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Case Report

Microcephaly, Deafness, and Renal Dysplasia: A Case of Barakat Syndrome

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ABSTRACT

Background: Barakat syndrome is a rare autosomal dominant disorder characterized by hypoparathyroidism, sensorineural deafness, and renal disease, collectively known as HDR syndrome. This disease is caused by the mutation of *GATA3* gene located on chromosome 10p15. *GATA3* is involved in the embryonic development of kidneys, inner ears, parathyroid glands, and central nervous systems.

Case report: Herein, we presented a 20-month-old female with seizure and microcephaly, congenital left kidney dysplasia, hypoparathyroidism, and bilateral sensorineural deafness. Her laboratory tests were consistent with hypoparathyroidism, and the chromosomal study revealed a deletion in chromosome 10. The patient was diagnosed as a case of Barakat syndrome based on her clinical and laboratory tests. The microarray-based comparative genomic hybridization study of the patient was compatible with the monosomy of 10p15.3p13 and trisomy of 12p13.33p13.33.

Conclusion: It is important to be aware of rare inherited conditions like Barakat syndrome (HDR syndrome) in a patient with abnormal presentations, such as seizure, neurodevelopmental delay, kidney defects associated with hearing loss, and clinical abnormalities associated with hypoparathyroidism.

Keywords: Barakat syndrome, Hypoparathyroidism, Microcephaly

Introduction

Barakat syndrome is a rare autosomal dominant disorder, which is known as a hypoparathyroidism, deafness, and renal dysplasia (HDR) syndrome (1). This disease was first described in siblings with hypocalcemia and proteinuria (2). Mutations in *GATA3*, a gene localized in 10p14-15, have been detected in the affected cases (3). *GATA3* is involved in the embryonic development of the kidneys, inner ears, parathyroid glands, and central nervous systems (4).

In this report, we presented a case of Barakat syndrome with microcephaly, neurodevelopmental delay, congenital left kidney dysplasia, hypoparathyroidism, and bilateral sensorineural deafness.

Case report

A 20-month-old baby was admitted to the hospital with fever, vomiting, and history of recurrent urinary infectious disease. The patient was a known case of microcephaly and neurodevelopmental delay. She had been experiencing recurrent admissions due to seizure within the first three months of birth.

She was born prematurely to non-consanguineous parents with gestational age of 36 weeks, and intrauterine growth retardation was diagnosed based on birth weight of 1800 g, head circumference of 31 cm, and length of 48 cm. She had a normal Apgar score and was fed with both breast milk and formula.

Neurological examination showed moderate

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Figure 1. Moderate ptosis affected both eyes

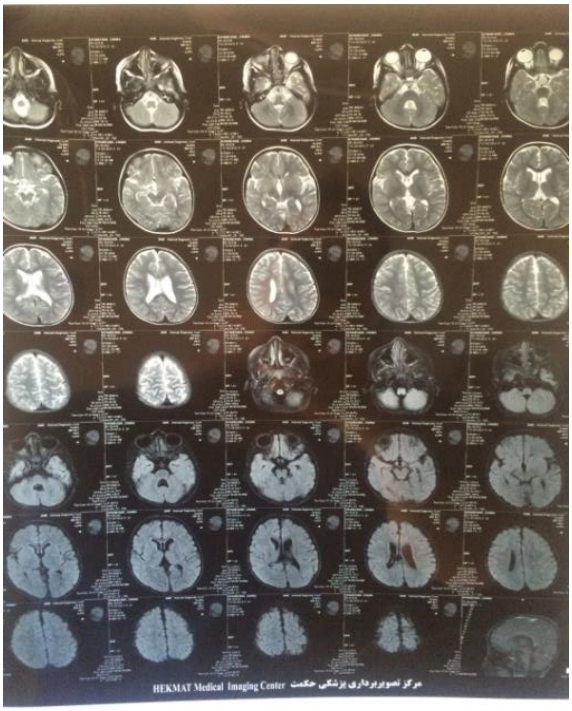

Figure 2. Computed tomography of the brain

ptosis affected both eyes and depression of deep tendon reflexes in lower extremities although electromyography and nerve conduction velocity tests showed normal results (Figure 1). Further history taking revealed a significant hearing loss (50 db) due to delay in verbal skills and developmental delay.

