Asian Journal of Case Reports in Medicine and Health

Volume 8, Issue 1, Page 5-10, 2025; Article no.AJCRMH.129502

Jacobsen Syndrome with 11q Deletion, Trigonocephaly, and MYBPC3 Mutation: A Unique Case Report

Nijalingappa.K.Kalappanavar [a++], Sonatta Monica Jose [b*], Sonoma Maria K.B [b] and Harshith M Pisale [b]

[a] Department of Pediatrics, SS Institute of Medical Sciences and Research Centre, Davangere-577004, Karnataka, India.
[b] Department of Pharmacy Practice, Bapuji Pharmacy College, Shamanur Road, SS Layout, Davanagere-577004, Karnataka, India.

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Article Information

DOI: https://doi.org/10.9734/ajcrmh/2025/v8i1211

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/129502

Case Report

Received: 04/11/2024
Accepted: 08/01/2025
Published: 14/01/2025

ABSTRACT

Jacobsen syndrome (JS), also known as 11q deletion disorder, is a rare chromosomal condition characterized by a wide range of congenital anomalies, developmental delays, and hematological abnormalities. This report presents the case of a 9-month-old female child with trigonocephaly, mild developmental delay, hypotonia, and ocular tracking issues. Initial examinations revealed a small atrial septal defect (ASD), a depressed and broad nasal bridge, epicanthic folds, low-set ears, overfolded helices, a smooth philtrum, and a high palate. Genetic testing, including clinical exome sequencing and chromosomal microarray analysis, identified a pathogenic heterozygous copy

[++] Professor and Head of the Department;
**Corresponding author: E-mail: pappasona2001@gmail.com;*

Cite as: *Nijalingappa.K.Kalappanavar, Sonatta Monica Jose, Sonoma Maria K.B, and Harshith M Pisale. 2025. "Jacobsen Syndrome With 11q Deletion, Trigonocephaly, and MYBPC3 Mutation: A Unique Case Report". Asian Journal of Case Reports in Medicine and Health 8 (1):5-10. https://doi.org/10.9734/ajcrmh/2025/v8i1211.*

number deletion in the 11q23.3-q25 region, confirming the diagnosis of Jacobsen syndrome. Additionally, mutations in the MYBPC3 and SYNE1 genes were identified. The MYBPC3 mutation is notable due to its association with cardiomyopathy, a finding that adds complexity to the cardiac profile typically observed in Jacobsen syndrome. Cardiomyopathy was diagnosed in the patient, emphasizing the importance of early cardiological evaluation. The diagnosis underscores the importance of early genetic evaluation in children with congenital anomalies and developmental delays. Comprehensive management involving genetic counseling, regular monitoring, and supportive therapies is essential to address the diverse needs of patients with Jacobsen syndrome. This case highlights the necessity for continued research and awareness to enhance understanding, treatment, and long-term outcomes for individuals affected by this rare chromosomal disorder.

Keywords: Jacobsen syndrome; trigonocephaly; 11q deletion; hypertelorism; developmental delay.

1. INTRODUCTION

In 1973, Petrea Jacobsen reported the first case of a patient with dysmorphic features, developmental delay, and congenital heart disease (atrial and ventricular septal defects) linked to an 11q deletion inherited from the father. Since then, more than 200 similar cases have been documented (Serra et al., 2021).

Jacobsen syndrome is a multi-congenital anomaly/mental retardation (MCA/MR) contiguous gene syndrome resulting from the partial deletion of the long arm of chromosome 11. It is estimated to occur in 1 out of every 100,000 births, with a female-to-male ratio of 2:1 (Blazina et al., 2016; Dalm et al., 2015; Jones et al., 1994). The most common clinical features include pre- and postnatal physical growth retardation, psychomotor delay, and distinctive facial dysmorphisms, such as skull deformities, hypertelorism, ptosis, coloboma, down-slanting palpebral fissures, epicanthal folds, a broad nasal bridge, a short nose, a V-shaped mouth, and small, low-set, posteriorly rotated ears. Abnormal platelet function, thrombocytopenia, or pancytopenia are typically present at birth (Mattina et al., 2009).

