*Cardiology in the Young*

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# What is pentalogy of Cantrell?

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**Brief Report**

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## Abstract

We present the unusual case of an 8-month-old female with tetralogy of Fallot, coarctation of aorta, and complete presentation of pentalogy of Cantrell. A meta-analysis of 236 cases of Cantrell's syndrome reported in the literature was performed to compare intracardiac findings.

## Case

An 8-month-old female presented for cardiovascular evaluation during a medical mission to Guyana due to a 1-month history of four cyanotic spells with short loss of consciousness. She had been started on propranolol 2mg/kg since the onset of the episodes. The patient was a 40-week gestational-age female born by vaginal delivery without complications. At birth, she had a thoracoabdominal midline defect (Figure 1a). Her birth weight was 2.9 kg (10$^{th}$ percentile), length 47 cm (25$^{th}$ percentile), and head circumference 34 cm (50$^{th}$ percentile). No relevant family history was reported. The patient arrived cyanotic, pale and in mild respiratory distress. Vital signs showed HbO2 saturation at 80%, respiratory rate at 22, heart rate at 116, and temperature at 36.2°C. Current weight was 6.2 kg (<5$^{th}$ percentile) and length 67 cm (25$^{th}$ percentile). On physical evaluation, a sternal cleft had spontaneously closed, with soft tissue and skin in the supraumbilical region. Paradoxical thoracic bulging was noted (Figure 1b). She had a systolic ejection murmur 3/6 in left sternal border, subcostal retractions, clear lungs bilaterally, and adequate peripheral pulses +2. Electrocardiogram showed right axis deviation, right atrial enlargement, and biventricular hypertrophy. Chest X-ray and chest CT showed sternal agenesis, cardiomegaly, and diaphragmatic eventration (Figure 1c,e). Coarctation of the aorta was seen distal to left subclavian artery with a length of 6.51 mm and width of 3 mm (Figure 1d). Echocardiography was remarkable for a ventricular septal defect of 7 mm with right to left shunt and a 20 mm gradient. There was an overriding aorta, right aortic arch with obstruction distal to subclavian artery, subvalvular pulmonary stenosis with a mean gradient 81 mm, and normal coronary arteries. Clinical findings were consistent with the complete pentalogy of Cantrell complicated by tetralogy of Fallot and aortic arch obstruction. Due to the limited resource setting, complex corrective surgery could not be performed. The patient was therefore referred to a tertiary centre where she was evaluated for surgical correction and underwent successful repair of tetralogy of Fallot and reconstruction of aortic coarctation. Three weeks later, the patient was able to go home on anticongestive management.

## Discussion

Cantrell's pentalogy was first described by Cantrell et al. in 1958. It comprises five major congenital defects at upper midline abdominal wall, lower sternum, anterior diaphragm, pericardial diaphragm, and intracardiac abnormalities.[1] A developmental failure of appropriated segments of the mesoderm is the embryologic background of the midline defects.[2] It occurs in approximately 1 in 65,000 to 200,000 live births globally.[3] Toyama's classification scheme categorises Cantrell's pentalogy into three classes. Class one involves a definite diagnosis with all five defects, while class two indicates a probable diagnosis with four defects, including ventral wall defect and intracardiac abnormalities. Class three signifies incomplete expression with a sternal abnormality and varied combinations of defects.[4] Incomplete expression of the syndrome has been well-recognised in the literature, while the full spectrum has been rare. Complete pentalogy of Cantrell carries a high mortality whether being treated surgically or not, with most patients expiring during the early days of life. The surgical approach must be customised to the patient's specific anatomy, acknowledging significant variations among cases. The primary goal is to achieve cardiopulmonary stability, which is usually already present. Next, it is crucial to cover the mediastinum to prevent sepsis, which, in cases such as ours, was present at birth due to in utero midline closure. Therefore, some patients may require staged surgery, while others can be corrected in a single procedure.

