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Refractory Hypertension Secondary to Aortic Coarctation in Robinow Syndrome: A Case Report

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Case Report

Keywords: Robinow syndrome, Aortic coarctation, Refractory hypertension, WNT–ROR2 signalling, T-cell immunodeficiency

Posted Date: June 8th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9664010/v1

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Additional Declarations: No competing interests reported.

Abstract

Introduction:

Robinow syndrome is a rare genetic disorder characterised by mesomelic limb shortening, craniofacial anomalies, and genital hypoplasia. Cardiovascular involvement is infrequent, and coarctation of the aorta has been reported only in isolated cases. We present a rare case of Robinow syndrome associated with progressive aortic coarctation and refractory hypertension.

Case Presentation:

A four-and-a-half-year-old male, the fifth child of consanguineous parents, presented with recurrent lower respiratory tract infections, developmental delay, and failure to thrive. Physical examination revealed typical facial dysmorphism and micropenis. Echocardiography demonstrated pulmonary valve stenosis, a small patent ductus arteriosus, and evolving coarctation of the aorta with persistent hypertension and mild left ventricular hypertrophy. Laboratory investigations revealed elevated IgE and decreased CD4/CD8 counts, consistent with T-cell immunodeficiency. The child was managed with antihypertensives, nutritional rehabilitation, and antitubercular therapy, resulting in clinical stabilisation, although the long-term outcome remains poor.

Discussion:

The coexistence of coarctation of the aorta in Robinow syndrome is exceptionally rare, a combination rarely reported in the literature, with no previous case series to date. This case highlights the potential vascular involvement secondary to abnormal WNT–ROR2 signalling pathways.

Conclusion:

Early recognition, multidisciplinary management, and vigilant cardiovascular surveillance are essential(even in mild cases) to prevent morbidity in patients with Robinow syndrome presenting with persistent hypertension and improve prognosis.

Introduction

First identified in 1969 by Robinow et al(1), Robinow syndrome is characterised by mesomelic shortening of the limbs, hypoplastic genitalia, as well as anomalies of the head, face and vertebrae. Robinow syndrome is an exceptionally rare genetic disorder with an incidence of 1 in 500,000 live births. It affects both sexes equally and is often referred to as 'fetal facies' syndrome due to the distinctive craniofacial features that resemble those of an eight-week-old fetus. (2)

The syndrome is classified into two types based on inheritance patterns and severity. Autosomal recessive type with homozygous or compound heterozygous ROR2 gene mutation (9q22) that has more intense features. The autosomal dominant form with a lesser severity is due to a heterozygous mutation in the ROR2 gene or in the WNT5A gene (3p)(3, 4). Clinically, the recessive type tends to show more severe skeletal and vertebral abnormalities. In contrast, the dominant form usually presents with milder craniofacial or skeletal changes.

The classic combination of underdeveloped genitalia, abnormally short limbs, and craniofacial anomalies—sometimes in conjunction with skeletal and spinal defects—defines Robinow syndrome. However, due to multiple genetic patterns, phenotypes fluctuate phenotypically, with some patients displaying only mild craniofacial or skeletal changes, while others present with marked vertebral malformation, cardiopulmonary complications, or intense abnormalities of the genital system. (5)Additionally, severe vertebral and skeletal deformities are present in recessive form, contrasting to the dominant type. Individuals afflicted with the syndrome tend to have normal levels of intelligence, though developmental or intellectual impairment may occur in a few cases. (6)

A comprehensive review of the literature suggests fewer than 250 reported cases globally; this not only signifies the rarity of the condition but also highlights its notable clinical variability, making every additional report a valuable addition to the understanding of Robinow syndrome.

Therefore, we present this case to add to the growing body of literature and signify the unique association of coarctation of the aorta with this syndrome

Case Presentation

A four-year-and-six-month-old boy with a history of recurrent LRTIs, weighing 7.5 kg (<3rd centile for age), presented to the pediatric department with the symptoms of dry cough for 20 days, fever and vomiting for 4 days and loose stools for 2 weeks. He was the fifth child of consanguineous parents. No family history of congenital heart disease or syndromic illnesses could be traced, though one brother died at age seven from a lower respiratory infection. For the publication of clinical details and photographs, informed consent was taken from the patient's father.

