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Pentalogy of Fallot in a preterm infant

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Title figure:
Étienne-Louis Arthur Fallot (1850 – 1911) was a French physician who in 1888 described in detail the four anatomical characteristics of tetralogy of Fallot, a congenital heart defect responsible for blue baby syndrome (Source: www.wikipedia.org).

INTRODUCTION

Pentalogy of Fallot is a rare form of cyanotic congenital heart disease, describing an association of atrial septal defect (ASD) with tetralogy of Fallot (TOF: ventricular septal defect (VSD), pulmonary stenosis, misplaced aorta and right ventricular hypertrophy). We report the case of a preterm female infant with pentalogy of Fallot and describe the complications following her surgery.

The mother, a healthy G3 / P1 in her early forties, had had an uneventful pregnancy until the discovery of a fetal cardiac malformation by prenatal ultrasound at 18 weeks of pregnancy. After discussion with her gynecologist and a pediatric cardiologist, the parents decided to continue the pregnancy. Corrective surgery was planned to be performed at around six months of life. Genetic testing for microdeletion 22q11.4 was negative.

At 33 1/7 weeks of gestational age, the mother developed pre-eclampsia and underwent emergency Cesarean section. The female infant was extracted with difficulties due to breech position. She was initially non-reactive, without spontaneous breathing and had a heart rate of < 30 bpm but responded well to standard resuscitation. Within the first minutes, she developed respiratory distress and needed respiratory support by CPAP with a maximum FiO_2 of 0.40. Apgar scores were 2, 9 and 10 at 1, 5, and 10 minutes, respectively. Umbilical cord pH values were within normal range (7.21 / 7.25).

Her birth weight was 1500 g (P5 – 10). Physical examination showed mild cyanosis and a 3 / 6 systolic ejection murmur at the second left intercostal space, radiating to the back. No other abnormalities were found.

Investigations included a chest X-ray, which showed the classic boot-shaped heart (Fig. 1), and echocardiography showing TOF with infundibular, valvular and supravalvular pulmonary stenosis, and a moderate secundum ASD, measuring 6 mm in diameter, with a left-to-right shunt. There was no patent ductus arteriosus.

