International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Barakat Syndrome: Case Report of A Rare Multisystem Genetic Disorder

Dr. Venugopal Reddy Iragamreddy[1], Dr. Sushma Abbani Manjunath[2], Dr. Abhishek S Aradhya[3], Dr. Dinesh Kumar Vuppu[4]

[1,2]Pediatrician, Pediatrics, Ovum Woman and Child Speciality Hospital
[3,4]Neonatologist, NICU, Ovum Woman and Child Speciality Hospital

Abstract
Barakat syndrome, also known as Hypoparathyroidism, Deafness, Renal disease (HDR) syndrome, is a rare autosomal dominant disorder. We report a case of a newborn female who presented with neonatal hypocalcemia, congenital hypothyroidism, and distinctive craniofacial features. Genetic testing confirmed a GATA3 mutation consistent with Barakat syndrome. Despite the absence of renal involvement at birth, the diagnosis was established based on clinical and genetic findings. This case highlights the variable presentation of Barakat syndrome and underscores the importance of early recognition, multidisciplinary evaluation, and genetic confirmation to guide long-term management and family counseling.

Keywords: Hypoparathyroidism, Hypocalcaemia, GATA 3 mutation.

Introduction

Barakat syndrome, also called HDR syndrome, is an autosomal dominant disorder characterized by a triad of hypoparathyroidism, sensorineural deafness, and renal disease (dysplasia, steroid-resistant nephrosis with progressive renal failure).

It has been attributed to monoallelic deleterious variants of GATA3, which encodes GATA-binding protein-3 (OMIM 131320), a transcription factor necessary for the embryonic development of the parathyroid glands, the auditory system, and the kidneys, as well as for the expression of genes encoding T-cell receptor subunits[1].

The parathyroid glands in these children are hypoplastic or absent. Hypocalcemia may occur during the newborn period or remain unnoticed until later childhood. Malformations of the uterus and vagina (didelphic uterus, septate vagina) can be present in females with this disorder.

Case report

Here is a case report of a female newborn born to a mother with a history of previous abortion through intrauterine insemination (IUI), from a non-consanguineous marriage.

The baby presented at 12 hours of life with stridor and hypocalcemia. No significant antenatal, perinatal, or family history was noted. On physical examination, microcephaly, hypoplasia of the depressor anguli oris, and bilateral microtia with preauricular skin tags were observed (Figure 1).

A comprehensive diagnostic workup was performed to uncover the aetiology of the baby's symptoms and physical findings and to confirm the diagnosis. Ionised calcium -1.03 mmol/L.

TSH – 44 micro IU/ml (elevated), USG Neck – Ectopic thyroid, Parathyroid hormone – 45 pg/ml (Normal range: 15-65 pg/ml). 2D Echo showed ostium secundum ASD. BERA at 3 months indicated normal hearing in the right ear, with peak V wave obtained up to 40 dBnHL, suggestive of normal bone conduction on the left side. USG kidneys were normal. Whole exome sequencing by next-generation sequencing (NGS) revealed GATA3 gene mutation (transcript number **NM 001002295.2**) in Exon 4, a heterozygous missense variation [Variant c.901C>g (p.Leu301Val)] indicating Barakat syndrome.

Hypocalcaemia and hypothyroidism were treated with IV calcium gluconate, followed by calcium and thyroid supplements respectively. The baby is currently 4 months old in follow-up and is being monitored for hypocalcemia and proteinuria.

Discussion

Barakat syndrome can occur at any age, and patients with this condition usually show symptoms related to hypocalcemia. It was first reported in 1977 by Barakat et al.[2] Mutations or terminal deletions of the zinc-transcription factor GATA3 gene (OMIM 131320) located on the telomeric region of chromosome 10p are responsible for the characteristic features of this syndrome. Beyond the typical manifestations of Barakat syndrome, larger deletions on chromosome 10p have also been linked to developmental delays, intellectual disabilities, autism spectrum behaviors, anomalies of the female reproductive tract, facial dysmorphism, congenital heart anomalies, and immune system deficiencies[3]. In the largest review to date, which included 180 cases, the majority (64.4%) exhibited all three hallmark features of the syndrome, with hearing loss being the most prevalent, observed in approximately 96.7% of patients. This was followed by hypocalcemia in 93.3% and renal involvement in 72.2% of cases[4].

