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## **PENTALOGY OF CANTRELL. A STILLBIRTH CASE REPORT**

**Keywords:** Pentalogy of Cantrell; Mesoderm; Gastroschisis.

**Palabras clave:** Pentalogía de Cantrell; Mesodermo; Gastrosquisis.

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## ABSTRACT

**Introduction:** Pentalogy of Cantrell is a rare congenital disorder characterized by midline birth anomalies. Its embryological origins are related to anomalies of the abdominal wall that prevent the closure of the thorax. Its etiology is not yet clear, but it has been associated with a failure of migration of the lateral plate mesoderm to the midline.

**Case description:** A stillbirth at 25.2 weeks of gestation diagnosed with pentalogy of Cantrell. The mother was a 14-year-old teenager with no relevant history of disease. An obstetric ultrasound was performed at 19 weeks of gestation and revealed findings suggestive of pentalogy of Cantrell. The mother was informed of the potential risks and future complications for the fetus, yet she chose to continue with the pregnancy. At 25.2 weeks of gestation, the mother went to the emergency department due to pain in the hypogastrium accompanied by moderate vaginal bleeding and absence of fetal activity. Once fetal death was confirmed by ultrasound, labor was induced, resulting in stillbirth with anencephaly, thoracic hypoplasia, gastroschisis, and eventration of the liver.

**Conclusions:** Adequate antenatal care, including strict ultrasound follow-up, is essential to detect future complications in the fetus; to provide advice on possible malformations incompatible with life, such as pentalogy of Cantrell; and to determine the best therapeutic approach.

## RESUMEN

**Introducción.** La pentalogía de Cantrell es una anomalía congénita rara que se caracteriza por malformaciones en la línea media del cuerpo, y cuyos orígenes embriológicos están relacionados con anomalías de la pared abdominal que impiden el cierre del tórax. Su etiología aun no es clara, pero se ha asociado con una falla de la migración de los pliegues del mesodermo lateral a la línea media.

**Presentación del caso.** Mortinato de 25.2 semanas de gestación diagnosticado con pentalogía de Cantrell. La madre era una menor de 14 años sin antecedentes patológicos. A las 19 semanas de gestación se realizó ecografía obstétrica que mostró imágenes sugestivas de pentalogía de Cantrell, y se le explicó a la gestante los riesgos y complicaciones futuras que presentaría el feto, pero esta decidió continuar con el embarazo. A las 25.2 semanas de gestación, la joven acudió al servicio de urgencias por dolor en hipogastrio acompañado de sangrado vaginal moderado y ausencia de actividad fetal. Una vez confirmada la muerte fetal mediante ecografía, se indujo el trabajo de parto, obteniéndose mortinato con anencefalia, hipoplasia de caja torácica, gastrosquisis y eventración del hígado.

**Conclusiones.** La realización de adecuados controles prenatales, en los cuales se realice un seguimiento ecográfico estricto, es fundamental para detectar futuras complicaciones en el feto; brindar asesoría sobre posibles malformaciones que sean incompatibles con la vida, como la pentalogía de Cantrell, y establecer las mejores alternativas de manejo.

## INTRODUCTION

Pentalogy of Cantrell was first described in 1958 when Cantrell *et al.* (1) published a series of five cases about this abnormality. It was defined as a collection of four midline body defects (specifically in the abdominal wall, sternum, diaphragm, pericardium and heart) accompanied by some intracardiac defect (2). Regarding intracardiac abnormalities, Madi *et al.* (3) state that ventricular septal and atrial septal defects are present in 100% and 53% of cases with this disorder, respectively, while tetralogy of Fallot and ventricular diverticula are found in 20% each (3).

This is a rare disorder considering that only about 250 cases have been reported worldwide (4). Thus, it is a rare syndrome with an estimated incidence that varies from 1 cases per 65 000 to 200 000 live births in the different reported series (5-7). Its spectrum is variable and depends on the five basic defects that define it: a midline supraumbilical abdominal wall defect, defect of the lower sternum, defect of the anterior diaphragm, defect in the pericardium, and intra-cardiac defects (8).

