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Joubert syndrome associated with new MRI findings and posterior reversible encephalopathy syndrome

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Abstract

Joubert syndrome (JS) is an inherited disorder characterized by transient episodic hyperpnea, ataxia, and vermian hypoplasia. Typical imaging findings of JS include hypoplasia or aplasia of the cerebellar vermis, thick and elongated superior cerebellar peduncles and an abnormally deep interpeduncular fossa with 'molar tooth sign'. We present a case of JS associated with deep cerebral sulci and fissures, polymicrogyria, and additional findings of posterior reversible encephalopathy syndrome associated with renal involvement.

Key words : Joubert syndrome ; Congenital vermian hypoplasia ; 'Molar tooth' brainstem ; posterior reversible encephalopathy.

Introduction

Joubert syndrome (JS) is an inherited disorder characterized by transient episodic hyperpnea, oculomotor abnormalities, ataxia, developmental delay and variable mental retardation (Joubert *et al.*, 1969). Renal (nephronophthisis), hepatic (fibrosis) and ocular (retinal dystrophy, ocular colobomas) diseases may be associated features of JS. Typical imaging findings of JS include hypoplasia or aplasia of cerebellar vermis, thick and elongated superior cerebellar peduncles and an abnormally deep interpeduncular fossa with 'molar tooth sign' (Blaser 2004 ; Maria *et al.*, 1997). Polymicrogyria and cortical dysplasia have also been reported in JS and related disorders (Blaser 2004 ; Dixon-Salazar *et al.*, 2004 ; Gleeson *et al.*, 2004).

In this report we present a case of JS associated with deep cerebral cortical sulci and fissures, polymicrogyria, and additionally clinical and imaging findings of posterior reversible encephalopthy syndrome (PRES) related to hypertension and renal involvement (nephronophtisis).

Case report

A 19-year-old man was admitted to the emergency department because of convulsions and unconsciousness. He had a history of chronic renal insufficiency and was undergoing hemodialysis twice a week since 6 years. His parents had second degree consanguinity with unremarkable family history. Vital signs included a temperature 36.6°C, pulse 88 beats/min, blood pressure 130/80 mmHg. Neurological examination revealed mental and motor retardation. Eye movements were limited in all directions (oculomotor apraxia). He had bilateral genu valgus deformity and had undergone surgery for this condition.

In laboratory tests, mild anemia (hemoglobin : 10.9 g/dl) associated with chronic renal failure was found. He had serum blood urea nitrogen of 123 mg/dL, creatinine of 13.25 mg/dL, and elevated liver enzymes (ALT : 65 IU/L, GGT : 138 IU/L).

Abdominopelvic ultrasonography revealed diffuse minimal granular appearance of the liver parenchyma and bilateral diffuse atrophic kidneys with cortical cysts. Cerebral magnetic resonance imaging showed abnormally deep interpeducular fossa, bilateral long and thick superior cerebellar peduncles compatible with a "molar-tooth" brainstem, high signal in the decussation of the superior cerebellar peduncles, enlarged "bat-wing" or "open umbrella" shaped fourth ventricle, enlarged cisterna magna, a small cerebellar vermian remnant and mild brainstem hypoplasia (Fig. 1a). Additional findings included bilateral deep cerebral sulci and fissures (Fig. 1b), and bilateral frontal polymicrogyria (Fig. 1c). Bilateral temporo-parieto-occipital cerebral cortical / subcortical and cerebellar hyperintense areas were observed suggesting PRES (Fig. 1d). Diffusion weighted MRI and apparent diffusion coefficient (ADC) mapping showed restriction of

