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A Rare Case of Tetralogy of Fallot with Snijders Blok Syndrome

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Abstract

Tetralogy of Fallot (TOF) is the most common cyanotic disease in the world. Anatomic heart defects that occur in this disease cause hypoxia and shortness of breath in the patient. Early diagnosis and treatment by surgery is necessary for infants. Snijders Blok Syndrome is a rare syndrome that affects nose, skull bones, ears and development of CNS, etc. Patients with this syndrome are often at the risk of seizure, FTT, etc. This case report emphasizes the importance of recognizing and managing the coexistence of Snijders Blok syndrome and TOF. The unique clinical presentation and genetic findings in this patient provide valuable insights into the complexity of overlapping genetic disorders and congenital heart defects. Further studies are needed to expand our knowledge and improve clinical management strategies for individuals with similar comorbidities. This comorbidity was not report before according to our best knowledge.

Keywords: Tetralogy of Fallot • Snijders Blok syndrome • Nuchal translucency • Microcephaly • Genetic variant

Introduction

Chromodomain Helicase DNA-binding (CHD) proteins are an important group of ATP-dependent chromatin remodeling proteins that play a crucial role in modulating gene expression by utilizing the energy derived from ATP hydrolysis to regulate chromatin structure [1,2]. In the past, several recognized syndromes have been associated with the CHD protein family, but none specific to CHD3 proteins. However, in 2018, Snijders Blok et al. identified a syndrome related to mutations in CHD3 proteins through a study involving 35 propends. This syndrome is characterized by intellectual disability, developmental delays, macrocephaly, impaired speech and language skills, and distinct facial features [3]. Further research and case reports have indicated that this syndrome may also be associated with additional symptoms such as idiopathic central precocious puberty, hyper sociability, joint laxity, and autism [4-6].

Tetralogy of Fallot (TOF) is a congenital heart disease that encompasses embryological, anatomical malformations, pathophysiological aspects, and management considerations [7,8]. This disease can be caused by several problems such as interventricular communication or ventricular septal defect, biventricular connection of the aortic root overriding the muscular ventricular septum, obstruction of the right ventricular outflow tract and right ventricular hypertrophy [9]. TF has a prevalence of 3 in 10,000 live births and is the most common cause of cyanotic cardiac disease in patients beyond the neonatal age [10]. Additionally, it accounts for approximately one out of ten deaths related to all congenital cardiac lesions patients with TF may present with symptoms ranging from severe cyanosis and ductus-dependent pulmonary circulation to subtle cyanosis in older patients [11]. The primary management approach for TF involves complete surgical repair of the defect, typically performed between 3 to 6 months of age. However, the timing of the surgery may be adjusted based on the adequacy of oxygenation of pulmonary blood, which may require a more complex approach [12].

In this report, we present a rare case of a patient with Snijders Blok syndrome and tetralogy of Fallot, which is a unique comorbidity based on our current knowledge.

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Case Presentation

We present a case report of a pregnant woman, gravid 2 abortions 0 and living child 1, who was referred to our hospital at 24 weeks of gestational age due to a high Nuchal Translucency (NT) measurement detected during routine sonography at 12 weeks of pregnancy. The patient underwent amniocentesis to rule out chromosomal abnormalities, which yielded negative results. The mother had no history of diabetes, hypothyroidism, or medication use during pregnancy. Although the parents were not related, there was a strong family history of cardiovascular disease. Fatal echocardiography was performed and revealed criteria consistent with Tetralogy of Fallot (TOF). The pregnancy continued until 39 weeks when the patient underwent a Normal Vaginal Delivery (NVD). After birth, the infant was examined (birth weight 3/100, head circumference 33/1, length 52 cm) and found to have low-set ears and microcephaly. However, the family did not seek further intervention at that time. Subsequent pediatric cardiology examinations confirmed the diagnosis of TOF based on the presence of a right ventricular outflow tract obstruction, overriding aorta, malalignment ventricular septal defect, and right ventricular hypertrophy. Cardiac surgery was scheduled for several months later.

Before the scheduled surgery, the patient experienced a tonic-clonic seizure and was referred to a neurologist. Additional examinations revealed hypotonic, failure to thrive, craniosynostosis, and facial deformities, including telecanthus (increased distance between the inner corners of the eyes) and a broad nasal bridge. Deep tendon reflexes were normal. The patient was treated with levebel for tonic–clonic seizures. Following seizure treatment, a genetic test was conducted due to the presence of seizures, microcephaly, and dysmorphic facial features. The test revealed a heterozygous variant in the *DDX3X* gene, which is known to cause intellectual developmental disorder, X-linked syndromic, Snijders Blok type.

This case highlights the coexistence of Snijders Blok syndrome and Tetralogy of Fallot, which is a rare comorbidity. Further research and clinical management are warranted to understand the underlying mechanisms and optimize treatment strategies for patients with this unique combination of conditions.

