A clue in the diagnosis of Cri-du-chat syndrome: Pontine hypoplasia

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A 5-month-old male patient was admitted with global developmental delay. He was the second child of consanguineous parents delivered through cesarean section after an uncomplicated second pregnancy, with a birth weight of 2530 g (<10th percentile), length of 47 cm (10-50th percentile) and head circumference of 31.4 cm (<10th percentile). There were no postnatal adaptation problems or history of asphyxia; family history was unremarkable. At 5 months, the patient had a weight of 6500 g (25th percentile), length of 63 cm (25-50th percentile) and severe microcephaly with a head circumference of 37.6 cm (<3rd percentile) (−3.9 standard deviation). Physical examination revealed a rounded face, hypertelorism, epicanthal folds, downslanting palpebral fissures, low-set ears and micrognathia. The patient made eye contact but was hypotonic with no head control. Deep tendon reflexes were normoactive. Systemic examination findings were normal and no abnormal crying was reported by the parents. Screening for inborn errors of metabolism (including anacylcarnitine profile from dried blood spot by tandem mass spectrometry [MS]), urine organic acid analysis by gas chromatography-MS, quantitative analysis of amino acids in plasma and biochemical test results (including thyroid hormones, B12 and creatine kinase) were all normal. Electroencephalography revealed no abnormalities. Auditory brainstem responses and eye examination were normal. Pons and brainstem hypoplasia was detected on cranial magnetic resonance imaging (MRI) [Figures 1 and 2] and compared with an age-matched healthy control [Figure 3]. The patient's syndromic face and MRI findings were suggestive of Cri-du-chat syndrome. The diagnosis was confirmed when karyotype analysis showed a deletion in the short arm of chromosome 5 consistent with the syndrome. The patient was prescribed physiotherapy and rehabilitation.

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Cri-du-chat syndrome is caused by a partial deletion, either terminal or interstitial, of the short arm of chromosome 5.[1] It occurs in 1 of every 50,000 live births and leads to global developmental delay. The main clinical features are a high-pitched cat-like cry (hence the name of the syndrome), distinct facial dysmorphism, microcephaly and severe psychomotor and mental retardation.[2] The clinical picture becomes less striking with advancing age[3] and the cat-like cry, the most differentiating feature of the syndrome, disappears as well. An important radiological feature of Cri-du-chat syndrome is hypoplasia of the brainstem mainly involving the pons, cerebellum, median cerebellar peduncles and cerebellar white matter, which can be detected by MRI.[4]

Pontine hypoplasia has been reported by MRI in a heterogenous groups of disorders including, e.g., pontocerebellar

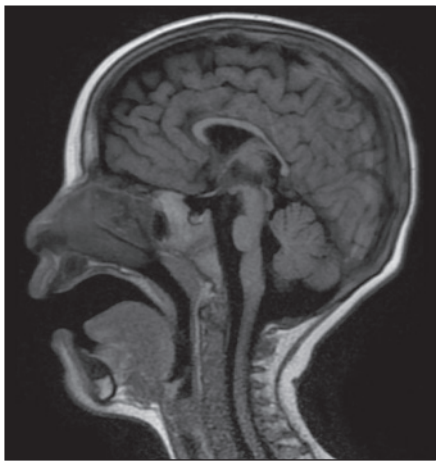

Figure 1: Pontine and brainstem hypoplasia on sagittal T1-weighted magnetic resonance image

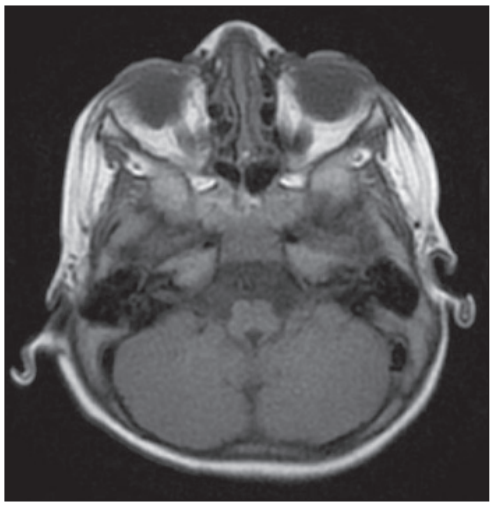

Figure 2: Brainstem hypoplasia on axial T1-weighted magnetic resonance image

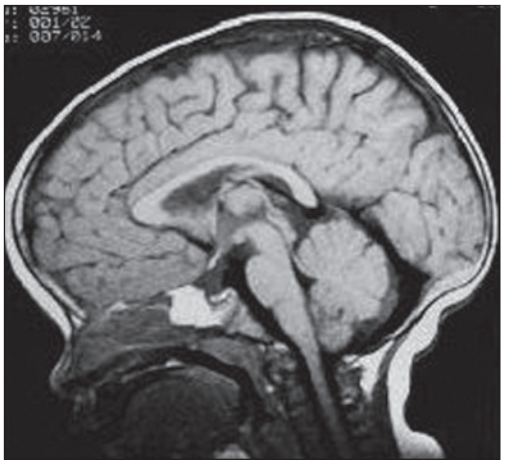

Figure 3: Brain stem of an age matched healthy control on T1-weighted sagittal cross-section magnetic resonance image

hypoplasias and congenital disorders of glycosylation, congenital muscular dystrophies and cerebellar disruptions in very preterm neonates.[5] Pontocerebellar hypoplasias as initially reported by Barth *et al*., are progressive disorders with prenatal onset.[6]

In conclusion, Cri-du-chat syndrome can be difficult to diagnose when clinical findings are not distinctive. Pontine and brainstem hypoplasia on MRI may play an important role in suggesting the correct diagnosis in Cri-du-chat syndrome.

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