Lissencephaly, cerebellar hypoplasia, and extrahepatic biliary atresia: an unusual association☆

Lisencefalia, hipoplasia cerebelar y atresia de vías biliares extrahepáticas: una asociación inusual

Dear Editor:

Lissencephaly is a brain malformation affecting the cerebral cortex, and is caused by a defect in neuronal development and migration.[1,2] In patients with lissencephaly, neurons are unable to migrate to the surface layers of the cortex, resulting in fewer convolutions, and accumulate in deep layers of the subcortical white matter, forming a subcortical layer of grey matter (band heterotopia). Lissencephaly has classically been divided into 2 types: type 1 is characterised by complete absence of gyri (agyria), which results in a smooth brain surface, or incomplete gyral formation, leading to broader gyri (pachygyria); type 2 features disorganised collections of neurons and loss of normal cortical lamination. Type 2 is associated with several genetic syndromes, including Fukuyama type congenital muscular dystrophy, Santavuori congenital muscular dystrophy, and Meckel-Gruber syndrome.[3] Lissencephaly may be associated with malformations of the central nervous system or other systems, for example in lissencephaly with cerebellar hypoplasia (LCH),[1,2,4–6] or with certain genetic syndromes, including Walker-Warburg syndrome.[3] LCH is reported to be linked to mutations in the *RELN* and *TUBA1A* genes. *RELN*, located on the long arm of chromosome 7 (7q22), encodes reelin, a protein involved in neuronal migration, synaptic plasticity, and transmission of nerve impulses. At least 6 autosomal recessive mutations in *RELN* have been described. *TUBA1A*, located on the long arm of chromosome 12 (12q13.12), encodes alpha-tubulin; this protein is a structural constituent of microtubules, which play a major role in cell division and movement. Ten autosomal dominant *TUBA1A* mutations have been described; these have been found in 30% of patients with LCH.[1]

Extrahepatic biliary atresia (EBA) is classified into 3 types depending on whether the condition presents in isolation (type 1), in association with other congenital defects but without being considered a polymalformative syndrome (type 2), or as a polymalformative syndrome (type 3).[7,8] Patients with type 2 and 3 EBA present cardiac, gastrointestinal, spleen, and genitourinary abnormalities.

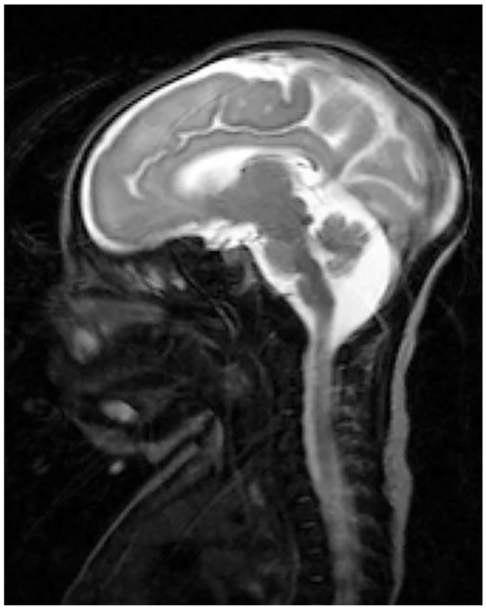

Fig. 1 Magnetic resonance imaging scan revealing LCH.

The case presented here was particularly challenging due to the presence of neonatal seizures secondary to a malformation of cortical development and fatal liver failure. This is the first reported case of an association between LCH and EBA.

