Case Report

A rare case of Joubert syndrome

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ABSTRACT

Joubert syndrome (JS) is autosomal recessive inherited disorder characterized by hypotonia, ataxia, developmental delay, intellectual disability with distinctive mid-hindbrain malformation (molar tooth sign), ocular abnormalities (e.g., pigmentary retinopathy, oculomotor apraxia, and nystagmus), renal cyst, and hepatic fibrosis. In our case, 7-year-old female child presenting with convulsion, both eye nystagmus, right eye exotropia, left eye ptosis, both eye papilloedema, developmental delay, magnetic resonance imaging brain suggestive "molar tooth appearance" of cerebellar peduncles, and "Bat wing appearance" of the prominent fourth ventricle. Chest X-ray showing cardiomegaly and C-reactive protein positive. The aim of our study is diagnosis and management of patient with JS and increase awareness about this disease and manage it as early as possible and prevent serious complication like visual impairment.

KEY WORDS: Joubert Syndrome; Nystagmus; Molar Tooth Appearance; Bat Wing Appearance

INTRODUCTION

Joubert syndrome (JS) is a rare autosomal recessive disorder, first described by Joubert in 1969. Estimated prevalence is between 1 in 80,000 and 1 in 100,000 live births.[1,2] JS is an autosomal recessive neurodevelopmental disorder, characterized by molar tooth malformation, a complex brainstem malformation that reflects aplasia and marked hypoplasia of cerebellar vermis, thickened and elongated superior cerebellar peduncles, and deepened interpeduncular fossa that is apparent on axial magnetic resonance imaging (MRI) at the midbrain–hindbrain junction. Clinically classic JS associated with neonatal hypotonia, ataxia, developmental delay,mental retardation, neonatal apnea, oculomotor apraxia and difficulty in initiating rapid horizontal eye movement.[3-7]

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CASE REPORT

A 7-year-old female child brought to Outpatient Department with complaint of convulsion for 30 min involving all limbs, associated with loss of consciousness, lethargic look, and uprowling of both eyeball. Patient had history of full-term normal vaginal hospital delivery with delay crying. At 1 year of age, she was diagnosed as developmental delay, cerebellar palsy with mental retardation. Patient had developed social smile at 5 months, walk with support at 6 years, not able to speak anything and not able to go school suggestive of developmental delay. Patient had one sibling and not significant family history. General examinations showing pallor and vitals were normal. Patient was semiconscious and all limbs tone, power was decreased. Abdominal, respiratory and cardiovascular examinations were normal. On ocular examination, involuntary eye movement was suggestive of nystagmus with right eye exotropia and left eye mild ptosis (Figure 1). Patient was uncooperative for visual acuity, and both eye retinoscopy showing +0.50 hypermetropia. Both eye fundus examination showing hyperemic disc with blurring of disc margins and mild attenuated blood vessels suggestive of papilloedema (Figure 2). Laboratory investigations

showing 6.0 gm/dl hemoglobin suggestive of anemia, C-reactive protein positive 0.6 mg/dl (latex agglutination), cerebrospinal fluid examination suggestive of predominant neutrophils, urine chemical examination showed trace albumin, and microscopic examination showed 3-4/hpf pus cells and 1-2/hpf red blood cells. Chest X-ray showing cardiomegaly (Figure 3), ultrasonography abdomen suggestive of 5 × 3 mm small medullary cyst in the lower pole of right kidney, and 6 × 5 mm small medullary cyst in the lower pole of left kidney.MRI brain showing prominent and elongated cerebellar peduncle with dysplastic vermis giving " Molar tooth appearance" (Figure 4). Bilateral superior cerebellum appears hypoplastic with prominent fourth ventricle giving "Bat wing appearance" (Figure 5).

