Joubert syndrome: the clinical and radiological findings

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Abstract

Joubert syndrome is a rare disease characterised by clinical and radiological findings. Among the classic clinical findings of JS are hypotonia, ataxia, mental-motor retardation, respiratory and opthalmological findings. The paediatric cases included in the study comprised nine patients. There was familial consanguinty in seven cases. Clinically, all cases had mental-motor retardation and hypotonia. Episodic hyperpnoea attacks were observed in one case. Facial dysmorphism was the most common additional systemic anomaly and four cases had additional opthalmic findings. Brain MRI examination revealed that all cases had molar tooth sign, bat-wing appearance and vermian cleft. The majority of cases also had vermian hypoplasia. Cerebellar folial disorganisation was observed in approxiamtely half of the cases. Three cases had corpus callosum anomaly and atretic occipital encephalocoele. No pathology was determined in other organs. This study aimed to evaluate the clinical and radiological findings of 9 patients diagnosed with Joubert syndrome.
Keywords: Joubert Syndrome, clinical findings, radiological findings, MRI.

Introduction

Joubert syndrome (JS) is an autosomal recessive transmitted disease characterised by cerebellar and brain stem malformations.[1] In classic JS, there are clinical findings such as ataxia, hypotonia, abnormal eye movements, hyperpnoea-apnoea episodes and mental-motor retardation. Radiologically, posterior fossa and brain stem anomalies are seen such as cerebellar vermian dysgenesis, expanded 4th ventricle, and thickened strained superior cerebellar peduncle.[2] Patients with JS may have varying clinical and radiological views. In addition to these classic findings, there may be central nervous system anomalies (occipital encephalosis, corpus callosum agenesis), ocular coloboma, retinal dystrophy, renal diseases (cystic dysplasia), polydactyly, hepatic fibrosis and tongue tumours.[3,4] This study aimed to evaluate the clinical and radiological findings of 9 patients diagnosed with JS.

Case Reports

The paediatric cases included in the study comprised 5 males (55.55 %) and 4 females (45.44 %) with a mean age of 4.66 years (range, 2-10 years). A retrospective evaluation was made of 9 paediatric patients diagnosed with JS by one experienced paediatrics neurologist and two experienced radiologists. There was familial consanguinty in seven cases. Clinically, all cases had mental-motor retardation and hypotonia. Episodic hyperpnoea attacks were observed in one case. Facial dysmorphism was the most common additional systemic anomaly and four cases had additional opthalmic findings. Epileptic seizure was present in four cases. In these patients, scalp electroencephalography (EEG) revealed generalized and focal epileptiform activity findings. Two of the patients were taking carbamazepine; two were taking sodium valproate+levetirasetam. Two cases died due to status epilepticus and recurrent lung infection. Physical therapy was initiated in the long-

term management of other patients with JS. The patient demographics, clinical findings and additional system anomalies are shown in Table 1.

Table-1: Patient demographics, clinical findings and additional system anomalies.

Patient	Age/Gender	Familial consanguinity	Clinical findings	Additional system anomalies
1	7 years/male	none	Hypotonia Ataxia Mental-motor retardation	Facial dysmorphism Inferior oblique overaction
2	6 years/female	1st degree	Hypotonia Ataxia Mental-motor retardation Episodic hyperpnea	Facial dysmorphism Scoliosis Alternan exotropia Limbal vernalis
3	2 years/male	1st degree	Hypotonia Ataxia Mental-motor retardation Nystagmus Epilepsy	None
4	3 years/male	1st degree	Hypotonia Ataxia Mental-motor retardation Nystagmus	None
5	3 years/male	1st degree	Hypotonia Mental-motor retardation Epilepsy	Facial dysmorphism Optic atrophy
6	10 years/female	2nd degree	Hypotonia Mental-motor retardation	None
7	5 years/female	None	Hypotonia Mental-motor retardation Epilepsy	None
8	2 years/female	2nd degree	Hypotonia Ataxia Mental-motor retardation Nystagmus	Facial dysmorphism
9	4 years/male	1st degree	Hypotonia Mental-motor retardation Epilepsy	Facial dysmorphism Stargardt disease

The cranial MRI findings of the patients are summarised in Table 2.

Table-2: Brain MRI findings.

