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Not Just a Posterior Fossa Abnormality: Imaging Diagnosis of Ritscher - Schinzel Syndrome

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Abstract: ***This report describes an antenatal case of Ritscher–Schinzel syndrome (cranio-cerebello-cardiac syndrome) diagnosed through characteristic imaging findings and supported by molecular findings. Prenatal ultrasonography demonstrated Dandy–Walker malformation with cerebellar vermian hypoplasia, cystic dilatation of the fourth ventricle, posterior fossa enlargement, and splaying of the cerebellar hemispheres, along with a choroid plexus cyst. Fetal echocardiography revealed a perimembranous ventricular septal defect, while thoracoabdominal assessment demonstrated congenital diaphragmatic hernia with herniation of abdominal contents into the thoracic cavity. Owing to extensive multisystem involvement and poor prognosis, pregnancy termination was performed. Post-abortion examination showed craniofacial dysmorphism with a prominent occiput. Genetic analysis identified a homozygous variant of uncertain significance in COMMD4, a gene recently implicated in Ritscher–Schinzel syndrome. The molecular findings, together with the characteristic antenatal imaging phenotype and parental carrier status, provided supportive evidence for the diagnosis. Correlation of antenatal imaging, postmortem findings, and molecular testing supported the diagnosis of Ritscher–Schinzel syndrome. This case highlights the importance of systematic prenatal imaging and broadens the recognised antenatal imaging phenotype of this rare syndrome.***

Keywords: Ritscher–Schinzel syndrome; 3C syndrome; prenatal diagnosis; Dandy–Walker malformation; congenital diaphragmatic hernia; ventricular septal defect; fetal echocardiography; COMMD4 gene.

1. Introduction

Ritscher–Schinzel syndrome (RSS), also known as cranio-cerebello-cardiac (3C) syndrome, is a rare autosomal recessive disorder characterised by craniofacial dysmorphism, cerebellar malformations, and congenital cardiac defects [1,2]. The syndrome exhibits marked phenotypic variability, with involvement of the central nervous system, cardiovascular system, and craniofacial structures [2,8].

Antenatal imaging frequently provides the first indication of the diagnosis, making radiologists pivotal in early recognition and prenatal characterisation of affected fetuses [3,4]. Accurate pattern analysis and systematic evaluation of associated anomalies are essential to differentiate RSS from other syndromic posterior fossa malformations and to guide genetic testing and counselling [5–7].

Recent studies have identified biallelic COMMD4 variants as a cause of a congenital multiple-organ malformation syndrome with significant phenotypic overlap with Ritscher–Schinzel syndrome [15]. Recognition of characteristic imaging findings and their correlation with molecular genetic abnormalities is important for establishing an accurate prenatal diagnosis.

2. Case Report

A 25-year-old consanguineously married woman with a significant adverse obstetric history was referred for evaluation following a targeted anomaly scan at 24 weeks gestation. Her obstetric history included a first pregnancy terminated at six months of gestation because of a fetal brain anomaly and a second pregnancy ending in a missed abortion at three months. The current pregnancy was her third gestation. Maternal serology showed Rubella IgG and CMV IgG positivity, consistent with previous exposure.

3. Imaging Findings

Antenatal ultrasonography demonstrated features of Dandy–Walker malformation, including cerebellar vermian hypoplasia, cystic dilatation of the fourth ventricle, enlargement of the posterior fossa, and splaying of the cerebellar hemispheres. An associated choroid plexus cyst was identified. Fetal echocardiography revealed a perimembranous ventricular septal defect. Thoracoabdominal assessment also demonstrated a congenital diaphragmatic hernia with herniation of abdominal contents into the thoracic cavity and associated mild mediastinal shift. The combination of posterior fossa, cardiac, and diaphragmatic abnormalities raised suspicion for an underlying syndromic disorder.

In view of the extensive multisystem involvement and unfavourable prognosis, medical termination of pregnancy

was undertaken. Post-abortion external examination demonstrated craniofacial dysmorphism in the form of a prominent occiput. Genetic testing identified a homozygous variant of uncertain significance in the COMMD4 gene, with both parents found to be heterozygous carriers. In view of the recently reported association of biallelic COMMD4 variants with a Ritscher–Schinzel syndrome–like phenotype and the concordant imaging findings, the variant provided supportive molecular evidence for the diagnosis, although its pathogenicity remains uncertain.

