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Case report

Arthrogryposis multiplex congenita with callosal agenesis and dentato-olivary dysplasia

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Abstract

We report the autopsy case of a boy with arthrogryposis multiplex congenita, associated with callosal agenesis and dentato-olivary dysplasia. The patient manifested with dysmorphic facial features and suffered from intractable epilepsy during the neonatal period. These sets of complications suggest that a common molecular mechanism may be involved in the development of corpus callosum and the folding of the dentate and inferior olivary nuclei. Deep brain structures, including the brainstem and the cerebellum, may be involved in the pathophysiology of symptomatic generalized epilepsy. The differential diagnoses for the clinical and pathological characteristics of this patient are discussed.

Keywords: Arthrogryposis multiplex congenita; Corpus callosum; Inferior olive; Dentate nucleus

1. Introduction

Arthrogryposis multiplex congenita (AMC) results from fetal hypokinesia due to various conditions involving the neuromuscular system. Ten to 60% of AMC cases are attributed to central nervous system abnormalities, including lissencephaly, metabolic disorders, hydrocephalus, and several genetic syndromes with brain malformations [1]. The clinical course and prognosis for individual AMC patients depends on the background disorder. In this report, we describe an AMC patient with an unknown congenital malformation syndrome. The association of callosal agenesis and dentato-olivary dysplasia, revealed by a neuropathological examination, may represent a subgroup of AMC patients with intractable epilepsy and a poor prognosis.

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2. Case report

The patient was a male born at 35 gestational weeks, after a pregnancy complicated with oligohydramnios. Birth weight was 1754 g. Respiratory distress was alleviated after surfactant administration and artificial ventilation, but following this treatment dysmorphic features were noticed. These included contracture of the extremities with rocker-bottom feet and camptodactyly, simian creases, overlapping fingers, widely-spaced nipples, diaschisis of the abdominal rectus muscle, cryptorchidism, prominent forehead, short palpebral fissures, broad and prominent nasal bridge, low-set ears, and micro-retrognathia. Ophthalmologic examination did not reveal any abnormalities. Cranial ultrasonography revealed absence of the corpus callosum, and possible calcifications in the periventricular white matter. Hypotonia and feeding difficulties were evident, and frequent tonic or myoclonic seizures appeared the day after birth. Electroencephalography showed a suppression-burst pattern during this period, which later developed into hypsarrhythmia at three months of age. These epileptic seizures were refractory to antiepileptics.

Only the myoclonic seizures responded partially to pentobarbital administration. The patient was weaned off artificial ventilation at the age of 46 days, but the epileptic seizures were further aggravated with accompanying bradycardia and cyanosis. He expired after a respiratory arrest following a tonic seizure at the age of three months. Investigations into the background condition of the patient, including urinary organic acid analysis, serum titer to rubella virus, cytomegalovirus, toxoplasma and herpes virus, blood amino acid profile and very long chain fatty acid analysis, and chromosomal analysis, were all negative. Metabolic acidosis was not present in the blood gas during the entire course of illness.

At autopsy the patient weighed 2500 g, and no abnormality was noted in the somatic organs. The lungs and kidneys were normal in size and histology. The brain weight was 410 g, which is proportional to the body weight. The cerebral gyri were normally formed, but showed poorly convoluted appearance. The cerebellum and brainstem were normal in size, but the pyramis in the medulla oblongata was small. Agenesis of the corpus callosum was noted (Fig. 1A), with accompanying elevation of the anterior horn of the lateral ventricle (Fig. 1B). There was a volume loss, marked myelination delay and gliosis in the cerebral white matter (Fig. 1C). Calcifications in the periventicular white matter, and lobulation of the caudate nucleus were also noted

