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Magnetic resonance imaging findings of two cases with West syndrome and hypomelanosis of Ito with hemimegalencephaly: a report of two cases

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Abstract

Background: Hemimegalencephaly is an unusual congenital non-familial malformation of the brain which is characterized by enlargement of the whole or part of one hemisphere due to neural proliferation and dysfunction in the cell migration. The brain stem and cerebellum may also be involved. There are also the common cortical malformation, unusual white matter proliferation, gliosis, and abnormal myelination in hemimegalencephaly. In addition, structural brain abnormalities like atrophy/hypertrophy, demyelination, gliosis, increased thickness of the cortical grey matter, increase signal intensity in the subcortical white matter, abnormal gyral patterns, blurring of the grey-white matter transition, and hamartomatous aspect can be observed on magnetic resonance imaging.

Case presentation: Two patients who underwent brain magnetic resonance imaging because of West syndrome and hypomelanosis of Ito were diagnosed as hemimegalencephaly. The first case was a 9-day-old male patient initially diagnosed with West syndrome. On the brain magnetic resonance imaging performed for epilepsy, right total hemimegalencephaly, diffuse polymicrogyria, and heterotopic grey matter foci on the right hemisphere were observed. In addition, right cerebellar dysgenesis, upward angulation in the lateral ventricle's anterior horn, and colpocephalic dilatation in the posterior horn were evident. The second case was a 2-year-old female patient with hypomelanosis of Ito disease. The main reason for her parents' hospital visit was the shortness of the right leg. Initial examination showed the hypopigmented lesions on the right side and hemihypertrophy in the left leg. Brain magnetic resonance imaging revealed mild hemimegalencephaly in the right cerebral hemisphere, T1-weighted isointense, T2-weighted hyperintense white matter lesions extending from the basal ganglia to the ventricular body and the periventricular fronto-parieto-occipital white matter, and dilatation of the lateral ventricle.

Conclusions: Hemimegalencephaly is a rare condition which may accompany syndromic cases with epilepsy or neurocutaneous disease. Brain magnetic resonance imaging should be performed in patients with a suspicious medical history in order to make the correct diagnosis of hemimegalencephaly and to determine the severity of brain involvement, if any.

Keywords: Case report, Hemimegalencephaly, Magnetic resonance imaging, West syndrome, Skin pigmentation

Background

Hemimegalencephaly is a rare hamartomatous congenital malformation characterized by asymmetric enlargement of a cerebral hemisphere. The hemimegalencephaly might even involve the brain stem and cerebellum [1, 2].

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Hemimegalencephaly was first defined it in 1835 by Sims and was thought to be associated with abnormal tissue and function based on 253 autopsy reviews. The most commonly recognized reason is the failure in neuroblast migration [2, 3].

There are three subtypes of hemimegalencephaly as isolated, syndromic and total that Hallervorden first described in 1923 [2, 4]. The isolated form has a better prognosis than syndromic hemimegalencephaly and the total form can be either isolated or syndromic. The subtypes have different incidence, cause, and involvement characteristics. Total hemimegalencephaly is the least frequent form and causes enlargement in the cerebrum, brainstem, and cerebellum [2]. Partial or complete body hemihypertrophy can occur in the syndromic hemimegalencephaly. It appears mainly related to neurocutaneous disorders including hypomelanosis of Ito, Proteus syndrome, Klippel–Trenaunay–Weber, neurofibromatosis, tuberous sclerosis, linear sebaceous nevus, and epidermal nevus [5].

Typical symptoms are severe, intractable early-onset epilepsy, developmental/psychomotor retardation, and contralateral hemiparesis [1, 2]. Hemimegalencephaly occurs in the early gestational period and the first neurologic findings can be macrocephaly and dysmorphic facial appearance which are usually seen at birth. On the other hand, the external appearance of the head may be normal in some patients. Treatment, of which seizure control is the main priority in patients, is crucial. Despite the high-risk procedure, hemispherectomy is the best therapeutic choice for intractable epilepsy [2].