As described by Mărginean *et al.* (9), pentalogy of Cantrell was classified by Toyama (10) into three classes according to the number of defects in each patient. Class 1 or definitive diagnosis has all 5 defects; class 2 or probable diagnosis involves 4 defects; and class 3 or incomplete expression comprises 3 defects.

Pentalogy of Cantrell or thoracoabdominal syndrome is characterized by the variable association of midline body defects with thoracoabdominal wall defects and its differential diagnosis is limb-body wall complex. Both conditions are of unknown cause and early origin but can be explained by an abnormal mesoderm development (11).

The available literature on pentalogy of Cantrell is scarce, mainly because it is a rare disease with great variability in its signs and symptoms of presentation. Reports on this subject are therefore a valuable resource, as they can serve as a basis for future research (12).

Periodic obstetric ultrasound is recommended to detect and treat fetal anomalies since it allows providing optimal perinatal care, considering that approximately half of structural anomalies can be detected in the first trimester. Some of anomalies include anencephaly, abdominal wall defects, holoprosencephaly, and cystic hygromas. However, due to the stages of embryonic development of some organs, it should be kept in mind that certain anomalies are observed at a later gestational age. Similarly, it is worth noting that, as stated by Saldarriaga-Gil *et al.* (13), the second trimester is the best stage for study to identify fetal structural anomalies.

The following is a case of pentalogy of Cantrell associated with craniofacial, limb and reproductive system defects, which was suspected by ultrasound at week 19 of gestation and confirmed *postmortem*. This is the seventh case of this anomaly reported in Colombia in the last 10 years and the second case in a female patient (8,9,14-17).

## CASE PRESENTATION

Stillbirth of 25.2 weeks in whom multiple malformations were identified at 19 weeks of gestation via obstetric ultrasound, leading to the suspicion of a diagnosis of pentalogy of Cantrell. The mother was a 14-year-old mestizo girl from the rural area of La Sierra, department of Cauca, Colombia. No degree of consanguinity with the father was determined, but it was established that this was the mother's first pregnancy.

The first antenatal check-up was carried out in September 2019, when the mother was 19.4 weeks pregnant, and the laboratory tests ordered at that time showed the following results: negative hepatitis B surface antigen; negative IgG and IgM toxoplasma antibodies; positive IgG and negative IgM antibodies against rubella; and positive IgG and negative IgM antibodies against cytomegalovirus. During this first check-up, an ultrasound was also performed, showing a fetus with anencephaly, ectopia cordis, hypoplastic left heart syndrome, diaphragmatic hernia, hyperlordosis, and equinovarus deformity in the right foot (findings compatible with pentalogy of Cantrell). Thus, counseling on voluntary termination of pregnancy was performed due to the severe malformations in the fetus and the risks and future complications; however, the mother preferred to continue with the pregnancy.

At 25.2 weeks of gestation, the mother was admitted to the emergency department of the Hospital Universitario San José de Popayán Empresa Social del Estado due to an 8-hour history of colicky abdominal pain in the hypogastrium accompanied by moderate vaginal bleeding and absence of fetal movements. Obstetric ultrasound was performed, which confirmed fetal death, so labor was induced.

A dead fetus was obtained after delivery, which was sent to the pathology service, where a female stillbirth with height of 23cm, weight of 555g and external malformations was identified. External malformations included amniotic bands attached to occiput and placenta; exencephaly; asymmetric, separated nostrils with ipsilateral nostril and hypoplastic nasal wings, suggesting arrested facial development; broad and flattened nasal bridge; cleft palate; low-set ears; short neck; hypoplasia of the right upper limb; right ectrodactyly; hypoplasia of the right side of the thoracic cage; gastroschisis; ventral hernia with liver content; equinovarus foot deformity; scoliosis with curvature of the spine to the right; and left ovary agenesis (Figures 1, 2, 3). The morphological detail of the images highlights the midline deviation in the face (Figure 1).

