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Anomalous origin of left coronary artery from pulmonary artery (ALCAPA): a case series and review of literature

Running title: ALCAPA

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Abstract

Introduction: Anomalous left coronary artery from the pulmonary artery (ALCAPA) is a rare Cardiovascular Disease presented with an incidence of 1:300000 live births.

Case Presentation: In this manuscript, four cases of ALCAPA in infancy were described. Two infants were presented with respiratory distress and two with heart a murmur. Their coronary artery was derived from the pulmonary artery. Two of them died, one after surgical procedure and one before surgical intervention. Of remained cases, one of them had a good surgical outcome and another was missed in follow up.

A brief review was done on case reports of ALCAPA in children. Eighteen manuscripts were found including 201 pediatric cases.

Conclusions: The vast majority of affected children will die within the first year of life if ALCAPA is not diagnosed and treated correctly.

Keywords: ALCAPA, Children, Cardiac, Bland White Garland Syndrome, Coronary Vessel Anomalies, Cardiovascular Diseases

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1. Introduction

Congenital coronary artery anomaly is a defect in one or more of the coronary arteries of the heart which may be present at birth and may be related to the origin, structure, and course of these arteries (1). Its incidence varies between 0.2 and 5.6% of the general population (2).

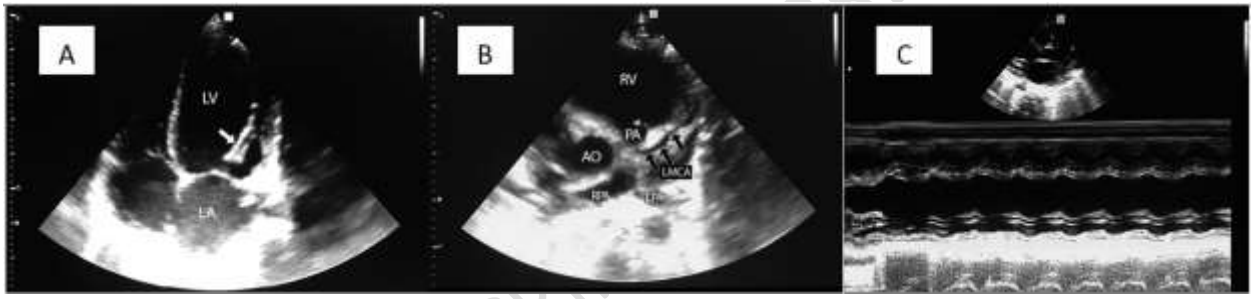
Anomalous left coronary artery from the pulmonary artery (ALCAPA) is a heart defect presented in 0.25-0.5% of the children (3) with an incidence of 1:300000 live births (4, 5).

The vast majority of affected children, up to 90%, die within the first year of life if ALCAPA is not diagnosed and treated in a timely manner (3, 4).

This anomaly was first described anatomically by Brooks in 1885 (6). Bland, White, and Garland described the first clinical features with an autopsy finding of ALCAPA in 1933 (7). This anomaly has thus been named the Bland-White-Garland Syndrome (8).

2. Case presentation

In this study, we report 4 pediatric cases of ALCAPA in the north of Iran, Mazandaran province, from March 2011 to 2016. The Informed Consent was taken from each cases' parent.



Case 1

A two-day-old boy was admitted to the neonatal intensive care unit due to respiratory distress and meconium aspiration. Cardiology consultation was performed on the 5th day of admission. Echocardiography showed severe right ventricle (RV) and left ventricle (LV) dysfunction in addition to pulmonary hypertension, Tricuspid regurgitation gradient (TR) was equal to 50 mmHg, and right to left shunt through a small atrial septal defect (ASD). The patient underwent heart failure treatment. During admission, barium swallow was performed due to frequent vomiting episodes which revealed severe gastro-esophageal reflux.

In the second echocardiography which was performed 5 days later, RV function was improved, TR= 40 mmHg, but the LV function was still reduced. The left coronary artery was connected to pulmonary artery in echocardiography, but due to the pulmonary artery hypertension, the diastolic flow was not detectable in the pulmonary artery. Figure 1.

The infant was referred to the heart surgery center with a primary diagnosis of ALCAPA. In follow up, the diagnosis was confirmed with CT-angiography then the infant operated but unfortunately, he died immediately after surgery.

Figure 1. (Case 1): Echocardiography, A: LV enlargement and increased density of papillary muscle (white arrow), B: Short axis view, LMCA (black arrows) from PA, C: Low LV ejection fraction. LV, left ventricle; RV, right ventricle; LA, left atrium; RPA, right pulmonary artery; LPA, left pulmonary artery

Case 2

A 3-month-old girl was admitted to the pediatric intensive care unit due to fever, respiratory distress, pneumonia and cardiomegaly on the chest radiogram. Cardiac consultation was requested due to cardiomegaly. The first emergency echocardiography revealed severe cardiac dysfunction and dilatation of the left ventricle, the ejection fraction (EF) was equal to 15%. Due to fever, cardiomegaly, severe cardiac dysfunction, and elevated troponin level, the patient underwent cardiac failure treatment with a primary diagnosis of myocarditis and also intravenous immunoglobulin was prescribed. She was intubated and in the second echocardiography on the next day, the left coronary to pulmonary artery connection was detected. Due to the patient's general condition, she could not be transferred to the cardiac surgery center. After improvement of the pneumonia and extubation, in the third echocardiography, a mild diastolic flow was seen in the pulmonary artery. Six days following the admission, she was extubated and on the next day, following an episode of vomiting, she underwent cardiopulmonary arrest and expired.