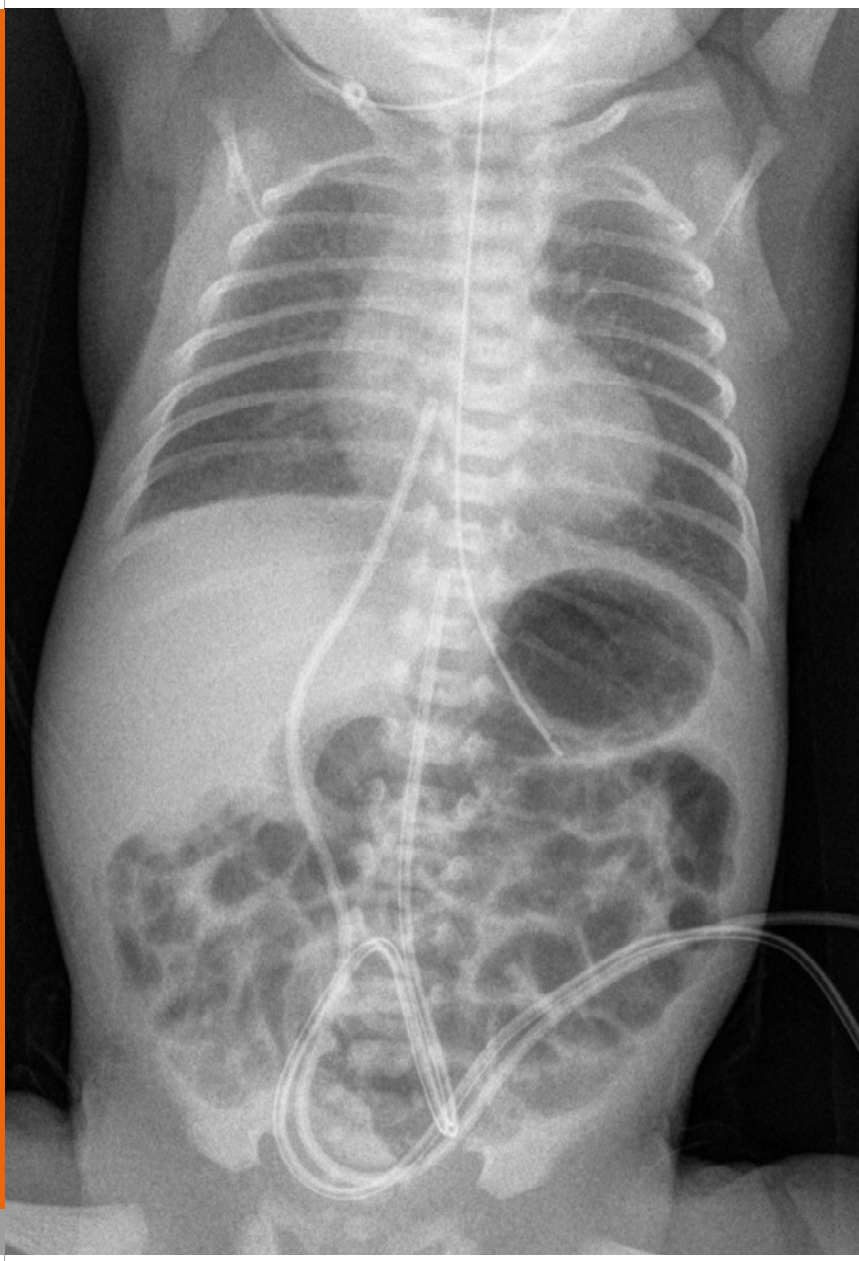

Fig. 1

Babygram following admission: boot-shaped heart and poor pulmonary perfusion.

She remained dependent on non-invasive respiratory support with nasal CPAP with a PEEP of 6 cmH_2O. As there was little effect of supplemental oxygen on the patient's oxygen saturation, it was decided to maintain the FiO_2 between 0.21 and 0.30 with a targeted oxygen saturation of > 60 %. The patient remained hypoxic with arterial paO_2 30 – 33 mmHg. Because of the low birth weight, surgical risks were considered to be too high, and a conservative approach was favored.

Propranolol was introduced at 2.5 mg/kg/dose every 6 hours to slow down the heart rate and to optimize diastolic filling time. This therapy was not effective and was therefore discontinued. Re-opening of the ductus arteriosus by infusion of prostaglandins (maximum dose of 60 ng/kg/min) was attempted in order to increase pulmonary blood flow, however this was ineffective as well, and the patient developed serious side effects (apnea, respiratory acidosis, cutaneous rash and diarrhea). An attempt at raising systemic vascular resistance, and thereby decreasing the right-to-left (R-L) shunt at the ventricular level by continuous infusion of phenylephrine (0.3 mcg/kg/min) was also without clinical benefit. Due to the worsening clinical condition, marked by persistent severe hypoxemia, surgical management was undertaken at 20 days of life (36 weeks of corrected age) with a bodyweight of 1955 g.

The procedure consisted of patch closure of the ventricular septal defect, enlargement of the right ventricular outflow tract with a transannular patch, and closure of the ASD with surgical fenestration. Cardiopulmonary bypass duration was 129 minutes and cross-clamp time was 89 minutes (Fig. 2; Video). Postoperatively, the patient remained intubated and the chest was left open.