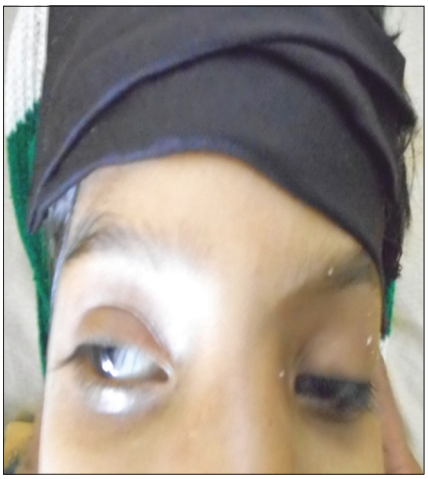

Figure 1: Both eye nystagmus, right eye exotropia, and left eye mild ptosis

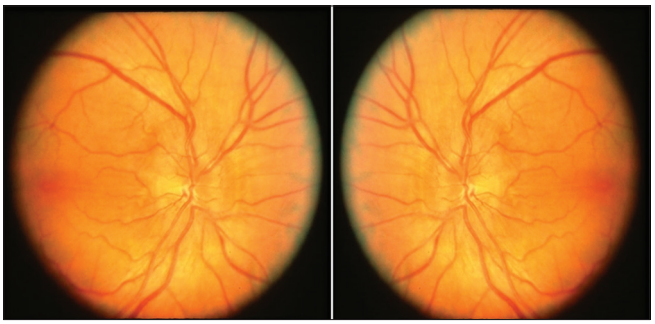

Figure 2: Both eye hyperemic disc with blurring of disc margins suggestive of papilloedema

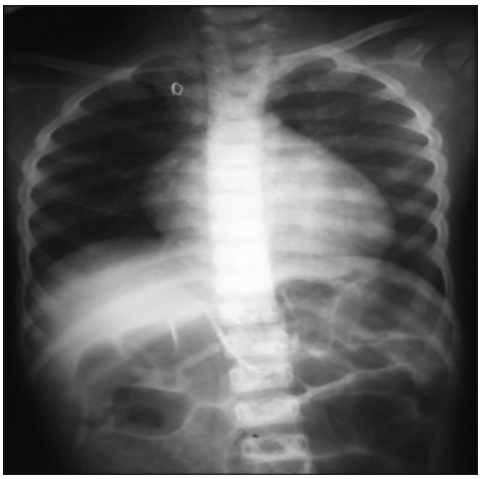

Figure 3: Chest X-ray posteroanterior view showing cardiomegaly

Treatment

Treatment line of convulsion was given by pediatrician. Inj. Mannitol (5 ml/kg/day) 6 hourly given to release intracranial tension. Refractive glasses for exotropia. Psychological and social support to patient and parents.Rehabilitation strategies for cognitive and behavioral difficulties.

Genetic Counseling and Prenatal Diagnosis

JS and related disorders (JSRD) transmitted in autosomal recessive pattern. Prenatal diagnosis is possible through chronic villus sampling at around 11 weeks' gestation. Recently fatal MRI has been acknowledged as method of choice to delineate posterior fossa malformation facilitating diagnosis of disease before 24 week of gestation.[8]

DISCUSSION

JS was first described by Joubert et al. in 1968, in four siblings with agenesis of cerebellar vermis presenting episodic hyperpnea, abnormal eye movements, ataxia, and intellectual

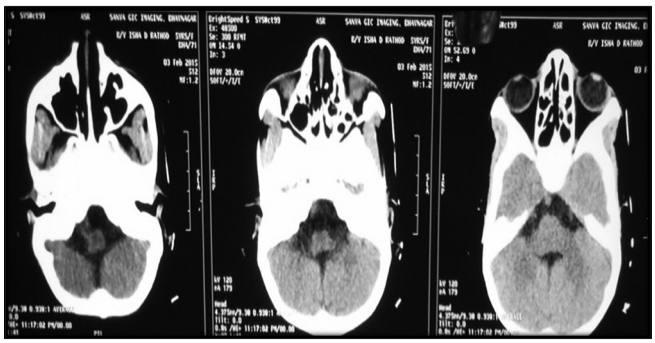

Figure 4: Magnetic resonance imaging cerebellar peduncles showing "molar tooth appearance"

