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Case Series

Congenital cardiac anomalies detected in fetal autopsies: a case series

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ABSTRACT

Congenital cardiac anomalies are among the most common structural malformations of the developing fetus and account for a high percentage of fetal morbidity and mortality. Timely detection and comprehensive assessment are important in prenatal care, allowing for appropriate parental counseling and directing possible therapeutic interventions. Although significant advances in prenatal imaging modalities, especially fetal echocardiography and ultrasonography, have increased the rate of antenatal detection, some of these anomalies are only diagnosed during post-mortem examinations. Fetal autopsy continues to be a useful means of validating prenatal diagnoses and revealing unsuspected anomalies, particularly in the setting of intrauterine fetal loss or pregnancy interruption after the detection of fetal abnormalities. The anatomical information obtained from fetal autopsy is essential in the comprehension of congenital cardiac malformations, their related anomalies, and the possible genetic and environmental determinants of their development. This paper is a collection of congenital cardiac defects identified at fetal autopsy and the very significant role of post-mortem examinations in improving diagnostic sensitivity and affecting future clinical management.

Keywords: Congenital cardiac anomalies, Fetal autopsies, Tetralogy of Fallot, Single ventricle, Patent ductus arteriosus, Hypoplastic left heart syndrome, Transposition of great arteries, DiGeorge syndrome, Amniotic band syndrome

INTRODUCTION

Congenital cardiac anomalies are the most frequent structural malformations in the developing foetus and represent one of the major causes of foetal morbidity and mortality.[1] As such, early detection and evaluation are of paramount importance in the application of prenatal care and parental counselling regarding possible therapeutic interventions.[2] Advances in prenatal imaging, mostly in foetal echocardiography and ultrasonography, have significantly improved antenatal detection rates, although some anomalies are detected only at post-mortem studies.[3] Foetal autopsy has remained a useful means for confirmation of prenatal diagnoses and detection of unsuspected anomalies in cases of both intrauterine foetal demise and termination of pregnancy after fetuses are found to have abnormalities.[1] The anatomic information from foetal autopsy forms the very important base for congenital cardiac malformations, their related anomalies, and their possible genetic and environmental causes.[3]

We present a spectrum of congenital cardiac anomalies diagnosed by foetal autopsy in a series of cases. These were examined in detail to illustrate the role that post-mortem studies may play in heightening diagnostic acumen and future clinical management.

This study was carried out retrospectively at the Department of Pathology in Sri Ramachandra Institute of Higher Education and Research to study the cardiac anomalies received for foetal autopsies for a period of 4

years (from January 2021 to March 2024). Institutional Ethics Committee approval was taken (IEC number-CSP-III/24/APR/04/135). A total of 352 foetal autopsies were carried out during this period out of which 16 presented with cardiac anomalies. In this paper, we aim to discuss 7 cardiac cases.

CASE SERIES

Case 1

A 37-year-old female was admitted to the hospital with a pregnancy complicated by suspected congenital cardiac anomalies in the foetus. At 21 weeks of gestation, a decision to terminate the pregnancy was made in view of abnormal foetal findings on prenatal imaging, raising concerns for major cardiac malformations. A foetal autopsy was thus performed to confirm the diagnosis and give further insight into the observed abnormalities.

Foetal autopsy findings

Gestational age

The gestational age was 21 weeks.

Foetal heart weight

The heart weight of foetus was 6 grams.

Heart measurements

The measurement of heart was 3.9×2×1 cm

Gross appearance

The heart was boot-shaped-a common feature when suspecting Tetralogy of Fallot. Furthermore, overriding of the aorta, right ventricular hypertrophy, a VSD, and a hypoplastic pulmonary artery were observed.

Vessels

Grossly, there was congestion with hypertrophy of muscles of the ventricular wall noted, especially in the right ventricle. This was in line with the RVH observed.

Ventricular wall

Myocardial fibers with thickened walls with evidence of hypertrophy appeared in histological sections, more so affecting the right ventricle, further in support of gross findings of RVH.

Diagnosis

The combination of boot-shaped heart, overriding aorta, ventricular septal defect, right ventricular hypertrophy, and hypoplastic pulmonary artery in the present case is highly suggestive of Tetralogy of Fallot.

