Group III Möbius Syndrome: CT and MR Findings

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Möbius syndrome is a congenital neuromuscular disorder characterized by both inability to abduct the eyes and facial weakness [1]. It is classified into four groups on the basis of whether the primary abnormalities are diffuse (group I), in the abducens and facial nerves (group II), or nuclei (group III), or lie outside the CNS (group IV) [2]. Although the radiologic findings of the musculoskeletal abnormalities associated with Möbius syndrome have been reported [3], no prior imaging studies of the primary CNS abnormalities have been published. We report a case of a child with clinical and pathologic evidence of group III Möbius syndrome whose CT and MR studies showed a hypoplastic brainstem and calcification in the abducens nerve nuclei. Radiologic-pathologic correlation is presented.

Case Report

A 2340 g boy was born at 38 weeks gestation to a 17-year-old woman whose pregnancy was complicated by polyhydramnios. The Apgar score at 1 min was 2 and at 10 min was 5. Owing to the lack of any respiratory effort he was intubated and received mechanical ventilation. The infant had several anomalies including cleft palate, micrognathia, and club foot. The neurologic evaluation revealed facial diplegia, external ophthalmoplegia, no suck or gag reflex, and a small tongue. There was decreased muscle tone in the trunk, and joint contractures at the ankles and knees. Spontaneous movements were reduced.

An EEG showed lack of differentiation of sleep stages. A brainstem auditory evoked response examination showed unilateral loss of pontine waves III, IV, and V. The child died at 6 weeks of age.

A CT scan (Fig. 1) at age 1 week demonstrated calcification in the region of the abducens nuclei bilaterally. Follow-up CT scans over the next 5 weeks showed no change. An MR image (Fig. 2) obtained at age 3 weeks demonstrated absence of signal due to the calcification within the abducens nuclei. Gradient-echo images (not shown) showed no evidence of magnetic susceptibility effect, which would imply associated hemorrhage. No other signal abnormality was demonstrated. Both CT and MR revealed a symmetrically hypoplastic brainstem and cerebellum.

At autopsy the brain weighed 410 g and had a normal gyral pattern. The brainstem and cerebellum appeared disproportionately small. Transverse sections of the brainstem at the level of the facial colliculi (Fig. 3) had evidence of focal calcifications in the region of the abducens nuclei and dark discoloration and shrinkage of the entire central portion of the brainstem extending from the floor of the fourth ventricle to the ventral surface. Similar discolored areas, some with small flecks of mineralization, were present in all levels of the medulla rostral to the obex. Microscopically, there were large foci of fibrillary gliosis and intense mineralization in the region of the abducens nuclei (Fig. 4). The entire central portion of the medulla at numerous levels was severely gliotic with nearly complete loss of normal architecture and obliteration of the nuclei of cranial nerves V, VI, VII, IX, X, XI, and XII. Despite the obliterative changes in the lower cranial nerve nuclei, there was gross and microscopic evidence of some preservation of peripheral elements (nerve roots and intraparenchymal radicles) of the involved cranial nerves. There also were numerous large-caliber, thin-walled vascular channels that coursed through the gliotic regions of the medulla (Fig. 4). There were smaller areas of gliosis and mineralization in the pons, midbrain, and medial hypothalamus that were not accompanied by the abnormal vascularization. An additional abnormality was the presence of neuronal-glial heterotopias in the leptomeninges of the ventral pons and medulla.

Discussion

Möbius syndrome consists of unilateral or bilateral palsies of the sixth and seventh cranial nerves manifested clinically by external ophthalmoplegia and facial paralysis. There may be associated musculoskeletal anomalies [3]. Towfighi et al. [2] classified the syndrome into four groups on the basis of the principal pathologic changes. Group I was characterized by simple hypoplasia or atrophy of cranial nerve nuclei, presumably as a result of embryonic maldevelopment. Group II resulted from primary lesions in the peripheral portion of the cranial nerves. Patients such as ours with focal necrosis in brainstem nuclei suggestive of fetal anoxia or infection comprised group III. Group IV consisted of patients without lesions in the CNS or cranial nerves who had a primary myopathy. Little is known about the pathogenesis of the syndrome, but intrauterine vascular, toxic, genetic, and infectious factors have been proposed as causative [4].

The histopathologic findings in our patient, with focal necrosis and calcification of the brainstem that was most severe in the abducens nuclei, are similar to the lesions reported by Thakkar et al. [5] in two patients with Möbius syndrome.

