Idiopathic infantile arterial calcification: prenatal diagnosis and postnatal presentation

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Summary

Idiopathic infantile arterial calcification (IIAC) is a rare disease of unknown etiology, which is characterized by arterial calcification. A 29-year-old primigravida at 33 weeks' gestation was referred for further evaluation for polyhydramniosis. An ultrasonographic examination revealed an intrauterine growth restricted fetus, pericardial effusion, increased renal cortical echogenicity with sparing of corticomedullary differentiation, and diffuse arterial calcifications involving the aorta, pulmonary artery, common iliac arteries, renal arteries, and common carotid arteries. At 35 weeks of gestation a cesarean section was performed because of fetal distress. A 1,900 g male infant was delivered. Postnatal examination confirmed the diagnosis of IIAC with dysmorphic features (clinodactily and low-set ears) and normal constitutional karyotype. The baby died when he was four months old in the newborn care unit. During routine obstetric ultrasonography, the combination of polyhydramniosis and intrauterine growth restriction may necessitate examination of the major vessels for presumptive a diagnosis of IIAC.

Key words: Artery; Calcification; Fetus; Prenatal Diagnosis.

Introduction

Idiopathic infantile arterial calcification (IIAC) is a rare disease characterized by arterial calcification and intimal proliferation of large and medium-sized arteries, with more than 160 cases described in the literature [1]. Most of these cases were diagnosed by postnatal radiologic demonstration or at autopsy. However, there are rare reports of prenatal diagnoses and postnatal follow-up and to our best knowledge no case of IIAC with dysmorphic features has been reported yet.

We describe a case of prenatal IIAC diagnosed by ultrasound with the findings of polyhydramnios, intrauterine growth restriction and major vessel calcifications and also dysmorphic features which were diagnosed postnatally.

Case Report

A 29-year-old primigravida at 33 weeks of gestation was referred to our School of Medicine from another hospital because of polyhydramnios. An ultrasonographic examination was performed using a Siemens ultrasound scanner with a 3-5 MHz multifrequency convex transducer (Antares, Germany).

The biparietal diameter measured 32.1 weeks, the femur length measured 27.5 weeks, and abdominal circumference measured 29.5 weeks, on ultrasound (US) examination. Fetal weight was estimated to be 1,400 g (3-5 percentile of birthweight for gestational age) on US examination. A biophysical profile was normal apart from a high (24 cm) amniotic fluid index. A small pericardial effusion, atrioventricular septal defect, increased renal cortical echogenicity with sparing of corticomedullary differentiation, and diffuse arterial calcifications involving the aorta, pulmonary artery, common iliac arteries, renal arteries, and common carotid arteries were noted (Figure 1a/b). We evaluated these findings as appropriate for IIAC and recommended close follow-up examinations for hydrops fetalis. Two doses of 12 mg of betamethasone were introduced intramuscularly for induction of fetal lung maturity. Maternal screening for structural abnormalities, metabolic disorders, anemia, and infections were unremarkable.

At 35 weeks of gestation, a cesarean section was performed under spinal anesthesia because of fetal distress. A 1,900 g male infant was delivered. The Apgar scores after 1 and 5 min were 3 and 5, respectively. The baby was intubated and ventilated because of the respiratory distress. On physical examination, low-set ears, bilateral clinodactily of the 2nd fingers, and a cardiac souffle were detected. Blood biochemistry showed normal values for calcium, phosphate, alkaline phosphate, and 25-hydroxyvitamin D. Renal function and hematologic parameters were normal. TORCH, VDRL, and HIV screens were negative.

A chest radiograph showed hilar enlargement and suspicious radio-opacities in the mediastinum. On echocardiography, calcifications of the aorta and the pulmonary arteries, mild tricuspid insufficiency, secundum type atrioventricular septal defect, and severe pulmonary hypertension were noted.

An abdominal US revealed marked calcification in the abdominal aorta and iliac arteries. Increased renal parenchymal echogenicity with sparing of corticomedullary differentiation was also detected.

