Case Report

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Newborn with multiple congenital anomalies in newborn, intensive care unit suggestive of joubert syndrome and related disorder with an atypical presentation

Garima Goyal*, Ajay Arya

Department of Pediatrics, Government Medical College Haldwani, Uttarakhand, India

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*Correspondence: Dr. Garima Goyal,

E-mail: dr.garimagoyal24@gmail.com

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ABSTRACT

Joubert syndrome (JS) is a rare autosomal recessive disorder with key finding of cerebellar vermis hypoplasia with a complex brainstem malformation that comprises the molar tooth sign on axial magnetic resonance images. This syndrome is difficult to diagnose clinically because of its variable phenotype. Molar tooth sign is not specific for JS. Another entity is termed as Joubert syndrome and related disorders (JSRD). Although the molar tooth sign and other important clinical features of the JS may be seen in these syndromes, they usually have supplementary prominent features. Author present a case of Joubert syndrome and related disorder in a term newborn delivered in the hospital of Government Medical College, Haldwani with multiple congenital anomalies. Macrocephaly, facial dysmorphism, polydactyly left hand and bilateral ballotable lumbar lump (multicystic dysplastic kidney). MRI showed molar tooth configuration of superior cerebellar peduncles, dilatation of lateral and third ventricles with aqueductal stenosis with arachnoid cyst (unusual association).

Keywords: Aqueductal stenosis, Arachnoid cyst, Joubert syndrome, Joubert syndrome and related disorder, Molar tooth sign

INTRODUCTION

Joubert syndrome (JS) is characterized by episodes of abnormal respiratory pattern, oculomotor findings, hypotonia, ataxia, developmental retardation with evidence of neuropathologic abnormalities of cerebellum and brainstem.¹ It has prevalence of <1 in 100,000. Only about 212 cases have been reported worldwide.² It is a syndrome with a variable phenotype making it difficult to establish the exact clinical diagnostic boundaries of the syndrome.

Another entity is termed as Joubert syndrome and related disorder (JSRD).³ JSRD is categorized into various phenotypic sub-groups. Although the molar tooth sign4

and other important clinical features of the JS may be seen in these syndromes, they usually have supplementary prominent features.

Clinical Details

A male baby was born out of non-consanguineous marriage through cesarian section (unbooked case) to primigravida mother with meconium stained liquor, non-vigorous. Resuscitation was done and revived. Baby was born with multiple anomalies, macrocephaly, facial dysmorphism (Figure 1).

On examination, following details were observed:

Heart rate: 150/minute, Respiratory rate: 56/min, Capillary refill time <3sec, Weight 3.25kg, Head circumference :42cm (Figure 2).



Figure 1: Facial Dysmorphism.



Figure 2: Head circumference measurement.

Facial dysmorphism (frontal bossing, microphthalmia, depressed nasal bridge, hypertelorism). Polydactyly left hand (post axial type 2) are observed (Figure 3).



Figure 3: Polydactyly left hand (post axial type2).

Respiratory assessment revealed tachypneoa with irregular respiration, bilateral air entry equal. Cardiovascular examination normal heart sounds heard. Abdomen was distended, soft, bilateral ballotable mass present in lumbar region.

Neurological examination revealed macrcephaly, wide anterior fontanelle with suture apart, hydrocephalus present. Moro's depressed, tone decreased, brisk deep tendon reflexes.

Spine and Genital examination

No anomaly detected

Auditory evaluation

OAE (Otoacoustic emission): Refer both the ears

Ophthalmological evaluation

Microphthalmos, fundus showing optic disc pallor with cilioretinal artery attenuation and features suggestive of retinal dystrophy. Investigations were carried out. Hemogram, renal function, metabolic workup was found normal. Ultrasound Abdomen: Multiple cysts in bilateral kidney, no evidence of hepatic fibrosis was present (Figure 4).



Figure 4: USG abdomen showing multicyclic dysplastic kidney.

CT Head

Dilatation of lateral and 3rd ventricles with cyst in posterior fossa was observed.

MRI Brain

Marked dilatation of lateral and third ventricles compressing the cerebral parenchyma with outward bowing of the visualised corpus callosum, distal narrowing of aqueduct was observed. Blood fluid level is seen in the right lateral ventricle, and possibility of an Aqueductal stenosis was observed.

A large CSF isointense area in the posterior fossa in retrocerebellar location compressing the cerebellum appears to be an Arachnoid cyst. Molar tooth sign is present (Figure 5).

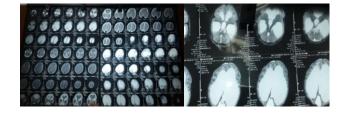


Figure 5: MRI Brain showing molar tooth sign and retro cerebellar cyst.

Echocardiography was normal. Infantogram was normal and Karyotyping revealed XY47.

