CASE REPORT

Persistent Crying in Infants: Not Always Colic

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Abstract

Persistent crying in infants includes a wide range of differential diagnoses, from benign causes to life-threatening situations. Anomalous left coronary artery from pulmonary artery syndrome is a rare congenital heart disease that presents as ischemia or heart failure in the first months of life and prompts urgent surgical treatment. A 5-week-old infant was taken to the emergency department due to inconsolable crying. Physical examination revealed a mitral systolic murmur. Chest X-ray evidenced cardiomegaly. The electrocardiogram and laboratory exams suggested myocardial ischemia. On the echocardiogram, he presented dilated left chambers, left ventricular dysfunction, and mitral regurgitation. An aortography was performed showing uncertain origin of the left coronary artery. A computed tomography angiography confirmed the diagnosis and reimplantation surgery was conducted with a favorable outcome. Although rare, anomalous left coronary artery from pulmonary artery syndrome can result in acute myocardial infarction and sudden death. A high rate of clinical suspicion and a thorough examination are key to diagnosis, treatment, and prognosis.

Keywords: Infant; Bland White Garland Syndrome/diagnosis; Bland White Garland Syndrome/surgery; Coronary Vessel Anomalies; Crying; Systolic Murmurs/etiology

Introduction

The anomalous left coronary artery from pulmonary artery (ALCAPA) syndrome, historically known as Bland-White-Garland syndrome,[1] is rare, accounting for less than 0.4% of congenital heart diseases.[2] There have been rather few studies assessing the epidemiology of this disorder in the general pediatric population. In an Irish birth cohort,[3] the incidence of ALCAPA was 0.023% and in a Polish study[4] it was 0.021%. However, it was 10 times higher in autopsy studies.[5] It usually occurs as an isolated defect but it can happen in conjunction with other congenital cardiac abnormalities such as atrial septal defect, ventricular septal defect, or coarctation of the aorta.[6]

In this anomaly, the myocardium is perfused by an abnormally arising left coronary artery from the pulmonary artery, which has a relatively low perfusion pressure and carries venous blood.[1] The physiopathology of ALCAPA carries a continuum of different stages.[6] In the first month of life, the perfusion and oxygenation of the myocardium are assured by the presence of physiological elevated pulmonary pressure and fetal hemoglobin. When pulmonary arterial pressure and vascular resistance fall, around the sixth week of life, a flow reversal from the left coronary artery occurs, resulting in a steal phenomenon.[7,8] At this point, if there are inadequate collaterals from the right coronary artery, a reduction in coronary perfusion and oxygenation ensues and chronic ischemia of the anterolateral wall develops. Consequent heart failure and associated mitral insufficiency lead to left ventricular dilation and remodeling of the myocardium over time. In this second phase, most infants become symptomatic.[1]

Rarely, if there is substantial collateral blood flow, ALCAPA can present in later childhood or adulthood as dilated cardiomyopathy or sudden death.[9] This is considered the third stage, where intercoronary collateral vessels develop, improving left coronary artery territory perfusion and myocardial function. A fourth and final stage relates to the presence of normal pulmonary arterial pressure and vascular resistance, with left coronary artery circulation supplied by the right coronary artery and a left-to-right shunt into the pulmonary artery, which causes subclinical myocardial ischemia with worsening mitral valve regurgitation and risk of sudden cardiac death.

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In symptomatic infants, periods of irritability or inconsolable crying associated with pallor, dyspnea, and diaphoresis that occur especially during feedings are typical.[9,10] Failure to thrive or wheezing are alternative presentations. A gallop or a short grade systolic murmur of mitral regurgitation may be found.

