

Joubert Syndrome Associated with Lissencephaly

Joubert syndrome (JS) is a rare autosomal recessive disorder characterized by clinical (hypotonia, ataxia and general developmental delay) and neuroradiological findings. Neuroimaging of JS reveals deeper than normal posterior interpeduncular fossa, prominent or thickened superior cerebellar peduncles, and vermian hypoplasia or dysplasia leading to the so called molar tooth sign(1).

Lissencephaly is a rare and severe cortical malformation that shows evidence of widespread incomplete neuronal migration. The spectrum ranges from complete absence of gyri (agyria) to broad gyri with reduced sulci (pachygyria), with an abnormally thick cortex(2).

The majority of JS cases have morphologically normal cerebrums and cerebellar hemispheres, but lateral ventricular enlargement due to atrophy, and corpus callosum dysgenesis were described. To our knowledge, JS associated with lissencephaly was very rarely reported(3,4).

A 3-year-old infant was admitted to our clinic because of seizures and marked psychomotor developmental delay. The patient was capable of head controlling, smiling to mother, and supportive sitting at 7, 8 and 10 months, respectively. He had also abnormal breathing pattern as alternating periods of predominantly hyperpnea and apnea within first month. His parents were first-degree cousins. His head circumference was normal. He was poorly contacting with surroundings. He could not sit without support. Axial hypotonia and spastic left hemiparesis were detected. Neuro-ophthalmological exami-

nation was within normal limits. Electroencephalogram and metabolic screening revealed no abnormalities. Abdominal ultrasound examination was normal. Cranial MRI showed characteristic imaging of JS including bat-wing shaped fourth ventricle, elongated and stretched superior cerebellar peduncles, hypoplasia of the cerebellar vermis (*Fig. 1*). Cerebellar hemispheres were normal. In addition, a flattened and thickened cerebral cortex with gyration anomalies predominantly in the frontotemporal areas with opercular hypoplasia and lissencephaly were noted. The patient was diagnosed as JS associated with lissencephaly. The patient was put on phenobarbital and physical therapy. At two years of age, he was hypotonic, and still could not sit without support, but his spastic left hemiparesis markedly improved. His head circumference did not reach to age-normal levels (46.5 cm, <5 p). Although the patient learned to sit without support approximately at three years of age, he did not talk and walk.

In a study of 21 unrelated and 6 related JS

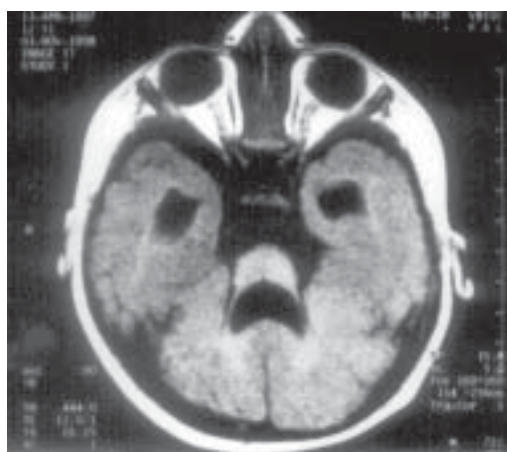


Fig. 1. Axial T1 weighted image demonstrates characteristic bat wing dilatation of fourth ventricle and elongated superior cerebellar peduncles.

families, both chromosome 9q34 and 17p11.2 JS loci were excluded in 26 JS families. They have also searched and excluded the candidate genes EN1, EN2, FGF8, and BARHL1 from a direct pathogenetic role in JS(5). Genetic studies and many variable phenotypes of JS suggest that there is heterogeneity in genetic basis of JS.

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X-Linked Adrenoleuko-dystrophy Presenting as Addison Disease

X-linked adrenoleukodystrophy (X-ALD) is a group of peroxisomal disorders characterized by an impaired beta-oxidation of very long chain fatty acids. This defect results in an extremely variable phenotype including presymptomatic form, isolated adrenal insufficiency and cerebral disease. An incidence of about 1: 10000 male subjects has been reported(1).

Two brothers (8 years and 5 years old), born of a non-consanguineous marriage were brought with complaints of progressively increasing pigmentation and darkening of

skin, starting from face since the age of 4 years. There was history of recurrent episodes of loose motions, vomiting and fever after the age of 4 years in the elder sibling for which he was hospitalized in a state of shock. Family history, perinatal history and developmental history were non-contributory. General and systemic examinations were unremarkable except for the generalized hyperpigmentation of the skin. Black colored spots were also noted on the tongue and oral mucosa.

Investigations revealed a normal hemogram. Basal serum cortisol levels were low [1.82 µg/dL and 2.8 µg/dL (normal= 9-25 µg/dL)] and response to ACTH was subnormal [5.86 µg/dL and 6.7µg/dL after ACTH stimulation test.]. Serum electrolytes, albumin,