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Indian Journal of Clinical and Experimental Ophthalmology

Journal homepage: www.ijceo.org

Case Report

Ritscher-Schinzel syndrome with venous sinus thrombosis: A rare association

Dinkar Yadav[1], **Renu Sharma**[1], **Neha Yadav**[2]*, **Suchi Bhalla**[3], **Kapil Bhalla**[1]

[1]*Dept. of Pediatrics, Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana, India*
[2]*Dept. of Ophthalmology, Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana, India*
[3]*Dept. of Microbiology, Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana, India*

ARTICLE INFO

Article history:
Received 23-01-2024
Accepted 20-05-2024
Available online 30-12-2024

Keywords:
3C syndrome
Autosomal recessive inheritance
Cardiac anomalies

ABSTRACT

Ritscher-Schinzel syndrome or Cranio-cerebello-cardiac syndrome (3C syndrome) is a rare disorder with autosomal recessive inheritance. Very few reported cases till now (<50 cases) and a prevalence of 1 in 1 million live births. It is characterized by cardiac defects, central nervous system anomalies like cerebellar hypoplasia, and craniofacial anomalies. Exact etiology is difficult to understand however mutation in chromosome 8q24 coding for strumpellin protein has been found. Index case presented with complaints of craniofacial abnormalities with abnormal cardiovascular examination. Typical clinical presentation, Echocardiography and Neuroimaging support the diagnosis of this rare syndrome.

1. Introduction

Ritscher - Schinzel syndrome or 3C syndrome is a rare disorder with cranio-facial, cerebeller and cardiac anomalies.[1,2] It is an autosomal recessive disorder with incidence of 1 in 1 million live births.[3] It is caused by mutation in chromosomes 8q24.13 which encodes for strumpllin protein.[4] Cardiovascular and cerebral anomalies are the most common cause of mortality. In this case report, we discuss the typical clinical presentation and diagnosis of this rare disorder.

2. Case Presentation

A 9 days old female baby of non-consanguineous marriage was referred to the tertiary care center from the district hospital because of lethargy and cleft palate. She was born as preterm birth (34 weeks gestation), to a primigravida mother, with a birth weight of 2.0 kg. by a normal vaginal delivery with no immediate complication at birth. In antenatal history, mentioned ultrasonographic findings were poorly formed cerebellun, undetectable vermis, and posterior fossa defects with mega cisterna.

The infant was on expressed breast milk with feeding done by Katori-spoon, had a weight loss of 340 gram. In the perinatal history were not found risk factors as smoking, alcohol intake, drug intake, substance abuse, x-ray exposure, diabetes mellitus, thyroid disease, fever or infectious disease, autoimmune disease, or any chronic illness. On examination, the index case presented with cleft palate, low set ears, prominent occiput, and micrognathia (Figure 1), murmur was audible on auscultation. Because of the anomalous antenatal scan, ECHO study and neuroimaging were planned. Neuroimaging revealed enlarged cisterna magna with cerebellar vermis aplasia (Figure 2) and an unusual finding of venous sinus thrombosis in left lateral sinus. Ophthalmological examination revealed megalocornea (Figure 2). ECHO study showed cardiac malformations expressed as double outlet right ventricle (Figure 3) with a large inlet ventricular septal defect, as

* *Corresponding author*.
E-mail address: dr.dinku2012@gmail.com (N. Yadav).

https://doi.org/10.18231/j.ijceo.2024.139

well as an atrial septal defect of osteum secundum type and patent ductus arteriosus. Detailed clinical examination as well as ultrasonogram and infantogram of the baby (for bone anomalies) were performed to screen for other anomalies.Ultrasonogram of the abdomen showed left kidney grade II hydronephrosis. Infantogram did not reveal any anomaly. Based on these clinical findings and imaging studies, Ritscher Schinzel syndrome was diagnosed in the index case.

The karyotyping in this index case was normal. Molecular diagnosis was not performed because it was not available due to high cost of the investigation. Cardiac surgery was planned, but the index case was discharged on the parent's request because of poor prognosis due to the multiple congenital anomalies. The patient has been included in a follow-up protocol and, one month after discharge he appears without any significant complication.