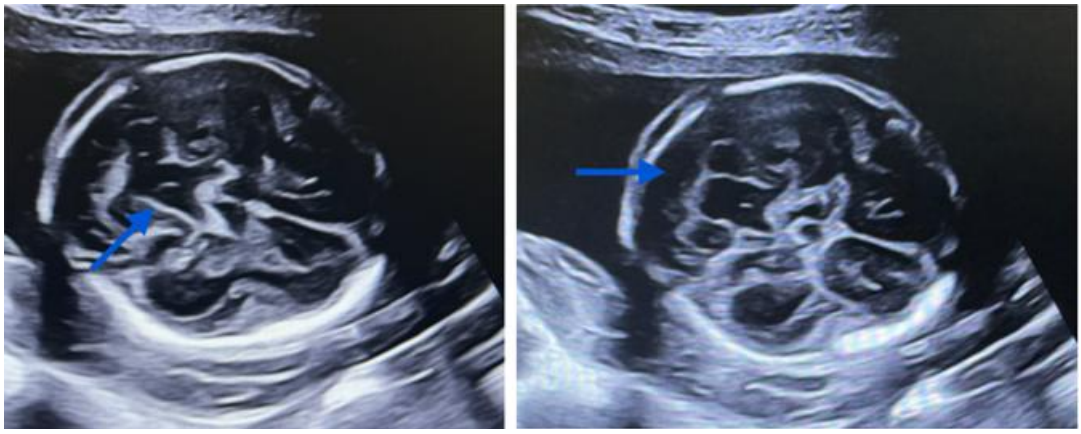
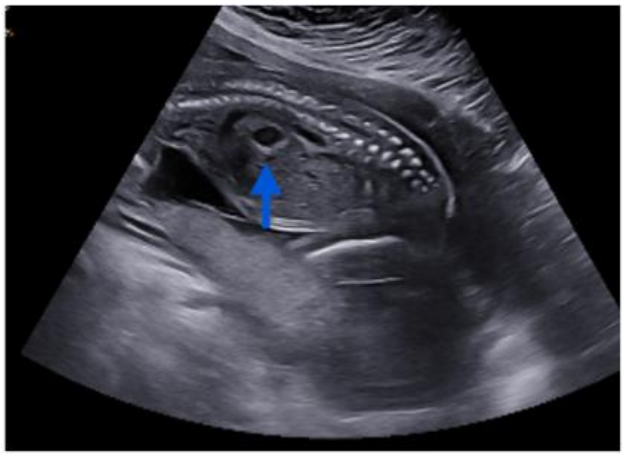
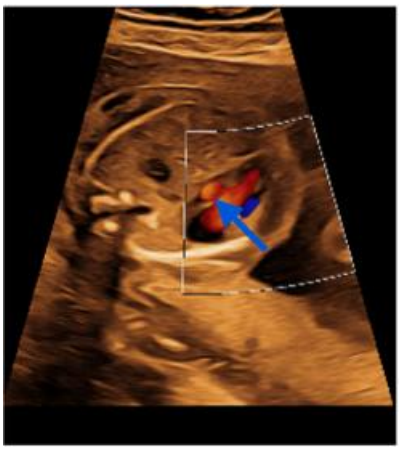


Figure 1: Ultrasonography demonstrated cerebellar vermian hypoplasia with widening and splaying of the cerebellar peduncles, together with cystic dilatation of the fourth ventricle and enlargement of the posterior fossa, consistent with Dandy–Walker malformation.