Jacobsen syndrome (JS) is usually not inherited, but an individual with the condition can transmit the deletion to their offspring (Ichimiya et al., 2018; Favier et al., 2015). According to published data, JS is linked to attention deficit-hyperactivity disorder (ADHD) and a higher prevalence of autism spectrum disorders. About a quarter of children with JS do not survive past infancy, with congenital heart diseases being the leading cause of death, followed by hematological disorders. Survivors require long-term specialized care, and the oldest known patient with JS is approximately 50 years old (Jurcă et al., 2017).

2. PRESENTATION OF CASE

Here is a 9 month old female child presented with trigonocephaly with metopic ridging at birth, mild developmental delay, hypotonia, eye tracking issue? hearing impairment? small ASD in the first ECHO scan, AF-admitting 1 finger nevus flammeus, depressed and broad nasal bridge, epicanthic folds, low set ears, overfolded helices, smooth philtrum, high palate, sacral dimple, mild lower length discrepancy, increased tone and jerky pursuits.

MRI of the brain showed T2/FLAIR hypo-intensities with cysts in the frontal region, simplified gyration (? mild polymicrogyria) only P1L1 is myelinated and T1 hypointense-corresponding hyperintensities.

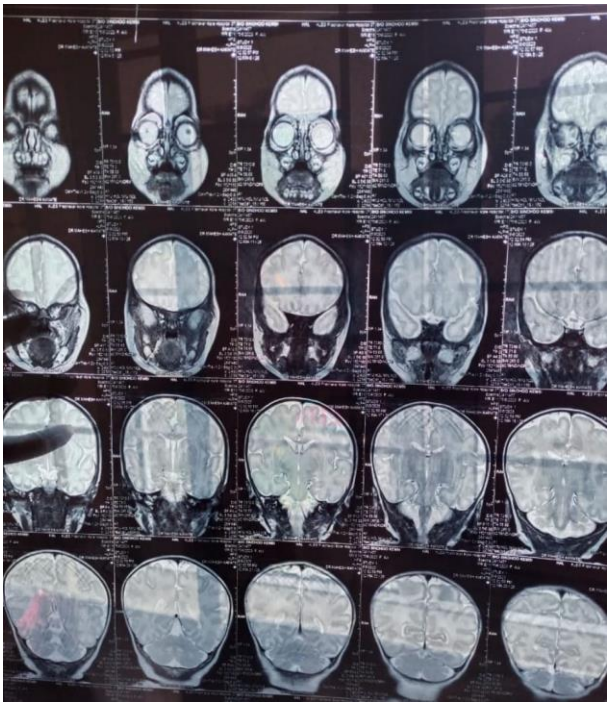
Clinical exome sequencing done elsewhere revealed a pathogenic variant in the MYBPC3 gene [c.33372C>A, p. Cys1124 Ter] and a variant of uncertain significance in the “SYNE1” gene [c.17938GA. p. Glu598Lys] and a likely pathogenic copy number deletion in the chromosome 11. Karyoseq with Karyotyping done elsewhere showed pathogenic CNV deletion (Chr 11: 120943729-135008516) (GRCh 37).

Whole exome sequencing done at NIMAHNS also revealed the same chromosome “11q23.3q25” copy number loss. She is suspected to be suffering from chromosome 11q, terminal deletion syndrome.

