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Short reports

Brainstem lesion revealed by MRI in a case of Leigh's disease with respiratory failure

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Abstract. This 6-year-old girl was admitted with insufficient involuntary breathing and generalized hypotonia. T_2-weighted MR images showed bilateral symmetrical tubular hyperintense lesions in the medio-caudal part of the medulla oblongata that correlated well with demyelination and gliosis in the regions of the reticular formation and the nucleus solitarius found at autopsy. The typical lesions of Leigh's disease in the basal ganglia were not present, which made the diagnosis uncertain prior to the histopathological findings. MRI was very helpful in deciding on further management of the patient.

Leigh's disease (subacute necrotizing encephalomyelopathy) is a rare autosomal-recessive disorder usually affecting infants and young children. The neurological symptoms are heterogeneous manifesting themselves in multiple deficits such as ataxia, spasticity, psychomotor regression, dysarthria, ophthalmoplegia, nystagmus, and respiratory difficulties. Although histopathologically well defined, Leigh's disease is not a biochemical entity, and various metabolic defects finally result in the same neuropathological condition [1]. Thus the in-vivo diagnosis is difficult. CT has enabled it in cases with marked symmetrical lesions in the putamen, but MRI proved to be superior [2].

We describe white matter lesions clearly visible in MRI mainly in the brainstem of an autopsy proven case of Leigh's disease, so far not typically reported in the MR literature.

Case report

The girl presented here was born in May 1982, 4 weeks prematurely weighing 2010 g. On the second day of life almost two thirds of the colon had to be removed due to necrotizing enterocolitis. At that time, serum lactate levels were not elevated. With appropriate diet and vitamin supplementation the subsequent clinical course and weight gain were satisfactory. Absorption parameters and blood levels of electrolytes and vitamins were monitored regularly and found to be within normal limits.

At the age of three years the following neurologic signs were noted: moderate truncal ataxia and tremor, mild bilateral ptosis as well as oculomotor apraxia (she was not able to follow fast moving objects), slightly elevated muscular tone and a symmetrical hyperexcitability of the tendon reflexes. Extensive laboratory investigations including liver function tests and intestinal absorption parameters were again normal. No abnormalities could be found in nerve conduction velocities and cranial CT, and physiotherapy was begun. In the following three years the neurological condition was fairly stable, did not deteriorate, and further developmental progress was noted.

At the age of 6 years, following a short febrile illness with diarrhea, she was sent to our hospital because of increasing lethargy, progressive unsteadiness, dysarthria and intermittent cyanosis with impaired consciousness. On admission, she presented with generalized muscular hypotonia, ptosis and somnolence. The tendon reflexes were symmetrically accentuated and the Babinski sign was negative. Respiration was shallow with poor chest movements, but no clinical evidence of dyspnea was noted. Capillary blood gases revealed a pH of 7.20 and a pCO_2 of 12.8 kPa. Although her condition was suggestive of a chronic slowly progressive disease process, she was intubated and artificially ventilated without difficulties. However, weaning her from the respirator a few days later was unsuccessful, resulting in immediate CO_2 retention and hypoxia. The following work-up was normal: complete blood count, electrolytes, liver function tests including coagulation parameters, analysis of cerebral spinal fluid, EEG and muscle biopsy (m. quadriceps).

MR imaging was then performed on a 2.35 tesla superconducing system (BRUKER/SPECTROSPIN). With the child still intubated and artificially ventilated, we obtained T_1- and T_2-weighted

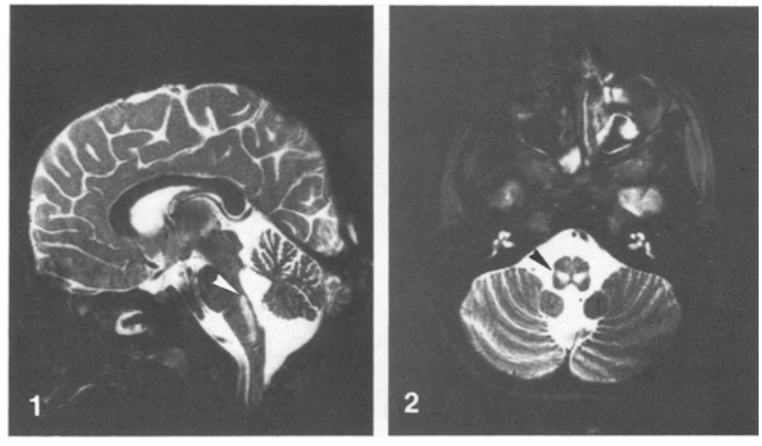

Fig. 1. Mid-sagittal T_2-weighted image revealing tubular shaped hyperintense lesion (arrow) in the medio-caudal part of the medulla oblongata (tegmentum)

Fig. 2. Axial T_2-weighted image at the level of the medulla oblongata showing two symmetrical hyperintense lesions near the floor of the 4th ventricle (arrow)

images (TR/TE 500/22 and 3000/120 msec) in the axial and sagittal plane with a slice thickness of 4 mm on an imaging matrix of 256 × 256. The T_2-weighted spin-echo sequences revealed two symmetrical hyperintense tubular lesions of 27 mm in length on sagittal view (Fig. 1), and of 6 mm diameter on axial view (Fig. 2) in the dorsal part of the medulla oblongata (tegmentum), beginning at the level of the 4th ventricle (floor) and extending caudally. In addition spotty subcortical hyperintense lesions, 3 to 5 mm in size, distributed in the parieto-temporal regions of both hemispheres were found. The caudal part of the vermis cerebelli appeared hypoplastic, the basal ganglia, however, were normal.

Further course: In view of these presumably irreversible brainstem lesions, the failure to wean the patient from the respirator and a worsening of her neurological status, it was decided in consent with the parents to stop the assisted ventilation three weeks after admission. Within a few hours after the extubation she died due to severe respiratory insufficiency.

The postmortem examination revealed the typical histopathologic findings of Leigh's disease: Sponginess of the brain tissue and vacuolisation of the neuropil with capillary proliferation of the central gray matter. These changes were found predominantly in the nucleus amygdalae, the corpora mammillaria, the substantia nigra, and the paramedian nuclei of the medulla oblongata. There was a marked gliosis and demyelination of the white matter symmetrically involving the paramedian dorsal tracts (fasciculus longitudinalis, and tractus solitarius in particular). Diffuse hypoxic-ischemic alterations of the cortex and the subcortical white matter are probably secondary.

Discussion

The gray and white matter lesions of the various regions of the brain described above appear as edema and gliosis, i.e. signal attenuation on T_1 and high signal intensity on T_2-weighted images. Since the MRI findings are nonspecific, similar lesions are found in multiple sclerosis [3], post asphyxia [4], or in central pontine myelinolysis [5], but they are either more diffuse, hemorrhagic or involve other structures, and show different clinical signs. In our patient the sites of the hyperintense lesions in T_2-weighted MRI findings corresponded well with the histopathological findings of spongiform degeneration, demyelination with glial proliferation and cystic necrosis, found in the brainstem at autopsy. In the literature, the typical lesions of Leigh's disease are described in the basal ganglia mainly putamen [6]. However, we found one case, where these areas were not involved, with only solitary lesions in the tegmentum and tectum, similar to our patient [2].

The MR findings in our patient, which correlated well with the neuropathologic lesions involving the region of the primary respiratory center, explained the insufficiency of her involuntary breathing. Thus we found MRI very helpful in facilitating the decision making for further clinical management of this girl.

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