Arterial tortuosity syndrome: relevance in pediatric surgery. A case report

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ABSTRACT

Introduction. Arterial tortuosity syndrome (ATS) is an extremely rare autosomal recessive disorder of the connective tissue. It is characterized by tortuosity and elongation of medium and large arteries, with multiple disorders associated with the widespread involvement of the connective tissue.

Clinical case. Newborn diagnosed with ATS, with multiple vascular malformations, hiatal hernia, and bilateral inguinal hernia.

He underwent surgery at three months of age. The hiatal hernia was closed, and bilateral inguinal hernia repair was performed. The inguinal hernias required up to 4 surgeries as a result of recurrences.

During follow-up, the patient had retrocardiac diaphragmatic hernia. It was operated on, with subsequent incisional hernia.

8 years later, he was admitted as a result of septic shock secondary to intestinal occlusion. Emergency surgery was scheduled, demonstrating gastric herniation in the right pleural cavity, with perforation of the fundus. The patient died at the ICU 24 hours later.

Discussion. The pediatric surgeon should be familiar with ATS, since it may cause multiple surgical pathologies, it is difficult to manage, and it is associated with a high risk of recurrence and complications.

KEY WORDS: Arterial tortuosity syndrome; GLUT10; SLC2A10; Aneurism; Pediatrics.

EL SÍNDROME DE TORTUOSIDAD ARTERIAL Y SU RELEVANCIA EN CIRUGÍA PEDIÁTRICA. A PROPÓSITO DE UN CASO

RESUMEN

Introducción. El síndrome de tortuosidad arterial (STA) es un trastorno autosómico recesivo del tejido conectivo muy infrecuente, caracterizado por tortuosidad y elongación de arterias de medio y gran calibre y múltiples trastornos derivados de la afectación generalizada del tejido conectivo.

Caso clínico. Neonato diagnosticado de STA, con múltiples malformaciones vasculares, hernia de hiato y hernia inguinal bilateral.

Intervenido a los tres meses, practicándose cierre de hernia de hiato y herniorrafia inguinal bilateral. Estas últimas requirieron hasta cuatro intervenciones por recidiva.

Durante el seguimiento presentó hernia diafragmática retrocardiaca, siendo intervenida, con posterior eventración.

A los ocho años ingresó por shock séptico secundario a oclusión intestinal. Se intervino urgente objetivando herniación gástrica en cavidad pleural derecha con perforación en fundus. El paciente falleció en la UCI tras 24 horas.

Comentarios. El cirujano pediátrico debe conocer el STA debido a la múltiple patología quirúrgica que puede presentar, difícil manejo, riesgo de recidiva y complicaciones.

PALABRAS CLAVE: Síndrome de tortuosidad arterial; GLUT10; SLC2A10; Aneurisma; Pediatría.

INTRODUCTION

Arterial tortuosity syndrome (ATS) is an extremely rare disorder of the connective tissue. It is caused by loss-of-function mutations in the SLC2A10 gene, which codes GLUT10 glucose transporter[1-7]. Estimated prevalence is below 1:1,000,000, with approximately 100 cases described in the literature. Male/female ratio is 1:1[8].

Clinical signs usually start during childhood, with severe tortuosity and abnormal elongation of medium and large arteries, along with predisposition to aneurism, arterial dissection, and stenosis, potentially involving the aorta and the pulmonary arteries[3]. Patients usually have craniofacial disorders, such as long face, high palate, crowded teeth, convex nose, micrognathism, descending palpebral fissures, and large ears[6,8]. The skin is typically hyperextensible and smooth, and it has traits characteristic of lax skin[9]. In some cases, healing can be delayed and cause atrophic scars, especially following any given surgery[10]. Additionally, ATS patients may present other signs of widespread connective tissue disorders, including abdominal

