Ocular manifestations in Joubert syndrome

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Abstract

Joubert syndrome and related disorder (JSRD) is a rare disorder of midline structure of brain having characteristic clinical and neuro-radiological findings. A 25 year old male was brought by his father to ophthalmic OPD with chief complaints of diminution of vision, irrelevant talk, agitation, sleep disturbances, drooping of eyelids. Neuroimaging revealed findings suggestive of Joubert syndrome and electroencephalography showed post ictal changes. He is also a known case of seizure disorder since 13 years & was on Levetiracetam. Ophthalmologists should be aware about the ocular signs of Joubert syndrome, as well as CNS malformations, neurological signs, psychiatric symptoms like epilepsy, intellectual disability which help in early diagnosis, so that the patient & his family are explained about the outcome, prognosis of the illness, need for psychoeducation, follow-up & social skills training.

Introduction

Joubert Syndrome is a rare autosomal recessive disorder that is diagnosed clinically and confirmed radiologically[1-5]. It is estimated to affect 1 in 1,00000 newborns. This neurodevelopmental genetic disorder is characterised by three primary findings: a midbrain malformation known as 'molar tooth sign'(MTS), hypotonia with subsequent development of ataxia and mental retardation. Ocular involvement can be developmental (coloboma) or degenerative (retinal dystrophy).

Additional clinical features like hepatic fibrosis, polydactyly, cystic kidney disease and nephronophthisis are now considered part of a clinical spectrum and classified under the wider term Joubert Syndrome and related disorders (JSRD[6].)

Joubert syndrome has a large range of clinical features and its prevalence is underestimated as it is likely underdiagnosed. This article is to create awareness about this rare disorder which has presented to our OPD so as to prevent late diagnosis and provide better treatment and counselling.

Case Report

A 25 year old male, a 7th grade dropout, born of second degree consanguinity was brought by his father to ophthalmic OPD with chief complaints of diminution of vision in right eye, irrelevant talk, agitation, sleep disturbances, drooping of eyelids. He is also a known case of seizure disorder since 13yrs & was on regular medication with Levetiracetam. There was no history of altered sensorium, substance abuse, abrupt onset of high grade fever or head injury.

On general physical examination he was emaciated, mentally retarded. Polydactyly and flattened hypothenar eminence was present. **Facial features:** Prominent right side malar bone with broad forehead (Figure 1), operated cleft lip, wide spaced eyes(Figure 2). On neurological examination right upper limb showed hypotonia with power of 3/5.

Figure 1: Prominent right side malar bone, broad forehead

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Figure 2: Operated cleft lip, wide spaced eyes, broad forehead

Microphthalmos, ptosis, unilateral right sided inferior iris coloboma. (Figure3)

Ophthalmic examination: Visual acuity : OD- 6/60 and no improvement with pinhole, OS- 6/6, near vision- N6. Colour vision was normal. Anterior segment : Fundus examination : unilateral inferonasal retinochoroidal coloboma.(Figure 4)

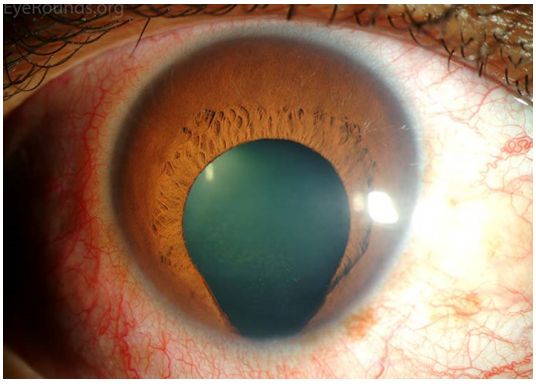

Figure 3: microphthalmos, ptosis, unilateral right sided inferior iris coloboma.

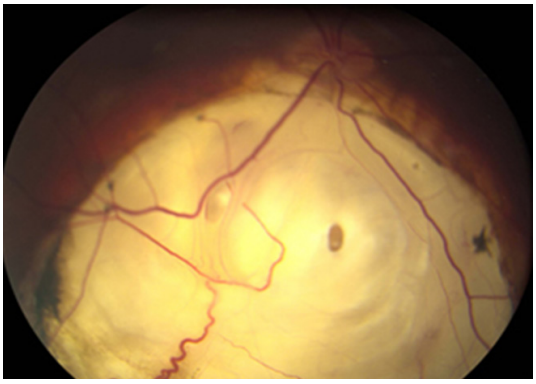

Figure 4: Fundus examination: unilateral inferonasal retinochoroidal coloboma.