Case Report

We report the case of a full-term, 5-week-old infant, taken to the emergency department of a district hospital for inconsolable crying. He had a cough and nasal obstruction for the previous three days, without fever or feeding problems. His family was from Kazakhstan, where pregnancy surveillance took place, but the baby was born in Portugal. Otherwise, his history was unremarkable. He had been exclusively breastfed with satisfactory weight evolution, around the 50th percentile. At admission, he was afebrile, hemodynamically stable with a heart rate of 160 bpm, blood pressure 76/48 mmHg (50th-95th percentile), and a respiratory rate of 65 bpm with peripheral oxygen saturation (SpO_2) of 100% (room air). He had mild substernal retraction and a systolic murmur (grade II/VI) was heard on the mitral focus. The remaining physical exam was normal. The chest X-ray revealed a significant cardiomegaly (Fig. 1). He was transferred to a tertiary hospital for further evaluation by pediatric cardiology (day two). Subsequent exams showed the elevation of cardiac enzymes and ST-depression with T wave inversion in leads V4-V6, I and aVL in the electrocardiogram. On an echocardiogram (Fig. 2), he had dilated left chambers – left ventricular end-diastolic diameter (LVEDD) 31 mm, *Z*-score +6.7 –, mild left ventricular dysfunction – left ventricular ejection fraction (LVEF) 50%, and moderate-to-severe mitral regurgitation. The left coronary artery was not identified by echocardiography. A restrictive patent *foramen ovale* with left-to-right shunt and the absence of patent *ductus arteriosus* were documented. He was started on diuretics (furosemide and captopril, both 1.3 mg/kg/day). On the next day (day three), an aortography was performed (Fig. 3) and showed normal positioning and distribution of the right coronary artery but was unable to identify the left coronary artery. Post-catheterization, he developed a femoral artery thrombosis and was admitted to the pediatric intensive care unit for fibrinolytic therapy (alteplase), on day four of disease, after having received a short-course heparin perfusion without improvement. A computed tomography angiography (Fig. 4) confirmed anomalous origin of the left coronary artery from the pulmonary trunk. Two days later (day six), an ALCAPA repair surgery was conducted. The left coronary artery, which originated from the lateral wall of the pulmonary trunk, was reimplanted into the aorta. Closure of the sternum was deferred, and the skin was closed with bovine pericardium. Prophylactic antibiotherapy with cefazoline was conducted for five days. He had good clinical evolution in the postoperative period, having started enteric nutrition after three days and with chest closure after six days. Inotrope and vasopressor support were maintained for nine days and invasive mechanical ventilation for 11 days after the surgery.

He was transferred to the cardiothoracic surgery ward at day 12 and discharged home after 23 days of hospital admission, with improvement of the ventricular size and function (LVEDD 25 mm, *Z*-score +2.39, LVEF 65%) maintaining moderate mitral regurgitation. At discharge, he was on furosemide (1.8 mg/kg/day), spironolactone (1.1 mg/kg/day), and acetylsalicylic acid (20 mg).

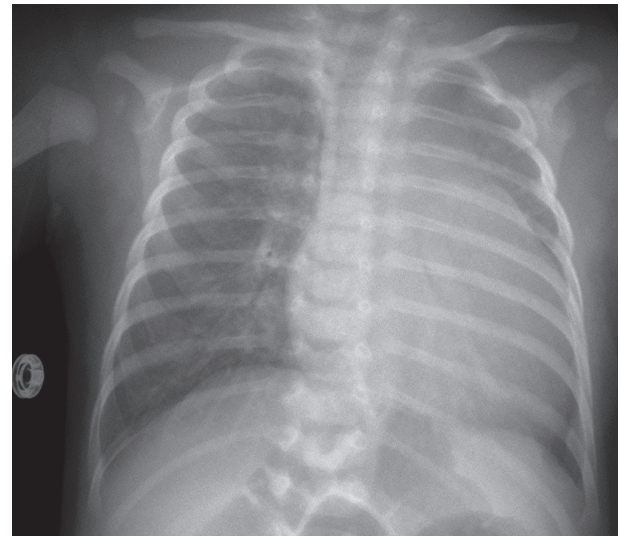


Figure 1. Chest X-ray at admission evidencing very significant cardiomegaly.