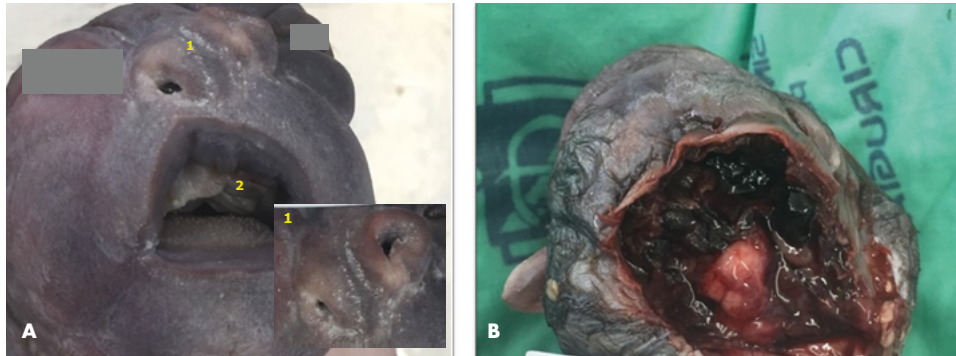


Figure 1. Photographic record of the head of the stillbirth. A) face (1. asymmetric and separated nostrils with ipsilateral hypoplasia of the nostril and nasal wings; and 2. cleft palate); B) medial parieto-occipital region (amniotic band).

Source: Photographs obtained during the study.

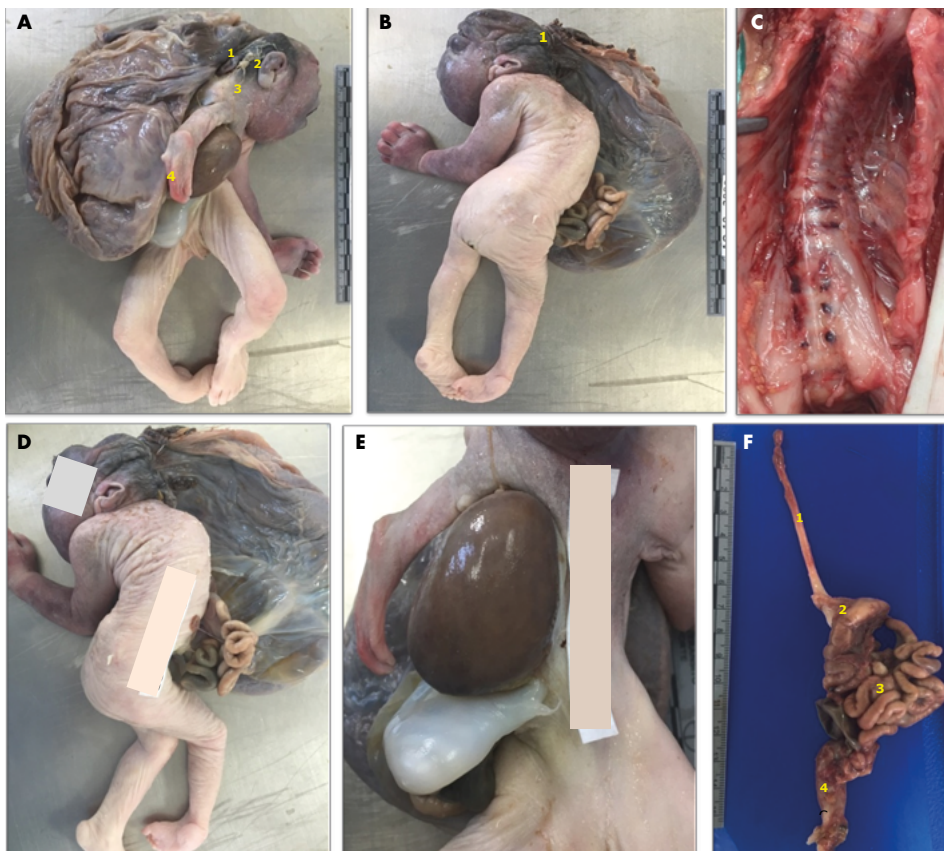


Figure 2. Photographic record of body defects of the stillbirth. A) right lateral view (1. amniotic bands attached to occiput and placenta, 2. low-set ears, 3. short neck, and 4. hypoplasia of the right upper limb ); B) left posterolateral view; C) anterior spinal dissection; D) right lateral view (gastroschisis); E) anterior view (liver outside the body and gastroschisis); F) dissection of the intestinal tract (1. esophagus, 2. stomach, 3. small intestine, and 4. rectum).

Source: Photographs obtained during the study.



