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Case report - Olgu sunumu

Joubert syndrome with oculomotor apraxia: a case report

Okulomotor apraksli Joubert sendromu: Bir olgu sunumu

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Abstract
In this paper, a 7 month old male case born to a first degree cousin marriage, referred to our department for oculomotor apraxia and hypotonia, diagnosed as having Joubert syndrome is discussed. Broad forehead, depressed nasal bridge, hypertelorism, hypotonia and oculomotor apraxia were found in physical examination. Pulmoner stenosis was reported in echocardiography. His peripheral blood cytogenetic analysis revealed 46, XY normal constitutional karyotype. "Molar tooth sign", a pathognomonic finding for this syndrome was observed in cranial magnetic resonance images. In Joubert syndrome; dysmorphic skeletal findings, liver and kidney problems can be observed. In early diagnosed cases, like our case, clinical follow up is important for detetion of the liver and kidney involvement.

Key words: Joubert syndrome, oculomotor apraxia, molar sign, hypotonia, hypertelorism.

Özet

Makalede 1. derece kuzen evliliği bulunan ailenin okulomotor apraksi şikayeti olan ve Joubert sendromu tanısı almış 7 aylık erkek çocuğu sunulmaktadır. Fizik muayenede geniş alın yapısı, basık burun kökü, hipertelorizm, hipotoni ve okulomotor apraksi saptanmıştır. Ekokardiyografi (EKO) pulmoner stenoz varlığını göstermiştir. Olgunun periferik kan sitogenetik analizinde 46, XY normal karyotip yapılanması bulunmuş olup, kranial MR sonucunda bu sendrom için tanı koydurucu olan "molar diş" görünümü saptanmıştır. Bu tanıyı alan olgularda dismorfik iskelet yapısı, karaciğer ve böbrek tutulumu bulguları da olabileceği göz önünde bulundurulmalıdır. Olgumuz gibi erken tanı konan hastalarda böbrek ve karaciğer tutulumu yönünden klinik takip önemlidir.

Anahtar sözcükler: Joubert sendromu, okulomotor apraksi, molar diş görünümü, hipotoni, hipertelorizm.

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Introduction

Joubert syndrome (JS) (OMIM #213300) is a rare autosomal recessive disorder. Cardinal manifestations are hypotonia, ataxia, oculomotor apraxia, retinal dystrophy, kidney cysts, fibrosis of the liver, polydactyly and mental retardation. Structural and functional deficiency of primary cilia are thought to play a role in the etiology of this disease. Cerebellar vermis hypoplasia is present in most cases and leads to the pathognomic " molar tooth" sign in cranial magnetic resonance imaging (MRI) [1, 2]. Mutations

involving the genes coding for ciliary proteins are thought to be responsible for the phenotype [2].
We describe a 7 month old male patient who was referred to Gulhane Military Medical Faculty Medical Genetics Department due to oculomotor apraxia and was diagnosed as having JS.

Case report

Second born to a first degree cousin marriage was referred to our department due to oculomotor apraxia and hypotonia. On physical examination, his height was 71 cm (75 p), body weight was 10.5 kg (90-97 p) and head circumference was 46 cm (90-97 p). The patient had an open anterior fontanelle of 4x4 cm. Depressed nasal bridge, hypertelorism and broad forehead were observed (Figure 1). The patient gained his head control at 5 months of age, had axial hypotonia and oculomotor apraxia in his neurological examination. Abdominal ultrasonography was normal. His echocardiogram revealed pulmonary stenosis. His karyotype was normal (46, XY). Cranial magnetic resonance imaging (MRI) revealed the pathognomic finding of “molar tooth” sign (Figure 2). The boy was diagnosed as having Joubert syndrome with these clinical features.

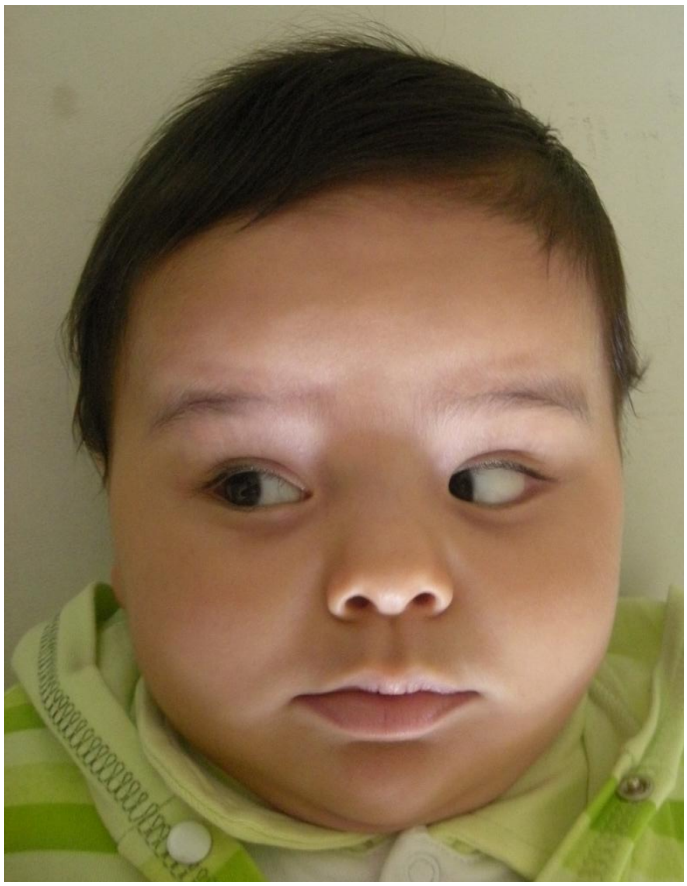

Figure 1. Dysmorphic features of the patient and oculomotor apraxia (Broad forehead, depressed nasal bridge, hypertelorism).