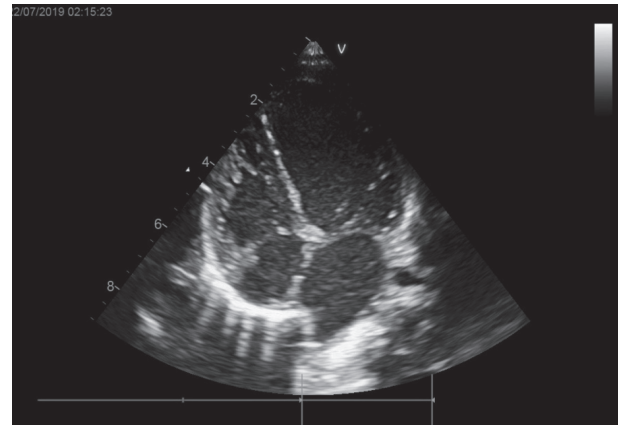


Figure 2. Echocardiogram at diagnosis, showing dilated left chambers (left ventricular end-diastolic diameter 31 mm, *Z*-score +6.7), mild left ventricular dysfunction (left ventricular ejection fraction 50%), and moderate-to-severe mitral regurgitation.

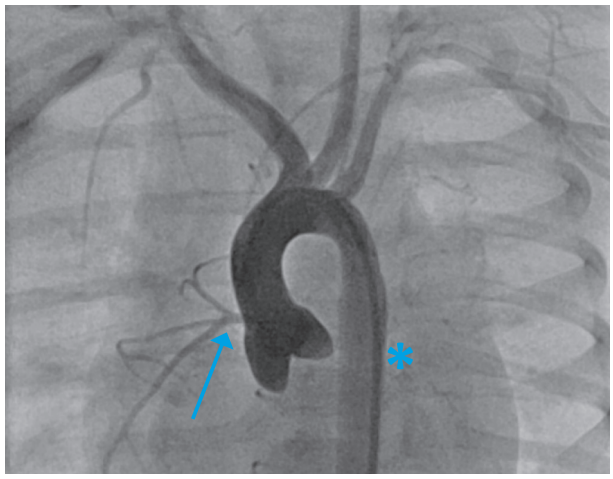
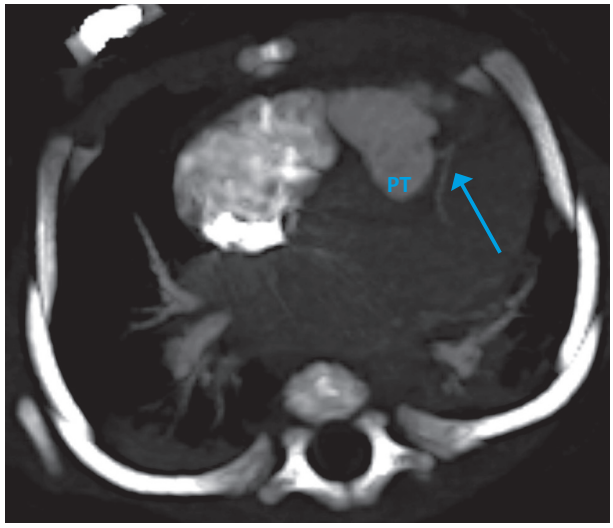


Figure 3. Aortography showing normal positioning and distribution of the right coronary artery (arrow) but without filling of the left coronary artery territory (asterisk).



PT - pulmonary trunk.

Figure 4. Computed tomography angiography confirming the anomalous origin of the left coronary artery from the left side strand of the pulmonary trunk (arrow), at 5 mm from the pulmonary valve plane, reflecting the anomalous left coronary artery from pulmonary artery syndrome.