It is a congenital heart defect with four main features, namely VSD, pulmonary stenosis, overriding aorta, and RVH. There is a possibility that the poor prognosis may partly be due to the fact that the anomaly was of a serious form, as evidenced by the hypoplastic pulmonary artery and significant vascular congestion.

Case 2

A 25-year-old female with pregnancy complicated by a suspected foetal cardiac anomaly presented at 14 weeks and 5 days of gestation. Due to the severity of the detected anomaly through prenatal ultrasound, it was decided to terminate the pregnancy. A foetal autopsy was performed after the termination of pregnancy to confirm the suspicion.

Foetal autopsy findings

Foetal age

The age of the foetus was 14 weeks + 5 days.

Heart weight

The weight of the heart was 2 grams.

Gross appearance

The foetus had normally positioned heart in thorax and normally related sinus, but with marked structural abnormalities of the heart. The major abnormality of the heart consisted of only one ventricle. There was only one inflow tract and one outflow tract and this is consistent with one of the most severe forms of congenital cardiac defect.

Ventricular morphology

The single maldeveloped ventricle thus did not possess any normally developed ventricular septation. The differentiation of one chamber into right and left chambers was also absent.

Inflow and outflow tracts

Only one inflow tract and one outflow tract were present, indicating an absence of cardiac septation.

Muscular structure

The myocardium was basically immature but appropriate for gestation age.

Diagnosis

These findings are consistent, in this case, with single ventricle congenital heart defect, a complex cardiac malformation characterized by a single functional ventricle and abnormal development of both the inflow and outflow tracts. The usual division between the right and left sides of the heart did not take place, leaving a single ventricle receiving both systemic and pulmonary blood flow.

Associated with a wide variety of other congenital heart defects, in the majority of cases it is incompatible with life without surgical intervention in the post-natal period.

Case 3

This was a 32-year-old female who presented with a pregnancy at 26 weeks of gestation, complicated by suspected congenital anomalies. Prenatal imaging raised concerns for a foetal cardiac abnormality.

Given the severity of these findings, the pregnancy was medically terminated, and a foetal autopsy was conducted in order to assess the cardiac and pulmonary structures.

Foetal autopsy findings

Foetal age

The foetal age was 26 weeks.

Cardiac findings

There was a widely patent ductus arteriosus. Normally, the ductus arteriosus closes shortly after birth. In this case, it remained widely open, indicating that the infant had a persistent pattern of foetal circulation.

Lung histology

Microscopic study of the lungs showed.

Hyaline membrane formation

Hyaline membranes lined the alveoli, with the classic appearance of hyaline membrane disease, better known as respiratory distress syndrome. This typically emanates from a deficiency of surfactant and presents with lungs of poor compliance and respiratory failure in the neonatal period.

Pulmonary oedema

Proteinaceous fluid was noted in filling the alveolar spaces, indicative of pulmonary oedema. This usually presents itself as a result of fluid overload or as an impaired cardiac function secondary to a congenital heart defect.

Vascular congestion

There is marked vascular congestion in the pulmonary vasculature that supports the diagnosis of pulmonary oedema.

Diagnosis

The autopsy revealed patent ductus arteriosus, a congenital cardiac anomaly characterized by failure of the foetal ductus arteriosus to close after birth. Though PDA is a normal foetal structure, persistence of this duct beyond birth or late gestation results in abnormal circulation between the pulmonary artery and aorta, complicating conditions like heart failure or pulmonary hypertension.

Findings in the lungs, ranging from hyaline membrane formation to pulmonary oedema, point towards respiratory distress syndrome. Although this is a common finding in preterm infants due to deficiency of surfactant, it can also relate to congenital heart diseases, like abnormal hemodynamic presented in this case due to PDA. The congestion and oedema in the lungs suggest that an inability of the heart to maintain circulation could be another cause for the respiratory compromise.

Case 4

The pregnant female patient was a 27-year-old admitted with a suspected foetal cardiac anomaly at a pregnancy age of 22 weeks and 5 days. Prenatal ultrasound revealed anomalies in the structure of the heart. The pregnancy was subsequently terminated after counselling. A foetal autopsy was performed to investigate the cardiac findings and confirm the prenatal diagnosis.

Foetal autopsy findings

Foetal age

The foetal age was 22 weeks + 5 days.