Course during Hospitalisation

Baby developed convulsions, started on antiepileptics. Ventriculoperitoneal Shunt surgery was done at day 20 of life. General condition of the baby improved slightly. But gradually respiratory distress was increased, and baby developed respiratory failure, so baby was put on ventilator. Baby did not maintain saturation in spite of very high settings, and ultimately could not be revived.

DISCUSSION

Joubert Syndrome

JS is a rare with autosomal recessive disorder characterized by clinical and characteristic neuroradiological findings. Exp neuroimaging features of JS include deep interpeduncular fossa, narrow isthmus (the ponto-mesencephalic junction), lack of decussation of superior cerebellar peduncles, dilated, distorted, and rostrally deviated fourth ventricle giving "Bat Wing" appearance, thick vertical superior cerebellar peduncles, rostral deviation of fastigium of fourth ventricle, wide foramen of Magendie and dysplastic vermis.

The brain stem, predominantly the medulla and upper cervical spinal cord, tends to be small. "Molar tooth sign" encompasses deeper than normal posterior interpeduncular fossa, prominent or thickened superior cerebellar peduncles, and vermian hypoplasia or dysplasia. The clinical features include episodic hyperpnoea and apnoea in the neonatal period, ocular abnormalities (oculomotor apraxia and ocular coloboma), hypotonia, truncal ataxia, developmental delay, intellectual impairment and abnormal facies.

Although the diagnostic criteria for JS have not been established, the clinical features frequently mentioned as essential for the diagnosis of classic JS comprise of:

- Hypotonia in infancy.
- Developmental delay/mental retardation.
- One or both of the following (not absolutely required but helpful for the diagnosis):
- 1. Irregular breathing pattern in infancy (intermittent tachypnea and/or apnea).
- 2. Abnormal eye movements.

Associated Features: Supratentorial anomalies are uncommon, but cerebral cortical dysplasia and gray matter heterotopias have been reported. Moderate lateral ventricular enlargement due to atrophy has been described in 6-20% of cases. Polydactyly (8%), ocular coloboma (4%), hamartomas of the tongue (2%), dysmorphic facies, microcephaly, tongue protrusion, multicystic kidney disease, congenital heart disease, unsegmented midbrain tectum, retinal dystrophy and agenesis of the corpus callosum are observed.

This syndrome is classified into two groups on the basis of retinal dystrophy. Patients with retinal dystrophy have a higher prevalence of multicystic renal disease and these patients also appear to have decreased survival rates compared with those of patients without retinal dystrophy.

Joubert Syndrome and Related Disorder

Joubert Syndrome-related disorders (JSRD)6 are defined based on associated multi-organ involvement (retinal dystrophy, nephronophthisis, hepatic fibrosis and polydactyly). Molar tooth sign is not specific for JS. JSRD is categorized into six phenotypic sub-groups:

- Pure JS.
- JS with ocular defect
- JS with renal defect,
- JS with oculorenal defects,
- JS with hepatic defect, and
- JS with orofaciodigital defects.

Although the molar tooth sign and other important clinical feature of the JS may be seen in these syndromes, they usually have supplementary prominent features. These are syndromes such as:

Coach syndrome: bilateral coloboma, hepatic fibrosis and renal calcification.

Varadi-Papp syndrome: mesaxial polydactyly, Y-shaped metacarpal, cleft lip or cleft palate, lingual hamartomas and vermian hypoplasia.

Dekaban-Arima syndrome: It is allied with Leber's congenital amaurosis and cystic dysplastic kidneys,

Senior-Loken syndrome: It is related with Leber's congenital amaurosis, retinitis pigmentosa and juvenile nephronophthisis.

Malta syndrome: It is related with molar tooth sign+, occipital encephalocele, hydrocephalus, cortical renal cysts with or without coloboma, and Leber's congenital amaurosis.

Inheritance of JSRD: It has usually autosomal reccesive inheritance (X-Linked Recessive rarely), genetically heterogeneous with one locus pointing to chromosome 9q. In addition, consanguinity has been documented in a few cases. Ten causative genes 7 have been recognized so far; every single one encoding for proteins of the primary cilium or the centrosome, making JSRD part of an expanding group of diseases called "ciliopathies".

This patient has evidence of retinal dystrophy with multicystic renal disease with polydactyly, dysmorphic facies, hydrocephalus. An unsual association was found by presence of arachnoid cyst in retrocerebellar area. Managment supportive and requires a multidisciplinary approach.

CONCLUSION

This patient had features suggestive of joubert syndrome and related disorder with additional features on MRI (aqueductal stenosis with arachnoid cyst in posterior fossa) having gross hydrocephalus, facial dysmorphism, polydactyly with multicystic dysplastic kidney.

Due to additional finding on MRI (Aqueductal stenosis with cyst in posterior fossa), it should either be incorporated in Joubert syndrome, or isolated nomenclature should be given.

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