



## Ocular Manifestations Leading to a Diagnosis of Joubert Syndrome Related Disorder

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### ABSTRACT

**Introduction:** Joubert syndrome is an inherited disorder of rare occurrence usually presenting as developmental delay, hypotonia, hyperpnea and ataxia. The diagnosis is confirmed by characteristic findings in neuroimaging. Involvement of ocular, renal and hepatic systems can be present. Joubert syndrome presenting first to an ophthalmologist is very uncommon.

**Case:** A twenty-one-year female, with history of delayed milestones, infantile hemiplegia with hearing and visual impairment was referred for visual assessment. On systemic examination, ataxic gait was present. CT head showed hypoplasia of postero-inferior portion of vermis with communication between 4th ventricle and cisterna magna with variable degree of cerebellar dysgenesis. The neurological, ophthalmological and radiological findings of this patient were consistent with Joubert syndrome related disorder.

**Conclusion:** We hereby report a case of Joubert syndrome related disorder with ocular involvement which after correlation with neurological findings and neuroimaging led us to the diagnosis of this rare disorder. The renal and hepatic functions in these patients need to be monitored.

**Key words:** Cerebellar dysgenesis, Chorioretinal coloboma, Hypoplasia of vermis, Joubert syndrome.

### INTRODUCTION

Joubert syndrome is a rare inherited disorder named after the French neurologist who described it in 1969 (Joubert et al, 1969). The manifestations are hypotonia, episodic hyperpnea along with progressive

ataxia, developmental delay and the diagnosis confirmed by distinctive neuro-radiologic findings of “molar tooth” sign (Saraiva et al. 1992). Involvement of other organs like eye, kidney, liver etc is grouped under Joubert syndrome related disorder (JSRD). JSRD has been associated with variable ophthalmic

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features namely primary gaze nystagmus, dystrophic retinal appearance, chorioretinal colobomas, abnormal optic nerve decussation (Khan et al, 2008), oculomotor apraxia, congenital ocular fibrosis (Appleton et al, 1989), Leber congenital amaurosis, strabismus, ptosis, amblyopia and third cranial palsy. We hereby report a case of bilateral retinal coloboma associated with ataxia and developmental delay which on imaging led to the diagnosis of JSRD.

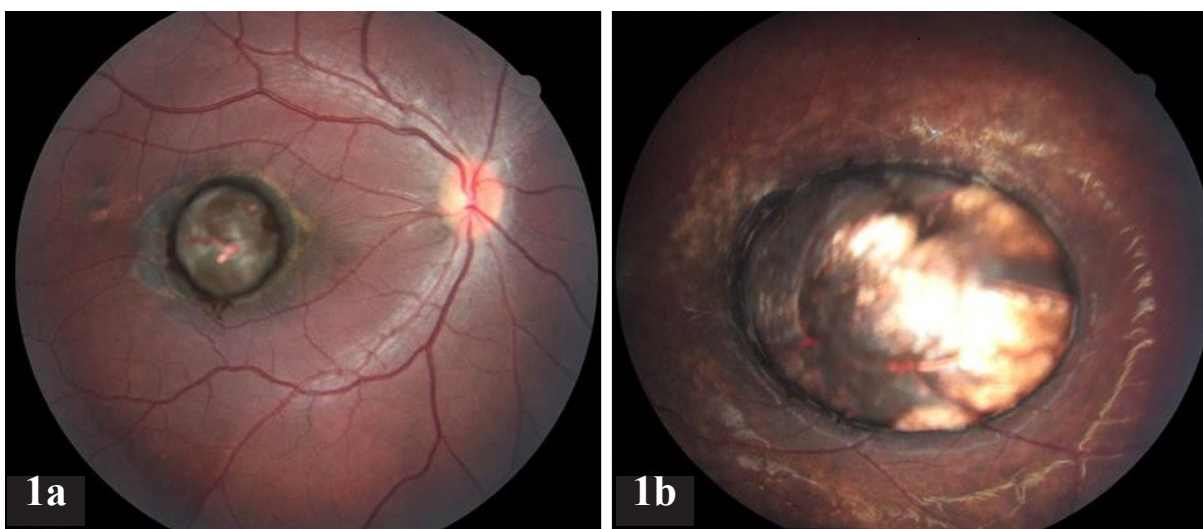
### CASE

A twenty-one-year female, with a diagnosis of obsessive-compulsive disorder, was referred to the ophthalmology department from the neurology ward for bilateral visual impairment since childhood. The patient was born of consanguineous marriage at full term without any perinatal issues. Later in infancy, the patient had delayed milestones and was diagnosed as infantile hemiplegia with hearing and visual

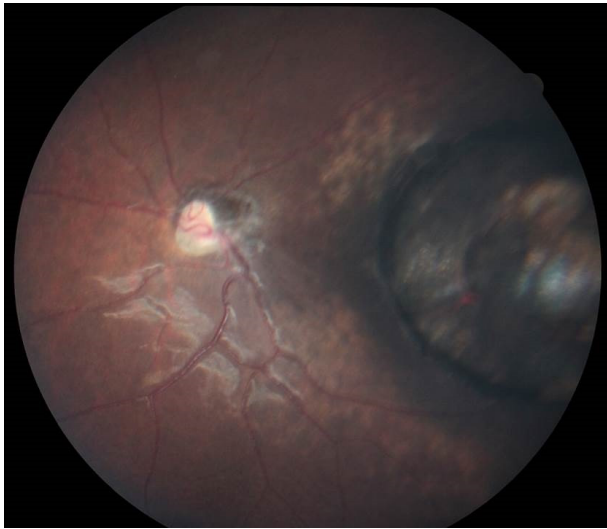
impairment. On systemic examination, ataxic gait was present. Patient had particular facies consisting of a long triangular face, high arched eyebrows, broad forehead, and prominent nasal bridge. No other phenotypic abnormalities like polydactyly or tongue abnormalities were noted. Best corrected visual acuity (BCVA) in the right eye was hand movements close to the face and the left had no perception of light. Bilateral nystagmus was present bilaterally. Left eye had micro-cornea & superior iris coloboma. Fundus examination revealed chorio-retinal coloboma (Figure 1a and 1b) in both eyes.