The degree of CHD is a source of major morbidity.[4] Thus, we performed our own meta-analysis using patients with pentalogy of Cantrell reported in the literature from PubMed and

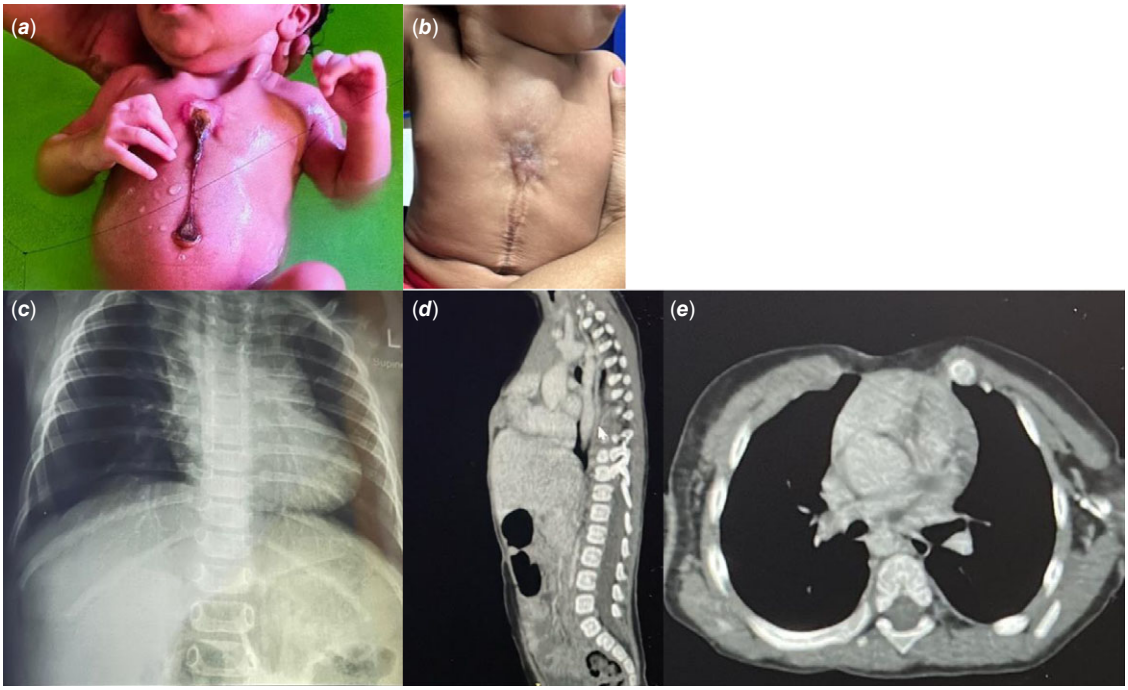


**Figure 1.** (***a***) Sternal cleft with soft tissue and skin in newborn patient (***b***) Sternal cleft with closed soft tissue skin in supraumbilical region and paradoxical thoracic bulging at 8-month-old. (***c***) Anteroposterior view remarkable for diaphragmatic hernia (***d***) Sagittal view shows diaphragmatic hernia and coarctation of the aorta (***e***)Transverse view shows sternal cleft.

Medline database to compare intracardiac findings, outcome of patients, and the most common associated malformations. With the following criteria, we included patients reported between 1972 and 2023, described in the English and Spanish literature. "Cantrell", "Pentalogy of Cantrell", "Cantrell's pentalogy", and "Cantrell syndrome" were used to search literature. We excluded patients reported in the literature without a definite diagnosis of Pentalogy of Cantrell, described in languages other than English or Spanish, and those reported after 2023 and not found using our literature search in PubMed or Medline. With these criteria, a total of 236 cases were included. 31% are female, 28% male, and 41% have an unreported biological sex. Of these cases, 22.5% were alive at the time of report, 39% were stillborn, 26.3% expired, and in 12.2%, the outcome was not reported.