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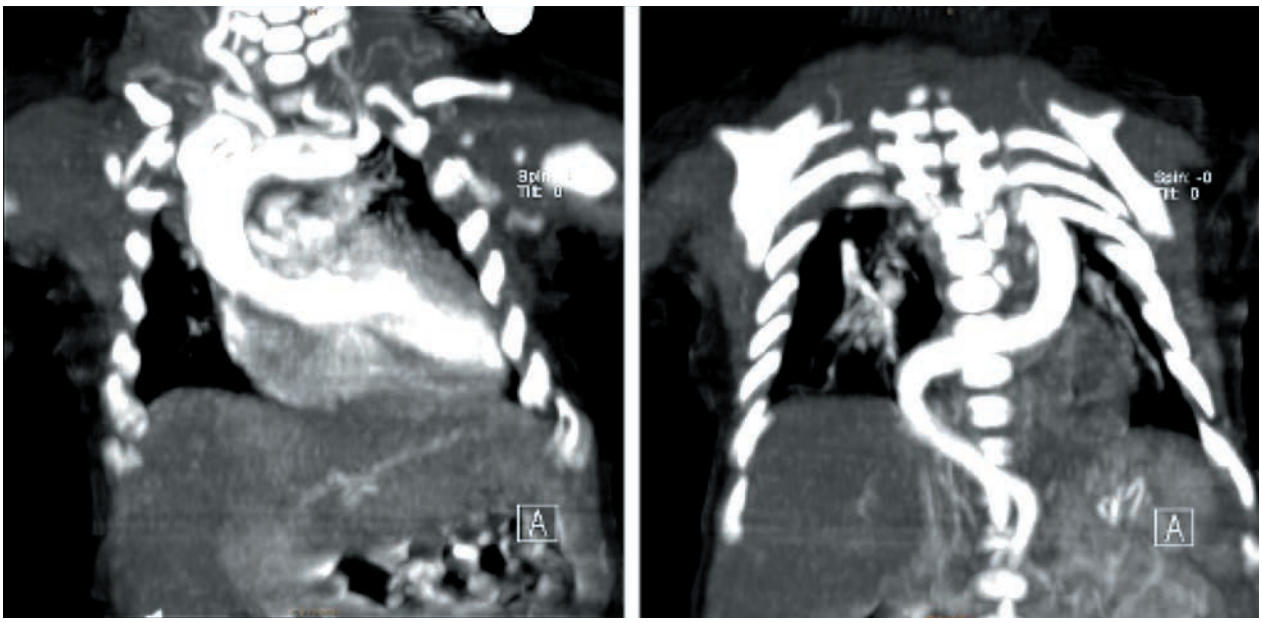

Figure 1. Thoracic CT-scan coronal cuts at 13 days of age. Redundant aorta.

wall hernia, inguinal hernia, hiatal hernia, diaphragmatic hernia, and skeletal and/or ocular disorders[6,9].

The objective of this work was to present the case of a newborn genetically diagnosed with ATS.

CLINICAL CASE

Male patient, without significant family history. Pregnancy remained under control, without complications. An emergency Cesarean section was carried out at gestation week 40 as a result of loss of fetal well-being. At birth, the patient had meconium aspiration syndrome, with respiratory insufficiency, which required orotracheal intubation in the first hours of life. Following neonatal ICU admission, blood pressure gradient was higher in the upper limbs than in the lower limbs, without aortic coarctation, and with bilateral inguinal hernia.

An echocardiogram and a thoracoabdominal CT-scan were carried out. The patient was diagnosed with moderate cardiomegaly, with severe abnormalities in the thoracic and abdominal vessels. The aorta was significantly redundant (Figs. 1 and 2), and the supra-aortic vessels had an abnormal origin, diameter, and trajectory. He also had severe hypoplasia of the pulmonary arteries, with moderate pulmonary hypoplasia, and a giant hiatal hernia causing frequent regurgitation.

Given the suspicion of ATS, a genetic study was conducted. It showed two heterozygous mutations in the SLC2A10 gene, thus allowing diagnosis to be confirmed.