The initial laboratory tests showed the serum calcium and serum phosphorus levels of 6.3 and 6 mg/dL, respectively. The level of serum intact parathyroid hormone was measured using immunoradiometric assay (5 ng/L: 15-60 ng/L). Other serum laboratory tests showed a BUN of 18 mg/dL, creatinine of 0.5 mg/dL, sodium of 137 mEq/L, and potassium of 4.5 mEq/L. Furthermore, the active urinary analysis was compatible with urinary tract infection. Additionally, erythrocyte sedimentation rate was 70 in the first hour.

Magnetic resonance imaging of the brain demonstrated mild prominancy of the ventricular system and global shrinkage of the cerebral cortex (Figure 2). Electroencephalography showed abnormal generalized spike and waves. Auditory Brainstem Response revealed bilateral severe-to-profound hearing loss. Abdominal ultrasonography demonstrated hypertrophic right kidney (86 mm in length) and undetected left kidney. The left kidney had globally decreased parenchymal mass, and the right kidney was detected with multiple cortical defects. Voiding cystourethrogram was performed, indicating grade 3 reflux in the right kidney.

Because of the simultaneous occurrence of hypoparathyroidism, deafness, and renal disease, the patient was diagnosed with HDR syndrome. However, the microarray-based comparative genomic hybridization study of the patient was compatible with the monosomy of 10p15.3p13 and trisomy of 12p13.33p13.33. After the treatment of the urinary tract infection, the patient was discharged while prescribing with sodium valproate, calcium syrup, and cefixime, and referred to audiometry for hearing aids.

Discussion

The HDR syndrome was first reported in 1977 by Barakat et al. (2). Subsequently, other cases were reported in the literature revealing the association of this syndrome with a wide characteristic spectrum consisting of hypoparathyroidism, microcephaly, sensorineural deafness, and renal disease (5-7). Patients may present with hypocalcemia or afebrile convulsions at any age. Renal disease in this case was compatible with other reports with hypoplasia and vesicoureteral reflux.

Nephrotic syndrome, cystic kidney, renal

dysplasia, aplasia, pelvicalyceal deformity, vesicoureteral reflux, chronic renal failure, hematuria, proteinuria, and renal scarring can be also observed among these patients (8-10). However, most of the patients show progression to chronic renal failure in adulthood and require renal replacement therapy (11). Deafness is a consistent feature of HDR syndrome, which is more severe at higher frequencies (12). Our patient also showed similar features on auditory brainstem response.

Hasegawa et al. reported 14 patients with 10p13 deletion, five, six, and two cases of whom had hypoparathyroidism or hypocalcemia, urinary tract abnormalities, and deafness, respectively (5). Fujimoto et al. reported a Japanese male with associated recurrent cerebral infarctions in the basal ganglia (13). Lichtner et al. performed molecular deletion analysis on two cases with partial monosomy 10p, hypoparathyroidism, deafness, renal dysplasia, cardiac defect, cleft palate, and reduced T-cell levels (14).

The diagnosis of this disease is based on the clinical findings. The tests that may improve diagnosis among the suspected patients include parathyroid hormone levels, audiogram or auditory brain stem response study, renal imaging studies, and DNA analysis (submicroscopic deletion on chromosome 10p). The treatment of this syndrome consists of managing the clinical abnormalities associated with hypoparathyroidism, deafness, and renal disease. Prognosis in this disease depends on the severity of renal disease.

Regarding this case presentation, to detect this extremely rare genetic disorder, patients with seizure or neurodevelopmental delay and kidney abnormality associated with hearing loss are suggested to be subjected to a parathyroid hormone.

Conclusion

It is important to be aware of rare inherited conditions like Barakat syndrome (HDR syndrome) in a patient with abnormal presentations, such as seizure, neurodevelop-mental delay, kidney defects associated with hearing loss, and clinical abnormalities associated with hypoparathyroidism.

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Conflicts of interests

None.

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