Case Report

Two Different Manifestations of Neonatal Vascular Injury: Dyke-Davidoff-Masson Syndrome and Crossed Cerebellar Atrophy

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Dyke-Davidoff-Masson syndrome (DDMS) was first described in 1933 as a clinical condition characterized by hemiatrophy, hyperpneumatization of paranasal sinuses, contralateral hemiparesis, facial asymmetry, seizures, and mental retardation.¹ DDMS can be of 2 types: congenital and acquired. The congenital type can be caused by various conditions experienced during fetal or early childhood development, including ischemia, infarction, trauma, infections, and hemorrhage. The acquired type is mostly associated with hemorrhage, trauma, and infections experienced after 1 month of age. DDMS can manifest alone or can be accompanied by crossed cerebellar atrophy (CCA) which is a newly discovered radiological marker characterized by prominent cortical sulci and loss of cerebellar parenchyma. The congenital type of DDMS is known to be accompanied by ipsilateral cerebellar atrophy and the acquired type is known to be accompanied by contralateral cerebellar atrophy.^{2,3} Supratentorial events may lead to destruction in the cortico-pontocerebellar pathways, mostly in the contralateral side of the body (80%) due to decussation.⁴ In this report, we present 2 cases of DDMS accompanied by CCA to emphasize the possibility that the DDMS cases with severe intrauterine hemorrhage can be accompanied by contralateral CCA and migratory abnormalities rather than ipsilateral CCA and clinical survey.

Key Words: Dyke-Davidoff-Masson—crossed cerebellar atrophy—intrauterine hemorrhage—supratentorial events—ipsilateral © 2019 Elsevier Inc. All rights reserved.

Case 1

A 15-year-old girl presented to our clinic due to recurrent seizures. Patient history indicated that the patient had been suffering from afebrile focal seizures in the right limbs since 1 week of age, the seizures recurred just before or during sleep, and the seizures recently became more frequent during the daytime and were mostly in the form of generalized tonic-clonic seizures. The patient had been born by normal spontaneous vaginal delivery and had no history of asphyxia. The patient also had no family history of epilepsy and neurological diseases and no parental consanguinity. On the third day after birth, ultrasonography showed chronic germinal matrix hemorrhage. Physical examination showed mild facial asymmetry, marked atrophy of the right half of the body, short limbs, and hemiparesis. On the right side, there was no Babinski sign, no extensor plantar response, and no clonus. Moreover, there was no hypo-/hyper-pigmentation on the face or body

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and no sandal gap. Head circumference was 52 cm (50th percentile). The patient could not walk, had little interest in her surroundings, and had an IQ of 30. Laboratory parameters were normal. Electroencephalography showed active epileptiform discharges from the left hemisphere. A 1.5-T cranial magnetic resonance imaging (MRI) scan showed bulk volume loss of white matter with cortical sulcal dilatation secondary to atrophy, marked calvarial thickening comparable to the symmetry of the left Sylvian fissure and the left lateral ventricle along with Wallerian degeneration, atrophy of basal ganglia and the posterior body and splenium of corpus callosum, bifrontal polymicrogyria, and hyperpneumatization of the ethmoidal, sphenoidal, and frontal sinuses (Fig 1). The patient was on a combination therapy of valproic acid, topiramate, levetiracetam, and clobazam. Based on the clinical signs and symptoms, the patient was diagnosed as having coexistence of congenital Dyke-Davidoff-Masson syndrome (DDMS), contralateral crossed cerebellar atrophy (CCA), and semptomatic generalized epilepsy and was treated accordingly. Based on the recurrence of intermittent seizures, the parents were recommended surgery.

Case 2

A 14-month-old girl was admitted to our polyclinic with a history of seizures. The patient had a body weight of 12 kg (25-50th percentile) and a head circumference of 44 cm (10-25th percentile). She had been born by normal spontaneous vaginal delivery at 37 weeks with a birth weight of 2600 g. Patient history showed that a fetal MRI scan performed at the last prenatal examination showed intracranial hemorrhage and thus the patient was transferred to the intensive care unit immediately after birth, and was initiated on phenobarbital therapy due to seizures on the second day after birth. Physical examination showed mild atrophy on the right side of the face and hemiplegia which was more pronounced in the right upper limb. No cerebellar pathology was detected. A neurological examination showed a shuffling gait in her right leg. After a 1-year seizure-free period, the patient had flexor spasms and the electroencephalography showed a run of 1.5-2 Hz spike-wave epileptiform discharges lasting 7-8 second per 10-second epoch in the fronto-centroparietal section of the right hemisphere. After the