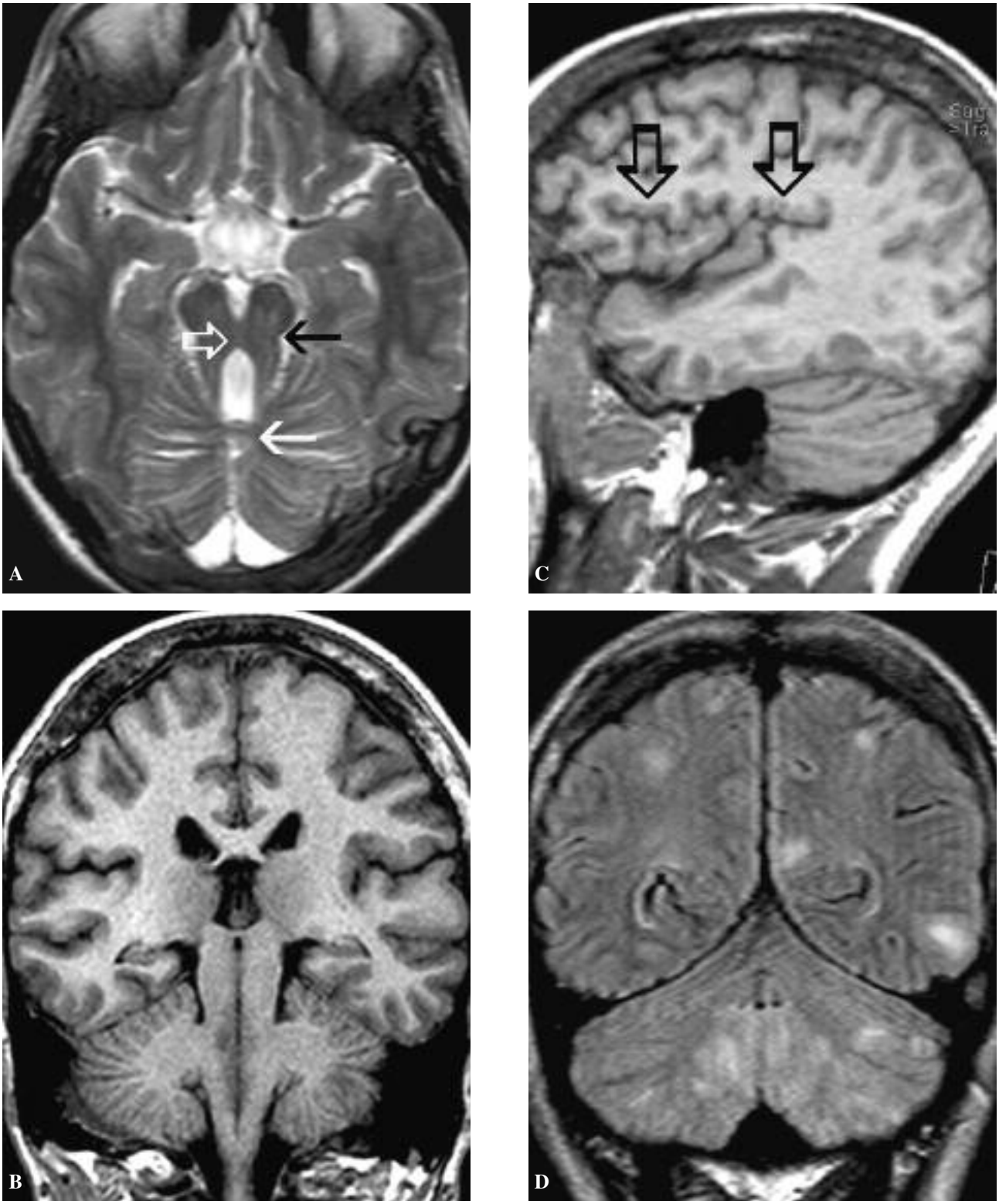

FIG. 1. — A. Axial T2 weighted magnetic resonance image (MRI) shows typical deep interpeduncular fossa and "molar tooth" appearances of the brainstem (arrow), high signal intensity in decussation of the superior cerebellar peduncles (open arrow). Small cerebellar vermian remnant (white arrow) is also seen. B. Coronal T1 weighted inversion recovery MRI shows deep cortical sulci and fissures. C. Sagittal T1 weighted inversion recovery MRI shows polymicrogyric cortex in right frontal lobe-perisylvian region (open arrows). D. Coronal FLAIR T2 weighted MRI shows multiple hyperintense areas in patchy distribution of the cerebral cortical / subcortical regions and cerebellum.

diffusion in bilateral parietal subcortical areas. Follow-up MRI obtained four months later revealed that the bilateral parietal subcortical areas with restriction of diffusion had disappeared. The follow-up MRI also showed disappearence of the parietal and temporal classical T2 hyperintense PRES lesions and new T2 hyperintense lesions in the bilateral cerebellar hemispheric subcortical areas.

