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Case Report

A case of Jacobsen syndrome with multifocal white matter lesions☆,☆☆

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ABSTRACT

Jacobsen syndrome is a rare disorder caused by partial deletions of the long arm of chromosome 11. The phenotype is variable with involvement of multiple organ systems, resulting in congenital heart defects, blood dyscrasias, and impaired growth. We describe a case of a 30-year-old man with multiple ophthalmic manifestations and brain magnetic resonance imaging (MRI) that was remarkable for multiple T2-hyperintense subcortical white matter lesions. It is important to be aware that patients with Jacobsen syndrome may have nonspecific white changes seen on MRI.

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1. Introduction

First described in 1973, Jacobsen syndrome (also referred to as 11q deletion syndrome) results from a partial deletion of the long arm of chromosome 11 [1]. Patients may demonstrate abnormalities involving multiple organ systems, including gastrointestinal, genitourinary, cardiovascular, and central nervous systems. The deletion usually ranges between 7 and 20 Mb in size, with a breakpoint at 11q23.3 in 70–80% of cases [2]. Interstitial deletions of 11q tend to present with less severe phenotypes than terminal ones. Herein, we describe a case of a young adult man with Jacobsen syndrome who was found to have multifocal white matter lesions on brain magnetic resonance imaging (MRI).

2. Case

A 30-year-old man with Jacobsen syndrome presented to our institution for further evaluation of worsening vision. The patient had a history of bilateral cataracts and had undergone left intraocular lens replacement and right cataract surgery. Bilateral optic atrophy was noted on fundus examination. Neurologically, no focal deficits were identified, although he was developmentally and cognitively impaired.

An MRI of the brain with intravenous gadolinium was obtained, which demonstrated multiple foci of T1 and T2 prolongation (Fig. 1). These lesions were situated along a predominantly subcortical distribution, with sparing of the U-fibers. A few pericallosal lesions were also seen. No lesions were identified in the posterior fossa. Following intravenous gadolinium administration, no significant contrast enhancement was observed. Serum chemistries and blood counts were within normal limits.

3. Discussion

Jacobsen syndrome has an estimated occurrence of less than 1 in 100,000 births, with a 2:1 female-to-male ratio. Affected patients present with a wide phenotypic spectrum, which includes impaired growth, hematological abnormalities, and congenital heart defects [3]. Characteristic dysmorphic features have been described such as macrocrania, broad nasal bridge, shortened neck, and trigonocephaly. Ophthalmologic manifestations, as seen in our patient, include hypertelorism, epicanthal folds, cataracts, retinal detachment, glaucoma, and optic nerve atrophy [1].

Abnormalities of the central nervous system are found in 65% of cases during perinatal imaging, and they include ventriculomegaly, cerebral parenchymal atrophy, and pachygyria [4]. Spina bifida, scoliosis, and other vertebral anomalies have also been reported [3]. Over 90% of patients suffer from some degree of mental as well as psychomotor retardation, the severity of which appears to have a direct relationship with the size of the chromosomal deletion [5]. Psychological disorders and seizures have also been described.

Our patient demonstrated multiple areas of T2 and T1 prolongation involving the subcortical white matter, with sparing of the posterior

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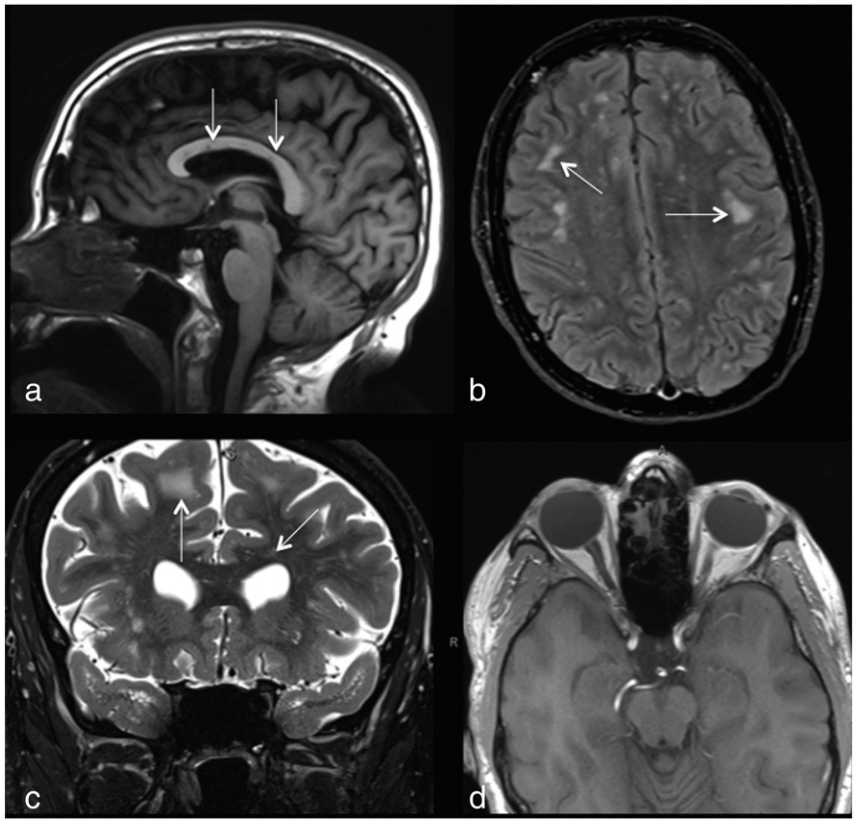

Fig. 1. Sagittal T1-weighted (a), axial FLAIR (b), and coronal T2-weighted (c) magnetic resonance images of the brain demonstrate multiple foci of T1 and T2 prolongation within the subcortical white matter and corpus callosum (arrows). There is sparing of the subcortical U-fibers. No significant contrast enhancement is seen on the axial T1-weighted postgadolinium image (d).

fossa. A few cases reports have noted similar findings in a deep or periventricular white matter distribution [6]. These lesions are thought to represent delayed myelination as opposed to a demyelinating process [7,8]. Magnetic resonance spectroscopy further supports this notion, demonstrating decreased myoinositol and NAA without increased choline as seen in demyelination [9].

The genes responsible for this phenotype remain an area for further investigation. Candidates include FEZ1 and RICS, which are involved in axonal growth and brain development, as well as HEPACAM (codes for hepatic and glial adhesion molecules) [10]. The latter of these are associated with megalencephalic leukoencephalopathy with subcortical cysts type 2 (MLC2, which is further divided into 2A and 2B types). Similar to MLC2B, the white matter lesions and neurological impairment in Jacobsen syndrome patients have been reported to stabilize or regress on follow-up imaging. The absence of classic MLC phenotypes might be attributed to variable penetrance and expressivity of the HEPACAM deletion, among other factors [10]. This may also account for the variable lesion distribution patterns observed in reported cases, including between siblings [11].

In conclusion, it is important for the radiologist to be aware that patients with Jacobsen syndrome can have multifocal white matter changes seen on MRI.

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