At 3 months of age, he underwent hiatal hernia surgery in the form of right thoracotomy as per the surgeon's

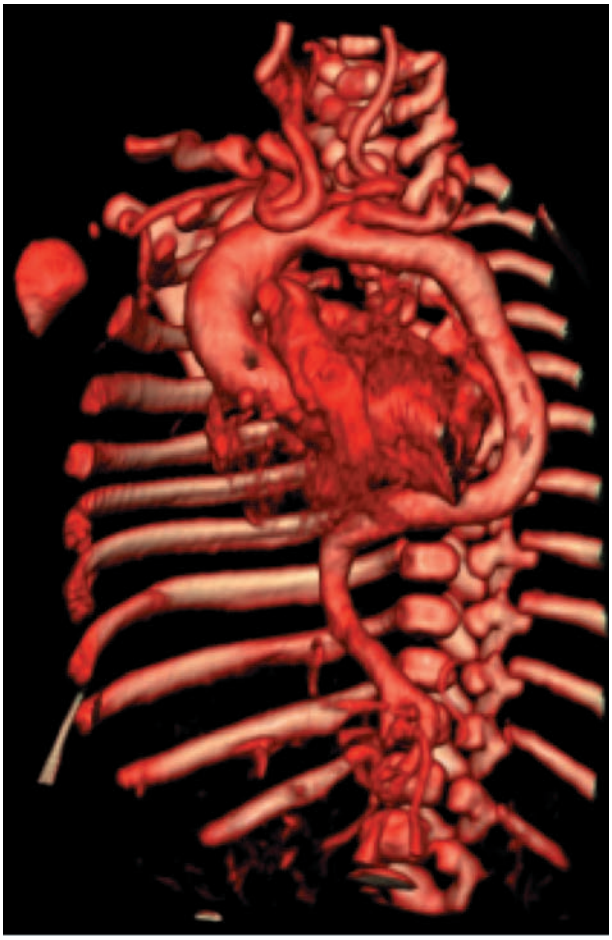

Figure 2. Thoracic CT-scan reconstruction at 13 days of age. Abnormal aorta and supra-aortic vessels.

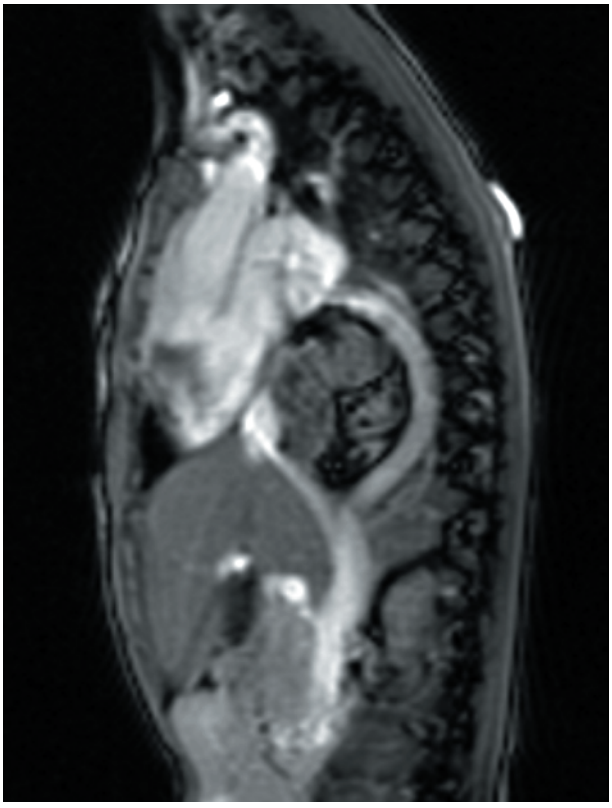

Figure 3. Retrocardiac diaphragmatic hernia. Thoracoabdominal CT-scan sagittal cut at 2 years and 9 months of age.

preference. The hernia was repaired, and a Belsey – Mark IV antireflux procedure was carried out.