Hemimegalencephaly can be detected by foetal magnetic resonance imaging (MRI) [2, 6]. In addition, video-electroencephalogram (EEG) monitoring, seizure semiology, single-photon emission computerized tomography, and positron emission tomography scanning are used in diagnosis. However, magnetic resonance imaging is the best way for a high-resolution structural image of the brain [6]. Magnetic resonance imaging findings are abnormal gyration, cortical dysplasia such as polymicrogyria, lissencephaly, pachygyria, schizencephaly, gyral thickening, poor grey/white matter differentiation, ventriculomegaly, and colpocephaly. Furthermore, "occipital sign" as displacement of the occipital lobe across the midline, gliosis, demyelination, and increased volume and heterotopia in the white matter of the involved hemisphere can occur [5, 6]. The most essential and unchanging signs are hamartomatous white matter abnormalities [6]. The affected side of the corpus callosum is generally broad but sometimes, may be bilaterally hypoplastic or none. The ipsilateral cerebellar hemisphere is displaced downwards relevant to enlargement in some cases. The magnetic resonance spectroscopy can show the decrease in glutamate and N-acetyl aspartate in white matter. A mild reduction of N-acetyl aspartate in the white matter of the contralateral hemisphere can also be observed [2]. The present study reports two cases with hemimegalencephaly, one of which underwent brain magnetic resonance imaging because of West syndrome and the other for hypomelanosis of Ito.

Cases presentation

MRI technique

MRI examinations were carried out using an 8-channel 1.5 T MRI machine (GE Signa Excite HD; GE Healthcare, Milwaukee, WI, United States, 2005). The MRI protocol included coronal 3D spoiled gradient-recalled (SPGR) T1-weighted images (repetition time (TR): 6.39 ms, echo time (TE): 2.28 ms, inversion time (TI): 450 ms, slice thickness: 4 mm, slice gap: 2 mm), axial and coronal fast spin echo T2-weighted images (TR: 5400 ms, TE: 86.2 ms, slice thickness: 5.5 mm, slice gap: 7 mm), axial and coronal fluid-attenuated inversion recovery (FLAIR) images (TR: 8000 ms, TE: 81.4 ms, TI: 2688 ms, slice thickness: 5.5 mm, slice gap: 6.5 mm), axial and sagittal spin echo T1-weighted images (TR: 640 ms, TE: 15 ms, slice thickness: 5 mm, slice gap: 6 mm), and B0 and B1000 diffusion-weighted images.

Patient 1

The first case is a 9-day-old male with macrocephaly diagnosed with West syndrome in the follow-up. He had magnetic resonance imaging of the brain in 2014 due to tonic–clonic contractions in his arms and legs (tonic–clonic epileptic seizures). Right total hemimegalencephaly (Fig. 1A–E), diffuse polymicrogyria, and heterotopic grey matter foci on the right hemisphere (Fig. 1A–C) were seen on axial T2-weighted and coronal T2 fluid-attenuated inversion recovery (FLAIR) images on the brain MRI performed for epilepsy. In addition, right cerebellar dysgenesis (Fig. 1F), upward angulation in the anterior horn of the lateral ventricle (Fig. 1A, D), and colpocephalic dilatation in the posterior horn (Fig. 1B, C, E) were evident.

Patient 2

The second case, a 2-year-old girl, was brought by her family due to shortness and thinning of the right leg in 2010. Three centimetres shortening of the right lower extremity and the hypopigmented lesions were detected on the right side, and hemihypertrophy was seen in the left leg (Fig. 2A). Brain magnetic resonance imaging revealed mild hemimegalencephaly in the right cerebral hemisphere (Fig. 2B, C) to the patient diagnosed with hypomelanosis of Ito disease in the follow-up. White matter lesions extending from the basal ganglia to the