Discussion

Joubert syndrome (JS) was first described in 1969 by Marie Joubert and colleagues, who reported a 6-month-old infant with an abnormal, rapid breathing pattern and developmental delay (Joubert *et al.*, 1969). The clinical signs and MRI findings of JS are not easily recognized especially in mildly affected individuals, so a direct estimation of the incidence of JS does not exist (Parisi *et al.*, 2007). It is a rare autosomal recessive disorder of the cerebellum with variable other features including skeletal, ophthalmologic, renal, hepatic and endocrine abnormalities. We demonstrated renal and hepatic failure, abnormal neurological findings and skeletal deformities in the clinical and laboratory examination of our patient.

Typical imaging findings of JS (prototype) include vermian hypoplasia / dysplasia of variable degrees, abnormal deep interpeduncular fossa with narrow isthmus, thickened, elongated and mal-oriented superior cerebellar peduncles giving the appearance of a "molar-tooth" (Blaser 2004 ; Gleeson *et al.*, 2004). Enlarged "bat-wing" or "open umbrella" shaped fourth ventricle and variable sized cerebellar vermian remnant with or without cleft are associated findings. Variable brainstem hypoplasia, midline anomalies such as holoprosencephaly, pituitary hypoplasia, and high signal in decussation of superior cerebellar peduncles, hamartomas or heterotopias may be seen (Blaser 2004). The absence of decussation of the superior cerebellar peduncles and of the pyramidal tract has been shown by using diffusion tensor imaging (Poretti *et al.*, 2007). In addition to the previously documented typical brain MRI findings of JS mentioned above, we found bilateral hemispheric deep cerebral cortical sulci and fissures in our case (Fig. 1b).

Moreover, typical T2 hyperintense lesions on MRI in posterior circulation areas including temporal lobes and cerebellum were observed suggesting PRES (Fig. 1d). PRES is usually described as reversible leukoencephaloapthy clinically manifested by headache, altered mental status, visual loss and seizures, and it primarily involves the parietal and occipital lobes (Hinchey *et al.*, 1996). Characteristic MRI findings of PRES are patchy cortical / subcortical hyperintense signal intensity areas on T2 weighted images in PCA territory. Main lesions in areas of the brain other than the parietal-occipital lobes have been also reported as atypical manifestations of PRES. Diffusion weighted imaging is usually normal, and markedly elevated signal with no restriction of diffusion is observed commonly on the ADC map. Less commonly high signal on DWI with "pseudonormalised" ADC values representing irreversible infarct can be seen (Thambisetty *et al.*, 2003). In our case bilateral parietal low ADC values consistent with restriction of diffusion in acute stage were seen on the first MRI examination. The pathophysiology of PRES is not entirely understood, but disordered cerebral autoregulation and endothelial damage, and a hyperperfusion state, with blood-brain barrier breakthrough, extravasation of fluid potentially containing blood or macromolecules, and resulting cortical or subcortical edema is suggested for the underlying mechanism (Hinchey *et al.*, 1996 ; Osborne 2004). It is associated with varied causes including hypertension, immunosuppressive drugs, thrombocytopenic syndromes, and various causes of renal failure. In PRES, the most common clinical presentations are headaches, mental abnormalities, seizures, and visual disturbances (Hinchey *et al.*, 1996). PRES associated with JS has not been previously described.

JS is a prototype of a group of genetic disorders in which variable radiological and clinical findings are associated (Maria *et al.*, 1997). Rarely encountered malformations besides the classic imaging findings and associated clinical features may be observed (Parisi *et al.*, 2007). The technological developments in MRI and new sequences provide better and more detailed images of these lesions.

In conclusion ; although polymicrogyria and cortical dysplasias in association with JS have been reported previously in the literature, deep cerebral sulci and fissures have not been reported yet. This finding may be related with JS and further research is required. Moreover, presence of PRES findings was another striking observation in this case.

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