Heart weight

The heart weight was 30 grams.

Gross description

The right side of the heart was grossly enlarged, suggesting dilatation of the right side. There were marked structural abnormalities further.

Mitral stenosis

The mitral valve was grossly narrow. This led to obstruction of blood flow from the left atrium into the left ventricle.

Hypoplastic left ventricle

There was underdevelopment of the left ventricle, therefore confirming HLHS. The underdeveloped size of the left ventricle is thus suggestive of an underdeveloped structure that cannot support the systemic circulation.

Dilated right ventricle

The right ventricle, on the other hand, was significantly dilated, thus compensating for the defects on the left side of the heart.

Right ventricular hypertrophy

The myocardial fibres of the right ventricle were thickened, consistent with hypertrophy and a compensatory response to the increased workload from left-sided heart dysfunction.

Thickening of endocardium

Generally, there was mild thickening of the endocardium, particularly around the mitral valve, which further supported the mitral stenosis diagnosis.

Diagnosis

The findings in this case include underdevelopment of the left ventricle, mitral stenosis, and compensatory dilation of the right ventricle, in a way compatible with hypoplastic left heart syndrome (HLHS). In HLHS, the left side of the heart is unable to support the systemic circulation adequately and, therefore, depends on the right heart to pump blood to the lungs and body. Without early surgical intervention, HLHS is uniformly lethal in the neonatal period.

The associated findings of mitral stenosis further accentuated the underdevelopment of the left side of the heart by further limiting blood flow into the hypoplastic left ventricle and likely contributed to the severity of the defect as a whole.

Case 5

This is a pregnancy of a 36-year-old female that complicated at 24 weeks of gestation by foetal cardiac anomalies identified during routine prenatal ultrasound. The pregnancy was thus terminated owing to the severity of the cardiac malformations. A foetal autopsy was hence performed to confirm the suspected cardiac defects and give further insight into the anatomical abnormalities.

Foetal autopsy findings

Foetal age

The foetal age was 24 weeks.

Gross cardiac findings

Pulmonary artery narrowing

Noticeable narrowing of the pulmonary artery was noticed both in the inflow and outflow tracts of the heart. This would have resulted in restricted blood flow from the right ventricle into the lungs.

Transposition of great arteries

Transposition of the great vessels was noted when the positions of the aorta and pulmonary artery were reversed. This is thus constituted of the aorta arising from the right ventricle and the pulmonary artery from the left ventricle, creating a separation between the systemic and pulmonary circulation.

Ventricular septal defect

There was a large VSD creating a direct communication between the right and left ventricles. This anomaly would have permitted the mixing of oxygenated and deoxygenated blood, usually serving as some type of compensatory mechanism when there is a transposition of the great vessels.

Narrowing of pulmonary artery

Histology confirmed marked narrowing of the pulmonary artery with thick-walled arteries and a reduced luminal diameter. This would further compromise the already poor pulmonary circulation.

Ventricular anatomy

VSD was well apparent, allowing abnormal flow of blood between the two ventricles.

Diagnosis

Foetal autopsy was then performed which showed TGA of great vessels with associated narrowing of the pulmonary artery and VSD. In TGA, the aorta and the pulmonary artery interchanges with each other.

This allows circulation of the venous blood through the body and arterial blood through the lungs without adequate exchange of blood across the two circulations.

This is usually incompatible with life unless there are other defects, such as a VSD, which allows some mixing of oxygenated and deoxygenated blood.

Narrowing of the pulmonary artery in this case would further restrict blood flow to the lungs and compound the hemodynamic difficulties imposed by the transposition. Unless surgically corrected early, these conditions are usually fatal in the neonatal period.

Case 6

The pregnancy of a 36-year-old woman was complicated with a suspected foetal cardiac anomaly, diagnosed in a routine prenatal ultrasound at approximately 22 completed weeks of gestation. Imaging studies indicated that the complex congenital heart defect was likely to be associated with other anomalies.

Because the findings were severe, the pregnancy was terminated and a foetal autopsy was performed in order to confirm the diagnosis and assess the nature of the cardiac and thoracic abnormalities.

Foetal autopsy findings

Foetal age

The foetal age was Approximately 22 weeks.

Cardiac findings

The aortic arch is to the right side of the thorax. This is an abnormal configuration that may be found in several congenital heart defects and in syndromic conditions such as DiGeorge syndrome.