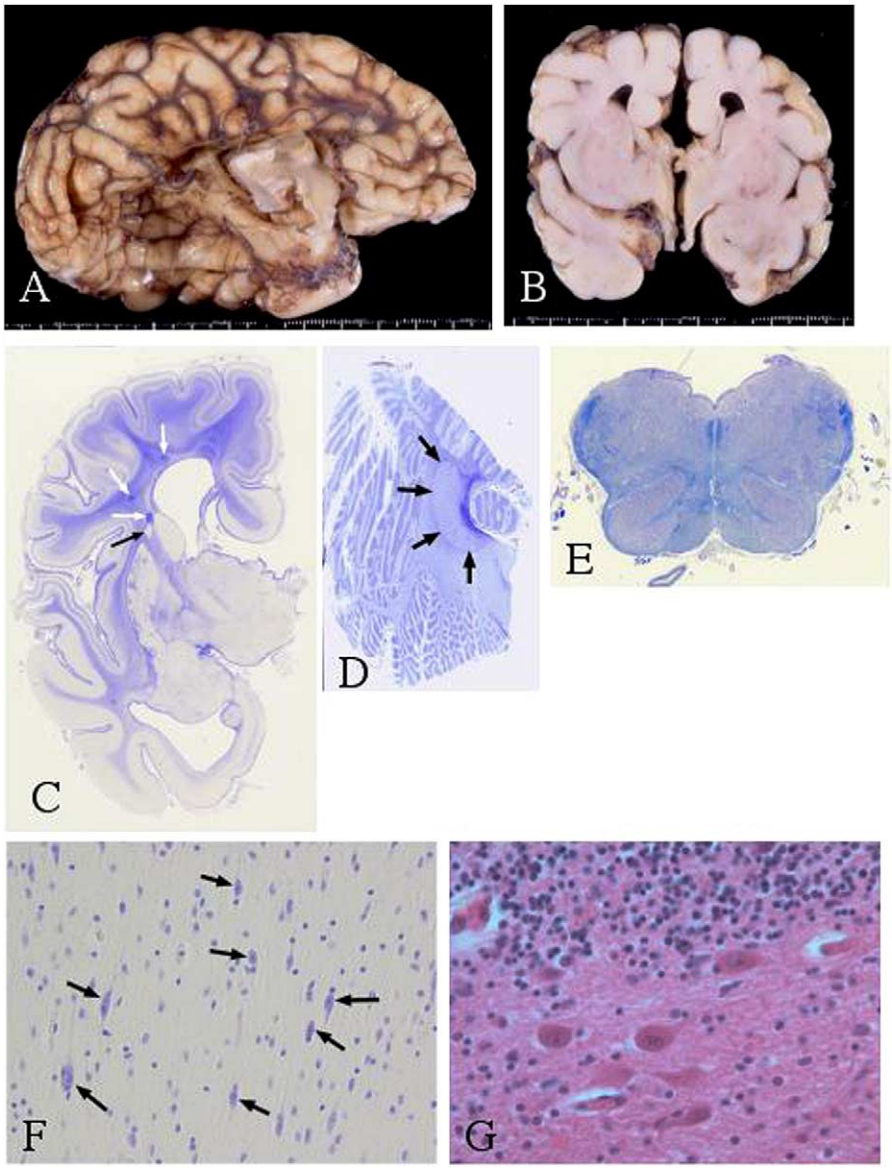

Fig. 1. (A and B): Sagittal (A) and coronal (B) sections of the brain. Callosal agenesis and elevation of the anterior horn of lateral ventricle (B) are noted. (C): Gliosis of cerebral white matter. Blank arrows: foci of calcification, filled arrow: lobulation of caudate nucleus. (D): The contour of dentate nucleus (arrows) appears round and lacks undulation. (E): Inferior olivary nuclei are C-shaped and undulations are simplified. (F): Ectopic neurons (arrows) are scattered in the subcortical white matter. (G): Ectopic Purkinje cells in the subcortical cerebellar white matter. (C and D): Hozler staining, E and F: Klüver–Barrera staining, (G): Hematoxylin–eosin staining, F and G: ×400.