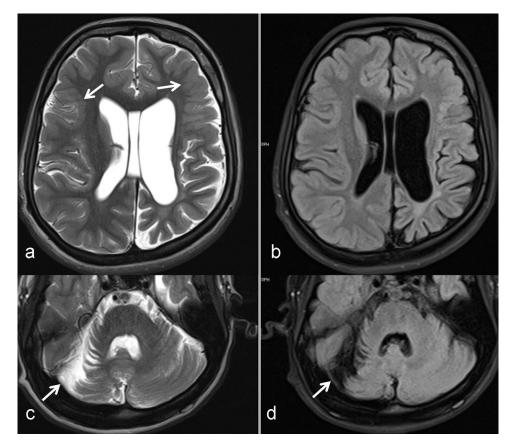


Figure 1. Axial T2-weighted MR image (a) reveals volume loss of the left cerebral hemisphere and bilateral frontal lobe polymicrogyria (arrows). Axial FLAIR MR image (b) shows dilatation of the left lateral ventricle and sulcal enlargement that consistent with left cerebral atrophy. Slight osseous calvarial hypertrophy in the left side of frontal bone is also seen. Axial T2-weighted MR image and FLAIR (c) and (d) show right cerebral atrophy (arrow).

detection of the burst-suppression pattern, the treatment was initiated immediately. A 1.5-T cranial MRI scan revealed asymmetric enlargement of the right ventricle, chronic hemorrhage in the right choroid plexus, asymmetric ventriculomegaly, atrophy of the right thalamus, loss of white matter volume in the right cerebral hemisphere, an abnormal pattern of cerebellar folia in the left cerebellar hemisphere, and left cerebellar atrophy (Fig 2). After the initiation of steroid therapy, the seizures disappeared. However, a repeat MRI showed persistence of previous abnormalities and thus the patient was diagnosed as having CCA.

Discussion

Cerebral atrophy may occur secondary to vascular injury/hemorrhage caused by a supratentorial event experienced in the pre- or perinatal period. Moreover, cerebral atrophy may manifest as the coexistence of DDMS and CCA.¹⁻⁸ Common clinical and radiological findings of DDMS include cerebral hemiatrophy, calvarial alterations, and hyperpneumatization of the sinuses. Cerebral atrophy can be congenital or acquired and is responsible for the destruction of the cortico-ponto-cerebellar and cerebello-rubro-thalamic pathways, multifocal

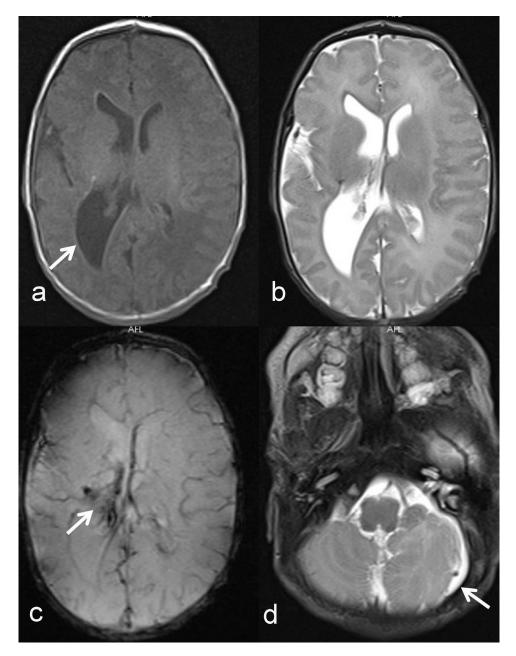


Figure 2. Axial T1-weighted MR image (a) show dilatation of the right lateral ventricle (arrow). Axial T2-weighted MR image (b) reveal volume loss of the right cerebral hemisphere and enlargement of sylvian fissure because of the cerebral atrophy. Axial GRE T2 star MR image (c) shows chronic hemorrhage of the right choroid plexus (arrow). Axial T2-weighted MR image (d) reveal left cerebral atrophy (arrow).

neuronal loss, loss of myelination, and loss of Purkinje cells. Moreover, it can be accompanied by the congenital type of DDMS in the ipsilateral side or can be accompanied by or manifest as acquired DDMS in the contralateral side.⁹ Although both of our patients were found to have congenital DDMS, they were diagnosed as having acquired DDMS since they had diffuse cerebral atrophy on the contralateral side.