Computed tomography (CT) of the chest, abdomen, and pelvis was performed using a Siemens Somatom Sensation (Erlangen, Germany) to facilitate a thorough evaluation and achieve a precise diagnosis. Multiplanar reformatted images were also obtained. There was diffuse calcification of the pulmonary arteries, ascending aorta, aortic arch, descending thoracic aorta, abdominal aorta, and common iliac arteries (Figures 2a/b). Cranial magnetic resonance imaging and skeletal survey were normal. Normal constitutional karyotype was found and no specific genetic abnormalities were noted. Although intensive newborn care support was given, the baby died when he was four months old because of sepsis.

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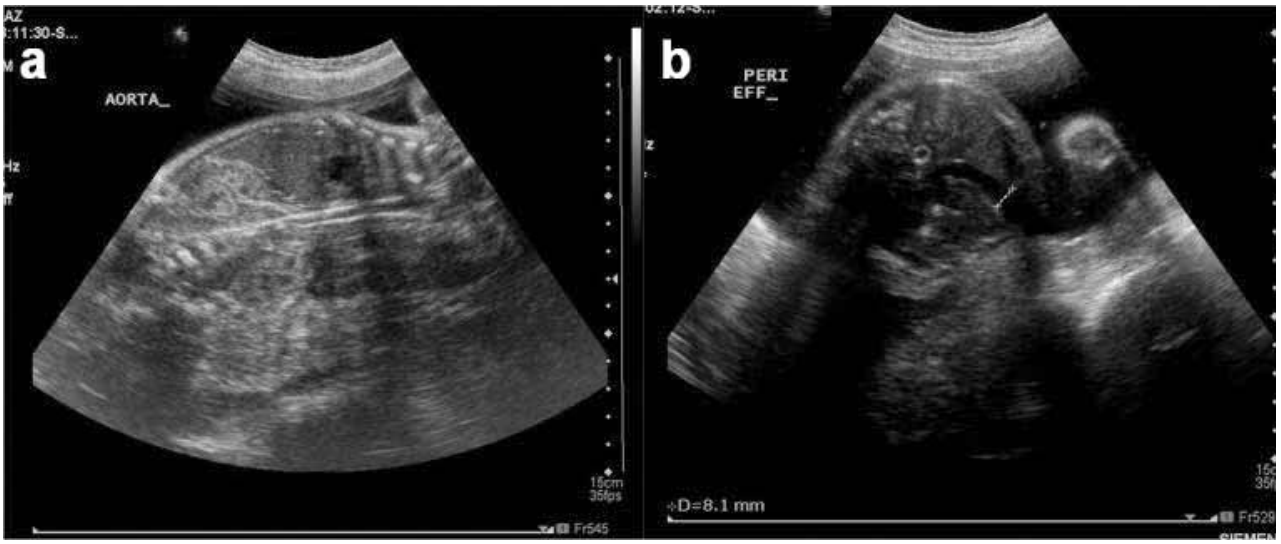