During the internal examination of the fetus, it was noted that hypoplasia of the thoracic cage was predominant with asymmetry on the right side and that the diaphragm separated the thoracoabdominal region, although it was displaced to the right and attached to the Glisson's capsule in the right lobe. It was also found that the liver protruded from the abdominal wall and that the area below the thoracic cage was adjacent to the psoas muscles, which were fused. The lungs weighed 3.5g and their overall size was reduced. The short inferior vena cava showed no intracardiac defects (Figures 3, 4, 5 and 6).

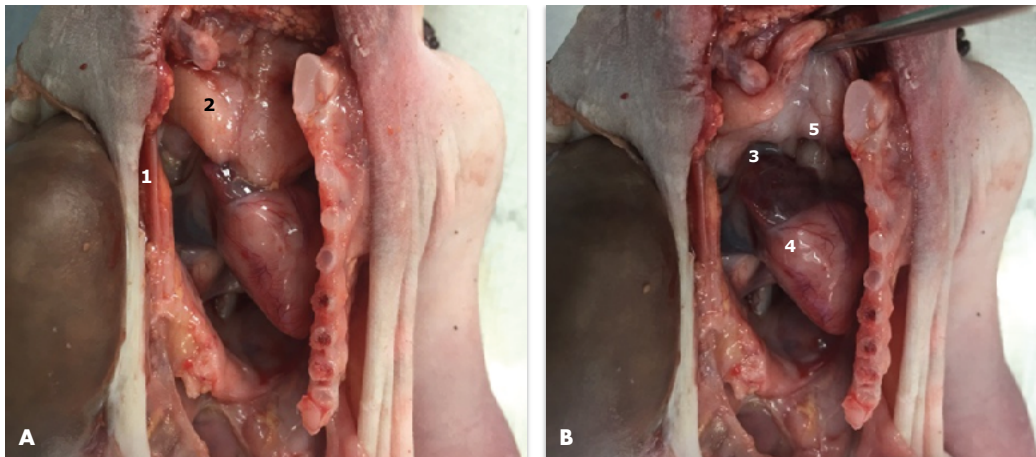


Figure 3. Thoracic cavity dissection. 1) hypoplasia on the right side of the thoracic cage; 2) thymus; 3) right atrium; 4) right ventricle; 5) normal arrangement of the main vessels. Source: Photographs obtained during the study.

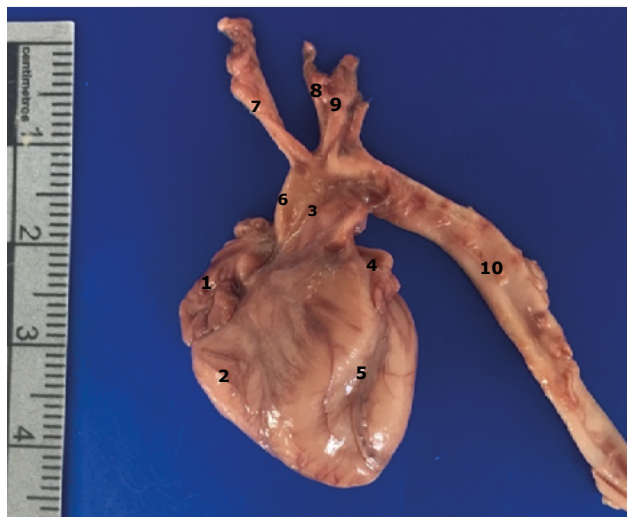


Figure 4. Heart and great vessels. 1) right atrium; 2) right ventricle; 3) pulmonary artery; 4) left atrium; 5) left ventricle; 6) ascending aorta; 7) brachiocephalic trunk; 8) left common carotid artery; 9) left subclavian artery; 10) descending aorta. Source: Photographs obtained during the study.



Figure 5. Viscera. 1) posterior aspect of the heart; 2) diaphragm; 3) inferior vena cava; 4) left liver lobe.

Source: Photographs obtained during the study.