Patient	Age/Gender	Molar tooth and batwing appearance		Vermian cleft	Vermian hypoplasia	Cerebellar folial disorganisation Additional findings
1	7 years/male	+	+	+	+	Retrocerebellar cyst
2	6 years/female	+	+	+	-	Pons atrophy
3	2 years/male	+	+	+	+	-
4	3 years/male	+	+	+	-	-
5	3 years/male	+	+	+	+	CC agenesis Colpocephaly Atretic occipital encephalocele Interhemispheric cyst
6	10 years/female	+	+	-	-	Cerebellar and vermis atrophy
7	5 years/female	+	+	+	+	CC hypoplasia Colpocephaly Retrocerebellar cyst
8	2 years/female	+	+	-	-	-
9	4 years/male	+	+	+	+	Atretic occipital encephalocele

Brain MRI examination revealed that all cases had molar tooth sign, bat-wing appearance and vermian cleft (Figure-1).

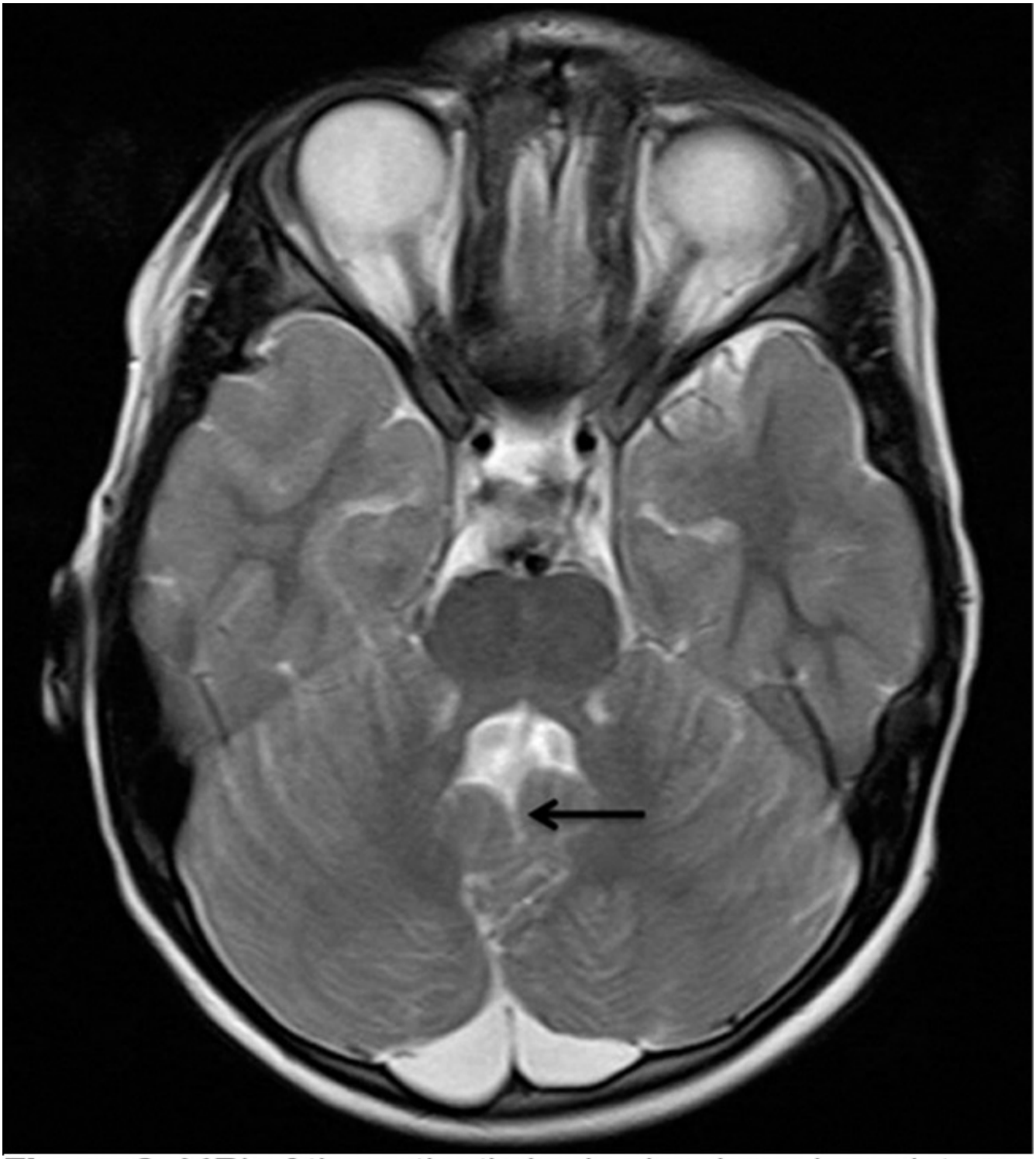

Figure-2: MRI of the patient's brain showing a hyperintense metastasis in the left temporal region.

Three cases had CNS anomalies (corpus callosum anomaly and atretic occipital encephalocele) (Figure-2 and 3).

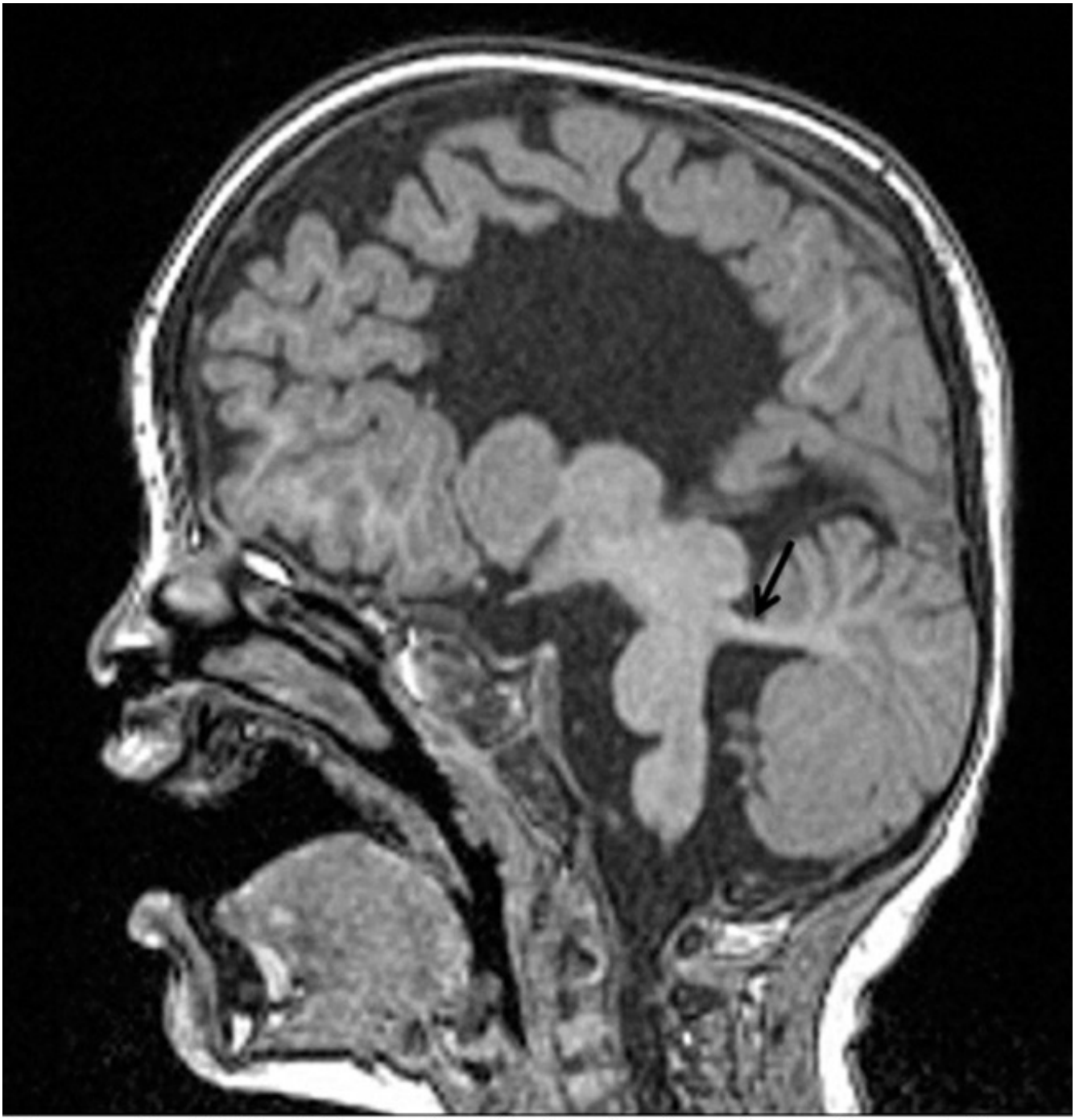

Figure-2: MRI of the patient's brain showing a hyperintense metastasis in the left temporal region.