The ductus arteriosus, which, in the foetus, is a vessel connecting the pulmonary artery to the aorta; in this case, it is situated on the left side and contributed to abnormal vascular arrangement.

Position and course of aortic arch not clearly outlined

Because of the compression and displacement of thoracic structures, the exact position and course of the aortic arch could not be finally outlined. This could well have been the result of associated abnormalities of the thorax or due to underlying structural constraints within the thoracic cage.

Associated findings

The lungs seemed to be underdeveloped, hence pulmonary hypoplasia may have been present. Pulmonary hypoplasia is a congenital malformation characterized by a reduction in the size and number of auriferous spaces. It often results in various types of congenital heart defects but especially in cases where space within the thoracic cavity is impeded.

Congenital anomaly

Given the cardiac and pulmonary findings, a syndromic association was suspected in particular, with the well-known DiGeorge syndrome associated with cono-truncal heart defects, including right-sided aortic arch and other thoracic malformations.

Lungs

Microscopic examination of lung tissue confirmed features of pulmonary hypoplasia with diminution of lung parenchyma and underdeveloped alveolar structures.

Cardiovascular

Except for the gross anomalies described, no significant cardiac and vascular histological changes were observed.

Diagnosis

The foetal autopsy findings are in line with a complex congenital anomaly of the foetal development: a right-sided aortic arch, left-sided ductus arteriosus, and possible pulmonary hypoplasia.

Malposition of the aortic arch and ductus arteriosus could be associated with underdeveloped lungs and may point to a syndromic condition, most likely DiGeorge syndrome, or 22q11.2 deletion syndrome, in association with such cardiovascular malformations.

Case 7

The pregnancy of a 37-year-old woman was complicated by the finding of multiple foetal anomalies on an early second-trimester ultrasound at 13 weeks of gestation. These included cardiac and skeletal abnormalities.

This raised the need for further evaluation, so the pregnancy was subsequently terminated due to these severe defects. A foetal autopsy was carried out in confirmation and for further elucidation of the underlying condition.

Foetal autopsy findings

Foetal age

The age 13 weeks.

Skin

The skin of the foetus had blackish discoloration, which might be due to ischemic changes or compression effects with regard to externalization of organs.

Abdomen

A large anterior abdominal wall defect was identified with herniation of abdominal contents through the defect. The herniated organs were covered by a thin membrane consistent with an omphalocele.

Ectopia cordis

The heart, weighing 0.2g, was located outside the thoracic cavity, thus presenting ectopia cordis.

The heart was placed directly under the skin, without any covering provided by the sternum. The heart was displaced anteriorly, lying external to the thoracic wall.

Thoracic findings

The left lung was not present and may indicate either pulmonary agenesis or severe underdevelopment of the lung.

Lower limbs

Left lower limb undeveloped. The right lower limb was incompletely developed, with only the right thigh being present and no structures found distal to the thigh.

Spine

The spine gave an impression of being short and angulated, evidencing a gross structural anomaly affecting the skeletal system.

Heart

The intrinsic cardiac muscle structure did not reveal any gross abnormality, though mispositioning of the heart outside the thoracic cavity was evident.

Other tissues

Underdeveloped limb structures and a poorly developed spine did show immature cartilaginous tissue that was appropriate in nature for this state of gestation.

Diagnosis

The findings are consistent with amniotic band syndrome, a rare congenital anomaly caused by the rupture of the amniotic sac, which results in the entanglement of parts of the body of the foetus by fibrous bands. This may cause a range of deformities depending on the site and extent of the constriction.

DISCUSSION

In general, congenital cardiac anomalies remain one of the most important contributors to foetal morbidity and mortality.[1]

Prenatal imaging with subsequent description of congenital heart defects and confirmation by foetal autopsy is highly useful for further understanding the nature, severity, and diversity of these anomalies.

It is a case series that epitomizes the spectrum of congenital cardiac anomalies seen in foetal autopsies, including Tetralogy of Fallot, single ventricle, patent ductus arteriosus, hypoplastic left heart syndrome, transposition of the great arteries, DiGeorge syndrome, and amniotic band syndrome. One important point revealed by this series is the complexity of CHD and the multidisciplinary approach to diagnosis and management.