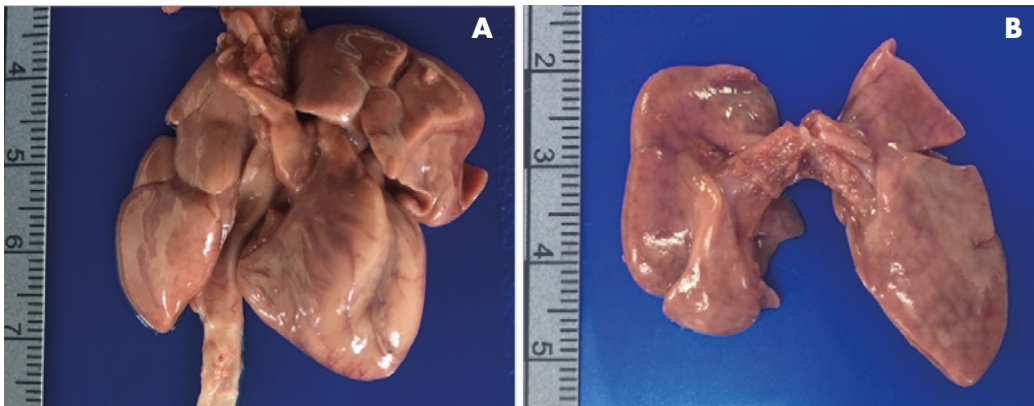


Figure 6. A) Right and left lungs, heart and great vessels; B) lungs.

Source: Photographs obtained during the study.

It was also evident that the reproductive system of the fetus was not fully formed and consisted of a uterus, right ovary and fallopian tubes hypoplasia, and agenesis of the left ovary (Figure 7).

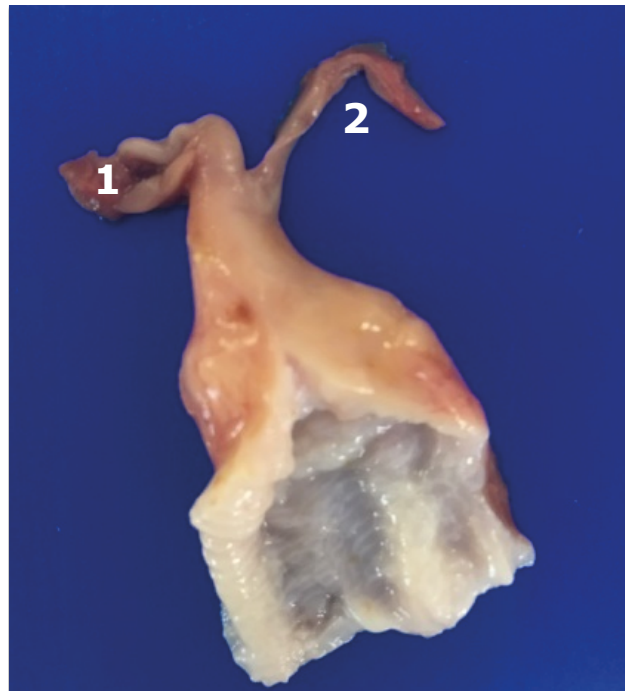


Figure 7. Uterus. 1) right ovary; 2) left fallopian tube.

Source: Photographs obtained during the study.

The histology of the organs showed that in the lung parenchyma there was a bilateral, but predominantly right, decrease in the alveolar surface area, with hypertrophy of the tunica media (Figure 8).