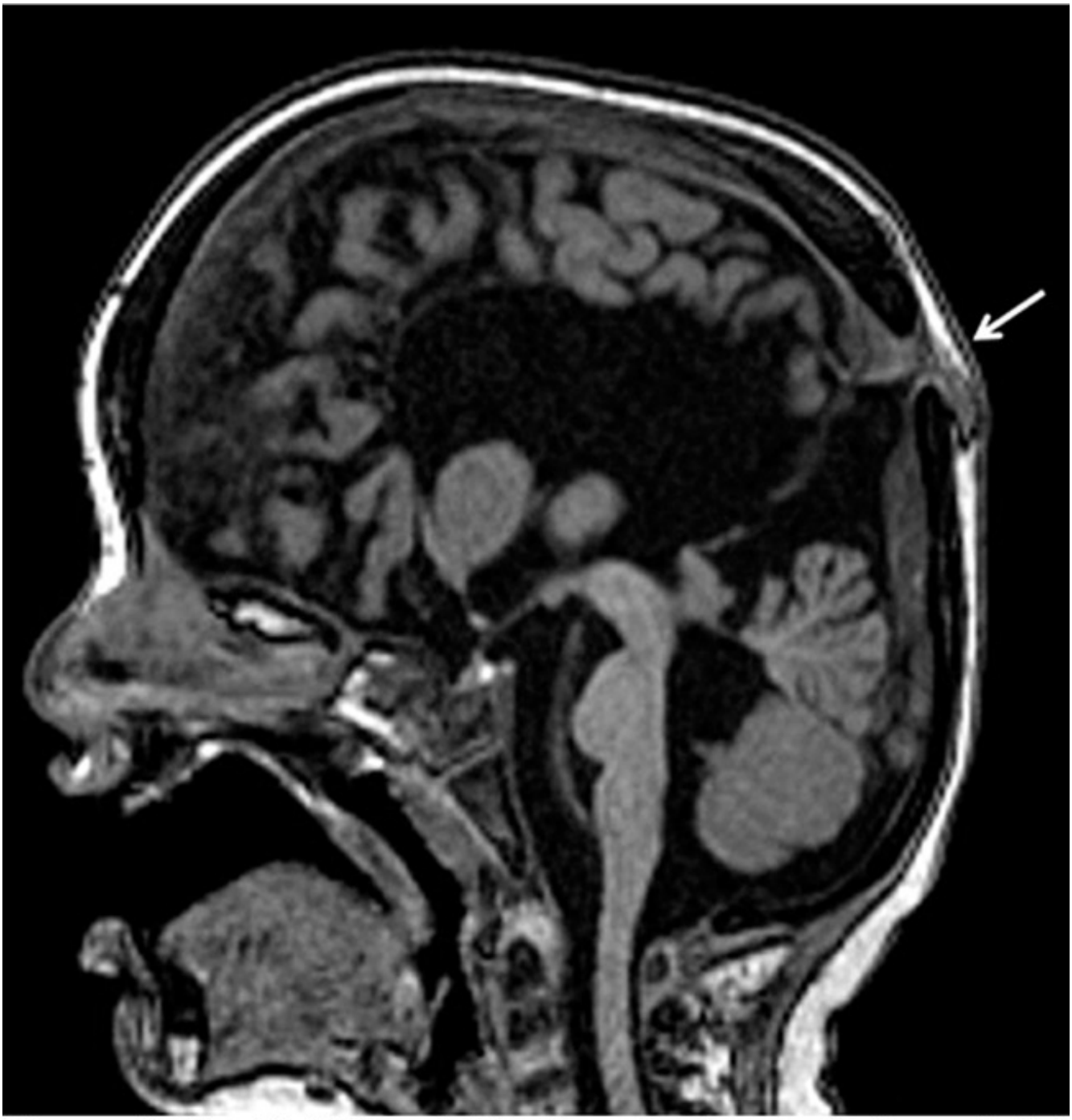

Figure-3: Sagittal T1-weighted image shows atretic occipital encephalocele (arrow).