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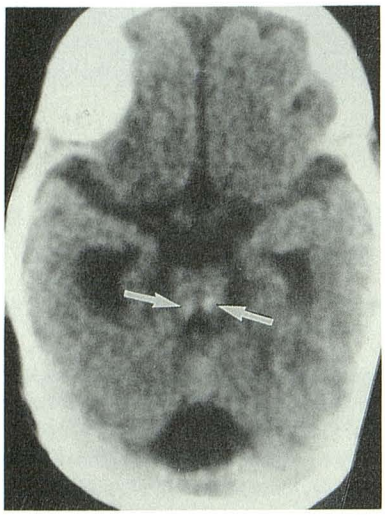

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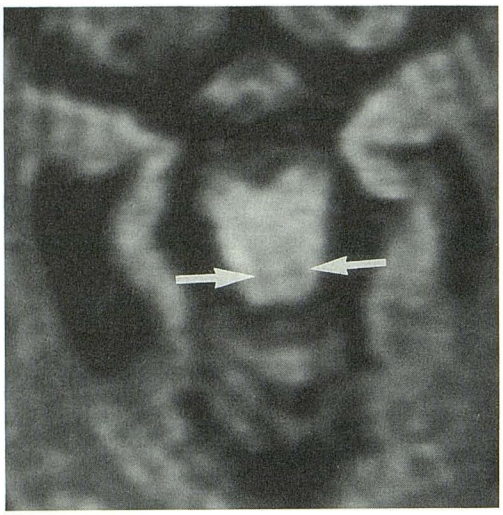

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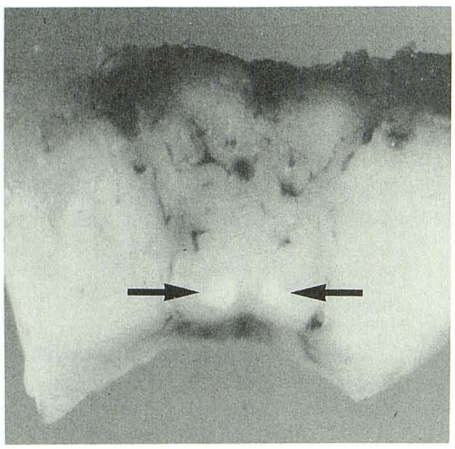
Fig. 1.—CT scan through brainstem without IV contrast material shows punctate areas of calcification bilaterally in the paramedian dorsal pons (*arrows*), just anterior to the floor of the fourth ventricle. This is the site of the abducens nuclei.

Fig. 2.—T1-weighted axial MR image through same location shows decreased signal (*arrows*) at site of punctate calcification. No corresponding T2 signal abnormality was seen.



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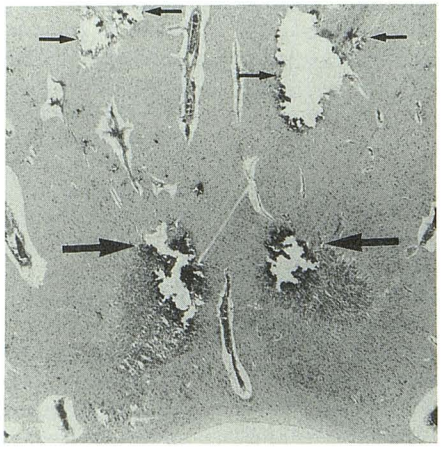

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Fig. 3.—Gross appearance of transversely sectioned brainstem at level of facial colliculi. There are bilateral foci of calcification in the region of the abducens nuclei (*arrows*). Note the discoloration and large vascular channels present in the central region. (×9)

Fig. 4.—Histologic appearance of brainstem at level shown in Fig. 3. Floor of fourth ventricle is at bottom of figure. There are bilateral calcifications and intense fibrillary gliosis in the region of the abducens nuclei (*large arrows*) and several smaller calcified foci (*small arrows*) ventrally. (H and E, ×30)

Other reports [6, 7] have described foci of brainstem necrosis and calcification in patients with this syndrome. All of these patients would thus be classified in group III of Towfighi et al. [2].

The brainstem calcifications seen on CT in this patient were bilateral, symmetric, and adjacent to the floor of the rostral fourth ventricle. This exactly corresponds with the pathologic findings of calcification within the abducens nuclei. Intracranial calcifications in neonates may be due to congenital infections such as toxoplasmosis or cytomegalovirus; these would not ordinarily be limited to brainstem nuclei. Similarly, most types of posthemorrhagic and postinfarction calcifications would have different distributions and configurations.

Calcification confined to the abducens nuclei is thus strongly suggestive of group III Möbius syndrome, and a clinical history of lateral gaze paralysis and congenital facial diplegia should be sought. Accompanying brainstem and cerebellar atrophy may also be demonstrated. In the case presented, Möbius syndrome was diagnosed clinically and subsequently confirmed by the specific CT, MR, and, ultimately, pathologic findings.

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