The most common intracardiac findings in patients with Pentalogy of Cantrell are ventricular septal defect (32.6%), atrial septal defect (26.7%), tetralogy of Fallot (12%), double outlet right ventricle (7.6%), ductus arteriosus (7.6%), left superior vena cava (6.8%), pulmonary stenosis (6%), truncus arteriosus (5.1%), and single ventricle (5.1%), depicted in Table 1. Other intracardiac findings are dextrocardia (4.3%), anomalous pulmonary veins return (4.2%), hypoplastic left ventricle (4.2%), transposition of great arteries (3.4%), tricuspid atresia (3.4%), coarctation of the aorta (3%), arch anomalies (3%), single atrium (2.6%), atrio-ventricular septal defect (2.1%), double superior vena cava (1.7%), and anomalous coronary artery origin (1.2%). Less than 1% of patients presented with Ebstein's anomaly, bicuspid pulmonary valve, atresia of aortic valve, hypoplastic right ventricle, mitral stenosis, pulmonary valve atresia, and single coronary ostium. One-fifth of patients had no specific intracardiac findings and one-tenth of patients had a normal cardiac examination. Extracardiac abnormalities were also reported including: ectopia cordis (45.8%), ventricular diverticulum (12.7%), aberrant common carotid artery (0.4%), and hypoplastic abdominal aorta (0.4%). The most common associated malformations seen with Pentalogy of Cantrell were exencephaly, spinal dysraphism, scoliosis, cleft lip, cleft palate, talipes equinovarus, limb agenesis, and low set ears. Although no specific genetic mutation has been identified as the cause of this syndrome, associations with trisomy 21, trisomy 18, Turner's syndrome, and severe Goltz-Gorlin syndrome were observed in a small percentage of patients in our study. The prognosis for pentalogy of Cantrell depends on the type and severity of associated malformations, presence of ectopic heart, and intracardiac anomalies. Patients who underwent surgical repair around 8 months of age tend to have a better prognosis, whereas most non-survivors were operated on the first day after birth.

The case highlights an unusual presentation of this syndrome as it is the first reported in literature to present with both tetralogy of Fallot and coarctation of the aorta. Intracardiac findings are a major prognostic factor in pentalogy of Cantrell; thus, comparing these findings across a 250-year span in our meta-analysis allows us to better understand the evolving patterns of cardiac anomalies associated with the syndrome. Through a comprehensive analysis of intracardiac findings over time, our aim is to refine patient care strategies and improve outcomes for patients diagnosed with pentalogy of Cantrell. Advances in research for pentalogy of Cantrell include a murine model developed by Aldeiri et al., in which genetic ablation of TGFβRII in Transgelin (Tagln) expressing cells results in midline closure anomalies similar to those seen in pentalogy of Cantrell. This establishes a reliable model to investigate the morphological alterations underlying Cantrell syndrome, providing the first mechanistic insight into the development of this syndrome.[5]

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**Table 1.** Prevalence of intracardiac and extracardiac findings in Cantrell syndrome

| Intracardiac findings | Prevalence (%) |
|---|---|
| Ventricular septal defect | 32.6 |
| Atrial septal defect | 26.7 |
| Tetralogy of Fallot | 12.0 |
| Double outlet right ventricle | 7.6 |
| Ductus arteriosus | 7.6 |
| Left superior vena cava | 6.8 |
| Pulmonary stenosis | 6.0 |
| Truncus arteriosus | 5.1 |
| Single ventricle | 5.1 |
| Dextrocardia | 4.3 |
| Anomalous pulmonary veins return | 4.2 |
| Hypoplastic left ventricle | 4.2 |
| Transposition of great arteries | 3.4 |
| Tricuspid atresia | 3.4 |
| Coarctation of the aorta | 3.0 |
| Arch anomalies | 3.0 |
| Single atrium | 2.6 |
| Atrioventricular septal defect | 2.1 |
| Double superior vena cava | 1.7 |
| Anomalous coronary artery origin | 1.2 |
| Ebstein's anomaly | <1 |
| Bicuspid pulmonary valve | <1 |
| Atresia of aortic valve | <1 |
| Hypoplastic right ventricle | <1 |
| Mitral stenosis | <1 |
| Pulmonary valve atresia | <1 |
| Single coronary ostium | <1 |
| No specific intracardiac findings | 20.0 |
| Normal cardiac examination | 10.0 |
| **Extracardiac abnormalities** | **Prevalence (%)** |
| Ectopia cordis | 45.8 |
| Ventricular diverticulum | 12.7 |
| Aberrant common carotid artery | 0.4 |
| Hypoplastic abdominal aorta | 0.4 |

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**Ethical standards.** Consent was given by Georgetown Public Hospital Corporation and parents. Institutional Review Board approval is not applicable for this study.

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