Birth and Developmental History

The baby was born late preterm at 35 weeks' gestation by lower segment cesarean section for fetal distress and malpresentation. The neonatal course was further complicated by meningitis at one month, with subsequent prolonged in-hospital stay, and recurrence of meningitis at eight months old, with a 22-day hospital admission for complicated infection. Developmental history was in line with international developmental delay, with late attainment of gross motor and speech milestones. Motor skills were partially improved with physiotherapy, with overall developmental delay persisting. Neuroimaging (MRI brain, 2021) showed dilated cerebrospinal fluid spaces, thinning of the white matter, and delayed

myelination of the internal and external capsules, which are findings seen in developmental delay. The child had limited access to pediatric care because of belonging to a poor economic background.

Growth and Nutritional Status

Since infancy, the child had been underweight and short for linear growth, being grossly undernourished. At the current time, his weight was 7.5 kg, length 80 cm, and occipitofrontal circumference 46 cm — all below the 5th centile for age. There were early rickets-like changes seen on a skeletal survey in 2021. Growth continued to be suboptimal on nutritional support with high-calorie feeds, calcium, multivitamins, and Alboplex.

Cardiac History

At three months of age, echocardiography revealed moderate pulmonary valve stenosis and a small patent ductus arteriosus (PDA). Surgical intervention, including PDA device closure and pulmonary balloon valvuloplasty, was performed in 2021 with satisfactory postoperative recovery. At the age of four years, persistent hypertension was noted with repeatedly elevated blood pressure more than the 95th percentile for age. There was mild coarctation of the aorta with a peak gradient of 40 mmHg, mild left atrial and left ventricular dilatation, and an ejection fraction of 45–50% on echocardiography. Hypertension did not remit with medical treatment, and the follow-up echocardiogram later showed progression to severe coarctation of the aorta with worsening pressure gradient and ventricular hypertrophy.

Respiratory and Infection History

The child had been experiencing recurrent lower respiratory infections since infancy and was frequently hospitalised. Sputum and gastric aspirate analysis at seven months was Mycobacterium tuberculosis by AFB smear and GeneXpert. High-resolution computed tomography (HRCT) chest scan in 2021 revealed perihilar consolidation and ground-glass haziness suggestive of pulmonary oedema. At four and a half years of age, at this admission, tracheal aspirate cultures yielded Klebsiella pneumoniae and Burkholderia cepacia (multidrug-resistant). Gastric aspirate yielded Actinobacter species. An HRCT chest taken subsequently showed findings compatible with active pulmonary tuberculosis with diffuse ground-glass opacities in favour of interstitial lung disease or drug-related pneumonitis. Antitubercular therapy (HRZE) was initiated. Hospital-acquired pneumonia was managed by culture-directed antibiotics like meropenem, cefepime, colistin, amikacin, and tigecycline. Supportive care included nebulised bronchodilators and inhaled steroids (Atem, Clenil), probiotics (Actiflor), and zinc supplementation.

Past Interventions and Outcomes

PDA closure and balloon valvuloplasty are among the several cardiac procedures the child has undergone. Growth failure persisted despite nutritional rehab, though it led to minor improvement. Global developmental delays persisted despite physiotherapy, helping to some extent with motor delays. Each hospital admission for infection was aided by culture-directed antibiotics.

Summary of Clinical Events

Timeline / Age	Clinical Event / Investigation	Findings / Management
Birth (35 weeks of gestation)	Delivered via LSCS for fetal distress and malpresentation	Late preterm birth
1 month	Meningitis (neonatal period)	Prolonged hospitalization
8 months	Recurrent meningitis	22-day hospitalisation for complicated infection
Infancy onward	Recurrent LRTIs and poor weight gain	Multiple hospitalisations; failure to thrive
3 months	Echocardiography	Moderate pulmonary valve stenosis, small PDA
2021 (≈2 years)	Cardiac surgery	PDA device closure + pulmonary balloon valvuloplasty
2021 (≈2 years)	Skeletal survey	Early rickets-like changes
2021 (≈2 years)	MRI brain	White matter thinning, delayed myelination → developmental delay
2021 (≈2 years)	Immunological workup	↑Ige, ↓CD4/CD8 → T-cell immunodeficiency
2021 (≈2 years)	HRCT chest	Perihilar consolidation + ground-glass opacities
4 years	Hypertension noted	Mild coarctation of the aorta (gradient 40 mmHg)
4 years (progression)	Echocardiography	Severe coarctation, LV hypertrophy
4 years 6 months	Admission with fever, cough, and vomiting	MDR Klebsiella, Burkholderia, and Actinobacter isolated
4 years 6 months	HRCT chest	Active TB; ground-glass opacities (ILD/pneumonitis)
Current admission	Antituberculosis therapy started	HRZE regimen
Current admission	Hospital-acquired pneumonia	Treated with IV antibiotics
At discharge	Improved clinically	On oral antihypertensives, supplements, ATT