Our patient was a full-term neonate with intrauterine growth retardation from week 34. The pregnancy was uneventful. The parents were nonconsanguineous and the baby was born by normal vaginal delivery. Birth weight was 2470 g (P2; −2.18 SD), length was 43 cm (P2; −2.3 SD), and head circumference was 30 cm (< P1; −3.21 SD). Two hours after birth, the child started to make sucking motions, which were subsequently associated with clonic movements of the face and left arm, lasting 4 min. The patient presented similar episodes during the first 24 h of life, which resolved with phenobarbital. We performed an aetiological study of neonatal seizures. A blood count revealed thrombocytosis and slightly elevated thyroid hormone levels. An electroencephalography study detected no alterations. Transfontanellar ultrasound revealed thinning of the corpus callosum and mega cisterna magna. In addition to these findings, a brain MRI scan (Fig. 1) also revealed partial atrophy of the cerebellar vermis and moderate sulcal underdevelopment in the frontal and occipital regions, compatible with LCH. The patient received treatment with phenobarbital, levetiracetam, and clobazam due to poor seizure control. A month and a half after birth, a follow-up blood test revealed cholestasis (total bilirubin 6.8 mg/dL, conjugated bilirubin 5.3 mg/dL, gamma-glutamyl transferase 2120 IU/L). An analysis of alpha-1 antitrypsin levels, a study of hormonal and metabolic function and infections, and an abdominal ultrasound revealed no abnormalities. We suspected EBA and

☆ Please cite this article as: del Castillo Velilla I, Martínez Jiménez MD, Martín MP, García Cabezas MA. Lisencefalia, hipoplasia cerebelar y atresia de vías biliares extrahepáticas: una asociación inusual. Neurología. 2020;35:502—503.

decided to administer conservative treatment due to the patient's poor prognosis. A genetic study of lissencephaly and congenital disorders of glycosylation yielded negative results. At 7 months of life, the patient was brought to hospital due to fever and decompensation of the underlying liver disease; despite medical treatment, she died due to cardiorespiratory arrest. A post-mortem liver biopsy confirmed the diagnosis of EBA. This is the first case of LCH associated with EBA to be reported in the literature. To date, no study has described mutations linking LCH and EBA.

Funding

This study has received no funding of any kind.

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11 December 2018

https://doi.org/10.1016/j.nrleng.2020.07.001
2173-5808/

Leriche syndrome as a rare cause of cauda equina syndrome*

Síndrome de Leriche como causa inhabitual del síndrome de la cola de caballo

Dear Editor:

Cauda equina syndrome is caused by lesions to the nerve roots emerging from below the conus medullaris (lumbar, sacral, and coccygeal nerve roots). It generally manifests as low back pain irradiating to the gluteus muscles, weakness of the lower limbs, saddle anaesthesia, and sexual and sphincter dysfunction. Cauda equina syndrome is an infrequent entity but requires urgent aetiological diagnosis and early treatment in order to minimise the potentially severe and irreversible sequelae.

We present the case of a 72-year-old man, a former smoker, with a diagnosis of arterial hypertension and atrial fibrillation treated with Sintrom® and antihypertensive drugs. The patient presented sudden weakness and hypoaesthesia of the lower limbs, accompanied by severe bilateral pain in the gluteus muscles, irradiating to both legs. He reported no history of intermittent claudication or changes in skin colour or temperature in the distal region of the lower limbs.

Neurological examination showed weakness of the lower limbs (hip flexion 3/5, knee flexion 3/5, knee extension 4/5, dorsiflexion and plantar flexion 0/5) and no weakness in the upper limbs. He presented tactile hypoaesthesia of the dorsal region of the feet and lateral region of the legs (L5), the external face of the thighs (L2—L3), and groin area (L1—L2); apallaesthesia up to the knees; and abolished positional sensitivity in the toes. The right Achilles and patellar reflexes were abolished, whereas the remaining stretch reflexes were normal. The plantar reflex was abolished bilaterally. The abdominal and cremasteric reflexes were absent on both sides. In conclusion, neurological examination findings were compatible with cauda equina syndrome. Furthermore, the peripheral pulses were not palpable.

Blood analysis revealed mild thrombocytopaenia, an International Normalised Ratio of 1.4, and prothrombin activity of 60%. An emergency lumbosacral spinal CT scan revealed no spinal cord anomalies or signs of haemorrhage. An MRI scan of the thoracolumbosacral spine detected no haemorrhages, spinal signal alterations, or cauda equina

* Please cite this article as: Casas E, Vázquez F, Witek NP. Síndrome de Leriche como causa inhabitual del síndrome de la cola de caballo. Neurología. 2020;35:503—504.