Discussion

The presented case report describes a unique combination of Snijders Blok syndrome and Tetralogy of Fallot (TOF). Snijders Blok syndrome is a rare X-linked genetic disorder characterized by intellectual developmental disorder and dysmorphic facial features. TOF, on the other hand, is a congenital heart defect involving malformations of the heart's structure. The coexistence of these two conditions in the same patient adds complexity to the clinical presentation and management.

In this case, the patient initially presented with high nuchal translucency during routine sonography, which prompted further investigations, including amniocentesis to rule out chromosomal abnormalities. The results were negative, suggesting that the observed abnormalities were not related to chromosomal anomalies commonly associated with high nuchal translucency.

Fetal echocardiography confirmed the diagnosis of TOF, characterized by a combination of right ventricular outflow tract obstruction, overriding aorta, malalignment ventricular septal defect, and right ventricular hypertrophy (Figures 1-5). This finding, in conjunction with the family history of cardiovascular disease, further supported the diagnosis. The patient's pregnancy progressed until 39 weeks, at which point a normal vaginal delivery was performed.

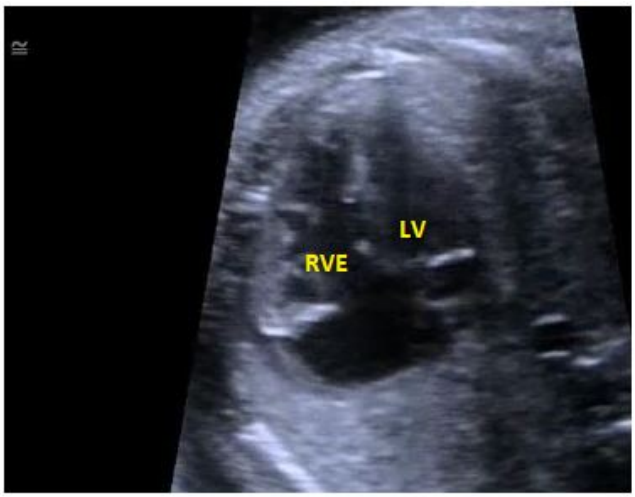

Figure 1. Apical four chamber view of fetal heart shows Right Ventricular Enlargement (RVE). LV: Left Ventricle.

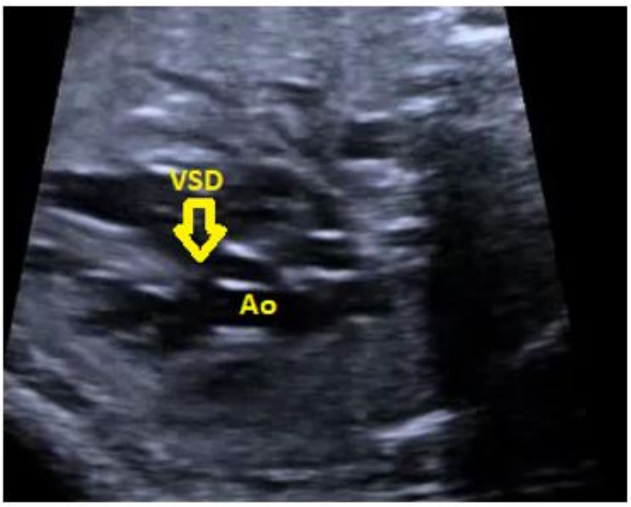

Figure 2. Septal view of the heart with slightly angulation shows a large Ventricular Septal Defect (VSD) and aortic overriding (yellow arrow). Ao; Aorta.

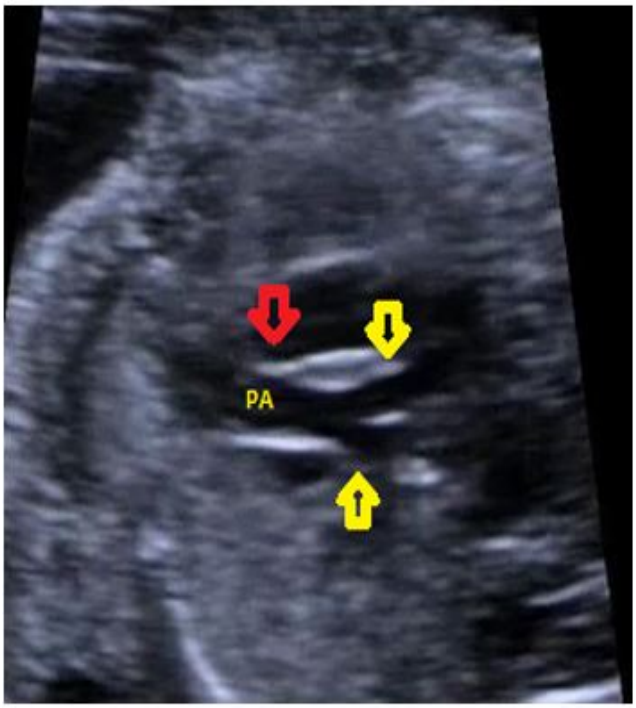

Figure 3. Short axis view of the great vessles shows a small Pulmonary Artery (PA, red arrow) and pulmonary branches (yellow arrows).