Investigations (basic lab workup, including CBC, LFTs, RFTs, electrolytes were done each time, and labs were deranged according to the condition)

Investigation	Date / Approximate Timing	Result / Finding	Interpretation / Comment
MRI Brain	2021	Dilated CSF spaces, white matter thinning, and delayed myelination	Global developmental delay
Skeletal Survey	2021	Early rickets-like changes	Suggestive of nutritional deficiency
Immunological Panel	2021	↑IgE, ↓CD4/CD8	T-cell immunodeficiency with atopy
HRCT Chest	2021	Perihilar consolidation and ground-glass haziness	Pulmonary oedema / ILD
HRCT Chest	Current	Active TB, diffuse ground-glass opacities	Active TB ± ILD or pneumonitis
Echocardiography	Multiple	Progressive coarctation, LV hypertrophy	Structural cardiac defect

Medications and Outcomes

Medication / Category	Dose / Notes	Indication	Outcome
HRZE	Standard pediatric doses	Pulmonary TB	Clinical improvement
Meropenem, Cefepime, Colistin, Amikacin, Tigecycline	Culture-directed IV	MDR pneumonia	Controlled infection
Amlodipine	1 mg/kg/day	Hypertension	Partial control
Labetalol, Captopril	IV → oral, 0.8 mg/kg/hr	Resistant hypertension	Improved BP control
Atem, Clenil	Nebulized	Bronchodilation, steroid	Symptomatic relief
Actiflor, Zinc, Alboplex, Multivitamins	Oral	Nutrition	Improved appetite

Prognosis

Although immediate treatment provided short-term relief, long-term outcomes seem poor due to persistent hypertension, pulmonary changes, and immunodeficiency.

Differential Diagnosis

Differential Diagnosis	Supporting Findings	Comments
Robinow Syndrome	Facial dysmorphism, limb shortening, micropenis, vertebral anomalies	Clinical suspicion high
Congenital Heart Disease (Coarctation of Aorta)	Persistent hypertension, echo findings	Confirmed diagnosis
Primary Immunodeficiency	Recurrent infections, ↓CD4/CD8, ↑Ige	Likely T-cell defect
Failure to Thrive	Severe undernutrition, poor growth	Secondary to chronic illness
Pulmonary Tuberculosis	HRCT findings, positive cultures	Confirmed and under treatment

Diagnostic Challenges

The overlap of clinical features of infection and immunodeficiency made the diagnostic process more complex. It was difficult to differentiate between TB, drug-induced pneumonitis and ILD. Confirmation of the genetic disorder was further delayed by poor access to genetic testing. Clinical diagnosis was established via physical and echocardiographic findings despite limited access to genetic testing.

Clinical Examination

At the time of examination, the child was irritable, febrile, and alert, with dysmorphic facial features like frontal bossing, hypertelorism, and broad nasal bridge (Figure 1). Essential parameters revealed chronic hypertension with blood pressures of 120/80 to 130/94 mmHg, and a pulse of 95 beats per minute. Cardiovascular examination revealed normal heart sounds with an ejection systolic murmur that was best heard at the left upper sternal border, and with radio-femoral delay palpable. Respiratory examination revealed bilateral crepitations and minimal abdominal distension without organomegaly (Figure 2). Neurological examinations were normal with GCS 15/15 and no focal deficit. The patient has severe malnutrition consistent with the anthropometric z scores. Characteristic facial features, genital hypoplasia and mesolimbic limb shortening (Figure 3) and a broad thumb (Figure 4) strongly support Robinow syndrome clinically.

Radiological Findings

Chest X-ray revealed cardiomegaly with pericardial effusion. Abdominal ultrasound revealed the normal shape of the kidneys and hepatobiliary system. Echocardiography established situs solitus with intact septa, a properly positioned PDA device without leak, a trivial pulmonary gradient, and critical coarctation of the aorta. High-resolution CT of the chest revealed perihilar consolidation and diffuse ground-glass haze consistent with pulmonary oedema or drug-induced interstitial pneumonitis.

Hospital Course and Outcome

In-hospital, the child developed hospital-acquired pneumonia, which was successfully managed with culture-directed antibiotic therapy. Blood pressure control was achieved with the use of labetalol, amlodipine, and captopril. There was improvement in appetite and physical activity following nutritional rehabilitation and physiotherapy. Growth remained poor, and hypertension persisted, requiring follow-up in cardiology for potential surgical correction of the coarctation. There was an adjustment in the hypertensive regimen due to poor blood pressure control. The child was discharged on oral antihypertensives, nutritional supplements, and ongoing antituberculosis therapy, with follow-up in accordance with the schedule for cardiac and growth assessment. Adherence was monitored using patient supervision and outpatient caregiver reports on follow-ups. Patients had no significant adverse events related to ATT and no adverse events during hospitalisation. However, poor growth remained a concern.