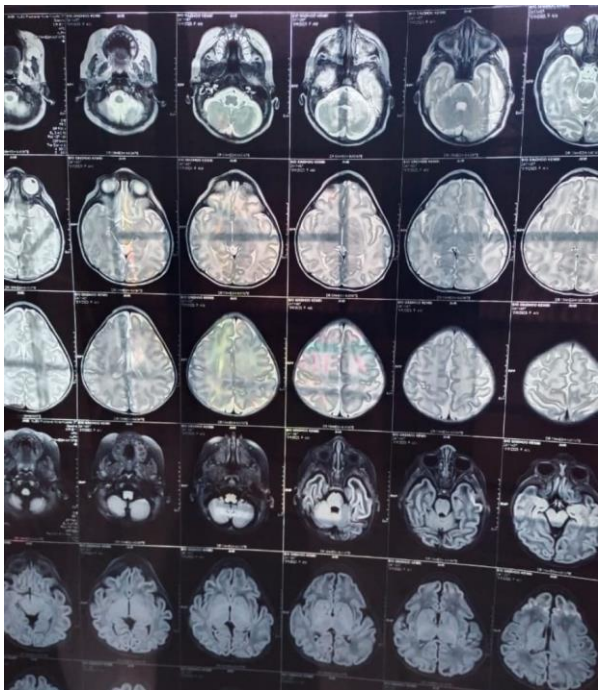
Chromosomal Microarray was done: Results were found to be positive – Pathogenic copy number loss relevant to the phenotype described in the subject was identified.

Table 1. Chromosomal Microarray

Type	Chromosome region	Size	Genomic coordinates	Zygosity	Classification
Copy no. Loss	11q23.3-11q25	14.07 Mb	Arr [GRCh 37] 11q23.3-11q25 (120864922-134944006X1)	Heterozygous	Pathogenic



(A)



(B)

Fig. 1(A-B). MRI outcome

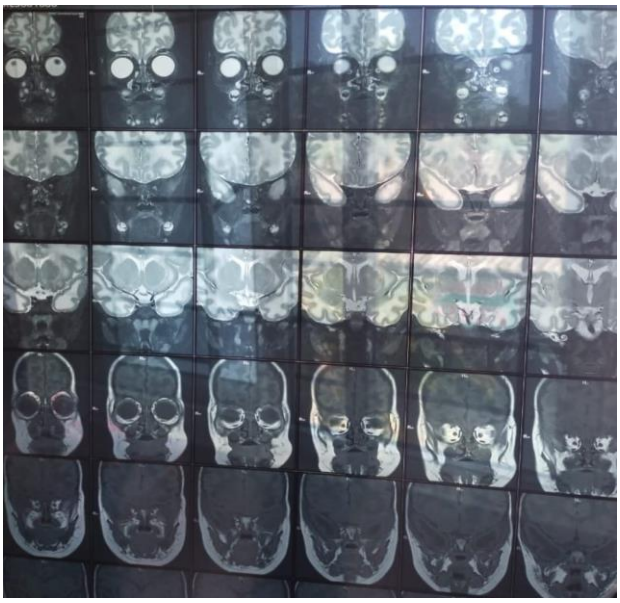


Fig. 2. MRI suggesting craniosynostosis (trigonocephaly) due to early fusion of the metopic suture

The figs. suggest Craniosynostosis (trigonocephaly) due to early fusion of the metopic suture as described

Report Summary – A heterozygous copy number loss. In 11q23.3-q25 region spanning the genomic coordinates chr11:120864922-134944006 was identified. Similar sized copy no. loss overlapping this region have been reported in DECIPHER associated with similar phenotypes. This region comprises of 156 genes including HEPACAM. The leukoencephalopathy phenotype is secondary to haploinsufficiency of the HEPACAM gene (MLC2) which is reported in literature. The same copy number loss was also observed in exome sequencing of the same proband. In addition, the clinical phenotype of the proband matches to that of the proband. In view of all the current evidence, this deletion is considered to be pathogenic.

Final Interpretation – In view of the presence of a heterozygous pathogenic deletion in 11q23.3-q25 along with the matching clinical phenotype, the diagnosis of "11q23.3-q25 deletion syndrome" is confirmed in the proband.