The inguinal hernias were indirect, and they required up to 4 surgeries in the first years of life as a result of multiple recurrences. A polypropylene mesh was placed in the last surgery.

During outpatient follow-up, and following a control thoracoabdominal CT-scan performed at 2 years and 9 months of age, a small retrocardiac diaphragmatic hernia was found (Fig. 3). Given its progression, it was operated on at the age of 7 by means of a right re-thoracotomy. The defect was sutured, and a Gore-Tex patch was placed.

Subsequent progression was good. However, at a control CT-scan carried out 11 months following surgery, partial recurrence of the diaphragmatic hernia was observed on the right side.

Given the patient's clinical stability and the lack of symptoms, non-urgent surgery was scheduled. However, a few weeks later, he was admitted with septic shock and intestinal occlusion, which had started 24 hours earlier.

At the time of emergency department admission, the patient was disoriented, with mucocutaneous paleness, hemodynamic instability, and widespread abdominal pain, as well as signs of peritonism.

Remarkable blood count findings included leukopenia (2.4×10^9/L) and increased CRP (19.3 mg/dl).

Resuscitation maneuvers were initiated, and an emergency thoracoabdominal CT-scan was carried out, which revealed a right giant diaphragmatic hernia, with small bowel, colon, and stomach loops. Additional findings included free air in the abdominal cavity and the right thoracic cavity, pleural and intra-abdominal free fluid, and intra-abdominal fecaloid material (Fig. 4).

Emergency surgery was performed in the form of a supraumbilical laparotomy, which demonstrated abundant free gastric content and a herniated gastric pouch in the thoracic cavity. The stomach was reduced, which showed a 3.5 cm perforation in the greater curvature and an isch-

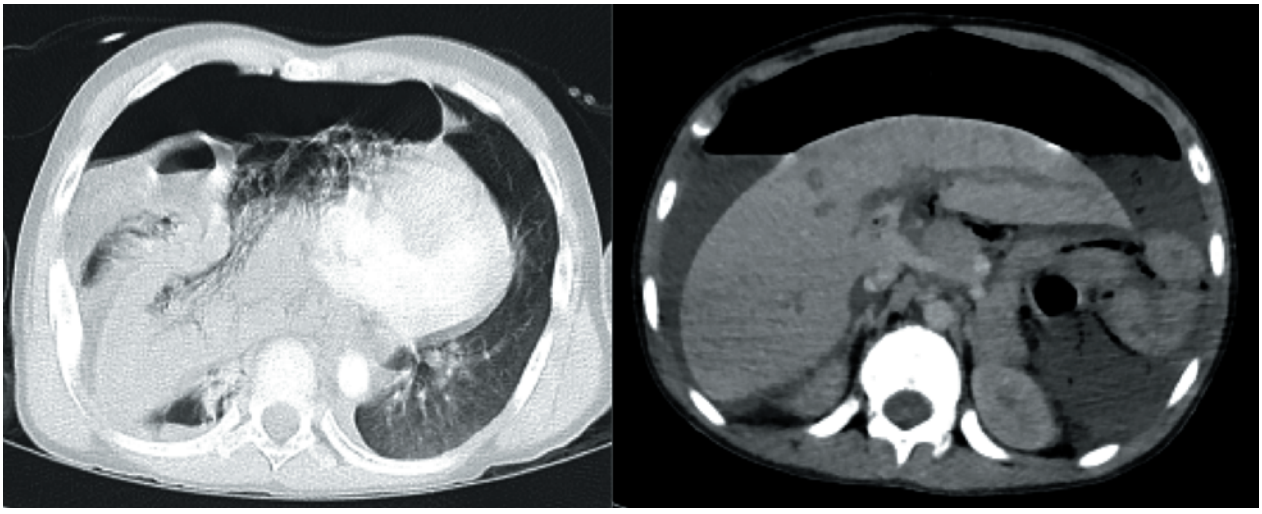

Figure 4. Thoracoabdominal CT-scan at 8 years of age.

emic gastric fundus, so partial gastrectomy was carried out. In addition, the patient had hypoperfusion of virtually the whole small bowel, as well as partial necrosis of the greater omentum.