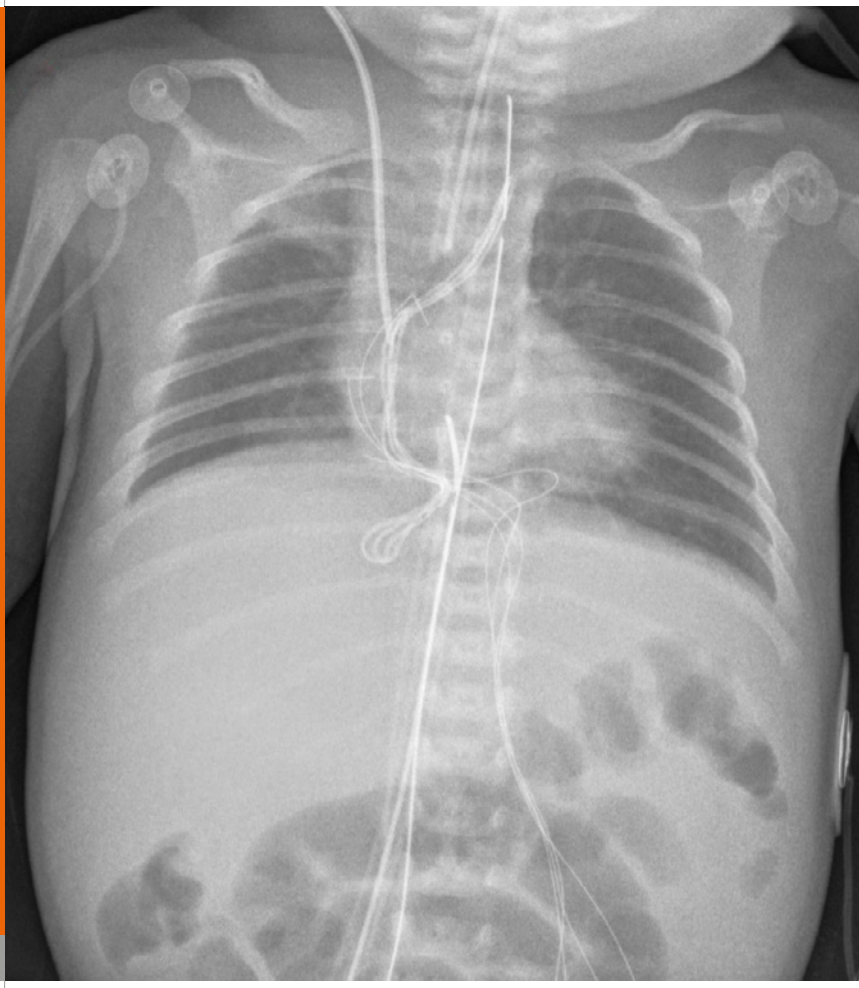

Fig. 2

Early post-operative chest X-ray.

Post-operative echocardiography showed a R-L inter-atrial shunt, biventricular hypertrophy with diastolic dysfunction of the right ventricle, a hypercontractile left ventricle, and free pulmonary insufficiency.

The course during the first post-operative days was marked by significant vasodilatation and capillary leak syndrome, leading to persistent edema. Continuous diuretic treatment was started, and inotropic support was gradually increased. Levosimendan infusion was administered for 48 hours, with good clinical response.

On the fifth post-operative day, the patient developed renal failure requiring peritoneal dialysis, followed by progressive recovery of renal function. In addition, a left-sided chylothorax was noted (Fig. 3 – 5). Treatment with chest tubes and octreotide was started without clinical improvement over a two-week-period. Finally, bilateral pleurectomies with ligation of the thoracic duct were performed. There was no recurrence of chylothorax after this procedure. The chest was closed on the 15th post-operative day.

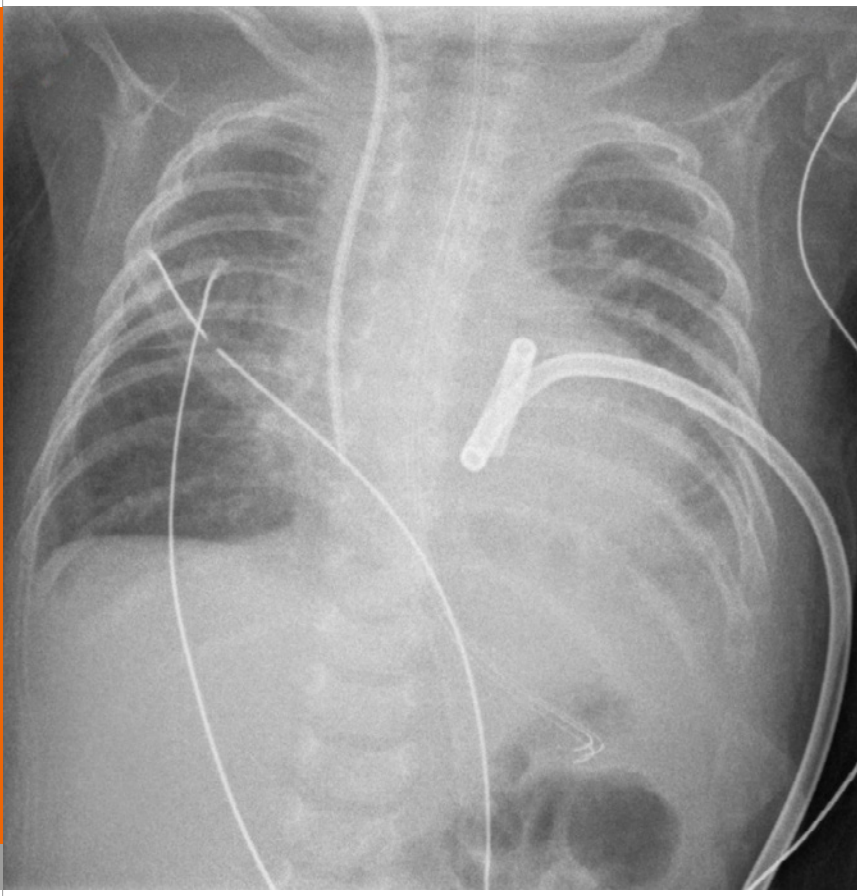

Fig. 3

Left pleural effusion (chylothorax) and chest drain.