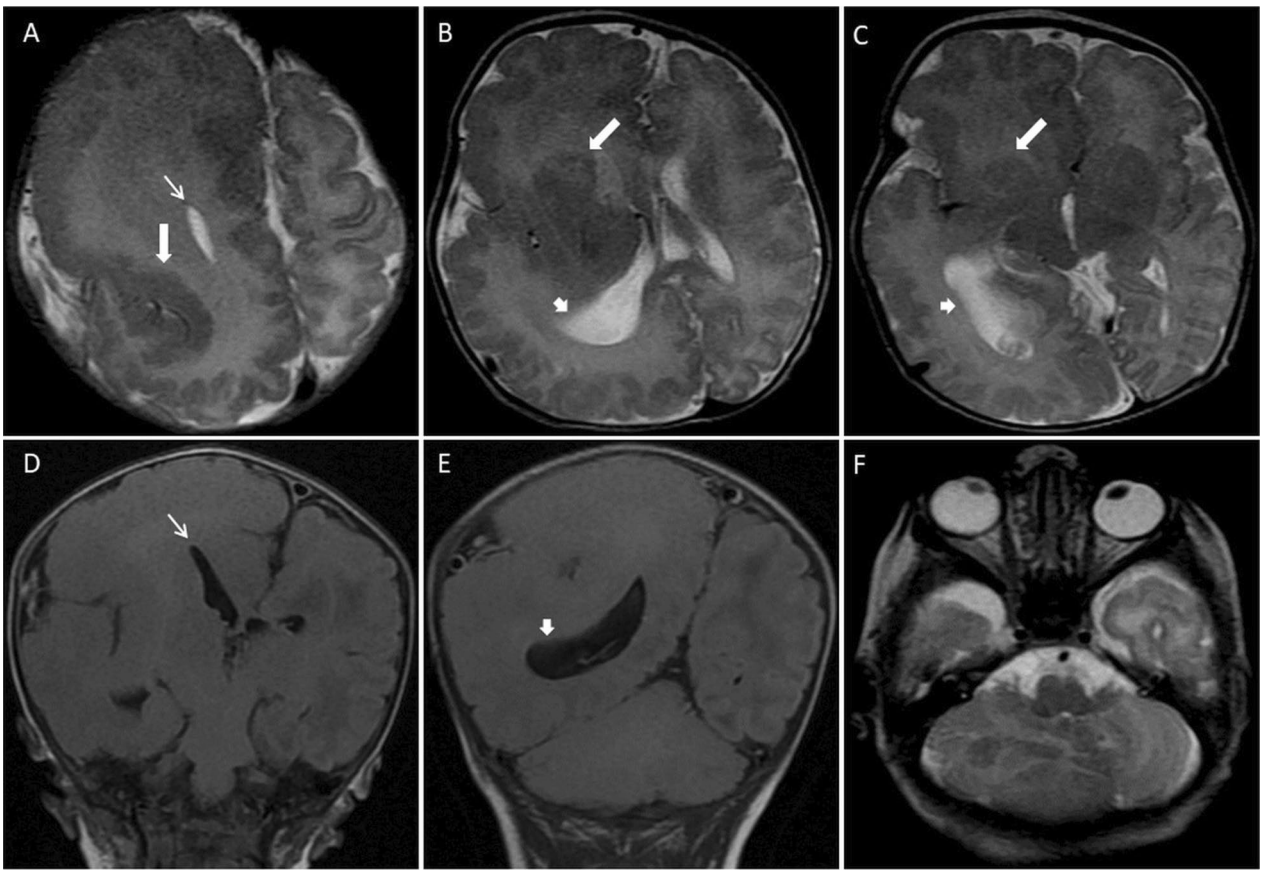

Fig. 1 MR images of a 9-day-old male with West syndrome and epilepsy (**a**), (**b**), (**c**), and (**f**) axial T2-weighted; (**d**) and (**e**) coronal T2 fluid-attenuated inversion recovery (FLAIR) series with right total hemimegalencephaly, diffuse polymicrogyria and heterotopic grey matter foci on the right (thick arrows), upward angulation in the frontal horn of the lateral ventricle (thin arrows) and colpocephalic dilatation (arrowheads) in the occipital horn and right cerebellar dysgenesis is shown

periventricular fronto-parieto-occipital white matter (Fig. 2B–E) were isointense in the T1-weighted series and hyperintense in the T2-weighted series. In addition, dilatation in the lateral ventricle (Fig. 2D, E) was observed.

Discussion

Hemimegalencephaly, also known as unilateral megalencephaly, is a rare [6]. Three grade of severity of hemimegalencephaly was described as mild–moderate–severe. In severe cases, neurologic prognosis is not good and expected life duration is only 1 year as they usually pass away in the first year of life. In moderate cases, the neurologic capacity depends on the severity of epilepsy. Mild cases can live almost normal. Therefore, there are usually moderate and severe cases reported in literature than mild cases [2]. Both cases had mild and moderate severity in this study. A male patient who was first diagnosed in his 9th day of life is now 7 years old, and the female patient is 13 years old, both continuing to live.

Hemimegalencephaly is a serious condition that requires a close follow-up of the patients. Hemimegalencephaly causes a real enlargement in the brain and can be confused with other diseases or conditions. Therefore, differential diagnosis is essential especially in some cases, such as Rasmussen encephalitis, Dyke–Davidoff–Masson syndrome, or Sturge–Weber syndrome, which cause one hemisphere not grow normally and remain smaller, making the normal hemisphere appear larger. In addition, other conditions which also cause an enlargement in the brain include gliomatosis cerebri, and other neuronal migration abnormalities that do not cause an overgrowth of the brain such as polymicrogyria, lissencephaly, agiri, pachygyria, should also be considered in the differential diagnosis [7].