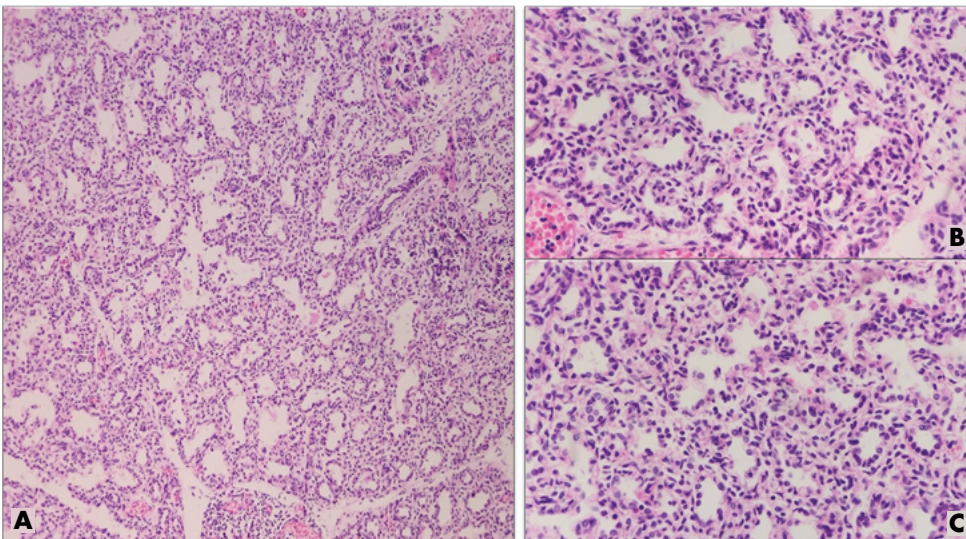


Figure 8. Hematoxylin and eosin staining of the right lung. A) 10X view; B) and C) 40X views.

Source: Photographs obtained during the study.



Microscopic examination of the placenta revealed 30% of tertiary chorionic villi with hyalinization, amniotic bands, chronic villitis, chorioamnionitis, and chronic deciduitis with microabscesses.

All the findings described here are part of the spectrum of partial expression or class 2 presentation of pentalogy of Cantrell (9,10), a syndrome suspected based on ultrasound findings and confirmed *postmortem*. The presence of craniofacial, musculoskeletal and reproductive system defects in the fetus also confirms the diagnosis, as they are described in the literature as additional and rare manifestations of this genetic anomaly (9,18,19).

## DISCUSSION

Pentalogy of Cantrell is a poorly described syndrome, but it has characteristic findings that allow to establish its diagnosis. Such findings comprise five basic defects: a midline supraumbilical abdominal wall, defect of the lower sternum, defect of the anterior diaphragm, defect in the pericardium, and intra-cardiac defects (19,20).

Embryological mechanisms involved in the development of pentalogy of Cantrell include abnormal mesoderm development (diaphragmatic, pericardial, and cardiac defects) and failure of fusion of lateral folds (sternal and abdominal wall defect) with changes in the development of a segment of the lateral plate mesoderm between 14 and 18 days of gestation. This leads to failure of the *septum transversum* to develop and failure of the somatic layer of the lateral plate mesoderm to migrate toward the midline, leaving the thoracoabdominal organs exposed (21).

Pentalogy of Cantrell is also characterized by damage to the amnion that may produce fiber-like bands that limit the development of the fetus, causing constriction on already formed structures (16,17). In the present case, a sternal defect with hypoplasia of the right side of the thoracic cage and thoracoabdominal midline defects, such as gastroschisis and liver eventration, were observed. Likewise, it was established that the fetus had ectopia cordis, although no pericardium defects or intracardiac anomalies were found, which does not rule out the diagnosis of pentalogy of Cantrell (10) because it has been proposed that this disorder has a wide spectrum of presentation, and its characteristics depend on the stage of development in which the defects occur (4).

Some of the causes described for pentalogy of Cantrell include aneuploidies such as trisomies 13 and 18; viral infections; mother's intake of teratogenic agents such as thalidomide, warfarin, and quinidine; vitamin A deficiency in the mother during pregnancy; and some type of familial tendency, with an X-linked dominant inheritance pattern and alteration of the region Xq25-Xq26,1, which is a characteristic of thoracoabdominal syndrome (8,15). However, no association with factors predisposing to malformations was evident in the present case. It should be noted that the patient did not undergo karyotype testing because the mother was young and reported no medical, pharmacological or intoxication history.

Pentalogy of Cantrell is more prevalent in men, with a 1.35:1 ratio (22,23), so this case is of great interest.

One of the described causes of pentalogy of Cantrell is amniotic rupture in cases of ectopia cordis (9), which was evidenced in the case reported here.

Routine ultrasounds performed during antenatal checkups (between 12 and 14 weeks and 19 to 24 weeks of gestation) are extremely helpful in diagnosing pentalogy of Cantrell (19,24). When this disease is suspected in the first trimester of gestation, it may be necessary to carry out complementary studies such as fetal echocardiogram, magnetic resonance imaging and biopsy of the chorial villi, which allows for G- or Q-banding karyotype testing. Such studies are essential, as they allow the identification of the full spectrum of disease presentation and offer the best advice regarding prognosis and follow-up (25). Moreover, early detection of congenital defects allows to offer interdisciplinary support from the beginning of pregnancy, as well as assistance in decision-making about anomalies incompatible with life.