Investigations: Routine blood investigations like CBC, RBS, Serum electrolytes, RFT, LFT were within normal limits. Electroencephalography showed post ictal changes with 4-5Hz,40-50 mV theta activity and 14-16Hz,10-20mV beta activity in the front leads. (Fig5) Ultrasonography of Abdomen and pelvis showed bilateral malrotated kidneys with extrarenal pelvis with mild raised cortical echogenicity. (Fig6)

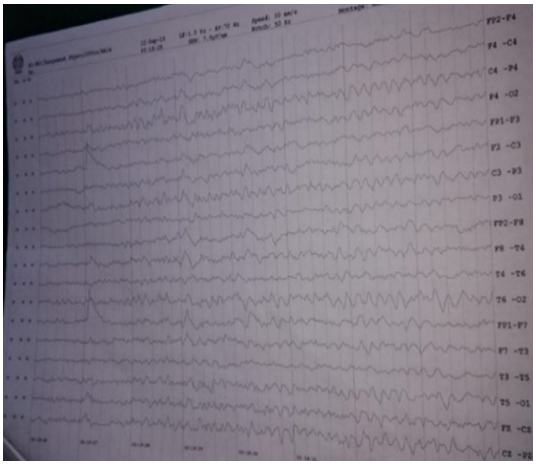

Figure 5: Electroencephalography changes with 4-5Hz,40-50 mV

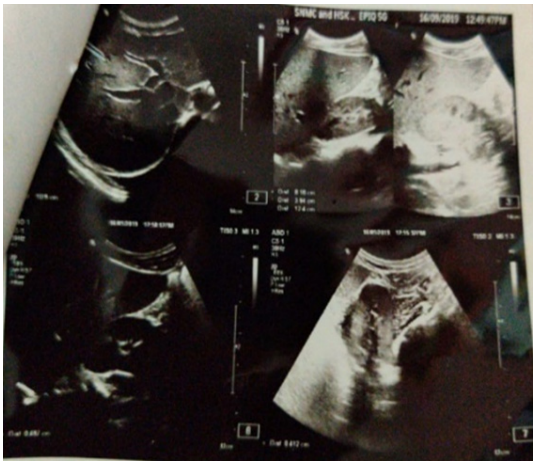

Figure 6: Ultrasonography of abdomen and pelvis showed bilateral mal-rotated kidney

MRI of Brain: Axial section at the level of brain stem showing lengthening of superior cerebellar peduncles and deep interpeduncular fossa giving rise to molar tooth appearance of mid brain with cerebellar hypoplasia. (Fig 7 & Fig 8) IQ assessment: Moderate intellectual disability - IQ 45.

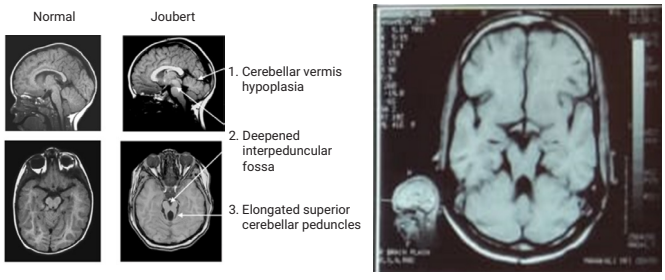

Figure 7: MRI of Brain: Axial section at the level of brain stem showing lengthening of superior cerebellar

peduncles and deep interpeduncular fossa giving rise to molar tooth appearance of mid brain with cerebellar hypoplasia

Discussion

Joubert Syndrome is a rare autosomal recessive disorder. Genetically heterogenous, with 3 loci – JBTS1(9q34.3); JBTS2(11p12q13.3); JBTS3(6q23)[7-9]. Clinical features include microphthalmos, abnormal pigmentation, ptosis, strabismus, nystagmus, myopia/hyperopia, ocular colobomas, extraocular muscles limitations, oculomotor apraxia(OMA), retinal dystrophy, polydactyly, renal dysfunction, mental retardation[10]. Other features are hepatic fibrosis, cystic kidney disease, nephronophthisis, epilepsy, developmental delay and speech deficits. Characteristic clinical findings like hepatic fibrosis, cystic kidney disease, ocular coloboma, retinal dystrophy, nephronophthisis are part of clinical spectrum & classified under wider term Joubert Syndrome & Related Disorders(JSRD). There are distinctive ocular characteristics of JS combined with systemic observations that helped in the diagnosis of Joubert syndrome. Difficulty in initiating saccades can indicate JS, and patients with OMA should get MRI of the brain done to look for the "molar tooth sign" even in the absence of other systemic findings. Coloboma, in addition to being frequently associated with hepatic manifestations of JS, can be an early ophthalmic indicator of JS in very young patients. Counselling and regular follow-up is required for early diagnosed patients.

Conclusion

Joubert syndrome is a multisystem disorder which require a multidisciplinary approach for management. Ophthalmologists should be aware about the ocular signs of Joubert syndrome, as well as CNS malformations, neurological signs, psychiatric symptoms like epilepsy, intellectual disability which aids in early diagnosis, so that patient & his family are explained about the outcome, prognosis of the illness, need for psychoeducation, follow-ups & social skills training.

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