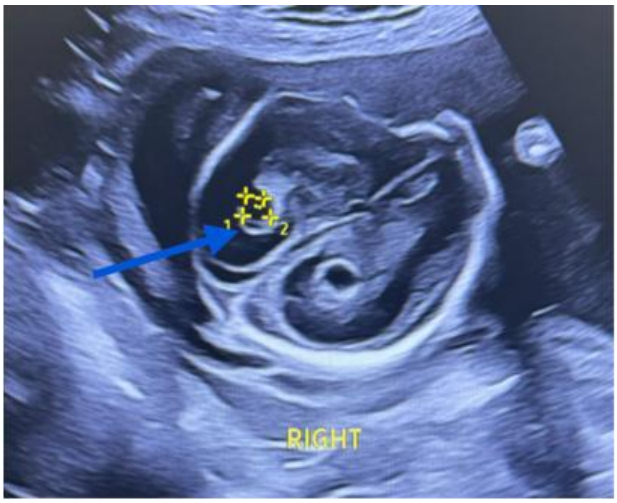
Image Gallery

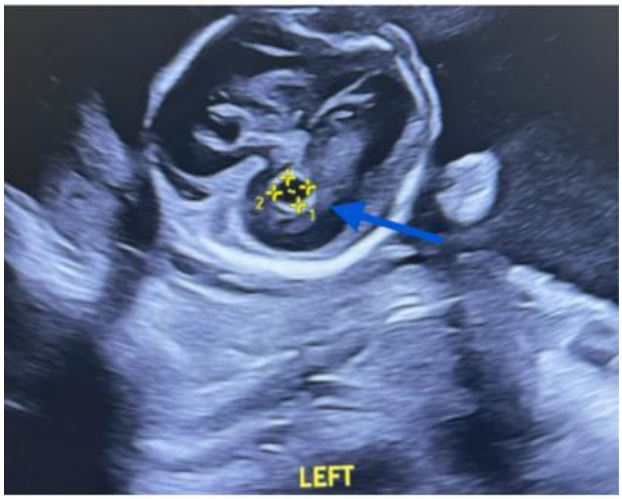


USG demonstrates stomach bubble inb the thoracic cavity- Congential Diaphragmatic Hernia



USG demonstrates Tiny peri Membranous VSD





4. Results

No Pathogenic or Likely pathogenic variants causative of the reported phenotype were detected

The maternal cell contamination testing done at MedGenome Labs Ltd Bangalore (Order ID: 1455080; Date: 26- Sep- 2025) was found to be negative.)

A homozgous variant of uncertain significance in the COMMD4 gene (c.1A>T, p.Met1) has been identified in the *POC* of (SID: 9408629), and this variant has been identified in parents, Mrs. (SID: 9408630) and Mr. (SID: 9408631) in heterozygous state. Biallelic mutation in COMMD4 gene has neen reported in patient affected with congentital multiple organ malformation syndrome, Ritscher- Schinzel Syndrome (medRxiv)

USG Demonstrates bilateral Choroid plexus cysts

Fetal Gross Specimen shows promoinent occiput

5. Discussion

Ritscher–Schinzel syndrome presents a diagnostic challenge due to overlapping features with other syndromic posterior fossa abnormalities [2,5]. Systematic antenatal ultrasonography remains the cornerstone of diagnosis, particularly in settings where fetal MRI is not routinely available [12,13]. In the present case, an organ-based imaging approach enabled early recognition of multisystem involvement**.**

Accurate posterior fossa pattern recognition is critical. The combination of vermian hypoplasia, enlarged posterior fossa, and fourth ventricular cystic dilatation favoured Dandy–Walker malformation over Blake pouch cyst or mega cisterna magna [10–13]. Although nonspecific, the presence of a choroid plexus cyst further supported a syndromic etiology and prompted a detailed search for associated anomalies.

Congenital heart disease represents a key diagnostic anchor in RSS and is among its most consistent manifestations [1,3,4,8]. Identification of a ventricular septal defect prompted focused evaluation for extracardiac anomalies. Detailed fetal echocardiography plays an important role in the prenatal assessment of fetuses with suspected syndromic disorders and facilitates comprehensive characterisation of associated cardiac defects [4,14].