Additionally, on the left side, optic disc hypoplasia was noted as shown in Figure 2.

Otorhinological examination showed profound neurosensory hearing loss in the left ear and moderate sensori-neural hearing loss on the right side. CT head of the patient showed hypoplasia of postero-inferior portion of vermis



**Figure 1: (a) Fundus photograph of right eye showing chorio-retinal coloboma; (b) Fundus photograph of left eye showing chorio-retinal coloboma and optic disc hypoplasia.**



**Figure 2: Fundus photograph of Left eye showing optic disc hypoplasia.**



**Figure 3: Axial CT scan showing hypoplasia of postero-inferior portion of vermis (arrow) with communication between 4th ventricle and cisterna magna with variable degree of cerebellar dysgenesis.**

with communication between 4th ventricle and cisterna magna with variable degree of cerebellar dysgenesis (Figure 3).

Renal function tests and liver function tests did not reveal any abnormalities. An ultrasonogram of the kidneys showed no abnormalities. The neurological, ophthalmological and radiological findings of this patient were consistent with JSRD. The patient was advised to have annual ocular examinations along with a close watch on her kidney and liver function tests semi-annually. Parents were explained the risks of respiratory depression during anaesthesia associated with this disorder.

## DISCUSSION

Joubert syndrome is a rare autosomal recessive syndrome with an incidence of 1 in 100,000. Its primary presentation to ophthalmologists is very rare. Classic Joubert syndrome is characterised by the presence of three primary findings: A distinctive cerebellar and brainstem malformation called the molar tooth sign (MTS), cognitive impairment and hypotonia. The Molar tooth sign is marked by dysgenesis of the isthmus, a part of the brainstem between pons and inferior colliculus and elongation and thinning of ponto mesencephalic junction, and deep interpeduncular fossa associated with

thickening of superior cerebellar peduncles and hypoplasia of vermis characterised by incomplete lobulation and enlarged fourth ventricles is seen (Saraiva et al, 1992). In Joubert syndrome incomplete fusion of the halves of the vermis creating a sagittal vermis cleft seen on axial or coronal MRI planes is also seen. Joubert syndrome related disorders (JSRD) can have additional findings like retinal dystrophy, ocular colobomas, occipital encephalocele, oral hamartomas, hepatic fibrosis, polydactyly, endocrine abnormalities and renal disease.

Ocular manifestations of JSRD include primary gaze nystagmus, dystrophic retinal appearance, chorioretinal coloboma, abnormal optic nerve decussation (Khan AO et al, 2008) oculomotor apraxia, Leber congenital amaurosis & congenital ocular fibrosis (Appleton et al, 1989), ptosis, strabismus, amblyopia and third nerve palsy. The syndrome is associated with retinal coloboma and retinal dystrophy in approximately 50% of cases (King et al, 1984; Lindhout et al 1980; Ivarsson et al 1993). Characteristic presentation of developmental delay, ataxia, oculomotor disorders with retinal dystrophy/coloboma should raise clinical suspicion and patients should be subjected to radiological investigations which will confirm the diagnosis. Ear abnormalities mostly conductive hearing loss have been associated in JSRD (Kroes et al, 2010), our case had sensorineural hearing loss in both ears which can be attributed to dysfunction of cilia which is said to be causative mechanism in this syndrome (Doherty, 2009).

The importance of recognizing Joubert syndrome is related to heterogeneous presentations, progressive nature of renal and hepatic disorders, outcome, its inheritance, and the potential complications during anaesthesia. The patients of Joubert syndrome are extremely sensitive to respiratory depressant effects of anaesthetic agents like Opioids and Nitrous oxide (Habre et al, 1997). The syndrome is predominantly inherited in an autosomal recessive manner, X linked and digenic inheritance has also been reported. Joubert syndrome is considered a part of ciliopathies, ten causative genes have been found encoding for proteins of the primary cilium or the centrosome (Doherty, 2009). Screening of siblings, genetic counselling and antenatal ultrasound/MRI is warranted in subsequent pregnancies.

Our case had most of the features viz- developmental delay, hypotonia as well as the characteristic radiological features in the brain. Ocular findings were bilateral chorioretinal coloboma and superior iris coloboma of the left eye which were consistent with the syndrome<sup>5</sup>. Since patients with retinal features have been found to be also having renal cystic disease in a majority of the cases, we performed a screening USG and KFT, both of which are normal. Although an MRI of the brain is the recommended study, CT scan was only available to us. Still the internal anatomy of our case matched with the previously described cases and hence is being presented as it adds to the literature in view of the rarity of this

anomaly. It also stressed through this report that ophthalmologists must have a high index of suspicion in patients of this kind of clinical profile to diagnose retinal dysplasia early in the course and if detected, to watch for renal abnormalities. The associated life-threatening

anaesthetic complications in an undiagnosed case also warrants an early diagnosis to prevent unwary consequences in future.



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