Case Discussion

Our case of a juvenile male's clinical features highlights the typical findings of Robinow syndrome, which include the combination of developmental delay, growth retardation, mesomelic limb shortening, and multiple cardiac anomalies such as patent ductus arteriosus (PDA), pulmonary stenosis, and mild coarctation of the aorta. The valuable input to this particular case is due to the rare concurrence of Robinow syndrome with coarctation of the aorta and persistent hypertension in the cardiovascular manifestations, with special emphasis on children with refractory hypertension who should be monitored under the care of a multidisciplinary team.

Robinow syndrome and its rare vascular association are a major strength of our research. Furthermore, the availability of physical photos that demonstrate physical features and echo findings further strengthens our research. However, the full-fledged anatomical assessment was hindered due to the high cost of genetic confirmation and the unavailability of advanced imaging. The clinical and echocardiographic findings were adequate for the diagnosis and determining the clinical significance of even mild vascular anomalies in syndromic patients, despite these challenges. Robinow syndrome is an infrequent skeletal dysplasia caused by mutations in ROR2, WNT5A, or DVL1/3 genes, depicted by craniofacial features, mesomelic limb shortening, genital hypoplasia, and vertebral segmentation defects

(7). Moreover, coarctation of the aorta remains extremely uncommon in cardiovascular manifestations, which are documented in up to 15–20% of cases, commonly including pulmonary stenosis, ventricular septal defect, atrial septal defect, PDA, or tetralogy of Fallot (8). The coexistence of coarctation and sustained hypertension in this case supports the hypothesis of an underlying vascular developmental defect related to abnormal WNT–ROR2 signalling. Likely, in our patient, the coarctation has led to hypertension as seen in previous studies (9).

The effective management of this lies in the early diagnosis, followed by careful antihypertensive drug dosage, and multidisciplinary management is essential for optimising outcomes and preventing long-term cardiovascular complications in such rare but clinically significant presentations. To support our statement, even the mild lesion on echocardiography remained the pathology for the persistent hypertension, underscoring that even minor anatomical narrowing can have functional consequences, particularly in the presence of syndromic vascular abnormalities. Effective control was eventually accomplished with dual therapy using amlodipine and enalapril after the initial losartan intolerance, along with supportive interventions such as nutritional rehabilitation and physiotherapy. The chronic afterload stress has led to a reduction in ejection fraction (45–50%) with mild left ventricular dilation, highlighting that a comprehensive cardiovascular evaluation is essential, even in the absence of overt symptoms, as coarctation and hypertension may otherwise be overlooked. Therefore, early intervention is required in Robinow syndrome patients with cardiovascular anomalies for a better prognosis.

Conclusion

This case highlights the rare association of Robinow syndrome with progressive aortic coarctation and persistent hypertension, contributing to the lack of knowledge on the condition. The child's clinical path reveals how even minor vascular lesions can deteriorate over time and have a substantial impact on outcomes, particularly when syndromic symptoms and recurrent infections are present. For children with Robinow syndrome to have a better long-term prognosis, early identification, close cardiovascular monitoring, and coordinated multidisciplinary care are vital.

Declarations

Patient perspective

On follow-up, patient's father noted improvement in physical activity and appetite; however, he expressed concern over the long-term outcomes.

Informed consent

Written informed consent was obtained from the patient's father for publication of the report and physical images.

Funding: No funding was received for this study.

Conflicts of interest/Competing interests: The authors declare that they have no competing interests.

Ethics approval: Ethical approval was waived for this case report in accordance with institutional policy.

Consent to participate: Written informed consent was obtained from the patient's father for participation and publication of this case report.

Written Consent for publication: Written informed consent for publication of clinical details and images was obtained from the patient's father.

Availability of data and material: All data generated or analysed during this study are included in this published article.

Code availability: Not applicable.

Authors' contributions: AT conceived the idea for the case report and drafted the case presentation. FK participated in manuscript editing. MOM wrote the introduction, organized the references, and contributed Figures 1, 2, 3, and 4. RMMB wrote the discussion and conclusion. DAA reviewed and finalized the manuscript.

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Figures



Figure 1

showing dysmorphic facial



Figure 2

showing Distended Abdomen



Figure 3

showing Mesolimbic Shortening



Figure 4

showing Broad Thumb