Hypoparathyroidism causes either symptomatic or asymptomatic hypocalcemia due to absent or inadequately low secretion of parathyroid hormone (PTH). Sensorineural hearing loss is a consistent finding, usually affecting both ears and being more prominent at higher frequencies. Auditory brain stem responses are normal initially. Distortion product auto-acoustic emissions (DPAEs) are typically absent, indicating an important role of outer hair cells in the etiology. Animal studies have confirmed these progressive morphological deteriorations. The severity of kidney involvement can vary greatly—from no detectable renal abnormalities to conditions such as renal dysplasia, hypoplasia, cystic kidneys, and vesicoureteral reflux. Many patients eventually develop advanced chronic kidney disease, often requiring renal replacement therapy[5].

Deafness or hypocalcemia caused by hypoparathyroidism is the initial feature of the syndrome. The complete HDR is observed in 64% of patients, ‘HD’ in 27%, ‘DR’ in 4%, ‘R’ in 1.7%, ‘HR’ in 1.7%, and ‘D’ in 0.6%, respectively[6]. Chenouard et al[7] reported a patient presenting with hypocalcemia due to hypoparathyroidism at 17 months old, who developed renal abnormalities and deafness by age 4. Aside from 2 patients by Nakamura et al[8], most patients experience onset of symptoms mainly in the second decade of life.

In our case, the neonate presented with hypocalcemia, congenital hypothyroidism, and microtia. Other features like hypoparathyroidism, deafness, and renal anomalies may develop later in life. Early genetic diagnosis will now help us to monitor for hypocalcemia, hypophosphatemia, hypercalciuria, and renal abnormalities. The plan is to get a bone-anchored hearing aid (BAHA) in follow-up. Early recognition is crucial for effective management, especially in preventing complications related to hypocalcemia and renal dysfunction. Genetic testing confirms the diagnosis and allows for appropriate counseling and

screening of at-risk family members. Supportive investigations in suspected cases include measuring parathyroid hormone (PTH) levels, serum calcium, ABER test, and renal imaging.

Conclusion

Barakat syndrome may not always display the full triad. Recognizing its incomplete forms is crucial, as early diagnosis and proactive management can greatly lessen long-term complications related to hypocalcemia and renal problems.

References

1. Shaw NJ. A Practical Approach to Hypocalcaemia in Children. Endocr Dev. 2015;28:84-100.
2. Barakat AY, D'Albora JB, Martin MM, Jose PA. Familial nephrosis, nerve deafness, and hypoparathyroidism. J Pediatr. 1977 Jul;91(1):61-4.
3. Lindstrand A, Malmgren H, Verri A, Benetti E, Eriksson M, Nordgren A, et al. Molecular and clinical characterization of patients with overlapping 10p deletions. Am J Med Genet A. 2010;152A:1233-43.
4. Zhu AS, Larrow DR, Cohen MS. Barakat syndrome presenting as isolated sensorineural hearing loss. Otolaryngol Case Rep. 2024;30:100573
5. Singh K, Sethi J, Bhargava V. Hyperkalemia unveiled: A case of Barakat syndrome. Indian J Nephrol 2020;30:135-6.
6. Barakat AJ, Raygada M, Rennert OM. Barakat syndrome revisited. Am J Med Genet A. 2018 Jun;176(6):1341-1348.
7. Chenouard A, Isidor B, Allain-Launay E, Moreau A, Le Bideau M, Roussey G. Renal phenotypic variability in HDR syndrome: glomerular nephropathy as a novel finding. Eur J Pediatr. 2013 Jan;172(1):107-10.
8. Nakamura A, Fujiwara F, Hasegawa Y, Ishizu K, Mabe A, Nakagawa H, Nagasaki K, Jo W, Tajima T. Molecular analysis of the GATA3 gene in five Japanese patients with HDR syndrome. Endocr J. 2011;58(2):123-30.

Figure legends:

Figure 1: A. Hypoplastic depressor anguli oris, B. Microtia and preauricular skin tags, C. skin tags