Tetralogy of Fallot

The classically presented four cardinal features of TOF are one of the most common cyanotic congenital heart defects, namely VSD, RVH, pulmonary stenosis, and overriding aorta.4 In this series, TOF was diagnosed with a boot-shaped heart with RVH, VSD, and pulmonary stenosis as classic presentation.

TOF results from an abnormal septation of the truncus arteriosus, resulting in impaired oxygenation of blood. Severe cases detected prenatally, despite advances in surgical repair, may result in foetal demise. Prenatal diagnosis and foetal autopsy confirmed not only the extent of anatomical disruption but also pointed out the need for early intervention when possible.[5]

Single ventricle

Single ventricle heart defects are a family of complex congenital heart anomalies characterized by only one functional ventricular chamber. We present a case series where a foetus diagnosed with single ventricle associated anomalies presented with single inflow and outflow tract. These conditions result in the mixing of oxygenated and deoxygenated blood, leading to profound circulatory compromise.

Generally, single ventricle physiology is incompatible with life without staged surgical intervention such as the Norwood procedure in the neonatal period.[6] The described features at the autopsy confirmed the diagnosis and demonstrated well the profound hemodynamic burden imposed by the condition.

Patent ductus arteriosus and hypoplastic left heart syndrome

Patent ductus arteriosus and hypoplastic left heart syndrome are critical CHDs that may present together or separately. In this case series, PDA is the diagnosis given to the condition whereby the ductus arteriosus, a vessel commonly present in all foetuses through which blood bypasses the lungs, does not close down after birth.

Although PDA would have been a normal intrauterine finding, its persistence into the postnatal period is abnormal and results in abnormal circulation.[7]

In this regard, PDA may be considered life-sustaining in utero in conditions such as HLHS, due to the allowance

of some systemic circulation in the presence of severe underdevelopment of left-sided heart structures. HLHS is always lethal without intervention and includes marked hypoplasia of the left ventricle, mitral valve, aorta, and aortic arch.[8]

These findings were confirmed at autopsy, which demonstrated the typical structural underdevelopment of HLHS, as well as a widely patent ductus arteriosus, emphasizing dependence on this foetal vessel for maintenance of flow.

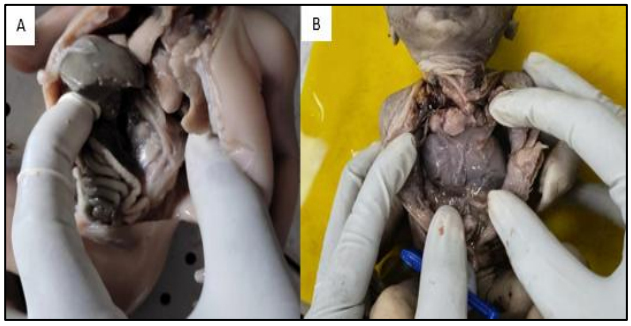

Figure 1: The gross view of the foetal dissection. (A) Displays the view of the abdominal cavity. (B) Displays the view of the thoracic cavity.

Transposition of the great arteries

Another complex congenital heart defect involves TGA, wherein the aorta and pulmonary artery are positioned in reverse, such that two parallel circulations take place, without allowing proper oxygenation of blood.[9] This needs to be corrected surgically as soon as it is born, since it would otherwise not be compatible with life.

The foetus in this case series had TGA with a ventricular septal defect that allowed for some degree of mixing between oxygenated and deoxygenated blood.[10] TGA is often associated with other defects of the heart; autopsy findings in the foetus confirmed the anatomic abnormalities, emphasizing the value of prenatal diagnosis for early postnatal surgical planning.[9]

DiGeorge syndrome

DiGeorge syndrome, also known as 22q11.2 deletion syndrome, results in the following cardiac defects: right-sided aortic arch, tetralogy of Fallot, and ventricular septal defects. In this case series, the foetus with the diagnosis of DiGeorge syndrome presented with a right-sided aortic arch, transposition of the great vessels, and pulmonary artery stenosis.[11]

DiGeorge syndrome is a multi-system disorder affecting the heart, immune system, endocrine glands, and facial development. Diagnosis was confirmed by autopsy findings and points to the syndromic nature of some congenital heart defects.