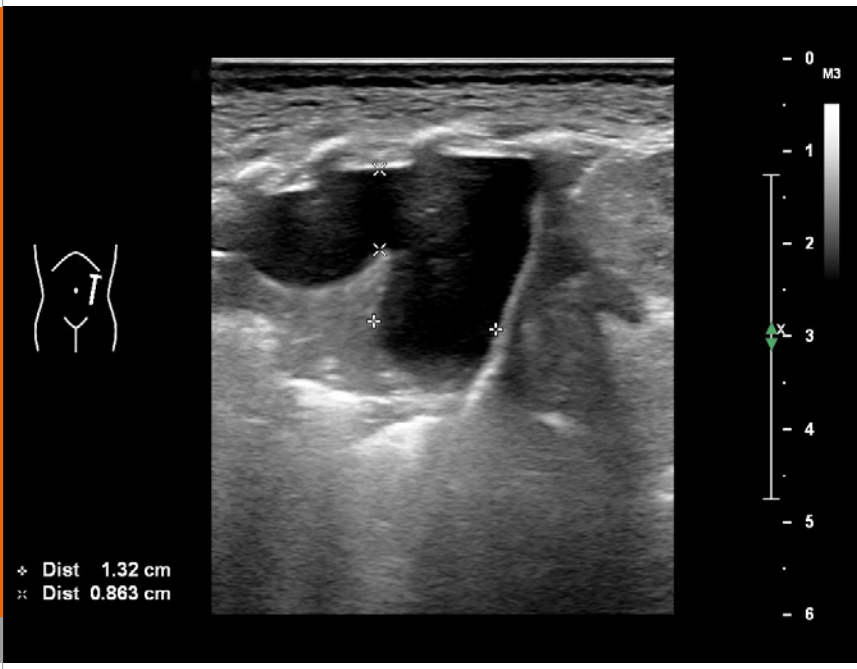

Fig. 4

US examination of the chest: anechoic pleural effusion; note atelectasis of the left lower lobe.

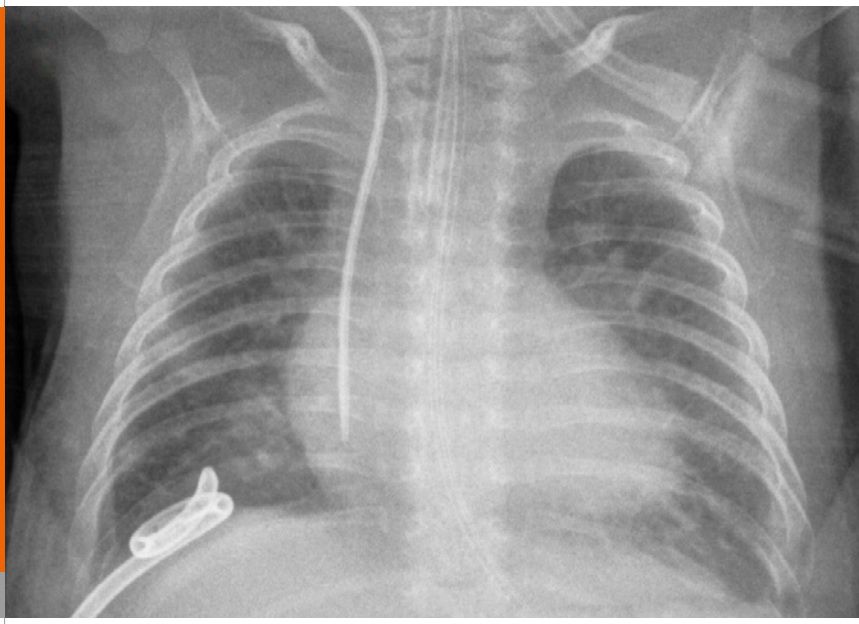

Fig. 5

Chest X-ray following pleurectomy procedure.

Respiratory evolution was marked by a prolonged duration of mechanical ventilation. An underlying BPD-like component was suspected, but corticosteroid treatment for 5 days had no effect.

Neurologic examination showed delayed development with hypotonia and abnormal eye movements. As nystagmus was observed, central blindness was suspected. Cerebral ultrasound and MRI examinations showed ischemic cortical post-central lesions (Fig. 6) and a small subacute stroke of the left caudate nucleus. EEG and auditory provoked potentials were normal.