Five months after surgery, he has a good weight evolution and is clinically asymptomatic. Electrocardiogram shows that there is no longer repolarization alterations and on the echocardiography there is clear improvement in the left ventricular dimensions (LVEDD 24 mm, *Z*-score -0.06) and function (LVEF 66%) as well as mitral regurgitation (mild). Left ventricular fibroelastosis and moderate stenosis of the pulmonary artery at the surgical site were described.

Discussion

Excessive crying in young infants is a common cause for seeking medical care. Although most causes are benign, there are a few life-threatening situations that should not be missed. The diagnosis of ALCAPA is challenging because a broad spectrum of clinical manifestations exists depending on the number and size of collateral vessels and the area of myocardium supplied by the right coronary artery, reflecting its complex physiopathology.[9] In infants, this anomaly mimics common situations such as infantile colic, gastroesophageal reflux or respiratory infections.[3,5]

A thorough history and physical examination are key to identifying the features that justify further investigation. Our patient presented with persistent crying, compatible with angina episodes. Typically, these are accompanied with diaphoresis or pallor, occur mostly during feeding time, and may impair weight evolution.[3,11] The absence of these characteristics made the diagnosis in our patient even more challenging. A complete cardiovascular exam must be included in the evaluation of the prolonged crying infant. Vital signs should be accessed and may provide diagnostic clues, like compensatory sinus tachycardia, which is frequent in left ventricle dysfunction. An alarm signal found at physical examination in our patient was the systolic murmur consistent with mitral regurgitation. A thorough examination including careful cardiac auscultation is, therefore, fundamental since low grade murmurs can be easily missed. However, this is a common and unspecific finding in infants and must be contextualized concerning the full clinical picture. Cardiovascular evaluation for signs of heart failure or shock must also be accessed in the evaluation of the prolonged crying infant.

If any of these concerns are found in the clinical history or abnormalities in the physical observation are found, a chest X-ray and electrocardiogram should be performed to rule out cardiomyopathy, although not being specific exams. In our patient, the thoracic imaging was performed mostly because of the respiratory symptoms. The pronounced cardiomegaly finding led to the subsequent investigation. In ALCAPA, the heart may be uniformly enlarged with a large left ventricle and frequently an enlarged left atrium, particularly in those patients with mitral insufficiency. Signs of pulmonary edema may be apparent. Electrocardiogram is another accessible exam that is helpful in the diagnosis of ALCAPA, since it shows ischemia signs in the majority of infants.[9] In case of alterations in cardiovascular examination or first line exams, prompt contact with pediatric cardiology and referral to a tertiary center must be accomplished.

Anomalous origin of the left coronary artery is usually detected by echocardiography,[12] an excellent, noninvasive tool to diagnose anomalous coronary arteries in young individuals.[6] However, in some cases, like in our patient, a poor acoustic window may not

allow for the full identification of the coronary artery origin. If an infant presents with cardiac failure with no obvious structural cause, or if an unexplained dilated left ventricle, depressed left ventricular function or mitral regurgitation are seen on echocardiography, ALCAPA should be suspected.[3,10] The hemodynamic study may occasionally be necessary to diagnose the disease or confirm the echocardiographic findings.[12]

Aortography is the gold standard diagnostic procedure with the injection of the contrast medium immediately above the aortic valve or directly into the right coronary artery.[9] When the left coronary artery function has an arterio-venous fistula, the dye will be seen passing via collaterals to the left coronary artery and, therefore, to the pulmonary artery. This did not happen in our patient, making the diagnosis by this technique difficult.