Early diagnosis of DiGeorge syndrome can be helpful in both prenatal counselling and postnatal management as it has implications on both cardiac and systemic health.[12]

Amniotic band syndrome

ABS is characterized by a condition wherein, after the rupture of the amniotic sac, entrapment of fibrous bands around foetus body parts causes deformities, ranging widely from limb defects to abdominal wall defects to even congenital heart anomalies.[13]

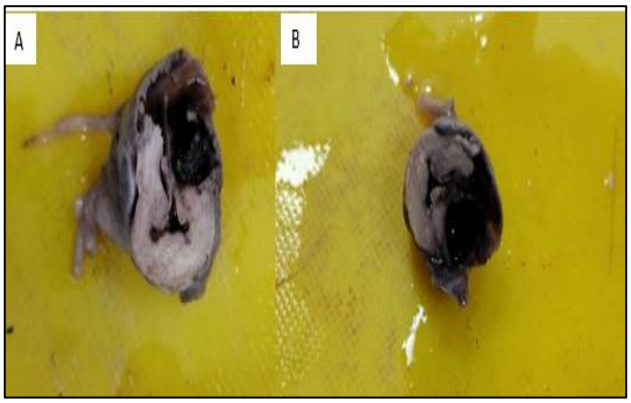

Figure 2 (A and B): The foetal dissection with two different views highlighting internal organs.

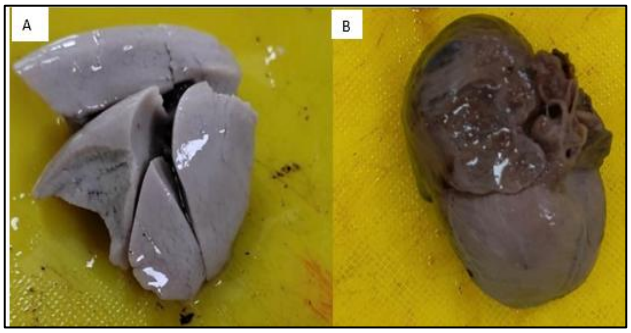

Figure 3: Two distinct specimens from the fetal dissection. (A) Shows the lung (both left and right lobes). (B) Shows the gross appearance of the heart.

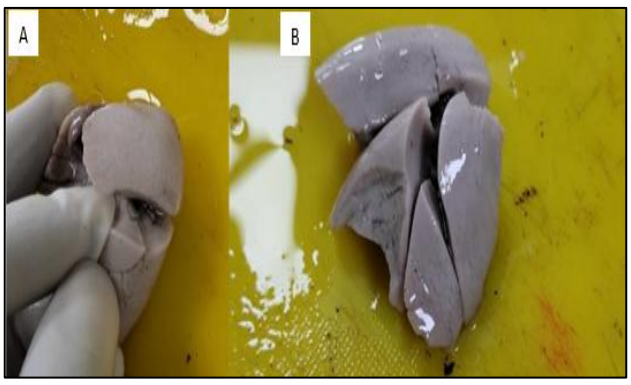

Figure 4 (A and B): Two different views of the gross appearance of the lung.

This series presented a foetus with ectopia cordis, omphalocele, and limb malformations-all classical features of severe ABS.

Ectopia cordis is a rare and usually fatal condition where the heart develops outside of the thoracic cavity and, thus, is very susceptible to external injury. The findings in this case of ABS serve dramatically to point out the impact of external compressive forces on foetal development in those instances in which vital organs, in this case the heart, are involved.[14]

CONCLUSION

This case series also provides a wide spectrum of congenital cardiac anomalies, which can be diagnosed on foetal autopsy, starting from an isolated heart defect like Tetralogy of Fallot to complex syndromic conditions such as DiGeorge syndrome and amniotic band syndrome. Each of these anomalies carries a different challenge for foetal and neonatal survival with various degrees of surgical or medical intervention. foetal autopsy has become necessary to confirm prenatal diagnoses, detail precise anatomy, and contribute significantly to the understanding of underlying pathology. It also serves to give appropriate genetic counselling and assessment of risk in subsequent pregnancies, more so in syndromic conditions like DiGeorge syndrome and amniotic band syndrome. There is improvement in these anomalies through advances in prenatal imaging and genetic testing; thus, the possibility for improved management and outcome.

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