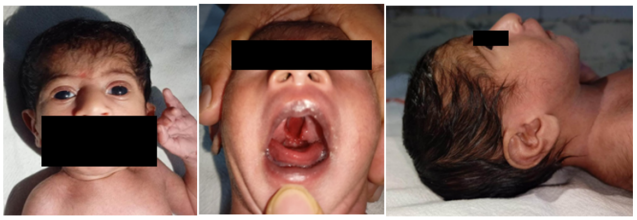

Figure 1: Showed clinical picture of megalocornea, cleft palate, low set ears with micrognathia (From left to right)

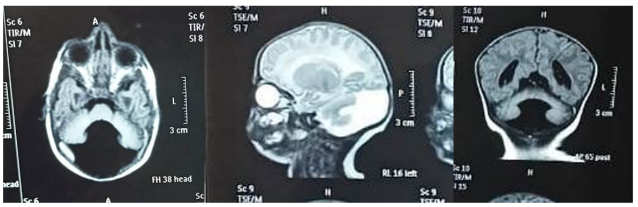

Figure 2: MRI brain showed enlarged cisterna magna, cerebeller vermis aplasia and venous sinus thrombus

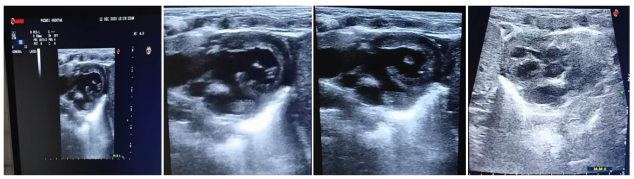

Figure 3: Echo study showed double outlet right ventricle with large inlet ventricular septal defect, atrial septal defect of osteum secundum type and patent ductus arteriosus

3. Discussion

Ritscher - Schinzel syndrome is inherited as an autosomal recessive disease (8q24 WASHC5). 8q24 WASHC5 encodes Strumpellin proteins of the family known as WAS Hopathies involved in actin polymerization and multiple endosomal transport process.[5]

The clinical presentation includes craniofacial features such as low-set ears, micrognathia, prominent occiput, ophthalmological issues like palpebral fissure down-slanting, hypertelorism, and cleft palate alone, or cleft lip with cleft palate.[6] The characteristic central nervous system anomalies are Dandy-Walker malformation or its variant. The cardiac anomalies are characteristically present as septal defects, valvular defects, and conotruncal anomalies. Macrocephaly is not a principal sign of the disease; if present, it is likely associated with hydrocephalous, warranting shunt surgery for hydrocephalus.[7] Macrocephaly without hydrocephaly may be present.Index case presented with complaints of craniofacial anomalies such as cleft palate, prominent occiput, migrognatia, megalocornea and low set ears with systolic murmur on cardiovascular examination.

Ritscher - Schinzel syndrome or 3C syndrome has an incidence of less than 1 per million live birth. To date, less than 50 cases have been reported. In the affected individual, this syndrome may manifest with more than one type of cardiac malformation. Diagnosis can be made by characteristic clinical findings with the appropriate radiological investigation. In Index case, diagnosis done on the basis of craniofacial anomalies with cardiac anomalies on echocardiography and cerebral anomaly on neuroimaging. Management includes evaluation of affected systems and treatment of pathologic manifestations. Management also involves multidisciplinary approaches, including individualized educational programs and specific rehabilitation programs, that aim at improving developmental disability and motor dysfunctions.[5] Cardiac malformation requires specific care, often through surgery. It is worth noting that cardiac and CNS malformations determine the outcome of the affected patient.[8]

4. Conclusion

Few cases, mostly sporadic, have been reported in the literature. Thence, a thorough understanding of this syndrome is essential for a correct postnatal diagnosis. Management requires a multidisciplinary approach, including advanced surgical support for cardiac and cranial malformations. Appropriate antenatal screening and molecular testing can be offered to such at-risk families who plan to have other babies.

5. Source of Funding

None.

6. Conflict of Interest

None.

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Author's biography

Dinkar Yadav, Senior Resident https://orcid.org/0009-0006-2566-7428

Renu Sharma, Junior Resident

Neha Yadav, Senior Resident

Suchi Bhalla, Professor

Kapil Bhalla, Professor

Cite this article: Yadav D, Sharma R, Yadav N, Bhalla S, Bhalla K. Ritscher-Schinzel syndrome with venous sinus thrombosis: A rare association. *Indian J Clin Exp Ophthalmol* 2024;10(4):802-804.