3. DISCUSSION

Jacobsen syndrome (11q23 deletion syndrome) is a rare genetic disorder caused by a deletion on the long arm of chromosome 11. This condition is associated with various congenital anomalies and intellectual disabilities. The clinical features of Jacobsen syndrome can vary depending on the size and location of the deletion. While craniosynostosis, particularly trigonocephaly due to early fusion of the metopic suture, is not a typical characteristic, it has been reported in a few cases. This case report highlights a rare presentation of Jacobsen syndrome with trigonocephaly, developmental delays, hypotonia, and distinct facial dysmorphisms, confirmed through chromosomal microarray and exome sequencing.

The proband in this case exhibited developmental delays, hypotonia, and facial dysmorphisms, including epicanthic folds, low-set ears, and a broad nasal bridge. Additionally, the patient had a small atrial septal defect (ASD), which is a common congenital heart defect seen in Jacobsen syndrome. These features align with previously reported cases of Jacobsen syndrome. However, the presence of craniosynostosis (specifically trigonocephaly) is a rare finding in this condition.

A review by Mattina et al. (2009) discussed the phenotypic variability in Jacobsen syndrome, highlighting congenital heart defects, intellectual disabilities, and distinct facial features as the most common clinical presentations. Craniosynostosis was not commonly reported, but some cases have shown a connection between large deletions and cranial anomalies like trigonocephaly. In this case, the early fusion of the metopic suture suggests that cranial development genes within the deleted region may play a role in this atypical presentation.

Further genetic studies have identified the HEPACAM gene, located within the 11q23-q25 deletion region, as a significant contributor to neurodevelopmental issues and motor delays. The loss of this gene could explain some of the developmental delays and hypotonia seen in the patient. This deletion pattern aligns with findings in genetic databases such as DECIPHER, strengthening the association between these genetic alterations and the observed clinical features (Mattina et al., 2009; Chatzimichali et al., 2015).

Despite the phenotypic variability in Jacobsen syndrome, hematological abnormalities, particularly thrombocytopenia, remain hallmark features, as described by Grossfeld et al. (2004). However, in this case, the absence of hematological issues highlights the condition's broad clinical spectrum. This variability underscores the need for genetic testing to accurately diagnose Jacobsen syndrome, especially in atypical cases.

Comprehensive management of Jacobsen syndrome requires a multidisciplinary approach involving specialists from neurology, cardiology, genetics, and craniofacial surgery. Early diagnosis through chromosomal microarray and exome sequencing is essential for identifying atypical features and ensuring appropriate interventions. This case contributes to the growing body of knowledge on Jacobsen syndrome by expanding the known phenotypic spectrum and emphasizing the importance of genetic testing in diagnosing rare presentations (Böhm et al., 2006; Noh et al., 2002; Gadzicki et al., 2006).

The findings stress the importance of genetic studies for improving diagnostic accuracy and tailoring patient management strategies. Identifying and reporting atypical cases can aid clinicians and researchers in better understanding the complexities of Jacobsen syndrome and improving care for affected individuals.

4. CONCLUSION

Jacobsen disease, also known as 11q deletion disorder, is a rare chromosomal condition with a spectrum of clinical manifestations. This case highlights the importance of early diagnosis and comprehensive management to improve the quality of life for affected individuals. Our patient presented with characteristic features such as developmental delays, congenital anomalies, and hematological abnormalities. The multidisciplinary approach involving genetic counseling, regular monitoring, and supportive therapies proved crucial in addressing the diverse needs of the patient. Continued research and awareness are essential to enhance understanding and treatment of Jacobson disease, ultimately paving the way for better prognostic outcomes.

CONSENT

As per international standards, parental written consent has been collected and preserved by the author (s).

ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

ACKNOWLEDGEMENTS

We would like to express our sincere gratitude to the patient's family for their cooperation and trust throughout the diagnostic and treatment process. we extend our appreciation to the medical team involved in the patient's care for their dedication and expertise. special thanks to the geneticists and laboratory staff for their crucial contributions to the diagnostic process. We acknowledge the support and guidance provided by Dr. N K Kalappanavar, Professor, Department of Pediatrics, SSIMS & RC in the preparation of this case report. Finally, we are grateful to our institution for providing the necessary resources and support to carry out this work.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

Blazina, Š., Ihan, A., Lovrečić, L., & Hovnik, T. (2016). 11q terminal deletion and combined immunodeficiency (Jacobsen syndrome): Case report and literature review on immunodeficiency in Jacobsen

syndrome. *American Journal of Medical Genetics Part A, 170*(12), 3237-3240.