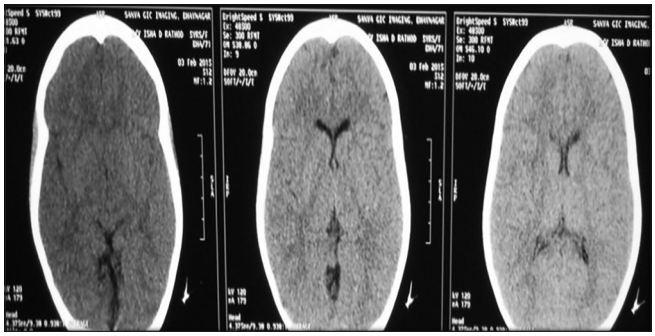

Figure 5: Magnetic resonance imaging of bilateral superior cerebellum appear hypoplastic with prominent fourth ventricle showing "bat wing appearance"

disability.[1] JS is rare autosomal recessive inherited disorder suspected by hypotonia, ataxia, developmental delay, intellectual disability with distinctive mid-hindbrain malformation (molar tooth sign), ocular abnormalities (e.g., pigmentary retinopathy, oculomotor apraxia, and nystagmus), renal cyst and hepatic fibrosis, hyperpnea alternating with periods of apnea.[9,10]

Once diagnosis of JSRD has been made, children should enter a diagnostic protocol to assess the possible multiorgan involvement. Ocular investigations include evaluation of visual acuity, ocular motility, fundus abnormality and possible electroretinogram, slit lamp examination disclose abnormalities of anterior segment of eye, kidney, and liver function should be tested.[9-11]

Valente, brancati, and dallapiccola proposed a clinical classification of JS in which molar tooth sign was consider as obligatory criteria and hypotonia, developmental delay, ataxia, abnormal eye movements were considered as primary criteria.

i. Pure JS: Only primary criteria.
ii. JS plus retinopathy, primary criteria and retinal abnormality (congenital leber amaurosis, pigmentary retinopathy, or unspecific retinitis).
iii. JS plus renal disease: Primary criteria and kidney involvement nephronophthisis, abnormal kidney ultrasound, or urinary concentration defect.
iv. Oro-facial-digital syndrome: Primary criteria plus orofacial abnormality (cleft lip/cleft palate, notched upper lip, tongue tumors, multiple frenula, etc.) plus mesaxial or pre-axial polydactylia.
v. Cerebellar vermis hypoplasia/aplasia, oligophrenia, ataxia, ocular coloboma and hepatic fibrosis, primary criteria, mental retardation, liver disorder (fibrosis and histological abnormalities), optic nerve or chorioretinal coloboma, nephronophthisis might be present.
vi. Cerebello-oculo-renal syndrome or senior-loken syndrome, primary criteria, retinal abnormality, and kidney involvement.

CONCLUSION

JS should be managed as early as possible before it results in serious complications such as decreased visual acuity due to pigmentary retinopathy, optic coloboma, retinal dystrophy, retinitis, nephropathy, renal cyst, elevated liver enzymes, hyperpnea, and apnea. Through clinical examination, laboratory and radiological investigations are necessary for early recognition and correct diagnosis. In neonates and infant, particular care should be taken managing respiratory and feeding problems related to either breathing abnormalities or hypotonia. Rehabilitation strategies planned for cognitive and behavioral difficulties. Any abnormal feature renal or hepatic failure carefully followed up over time.[10,11] Soon after birth, prognosis is related to the extent and severity of breathing dysregulation. In most cases, respiratory abnormalities resolve spontaneously in first month or years of life afterward, prognosis depends mostly on ocular, renal, and hepatic complication.

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