The presence of congenital diaphragmatic hernia appears to be an uncommon association and may broaden the antenatal imaging spectrum of RSS. It also underscores the importance of meticulous thoracoabdominal assessment in fetuses with posterior fossa abnormalities [6,7]. Although cerebellar and cardiac abnormalities are well-recognised features of RSS, diaphragmatic defects have rarely been described. The coexistence of Dandy–Walker malformation, ventricular septal defect, and congenital diaphragmatic hernia in a case supported by molecular genetic findings broadens the prenatal imaging phenotype of this rare syndrome and may facilitate earlier antenatal recognition [6,7].

To our knowledge, prenatal diagnosis of Ritscher–Schinzel syndrome associated with congenital diaphragmatic hernia and a homozygous COMMD4 variant has not been widely reported. This case expands the recognised antenatal imaging spectrum of the disorder and highlights the role of prenatal imaging in identifying multisystem involvement suggestive of an underlying genetic syndrome. The observation may represent an expansion of the recognised prenatal imaging phenotype of RSS and underscores the value of integrating detailed antenatal imaging with molecular genetic analysis in suspected syndromic disorders [15].

Temtamy syndrome was considered in the differential diagnosis because of its association with posterior fossa abnormalities [5]. The absence of limb anomalies, the characteristic imaging constellation, and the molecular findings were consistent with the diagnosis of RSS [6,7]. Other differential considerations for antenatally detected Dandy–Walker malformation include isolated Dandy–Walker malformation, Joubert syndrome, and other syndromic cerebellar malformations, emphasising the importance of systematic evaluation for associated extracranial abnormalities [10–13].

Although Joubert syndrome was considered in the differential diagnosis because of overlapping posterior fossa imaging features, the associated cardiac defect, craniofacial abnormalities, congenital diaphragmatic hernia, and supportive COMMD4 molecular findings favoured Ritscher–Schinzel syndrome. The presence of parental consanguinity in our case further supports an autosomal recessive mode of inheritance. In addition, the patient's adverse obstetric history raises the possibility of recurrence of an underlying genetic disorder and highlights the importance of prenatal screening, genetic counselling, and targeted molecular testing in subsequent pregnancies [9].

Recent evidence has identified biallelic COMMD4 variants in individuals with a congenital multiple-organ malformation syndrome showing substantial phenotypic

overlap with Ritscher–Schinzel syndrome [15]. Affected individuals demonstrate cerebellar abnormalities and multisystem developmental anomalies resembling the clinical spectrum of RSS [15]. In our case, a homozygous COMMD4 variant was identified, while both parents were heterozygous carriers, supporting an autosomal recessive inheritance pattern [9,15]. Although classified as a variant of uncertain significance, the molecular finding, together with the characteristic antenatal imaging phenotype and parental carrier status, provided supportive molecular evidence for the diagnosis while remaining insufficient to establish causality independently [15].

6. Conclusion

Recognition of characteristic antenatal imaging patterns and associated extracranial abnormalities, combined with comprehensive evaluation of associated anomalies and molecular genetic testing, is essential for accurate diagnosis of Ritscher–Schinzel syndrome [3,4,6,7,13]. When a posterior fossa malformation is identified, careful assessment of the cardiovascular and extracranial systems should be undertaken to detect associated syndromic abnormalities [3,4,10–13]. The association of Dandy–Walker malformation, ventricular septal defect, and congenital diaphragmatic hernia in our case broadens the antenatal imaging phenotype of RSS and highlights the value of integrating imaging findings with molecular genetic data [15]. This case expands the recognised prenatal imaging phenotype of Ritscher–Schinzel syndrome and highlights the importance of integrating antenatal imaging findings with molecular diagnostics for accurate diagnosis, prognostication, and genetic counselling.

7. Teaching Points

- When a posterior fossa malformation is detected antenatally, systematic evaluation of the cardiac, thoracoabdominal, and extracranial structures is essential to identify syndromic associations such as Ritscher–Schinzel syndrome [1–4].
- When Dandy–Walker malformation coexists with congenital heart disease, a targeted search for additional anomalies and prompt consideration of syndromic diagnoses and molecular genetic testing are warranted [1–4].
- Recognition of multisystem involvement, including uncommon associations such as congenital diaphragmatic hernia, can facilitate accurate prenatal diagnosis, prognostication, and parental counselling [6,7,15].

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