Böhm, D., Hoffmann, K., Laccone, F., Wilken, B., Dechent, P., Frahm, J., Bartels, I., Bohlander, S. K. (2006). Association of Jacobsen syndrome and bipolar affective disorder in a patient with a de novo 11q terminal deletion. *American Journal of Medical Genetics Part A, 140*(4), 378-382.

Chatzimichali, E. A., Brent, S., Hutton, B., Perrett, D., Wright, C. F., Bevan, A. P., Hurles, M. E., Firth, H. V., & Swaminathan, G. J. (2015). Facilitating collaboration in rare genetic disorders through effective matchmaking in DECIPHER. *Human Mutation, 36*(10), 941-949.

Dalm, V. A., Driessen, G. J., Barendregt, B. H., van Hagen, P. M., & van der Burg, M. (2015). The 11q terminal deletion disorder Jacobsen syndrome is a syndromic primary immunodeficiency. *Journal of Clinical Immunology, 35*, 761-768.

Favier, R., Akshoomoff, N., Mattson, S., & Grossfeld, P. (2015). Jacobsen syndrome: Advances in our knowledge of phenotype and genotype. *American Journal of Medical Genetics Part C: Seminars in Medical Genetics, 169*(3), 239-250.

Gadzicki, D., Baumer, A., Wey, E., Happel, C. M., Rudolph, C., Tönnies, H., Neitzel, H., Steinemann, D., Welte, K., Klein, C., & Schlegelberger, B. (2006). Jacobsen syndrome and Beckwith-Wiedemann syndrome caused by a parental pericentric inversion inv(11)(p15q24). *Annals of Human Genetics, 70*(6), 958-964.

Grossfeld, P. D., Mattina, T., Lai, Z., Favier, R., Jones, K. L., Cotter, F., Jones, C., & 11q Consortium. (2004). The 11q terminal deletion disorder: A prospective study of 110 cases. *American Journal of Medical Genetics Part A, 129*(1), 51-61.

Ichimiya, Y., Wada, Y., Kunishima, S., Tsukamoto, K., Kosaki, R., Sago, H., Ishiguro, A., & Ito, Y. (2018). 11q23 deletion syndrome (Jacobsen syndrome) with severe bleeding: A case report. *Journal of Medical Case Reports, 12*, 1-4.

Jones, C., Slljepcevic, P., Marsh, S., Baker, E., Langdon, W. Y., Richards, R. I., & Tunnacliffe, A. (1994). Physical linkage of the fragile site FRA11B and a Jacobsen syndrome chromosome deletion breakpoint in 11q23.3. *Human Molecular Genetics, 3*(12), 2123-2130.

Jurcă, A. D., Kozma, K., Ioana, M., Streaţă, I., Petcheşi, C. D., Bembea, M. A., Jurcă, M. C., Cuc, E. A., Vesa, C. M., & Buhaş, C. L. (2017). Morphological and genetic abnormalities in a Jacobsen syndrome. *Romanian Journal of Morphology and Embryology, 58*(4), 1531-1534.

Mattina, T., Perrotta, C. S., & Grossfeld, P. (2009). Jacobsen syndrome. *Orphanet Journal of Rare Diseases, 4*, 1-0.

Noh, J. H., Park, I. S., Lee, H. K., & Kim, Y. C. (2002). A case of Jacobsen syndrome. *Journal of the Korean Society of Neonatology, 9*(2), 211-214.

Serra, G., Memo, L., Antona, V., Corsello, G., Favero, V., Lago, P., & Giuffrè, M. (2021). Jacobsen syndrome and neonatal bleeding: Report on two unrelated patients. *Italian Journal of Pediatrics, 47*, 1-8.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/129502