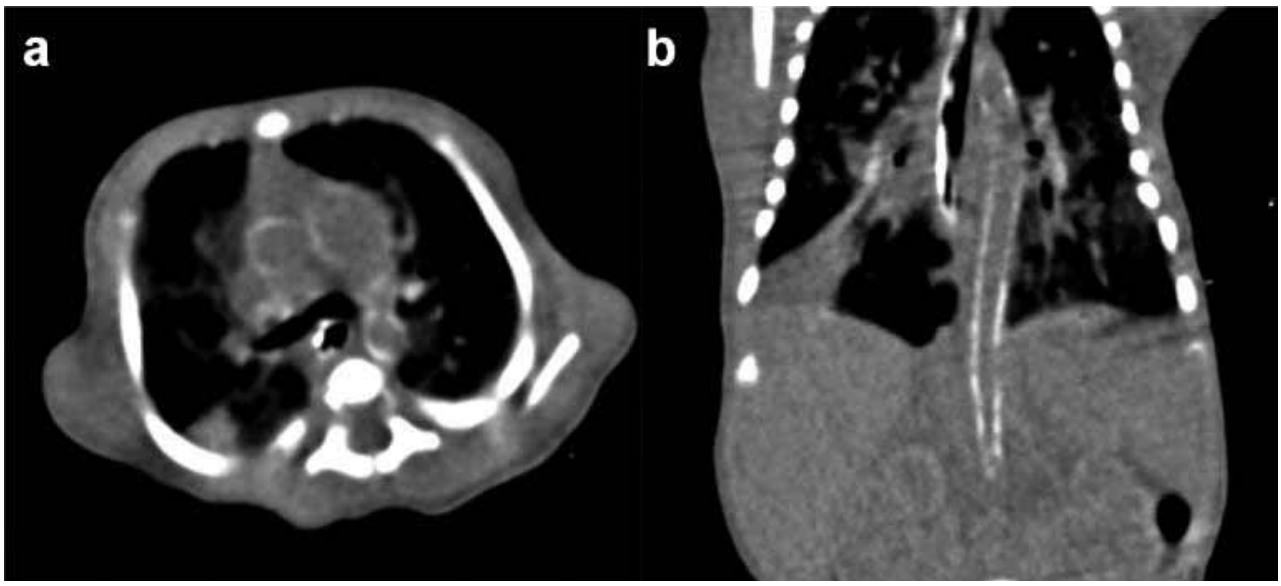

Figure 1. — a) Prenatal sonogram showing the hyperechogenic renal artery and abdominal aorta, interpreted as calcifications. Increased renal echogenicity is also seen, b) Pericardial fluid and descending aorta calcification can be seen.
Figure 2. — a) Axial CT image of the thorax showing circumferential calcification of the ascending and descending aorta, and the pulmonary trunk, b) Coronal reformation shows aortic calcification.

Discussion

IIAC, characterized by medial calcification and intimal proliferation of large and medium-sized arteries, was first described in 1901 [2, 3]. The etiology of this disease is not known. The inheritance pattern is thought to be autosomal recessive. Rutsch *et al*. [4] and Numakura *et al*. [2] reported that mutations within the ecto-nucleotide pyrophosphatase/phoshodiesteterase 1 (ENPP1) gene (chromosome 6q22-q23) gave rise to inactivation of ENPP1 and were associated with the disorder [5]. ENPP1 is an essential physiologic inhibitor of calcification [6].

Generalized arterial calcification can occur from hyperparathyroidism secondary to chronic renal disease, antepartum hypervitaminosis D of the gravida, a disorder of calcium-phosphorus metabolism, or arteritis due to an intrauterine infection [7]. These disorders should all be excluded prior to establishing a diagnosis of IIAC. In the case presented here there were no abnormalities linked to these disorders.

The co-occurrence of IIAC with dysmorphic features has not been reported in the literature. We demonstrated low-set ears and clinodactily of the 2nd fingers in our case. These findings may be shown to represent the characteristics of a novel syndrome, pending reports of new cases with similar findings.

The gold standard for diagnosis of IIAC in living patients is arterial biopsy, while in postmortem cases the diagnosis is made at the time of autopsy. Radiologic modalities, such as CT and US, aid in the diagnosis without using invasive procedures [8]. The widespread

use of US facilitates the prenatal diagnosis of IIAC. IIAC may present as hydrops fetalis, polyhydramniosis, and arterial calcification on prenatal US [7]. Additional secondary findings include hepatomegaly, cardiomegaly, and increased renal echogenicity [9].

Although most patients die within the first six months of life, generally because of cardiac failure, there have been rare reports of long-term survival in the literature [4, 8]. Some have reported spontaneous resolution of the calcifications [10, 11], and others have identified successful medical therapy with bisphosphonates [8, 12, 13]. Van der Sluis *et al*. [8] described long-term follow-up with etidronate therapy for up to 25 years.

In conclusion, prenatal diagnosis of IIAC may provide the opportunity to refer such cases to tertiary centers for close supervision by an obstetrician, neonatologist, radiologist and pediataric cardiologist. US is an easily accessible diagnostic tool which aids in the prenatal diagnosis and postnatal evaluation of this disorder, while CT easily reveals calcifications in the larger and smaller arteries, without the need for invasive procedures, like arterial biopsy or autopsy. During routine obstetric US, the combination of polyhydramniosis and intrauterine growth restriction may necessitate examination of the major vessels for a presumptive diagnosis of IIAC.

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