Finally, it is important to mention that during autopsies it is essential to make a detailed macroscopic and microscopic documentation of the findings, that is, a complete record of the malformations of the body must be made so that this, together with the pathologist's report, allows to establish the diagnosis that caused the death. In the present case, the findings corroborated at the autopsy highlight the importance of performing this procedure in cases of multiple congenital anomalies, as it allows the family and even the scientific community to learn about the complications that led to the termination of a pregnancy (26-28).

## CONCLUSIONS

Adequate antenatal care, including strict ultrasound follow-up, is essential to detect future complications in the fetus, as well as to provide advice on possible malformations incompatible with life, such as pentalogy of Cantrell, and to determine the best therapeutic approach. Furthermore, autopsies on fetuses with multiple congenital anomalies are indispensable because, as in this case, they allow for the identification of alterations not detected on ultrasound or external physical examination.

## ETHICAL CONSIDERATIONS

The informed consent of the legal guardian of the 14-year-old girl who gave birth to the stillborn that is the subject of this report was obtained.

## CONFLICT OF INTEREST

None stated by the authors.

## FUNDING

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## REFERENCES

1. Cantrell JR, Haller JA, Ravitch MM. A syndrome of congenital defects involving the abdominal wall, sternum, diaphragm, pericardium and heart. *Surg Gynecol Obstet.* 1958; 107: 602–614
2. Kaouthar H, Jihen A, Faten J, Hela M, Fatma O, Lilia C, et al. Cardiac anomalies in Cantrell's pentalogy: From ventricular diverticulum to complete thoracic ectopia cordis. *Cardiol Tunis.* 2013;9(1):94–7
3. Madi JM, Festugatto JR, Rizzon M, Agostini AP, Araújo BF, García RMR. Ectopia Cordis Associated with Pentalogy of Cantrell—A Case Report. *Rev Bras Ginecol Obstet.* 2019;41(5):352–6. <https://doi.org/hmfb>.
4. Williams AP, Marayati R, Beierle EA. Pentalogy of Cantrell. *Semin Pediatr Surg.* 2019;28(2):106–10. <https://doi.org/hmfc>.
5. Türkçapar AF, Sargin Oruc A, Öksüzoglu A, Danişman N. Diagnosis of Pentalogy of Cantrell in the first trimester using transvaginal sonography and color Doppler. *Case Rep Obstet Gynecol* 2015;2015:179298. <https://doi.org/gb589h>.
6. Carmi R, Boughman JA. Pentalogy of Cantrell and associated midline anomalies: a possible ventral midline developmental field. *Am J Med Genet.* 1992;42(1):90–5. <https://doi.org/b7sgqz>.
7. Vazquez-Jimenez JF, Eberhard GM, Daebritz S, Keutel J, Nishigaki K, Huegel W, et al. Cantrell's syndrome: a challenge to the surgeon. *Ann Thorac Surg.* 1998;65(4):1178–85. <https://doi.org/csn85k>.
8. Saldarriaga W. Pentalogía de Cantrell. Reporte de caso. *Salud Uninorte. Barranquilla.* 2014;30(3):505–12.
9. Mărginean C, Mărginean CO, Gozar L, Meliț LE, Suci HT, Gozar H, et al. Cantrell Syndrome—A Rare Complex Congenital Anomaly: A Case Report and Literature Review. *Front Pediatr.* 2018;6:201. <https://doi.org/gdxdn2>.
10. Toyama WM. Combined congenital defects of the anterior abdominal wall, sternum, diaphragm, pericardium, and heart: a case report and review of the syndrome. *Pediatrics.* 1972;50(5):778–92.
11. Ayala-Zapata S, Perlaza NA, Calle A, Saldarriaga W. Síndrome toracoabdominal: reporte de un caso en un museo de morfología. *Rev. Cienc. Salud.* 2017;15(2):293–9. <https://doi.org/hmfd>.
12. Edwards L, Hui L. First and second trimester screening for fetal structural anomalies. *Semin Fetal Neonatal Med.* 2018;23(2):102–11. <https://doi.org/gdg9nx>.
13. Saldarriaga-Gil W, Ayala-Zapata S, Ramírez-Cheyne JA, Isaza C. Pentalogy of Cantrell and amniotic bands: A case report and review of the literature. *Rev Colomb Obstet Ginecol.* 2014;65(3):243–9. <https://doi.org/hmdq>.
14. Riaño CE, Otoya JP, Gentile JI, Mosquera W, Socarrás JA, Castro JM, et al. Pentalogía de Cantrell (ectopia cordis): reporte de un caso. *Rev Colomb Cardiol.* 2010;17(6):286–90.
15. Morantes J, Morales C, Gómez-Hoyos D, Roza JP. Pentalogía de Cantrell, sobrevida a 6 meses. Reporte de un caso y revisión de la literatura. *Ciencia y Gestión.* 2019 [cited 2022 Mar 18];1:29–34. Available from: <https://bit.ly/36847Gg>.
16. Pachajoa H. Pentalogía de Cantrell en el primer gemelo de un embarazo gemelar monocigótico: presentación de un caso y revisión de la literatura. *Rev Colomb Obstet Ginecol.* 2011;62(1):94–7. <https://doi.org/hm28>.
17. Siega-Riz AM, Herring AH, Olshan AF, Smith J, Moore C. The joint effects of maternal pre-pregnancy body mass index and age on the risk of gastroschisis. *Paediatr Perinat Epidemiol.* 2009;23(1):51–7. <https://doi.org/fhc4x7>.