Without treatment, this anomaly carries a 90% mortality in the first year of life[6] due to ischemic cardiomyopathy and endocardial fibrosis from a decreased oxygen supply in the left coronary artery territory. Anticongestive therapy is used temporarily but surgical correction is advised as soon as possible in order to preserve the myocardium.[12,13] Starting with left coronary artery ligature, first reported in 1959,[14] considerable advances have been made in the surgical techniques employed, including myocardial revascularization, anastomoses of the left coronary artery to the right or left subclavian artery,[11,15-17] or the Takeuchi technique, described in 1979,[18] where a tunnel is constructed within the pulmonary artery in order to allow the communication of the left coronary artery with the aorta through an aortopulmonary window. Nowadays, the preferred surgical method is the left coronary artery translocation, with good outcomes even in patients with severe left ventricular dysfunction and mitral insufficiency.[6] Our patient was operated on very soon after the diagnosis, with good immediate clinical evolution, improvement of ventricular function and of mitral regurgitation, and remaining stable a few months after surgery. However, long-term follow-up with electrocardiogram to look for arrhythmias and echocardiogram for monitoring left ventricular function and mitral regurgitation is needed.[12]

In conclusion, this case stands out for its presentation with only persistent crying and for its early diagnosis, made in the first attempt to seek medical help. Most patients are identified later, when clear signs of cardiac failure are already present.[3,4] Feeding problems or failure to thrive are normally reported, and frequently patients have been observed before without the diagnosis having been established.[3]

With this case report, the authors intend to improve clinical awareness for ALCAPA syndrome. There should be a high suspicion index among pediatricians, trainees, and general practitioners. Although rare, given its bad prognosis when not treated in a timely manner, it is important to look for this anomaly in the right settings.[1,9] Anomalous left coronary artery from pulmonary artery syndrome should be suspected in any children with symptoms of heart failure, electrocardiogram abnormalities, and decreased left ventricular systolic function with unknown cause. Considering that there are no populational studies to ascertain its real prevalence, it is probably underdiagnosed. Its prompt recognition and referral to a tertiary cardiac center to enable early surgical intervention is essential for improving the prognosis of these children.[3]

WHAT THIS CASE REPORT ADDS

- Persistent excessive crying in infants may be a sign of a severe underlying abnormality.
- A thorough history and physical examination should be carefully performed to identify alarm signs that justify further investigation.
- Considering the cardiovascular alterations, chest X-ray, and electrocardiogram are simple first line exams that may identify cardiomyopathy.
- Anomalous left coronary artery from pulmonary artery syndrome should be suspected in any child with heart failure symptoms, electrocardiogram abnormalities, and depressed left ventricular systolic function with unknown etiology.
- Early diagnosis and surgical repair are associated with a better prognosis.

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

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Confidentiality of data

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

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Choro Persistente em Crianças: Nem Sempre Cólicas

Resumo

O choro persistente no lactente inclui uma ampla gama de diagnósticos diferenciais, desde causas benignas até situações ameaçadoras da vida, como a síndrome de origem anómala da artéria coronária esquerda do tronco pulmonar, uma doença cardíaca congénita rara que se apresenta como isquemia ou insuficiência cardíaca nos primeiros meses de vida e exige tratamento cirúrgico urgente. Um lactente de 5 semanas foi levado ao serviço de urgência por choro inconsolável. O exame físico revelou um sopro sistólico mitral. A radiografia de tórax revelou cardiomegalia, o eletrocardiograma e os exames laboratoriais sugeriram isquemia miocárdica. Ao ecocardiograma, apresentava câmaras esquerdas dilatadas, disfunção ventricular esquerda e regurgitação mitral. Realizou aortografia mostrando origem incerta da artéria coronária esquerda. A angiotomografia confirmou o diagnóstico e foi realizada uma cirurgia de reimplante, com resultado favorável. Embora rara, a síndrome de origem anómala da artéria coronária esquerda do tronco pulmonar pode resultar em enfarte agudo do miocárdio e morte súbita. Um elevado grau de suspeita clínica e um exame minucioso são essenciais para o diagnóstico, tratamento e prognóstico.

Palavras-Chave: Anomalias dos Vasos Coronários; Choro; Lactente; Síndrome de Bland-White-Garland/diagnóstico; Síndrome de Bland-White-Garland/cirurgia; Sopros Sistólicos/etiologia