Atalar et al investigated differences between congenital and acquired DDMS and reported that calvarial changes were detected in 12 patients with congenital DDMS while no calvarial changes were seen in patients with acquired DDMS. Moreover, the authors considered that Wallerian degeneration, which was also seen in both of our patients, was associated with axonal intrauterine injury.¹⁰ On the other hand, some postmortem pathological studies found moderate basal ganglia atrophy in patients with acquired DDMS rather than in patients with congenital DDMS.² Interestingly, both in the study by Unal et al and in our study, cerebral hemiatrophy was accompanied by left hemisphere dominance, basal ganglia atrophy, and Wallerian degeneration and was mostly seen in girls rather than boys.^{10,11}

The cerebral atrophy occurring before the completion of neurodevelopment (ie, prior to myelination) may manifest in the form of reversible diaschisis; however, if it occurs secondary to such causes as hemorrhage and infarction, these causes may be irreversible and may result in permanent cerebral atrophy. The most probable pathophysiological mechanism of CCA involves the enhancement of excitatory synaptic transmission and anterograde transneuronal degeneration. Fetal MRI has been shown to be useful in the diagnosis of temporary or permanent CCA associated with ischemia and hemorrhage.^{7,8} In our second patient, a fetal MRI scan that had been performed due to a suspicion of hemorrhage showed clinical findings suggestive of permanent cerebral atrophy and these findings provided an insight into the probable postpartum neurological complications. Moreover, the findings also helped us to rule out other causes of neonatal cerebral atrophy that could have complicated the diagnosis, such as hemiatrophy, hemiplegia, and epilepsy.

Uduma et al suggested that the brain injury occurring before the completion of bone maturation (ie, in the first 2 years of life) can be relatively more pronounced in patients with DDMS.⁵⁻¹² Limperopoulos et al reported that the immature cerebellum is highly vulnerable during late gestation and can be affected by contralateral cerebral injury, thereby leading to cerebral atrophy.¹³ Intrauterine vascular occlusion has been reported as the most common cause of congenital DDMS.^{5,13,14} However, although both DDMS and CCA have been attributed to neonatal vascular events, the exact causes of the coexistence or isolated manifestation of these 2 conditions remain unknown. Nevertheless, in light of the clinical findings of our patients, we consider that both the coexistence and the isolated manifestation of these 2 conditions can be associated with the extent of the primary injury and to the fact that both of our patients were in their early developmental stages at the time of injury. In terms of this distinction, fetal cranial MRI provided excellent results for the evaluation of our patients.

Intrauterine events can be accompanied by migratory abnormalities as well. Shubhakaran et al reported that 7 cases of cerebral hemiatrophy were associated with ipsilateral large schizencephalic cleft and 2 patients had porencephaly.^{3,15} In our study, for the first time in the literature, neuronal migratory abnormalities were found to be accompanied by bifrontal polymicrogyria, cerebral atrophy, and CCA.

Treatment of DDMS and CCA is often longitudinal and symptomatic, primarily including physical therapy, speech therapies, vocational therapies or the control of seizures via vagal nerve stimulators or epileptic surgery. In a previous case report, Park et al found no significant relationship between resistant and infrequent seizures in the DDMS patients with a vascular etiology.¹⁶ Both of our patients had resistant seizures that decreased their quality of life, of whom 1 patient was recommended epileptic surgery and the other was recommended vagal nerve stimulation.

Conclusion

Patients with a history of pre- or peri-natal vascular injuries may clinically present with resistant seizures, hemiplegia, hemiatrophy, facial atrophy, and mental retardation. In patients presenting with cerebral atrophy, the differential diagnosis should also involve the coexistence of DDMS and CCA. MRI is highly useful in the diagnosis of such patients. Patients diagnosed with congenital DDMS may additionally present with CCA. However, it remains unclear as to why DDMS can be present in some patients and not in the others despite all of them having the same etiology; therefore, both the coexistence of DDMS and CCA and the isolated manifestation of CCA should be kept in mind in patients presenting with supratentorial conditions. In children detected with cerebral atrophy in the neonatal period, the fetal MRI scan performed in the antenatal period provides useful diagnostic information both for the differential diagnosis and the treatment of the patients. On the other hand, polymicrogyria, which is a rare condition accompanying the congenital form of DDMS, was first reported in our patients. Accordingly, this rare condition should be kept in mind in patients presenting with resistant seizures.

In conclusion, we present 2 cases of DDMS accompanied by CCA to emphasize the possibility that the DDMS cases with severe intrauterine hemorrhage can be accompanied by contralateral CCA and migratory abnormalities rather than ipsilateral CCA and their clinical survey.

A written consent was obtained from the parents with regard to the publishing and dissemination of the images of the patients.

Conflicts of interest

All authors declare that they have no conflict of interest about this study.

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