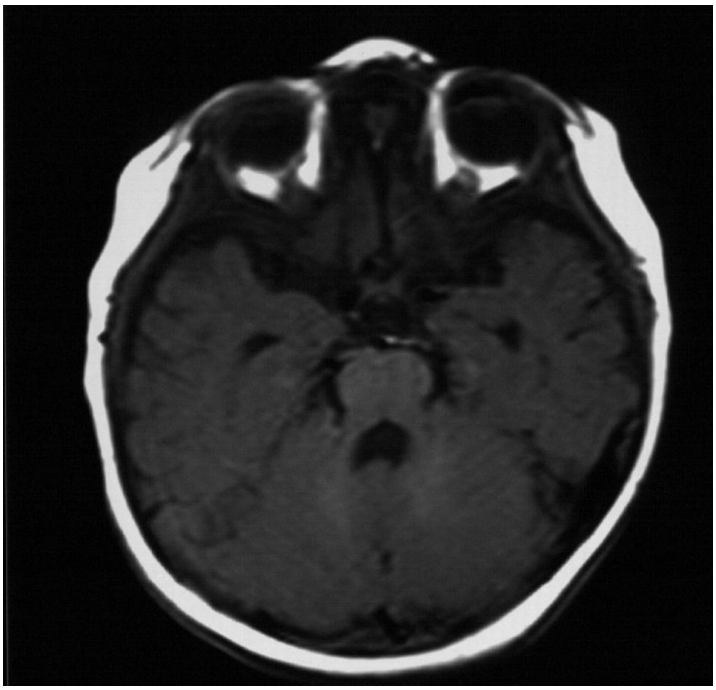

Figure 2. " Molar tooth" sign at cranial MRI (axial plane).

Discussion

Joubert syndrome is characterized by a unique congenital malformation of the hind brain and defects in the structure and function of primart cilium. It is an autosomal recessive syndrome exhibiting various congenital anomalies and mental retardation [1].

The fact that the couples are first degree cousins is a supporting evidence that our case is affected by Joubert syndrome- an autosomal recessive disorder. The diagnosis is largely based on the presence of cerebellar vermis hypoplasia, thickened interpedincular fossa, elongated superior cerebellar pedincules at axial planes of cranial MRI that make up the "molar tooth" sign [3]. Our case also had the same radiologic findings. Studies have showed that hypotonia and irregularities at breathing pattern could be linked to vermis hypoplasia seen in JS patients [3]. The hypotonia in our case could be a result of this structural brain anomaly.

Nystagmus, oculomotor apraxia, strabismus and ptosis are the ophtalmologic findings observed in JS [5]. In our case, we observed oculomotor apraxia and hypertelorism. Nearly one third of patients with JS have kidney anomalies including cystic dysplasia and juvenile nephrophtysis [6, 7]. In our case, urinary biochemical findings and abdomen ultrasonography were within normal limits.

Approximately %9 of JS patients have accompanying hepatic disorders, mostly being hepatic fibrosis. Liver function tests and ultrasonography findings of our case were within normal limits. Skeletal abnormalities are commonly seen in JS, %16 of patients demonstrate postaxial polydactyly [6]. Our case did not have any accompanying skeletal abnormalities.

As a result, our case was diagnosed as JS due to oculomotor apraxia, characteristic facial appearance, hypotonia and "molar tooth" sign on cranial MRI. Patients who are diagnosed as having JS should be screened for skeletal as well as liver and kidney anomalies. Cases diagnosed early like ours, should be followed up for the liver and kidney problems.

References

1. Parisi MA. Clinical and molecular features of Joubert syndrome and related disorders. Am J Med Genet C Semin Med Genet 2009 15;151:326-40.

2. Doherty D. Joubert syndrome: insights into brain development, cilium biology, and complex disease. Semin Pediatr Neurol. 2009; 16: 143-54.
3. Maria BL, Bolthauser E, Palmer SC, Tran TX. Clinical features and revised diagnostic criteria in Joubert syndrome. J Child Neurol. 1999; 14: 583-90.
4. Gleeson JG, Keeler LC, Parisi MA, Marsh SE, Chance PF, Glass IA, Graham JM, Jr, Maria BL, Barkovich AJ, Dobyns WB. Molar tooth sign of the midbrain-hindbrain junction: occurrence in multiple distinct syndromes. Am J Med Genet. 2004; 125A: 125-134.
5. Hodgkins PR, Harris CM, Shawkat FS, Thompson DA, Chong K, Timms C, Russell-Eggitt I, Taylor DS, Kriss A. Joubert syndrome: long term follow-up. Dev Med Child Neurol. 2004; 46: 694-9.
6. Saraiva JM, Baraitser M. Joubert syndrome: a review. Am J Med Genet. 1992; 43: 726-31.
7. Saunier S, Salomon R, Antignac C. Nephronophthisis. Curr Opin Genet Dev. 2005; 15: 324-31.