Case 3

A 7-month-old male infant was referred to the cardiac clinic due to failure to thrive (FTT) and a heart murmur. Echocardiography showed dilated cardiomyopathy, EF=20%, in addition to mitral insufficiency. A careful evaluation revealed left coronary artery to pulmonary artery connection and obvious retrograde flow was detected in the left coronary artery. The condition was described for the parents and admission was advised but they did not refer and follow up evaluation was impossible maybe due to referring to another center.

Case 4

A 35-day-old boy was referred to the cardiac clinic due to cardiac murmur. The left ventricle function was decreased in echocardiography, EF=40%, and moderate mitral insufficiency was detected. Evaluation of coronary arteries showed left coronary artery to pulmonary artery connection and obvious diastolic flow and reversal flow were not detected in left coronary artery. The patient was referred to a cardiac surgery center with an initial diagnosis of ALCAPA. In follow up, ALCAPA was confirmed and the patient was operated. After successful heart surgery, the patient has been following up to now.

3. Discussion

In fetal life, the pressure of the pulmonary artery is equal to systemic pressure, allowing for enough myocardial perfusion from the pulmonary artery derived from the anomalous coronary artery (4).

However, after birth, the pulmonary artery contains desaturated blood at a pressure that rapidly falls below systemic pressure (9). Hence, the left ventricle is perfused with desaturated

hemoglobin at low pressure. This predisposes the heart's muscle to ischemia, especially during activities like feeding or crying (4).

After birth, as the resistance of pulmonary arteries decreases, the flow in the left coronary artery and the collateral, tends to pass into the pulmonary artery rather than into the myocardial blood vessels because the pressure in the pulmonary arteries is lower than the coronary. So, a "coronary artery steal" takes places from the coronary arteries into the pulmonary artery (10).

This steal phenomenon further leads to the myocardial ischemia and the ischemia worsens during activities such as feeding and crying (4).

Heart failure may occur because of myocardial infarction in the anterolateral region and/or mitral valve dysfunction due to ischemia of anterolateral papillary muscle (11).

The heart enlarges and congestive heart failure often worsens by myocardial infarction in the anterolateral region and mitral valve dysfunction secondary to a dilated mitral ring or infarction of the papillary muscle (11).

The ALCAPA syndrome has two types: the adult type and the infantile type. Patients with good collateral vessels have the adult type of ALCAPA, and those without well-established collateral vessels have the infantile type. The manifestations and outcomes of these two types of ALCAPA are different (12).

ALCAPA is often isolated but may be associated with other anomalies including patent ductus arteriosus, ventricular septal defect, tetralogy of Fallot, pulmonary atresia, hemitruncus, and coarctation of the aorta (CoA) (3, 4, 11).

The affected Infants experience pneumonia and heart failure in the early weeks and months after birth (13). Dyspnea, feeding intolerance, diaphoresis and FTT are common symptoms that may resemble those of infantile colic, gastroesophageal reflux, and bronchitis (4).

Signs: Infants have episodic attacks of restlessness which are equivalent to angina pectoris (11).

In infancy and early childhood, ALCAPA is characterized by heart failure symptoms (14). While in late childhood and adolescence, mitral insufficiency (due to papillary muscle infarction), and sudden cardiac death are common manifestations of the disease (14)

Dilated cardiomyopathy (DCM) is an important differential diagnosis for ALCAPA and this vascular anomaly should be considered in all children with DCM or isolated mitral insufficiency (11).

Diagnosis: An obvious cardiomegaly and evidence of pulmonary edema are seen in the chest radiogram (4, 13). Abnormal Q wave and inverted T in Lead I and AVL and V4-V6 Leads are found in EKG which can help the diagnosis (13).

2D echocardiography and color Doppler are diagnostic and there is no need for angiography (4). Color Doppler evaluation shows retrograde flow from an aberrant left coronary artery into the pulmonary artery (4). Other findings including hyper-density of the mitral papillary muscles, increased septal collateral flow in color Doppler and significant right coronary artery dilatation help the diagnosis (13). Other diagnostic modalities include CT angiography and MRI (4).

ALCAPA is a rare disease that needs a cardiac operation, but in the case of inappropriate treatment, its mortality reaches up to 90% within the first year of life (3). Of four reported cases in this study, 2 cases expired. One of them died before the surgery and another one immediately after the operation, one case is alive now and we miss follow up of the latter one.

4. Review protocol

A short review was made on online databases for articles in the English language that reported ALCAPA cases in pediatric age. We searched for "children", "pediatric", "ALCAPA", "Anomalous left coronary" and "Bland White Garland Syndrome" in the Google Scholar and PubMed without time limitation. Finally, we found 18 published case reports including 201 cases. See Table 1.