18. Trejo-González AA, De los Santos-Sánchez DJ, Trejo-Gonzalez PC. Pentalogía de Cantrell. *Revista Médica MD*. 2018;10(1):53-5.
19. Cuesta-Guardiola T, Aluja-Méndez A, Pérez-Fernández-Pacheco R, Gámez-Alderete F, Ortiz-Quintana L, De León-Luis J. Diagnóstico prenatal de Pentalogía de Cantrell. *Prog Obstet Ginecol*. 2016;59(3):170-4. <https://doi.org/f3jgst>.
20. Jnah AJ, Newberry DM, England A. Pentalogy of Cantrell: Case Report With Review of the Literature. *Adv Neonatal Care*. 2015;15(4):261-8. <https://doi.org/hm3c>.
21. Caici D, Sepúlveda W. Ultrasonografía en obstetricia y diagnóstico prenatal. 2<sup>nd</sup> Ed. Buenos Aires: Journal; 2018.
22. Amorim E, Filho NAS, Sarmiento PA, Lacerda JS, Ferreira WC, Mocelin PR, et al. Pentalogy of Cantrell with Sternum Agenesis — A Case Report. *Open Journal of Thoracic Surgery*. 2020;10:1-5. <https://doi.org/hm3d>.
23. Chen CP, Hsu CY, Tzen CY, Chern SR, Wang W. Prenatal diagnosis of pentalogy of Cantrell associated with hypoplasia of the right upper limb and ectrodactyly. *Prenat Diagn*. 2007;27(1):86-7. <https://doi.org/b3wwc7>.
24. Saldarriaga W, Artuz A. Ayudas Diagnósticas en Obstetricia. In: Fundamentos en Ginecología y Obstetricia. Cali: Programa Editorial Universidad del Valle;2010. p. 265-277.
25. Madi JM, Festugatto JR, Rizzon M, Agostini AP, Araújo BF De, Garcia RMR. Ectopia Cordis Associated with Pentalogy of Cantrell—A Case Report. *Rev Bras Ginecol Obstet*. 2019;41(5):352-6. <https://doi.org/hmfb>.
26. Connolly AJ, Finkbeiner WE, Ursell PC, Davis RL. Autopsy Pathology: A Manual and Atlas. 2nd ed. Philadelphia: Elsevier; 2009.
27. Olaya-Contreras M. Introducción a la Patología Perinatal. Bogotá D.C.; 2014 [cited 2022 mar 24]. Available from: <https://apple.co/3uxb7F8>.
28. Pineda-Leguizamo R, Miranda-Navales G, Villasís-Keever MA. La importancia de los reportes de casos clínicos en la investigación. *Rev. alerg. Méx*. 2018;65(1):92-8. <https://doi.org/gg5qmm>.