ultrasound at the seventh month of pregnancy, showed intrauterine growth restriction. Her mother deny any history of

any chronic medications. No family history of similar Presentation.

The diagnosis of CDP associated with HG based on history, clinical and radiological criteria.

Discussion

CDP was first described by Conradi in 1914⁽⁶⁾. It is a heterogeneous group of disorders associated with a range of pathologies characterized by systemic disorder of chondrogenesis. Thus, it is not a disease on itself but a sign seen in many either genetic or non-genetic conditions.^(1, 5, 12)

A number of studies suggested that the enzyme arylsulfatase E (ARSE) plays an important role in cartilage and bone composition and development, thus any deficiency or alteration in the this enzyme was believed to be the underlying CDP^(9, 13).

The ARSE gene which provides instructions for production of the ARSE and its biochemical properties, is located at Xp22.3^(9, 13, 14). Inherited cases of CDP usually caused by mutations of this gene and thus responsible for the different clinical phenotypes^(7, 9).

It is proposed that gene ARSE codes for arylsulfatase-E is vitamin K dependent

enzyme^(4, 7). Its activity is inhibited in conditions of coagulopathy in which decrease the amount of active vitamin K or defects in its metabolism and function. These conditions include warfarin embryopathy, vitamin K deficiency embryopathy and maternal autoimmune disease and other causes.^(5, 13)

Vitamin K deficiency embryopathy can occur due to various causes of maternal malabsorption or malnutrition through different pathologies⁽¹⁵⁾ Malnutrition may occur in cases of severe HG associated with deranged vitamin K metabolism^(11, 16). Andrew S. e.l.,2015, reported the earliest diagnosed case of vitamin K deficiency embryopathy due to HG⁽¹¹⁾. Helga V. T. e.l., 2013, reported eight patients with a Binder phenotype with or without CDP who all shared a known or suspected maternal deficiency of vitamin K⁽¹⁰⁾. So CDP may be seen in infants of mother with severe HG as a result of maternal-fetal vitamin K deficiency^(4, 9-11, 17). This is hypothesized to occur between 6-9 weeks gestation⁽⁴⁾

Interestingly, both acquired and genetic cases have been described, presenting with similar phenotype⁽⁷⁾. The most prominent clinical manifestations of patients with CDP are low birth weight, short stature, growth abnormality and short distal phalanges of fingers and toes (brachytelephalangy). Usually associated with characteristic facial appearance, (Binder phenotype) particularly a short flat nose, depressed nasal bridge and large prominent forehead. Other clinical manifestations include, short neck, with cutaneous changes as ichthyosis and coarse, sparse and lusterless hair⁽¹⁸⁾.

Radiologically, CDP characterized by abnormal calcification, most often located in the epiphyses of long bones (stippled epiphyses) and vertebral column. Stippling is usually symmetric and tends to disappear radiologically at the preschool age when the epiphyses ossify^(6, 9). Extra osseous calcifications some time can occur in sites like the larynx, trachea, and bronchi.^(1, 5, 17)

The pattern of the punctata together with full skeletal survey and chromosomal analysis aid in making the correct diagnosis.

Prognosis, CDP ranged from minimal disorder that get better by adulthood to more health problems including respiratory difficulties, cervical spine stenosis, hearing loss, cataract, cardiac abnormalities and intellectual disability^(6, 17). In severe cases, it leads to antenatal or early childhood mortality⁽¹⁹⁾. There is no cure for CDP and the management is symptomatic and supportive as physiotherapy and orthopedic procedures to improve function. Some of complications have led to early death.⁽¹⁷⁾

Conclusion and Message

CDP is very rare present in pediatric age group. It may be seen in infants of mothers with HG. We hope to increase awareness about the maternal risk factors, especially HG, which lead to nutritional deficiency. This CDP phenotype may be preventable with maternal vitamin K supplementation early in the course of HG.

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