No pathology was determined in cardiac or abdominal organs from the echocardiography and abdominal US examinations.

Discussion

JS is a rare disease characterised by clinical and radiological findings. Among the classic clinical findings of JS are hypotonia, ataxia, mental-motor retardation, and respiratory findings such as

apnoea/hyperpopnoea, and opthalmological findings as ocular motor apraxia.[1,5] In the patients with JS, some studies determined that the respective frequency of anomalies as tongue protusion, tongue tumours, polydactyly, kidney anomalies, megalocephaly, microcephaly, ocular coloboma, retinal dystrophy, esophageal reflux, pectus excavatum, hepatic anomalies, hydrocephaly, bradycardia, cardiac failure, cerebral palsy, asthma, webbed feet and cleft lip.[3,4,6] As JS is an autosomal recessive transmitted disease, there is a risk to other children of a couple to be affected.[7,8]

In the current study, hypotonia and mental-motor retardation were present in all the cases. Ataxia was seen in more than half of the cases. Of interest is that one case had hyperpnoea episodes, which are often defined as a prominent factor of JS. Most cases had findings of facial dysmorphism and four cases had opthalmological findings, the most noticeable of which was optic atrophy. There was familial consanguinity in a total of seven cases, two at 2nd degree and five at 1st degree. One family was found to have two children with JS.

The principal MRI findings of Joubert syndrome are deep interpeduncular fossa together with a narrowing of the isthmus, thickening of the superior cerebellar peduncle, fourth ventricle deformity together with hypolplasia of the vermis, fastigumun rostral shift and sagittal vermian cleft originating from the incomplete union of the two halves of the vermis. These neuroradiological characteristics form the molar tooth sign. This finding is seen in 85% of patients and is accepted as pathognomonic. In the absence of vermis, a cleft forms between the two normal cerebellar hemispheres. Associated with this, is the 4th venticle bat-wing appearance seen on CT and MRI.[9] The molar tooth sign, vermian cleft and bat-wing appearance are the basic radiological findings of JS. In another study, several brain structural anomalies were reported besides the basic radiological findings of JS. The most remarkable of these anomalies were cerebellar folial disorganisation, temporal lobe hypoplasia, ventriculomegaly, occipital encephalocoele, atretic encephalocoele, callosal dysgenesis, periventricular and subcortical heterotopia and hypomyelination. [3,4,10]

In the current study, all cases had the basic radiological findings of JS. The majority of cases also had accompanying vermian hypoplasia, and cerebellar folial disorganisation was observed in approximately half of the cases. Three cases had additional corpus callosum anomaly and atretic occipital encephalocele.

The prognosis of patients with JS is related to the severity of respiratory impairment immediately after birth. Especially long-lasting, life-threatening repeated attacks of apnoea create a need for mechanical ventilation. In addition, feeding problems are a significant health problem for many patients. If renal and hepatic complications are not treated in time, they may be life-threatening.[4] None of the cases in the current study had clinical apnoea. Only one case had episodic hyperpnoea but there was no requirement for respiratory support. All the cases had normal kidney and liver function test results. The patients with JS were taking medications. Physical therapy was initiated in the long-term management of other patients with JS. Patients diagnosed with JS should be examined for possible multi-organ pathologies. The ocular evaluation should include visual acuity, eye movements and fundus oculi examination. Kidney and liver function tests should determine whether or not there are abnormalities. The kidney parencyhma echogenicity and cysts and liver fibrosis should be evaluated by abdominal US. If there is ever any suspicion of abnormal changes in the liver, MRI examination should be applied. Biopsy is recommended when necessary. Investigations should be made for other accompanying pituitary defects, cleft palate, congenital heart defects, situs inversus and Hirschsprung disease.[4]

Conclusion

Brain MRI examination, eye examination, abdominal US and echocardiography examinations should

be made in paediatric cases with clinical suspicion of JS. Attention should be taken in respect of other multisystem pathologies and additional brain anomalies.

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