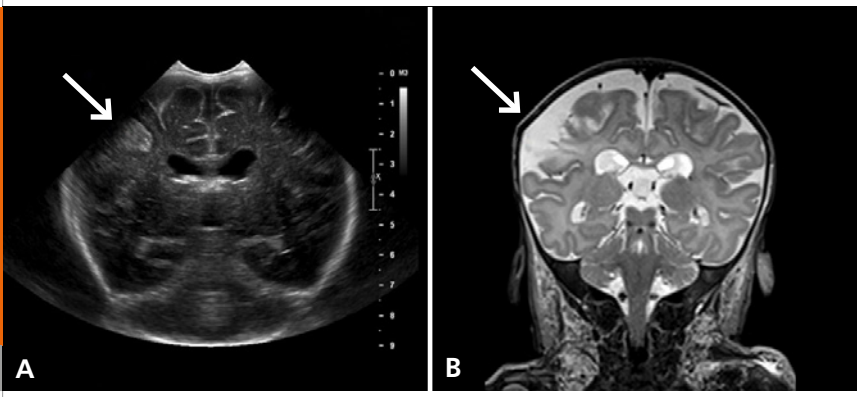

Fig. 6

A) Cerebral ultrasound examination: hyperechoic lesion of the right post-central gyrus (arrow);
B) MRI: coronal T2-weighted images of the chronic ischemic lesion (arrow) shown in Fig. 6 A (10 weeks after surgery).

Due to all these features, with absence of a deletion of 22q11, further genetic examinations were performed by high throughput sequencing of DNA extraction from jugal epithelial cells. However, there was no pathogenic variant in the panel of genes that could explain the clinical features (mutations in the genes of the RAS subfamily).

At 4 and 6 months of adjusted age, examinations showed moderate global developmental delay as well as axial hypotonia. Regular neurodevelopmental follow-up is planned.

DISCUSSION

Congenital heart defects (CHDs) are found in approximately 0.8 – 1 % of live-born infants (1). Owing to advances in prenatal diagnosis, prenatal care, and surgical treatment, the prognosis of these patients if born at term has vastly improved (2). However, extensive literature documents higher risks of mortality, morbidity, and long-term adverse outcomes related to preterm birth in infants with CHDs (3).

A study conducted by 'The New England Regional Infant Cardiac Program' concluded that there is a direct relationship between mortality and birth weight of less than 2 kg for selected types of cardiac surgery. In this study, calculated mortality rates in the less than 2 kg group ranged from 70 % to 100 % compared with 27 % to 86 % for the same diagnostic severity groups in babies born at term (4).

A study published by the Society of Thoracic Surgeons (STS) regarding congenital heart surgery also suggests that body weight of less than 2.5 kg at surgery is consistently associated with a 1.5 to 3 times higher mortality rate in specific cardiovascular procedures in all levels of "Risk Adjustment for Congenital Heart Surgery, RACHS-1" (5). Another study conducted by the STS showed that outcome is worse even for neonates born at early term (37 to 38 weeks of gestation) compared to those born late term (at 39.5 weeks of gestation). These early-term infants have a higher mortality, more post-operative complications and prolonged hospital stay (6).

The main post-operative complication in our patient was chylothorax. Analysis of a multi-institutional database estimates its overall incidence at 2.8 % in children after congenital heart surgery and a rate of 4.2 % in neonates (7). This higher rate in the neonatal population is explained by the more complex lymphatic system and a different and technically more complicated surgical approach. A study published in 2017, comparing different treatment strategies for chylothorax, suggested an increased success rate by the combination of fasting, total parenteral nutrition and octreotide (8). Unfortunately, the failure of this conservative management led to double pleurectomy in our patient.

The presented case of a premature baby with severe CHD demonstrates how difficult it might be to make a decision regarding appropriate treatment and timing for surgery in preterm infants. On the one hand, surgical experience might suggest that it is better to delay surgery until the patient reaches a higher weight, in order to decrease the risk of bypass-related morbidities. On the other hand, there is an increased risk of mortality and morbidity if conservative treatment is ineffective and duration of unacceptable hemodynamics and oxygenation is prolonged (9,10).

Usually, in infants born at term with TOF, surgery is performed between three and six months of life, but it is worth noting that more and more centers advocate

for even earlier primary intervention, in particular in symptomatic patients (8,11).

In summary, premature neonates with CHD represent a high-risk population for morbidity and mortality. It is often difficult to determine the best treatment strategy for a premature patient with CHD. This type of clinical situation requires the collaboration of many specialists, and the decision should be made after balancing all potential risk factors.

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