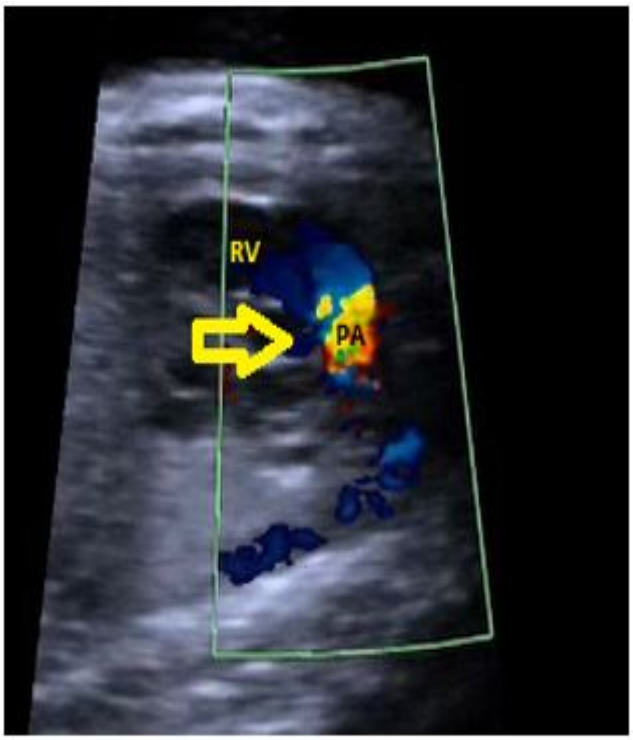

Figure 4. Color Doppler employment in pulmonary artery shows flows acceleration (yellow arrow), indicating a significant stenosis in pulmonary. RV: Right Ventricle.

Figure 5. The patient shown microcephalus, low set ear, board bridg nose, etc.

Postnatal, the infant exhibited additional clinical features, including low-set ears, microcephaly, and facial dysmorphic. Although these findings were consistent with Snijders Blok syndrome, the family did not initially seek further intervention. However, subsequent pediatric cardiology examinations confirmed the diagnosis of TOF.

The patient's clinical course was complicated by the occurrence of seizures, which led to a referral to a neurologist. The patient exhibited hypotonic, failure to thrive, craniosynostosis, and additional dysmorphic facial features. Genetic testing revealed a heterozygous variant in the *DDX3X* gene, which is associated with Snijders Blok syndrome.

The coexistence of Snijders Blok syndrome and TOF poses challenges in terms of clinical management and treatment planning. Each condition requires specialized care from different medical disciplines. In this case, cardiac surgery for TOF repair was scheduled for a later date, but the occurrence of seizures and the patient's overall clinical presentation necessitated an interdisciplinary approach involving neurology and genetics. The identification of the *DDX3X* gene variant further contributes to our understanding of the underlying genetic mechanisms associated with Snijders Blok syndrome. However, more research is needed to elucidate the specific genotype-phenotype correlations and the impact of the identified variant on the patient's clinical presentation.

This case report highlights the importance of a multidisciplinary approach in the management of complex medical conditions. Collaboration between specialists from various fields, such as cardiology, genetics, and neurology, is crucial for comprehensive care and optimal treatment outcomes for patients with rare and overlapping conditions. Future research efforts should focus on unravelling the underlying genetic and molecular mechanisms linking Snijders Blok syndrome and TOF, which may lead to improved diagnostic strategies and targeted therapeutic interventions for affected individuals.

Conclusion

In conclusion, the presented case report describes a rare and intriguing combination of Snijders Blok syndrome and Tetralogy of Fallot (TOF). This unique comorbidity highlights the complexity of overlapping genetic disorders and congenital heart defects. The patient's clinical presentation, including high nuchal translucency, microcephaly, dysmorphic facial features, and the diagnosis of TOF, posed challenges in terms of diagnosis and management.

The identification of a heterozygous variant in the *DDX3X* gene, associated with Snijders Blok syndrome, further contributes to our understanding of the genetic basis of this condition. However, more research is needed to establish the precise genotype-phenotype correlations and the impact of the identified variant on the patient's clinical features.

The management of this case required a multidisciplinary approach involving cardiology, genetics, neurology, and other relevant specialties. Collaboration between different medical disciplines was essential for comprehensive care and treatment planning.

This case report underscores the importance of further research to elucidate the underlying genetic and molecular mechanisms linking Snijders Blok syndrome and TOF. A better understanding of these mechanisms may lead to improved diagnostic strategies, tailored treatment approaches, and enhanced outcomes for patients with similar comorbidities.

In summary, this case report provides valuable insights into the complexity of overlapping genetic conditions and congenital heart defects. It highlights the need for interdisciplinary collaboration and ongoing research to advance our knowledge and optimize the management of individuals with rare and overlapping conditions such as Snijders Blok syndrome an d TOF.

Conflict of Interest

The authors have no conflict of interest to disclose.

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