Zheng et al. reported 19 cases during 16 years (12 boys and 7 girls). The age range of them was 2.5 months to 13 years, average of 12 months. Operation mortality was 5 (26%) patients (13).

In Uysal et al.'s study during 20 years, 7 ALCAPA cases were reported and 5 of them were girls while 2 of them were boys. In 5 patients, the clinical manifestation was as heart failure and all of them aged less than 6 months and two of them were referred due to heart murmur (15).

In the case series of Brotherton et al., (11) 5 patients were reported for 5 years, 3 girls and 2 boys, and all of them were under 5 years old. In our case series during 5 years, 4 ALCAPA cases, 3 boys and a girl, were reported and all of them aged less than one year old and two of them were neonate.

Some cases of adulthood ALCAPA were reported by Fierens et al. (16) a 73-year-old woman and Selzman et al. a 23-year-old woman (14).

Symptoms of the disease in infancy are various and can resemble common complications of infancy including colic, gastroesophageal reflux, lactose intolerance, and pneumonia.

The ALCAPA diagnosis can be mistaken by DCM and endocardial fibroelastosis (13).

In the study by Ojala et al., during 27 years, 29 cases were reported of which 4 patients were admitted with the initial diagnosis of pulmonary infection (3).

In our reported patients, an infant was diagnosed due to pneumonia and cardiac insufficiency. In another neonate, the ALCAPA was diagnosed due to cardiac insufficiency and another one due to a heart murmur and FTT. One infant was diagnosed due to the detection of a heart murmur.

For diagnosis of ALCAPA, 2D and color echography are diagnostic and in color Doppler, retrograde flow in the pulmonary artery is observed (4).

In this case series, in the first case, aberrant coronary artery was detected in 2D echocardiography but due to some degrees of pulmonary hypertension, reversed flow was not detected in the pulmonary artery.

In the second case, the aberrant coronary artery was detected too and similarly, the reversed flow was not observed in the pulmonary artery. Some days later, following recovery from pneumonia and extubation, a mild reversed flow was detected in the pulmonary artery.

A clear inverted flow was reported in the third case who was a 7-month-old infant who is justified according to the age of the infant and decreased pulmonary hypertension.

In the first and second cases, ALCAPA was diagnosed in the second echocardiography, it seems that it was due to heart failure and precision in the connection of coronary arteries.

All of our cases had evidence of heart failure and didn't have any other congenital heart disease.

Table 1. Pediatric cases of ALCAPA					
Study Year	Ref.	Location	Cases	Male (%)	Prognosis
Ma 2017	(17)	China	3	2 (67%)	All had post-operative good outcome
Zhang 2017	(18)	China	50	29 (58%)	Overall, the midterm follow-up showed satisfactory recovery of cardiac function after the successful restoration of a dual-coronary arterial system
Walker 2016	(19)	United state	1	0 (0%)	post-operative good outcome
Moeinipour 2016	(12)	Iran	5	4 (80%)	All had post-operative good outcome
Rodriguez 2015	(20)	United state	12	2 (33%)	the overall survival rate was 83%; in the older, asymptomatic children, it was 100%
Muzaffar 2014	(21)	India	53	29 (55%)	There were 5 postoperative hospital deaths with an overall mortality rate of 9.6%
Molaei 2014	(22)	Iran	2	0 (0%)	No follow up
Aliku 2014	(23)	Uganda	1	1 (100%)	Died before operation
Uysal 2013	(15)	Turkey	7	2 (28%)	Three cases have died. Two of these patients died during the postoperative period, and the remaining patient died suddenly during the preoperative period at home.
Szmigielska 2013	(24)	Poland	1	1 (100%)	post-operative good outcome
Smith 2013	(25)	United state	1	1 (100%)	No follow up
Secinaro 2011	(5)	United kingdom	6	3 (50%)	No follow up
Zheng 2010	(13)	China	19	12 (63%)	In addition to the 5 perioperative deaths, 13 patients survived postoperatively without overt symptoms during follow-up period
Ojala 2009	(3)	Finland	29	--	Early postoperative mortality (<30 days) was 17%. No late mortality (>30 days) was detected
Brotherton 2005	(11)	Ireland	5	2 (40%)	Three had post-operative good outcome, one diagnosed post mortem and one died post operation.
Bland 1993	(8)	United state	1	1 (100%)	diagnosed post mortem
Salzer 1993	(26)	Austria	3	2 (67%)	No follow up
Brooks 1885	(6)	Ireland	2	--	No follow up

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5. Conclusions

Although it is rare, in infants and children who were presented with dilated cardiomyopathy, decreased heart function or myocardial infarction, ALCAPA should be considered as an important differential diagnosis and the connection of coronary arteries to aorta should be carefully checked in echocardiography.

6. Foot notes

Author Contributions: Study concept and design: H R Gh., and M R N. Review of data: K B. Drafting of the manuscript: H Z. Critical revision of the manuscript for important intellectual content: H R Gh.

Conflict of Interests: There is not any conflict of interest.

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