In the immediate postoperative period, he was admitted at the pediatric ICU. The patient died as a result of septicemia in the following hours.

The histopathological study and the autopsy confirmed ATS, with aortic arch, supra-aortic trunks, abdominal aorta, and tortuous Willis polygon vessels. Other relevant anatomical findings included superior vena cava dilatation and venous sinus; left ventricle hypertrophy and pulmonary artery infundibulum dilatation; permeable oval foramen; double renal arteries; and a 3 x 2 cm diaphragmatic hernia with a leftward, downward trajectory towards the right cavity.

Histological study demonstrated elastic fiber disruption, disorganized fibers of various calibers, and presence of myxoid material and collagen deposits within the elastic fibers in the larger vessels.

DISCUSSION

ATS is an extremely rare entity. Clinical signs vary according to the arteries involved and the disorders caused by connective tissue involvement.

Transmission is autosomal recessive. ATS is caused by mutations in the SLC2A10 gene (20q13.12), which codes GLUT10 glucose transporter[1-7]. Up until now, 23 mutations in the SLC2A10 gene have been described in 102 families[7].

Prenatal diagnosis can be achieved by means of ultrasonography following delayed intrauterine growth, oligohydramnios, and especially, aortic tortuosity[7]. Genetic study of amniocytes or chorionic villus cells allows definitive diagnosis to be established.

Postnatal diagnosis and study require a comprehensive assessment, including thorough clinical examination, echocardiogram, magnetic resonance angiography, and/or CT-angiography. Ophthalmological examination using keratometry and renal ultrasonography is recommended in all patients diagnosed with ATS[7].

Histopathological examination of the vessel walls involved reveals disorganization and fragmentation of the internal elastic lamina and the elastic laminas of the tunica media of the large arteries[4,7,8], as evidenced in our case.

Differential diagnosis should include type 1a, 1b, and 1c lax skin, Loeys-Dietz syndrome, vascular Ehlers-Danlos syndrome, Marfan syndrome, and occipital horn syndrome – lax skin being associated with *ATP7A*[8].

Patients have an increased risk of aneurism formation and dissection at any given age, both at the aortic root and the whole arterial tree[9-13], with the cardiovascular system being the main cause of morbidity and mortality. Therefore, regular follow-up using EGC, MRI, and/or CT-scan is recommended. In terms of surgery, aortic root replacement (in the presence of aneurism) and pulmonary artery reconstruction may also prove beneficial.

In addition, ATS patients have an increased risk of cerebrovascular and abdominal ischemic events at all ages[8].

Pregnancy in the presence of ATS requires intensive monitoring both of the mother and the fetus, Cesarean section, and cross-disciplinary post-birth care. The main risks for the mother include aortic root dilatation and dissection. Consequently, closer surveillance is recommended during pregnancy and following delivery as a result of having a greater risk of progressive aortic root dilatation, and also due to the previous aneurisms[8].

Mortality was initially estimated at 40% before 4 years of age[12]. However, later studies with molecularly confirmed patient series suggest lower mortality rates[9]. Even so, prognosis can be severe. The main causes of death include respiratory insufficiency, ventricular hypertrophy leading to widespread cardiac insufficiency, myocarditis, and ischemic events.

Ours is a single case, which means it cannot be extrapolated to all clinical presentations. However, in our view, considering how poor progression was in our patient, this is a highly complex pathology requiring a cross-disciplinary approach.

The recurrences found in inguinal hernias seem to support a more radical surgical treatment from the beginning with the help of prosthetic material, which would make up for the faulty connective tissue itself.

The pediatric surgeon should be familiar with ATS owing to the multiple potentially surgical pathologies it can be associated with, and considering management difficulty and recurrence and complication risks.

In our opinion, close follow-up and a radical surgical approach can prevent the risk of complications.

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