The first patient had West syndrome in the present case report. West syndrome includes infantile spasms, hypsarrhythmia on electroencephalogram, and mental retardation and has two subgroups as symptomatic (with Hemimegalencephaly) and unknown aetiology cytotoxic

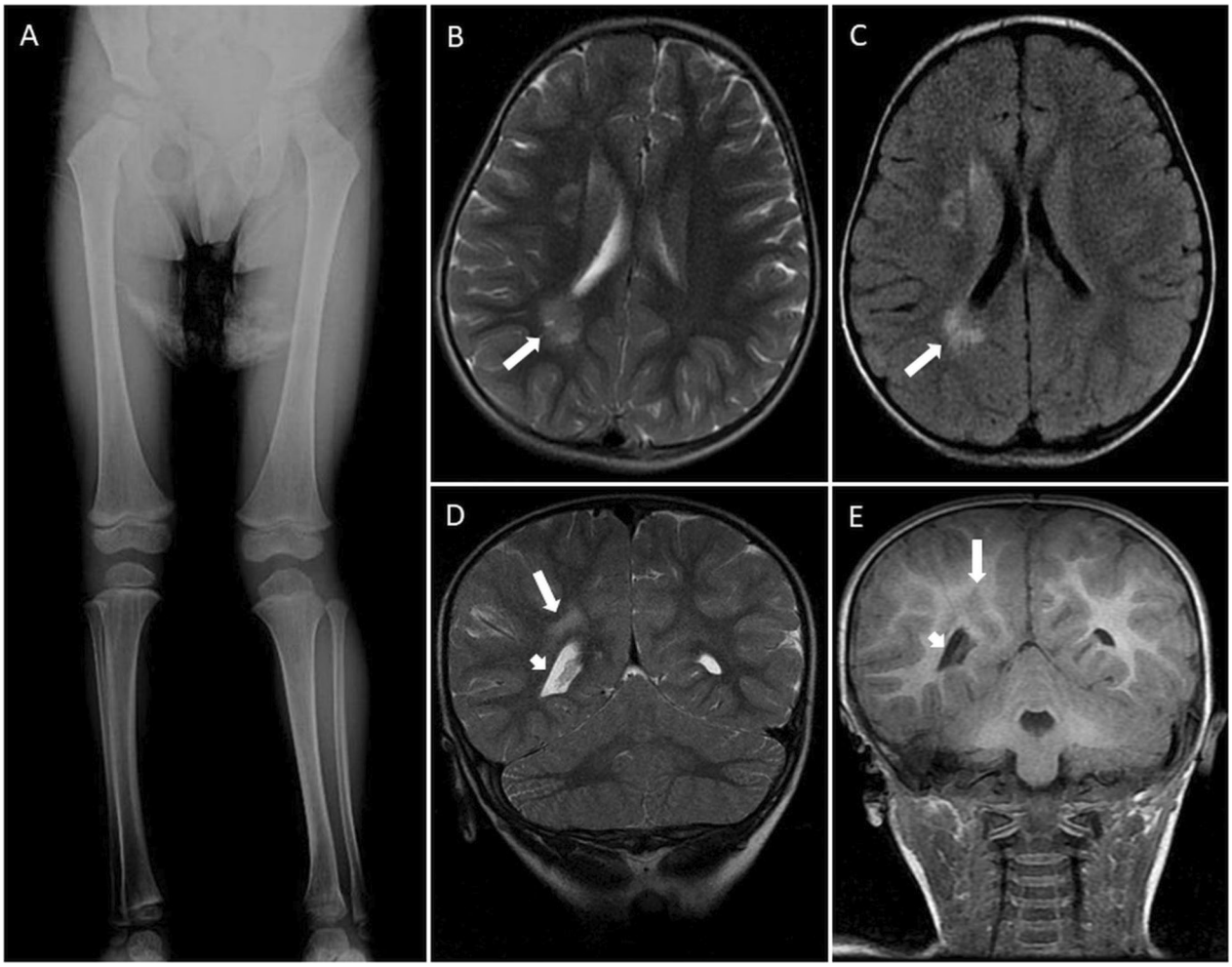

Fig. 2 MR images of a 2-year-old female mild hemimegalencephaly in the right cerebral hemisphere with hypomelanosis of Ito. (**a**) Direct X-ray of the lower extremity shows hemihypertrophy in the left lower extremity. (**b**) axial T2-weighted; (**c**) axial FLAIR; (**d**) coronal T2-weighted series show amorphous, hyperintense white matter lesions extending from the basal ganglia to the ventricular body and the periventricular fronto-parieto-occipital white matter (thick arrows). (**e**) Coronal 3D spoiled gradient-recalled (SPGR) T1-weighted series shows isointense lesions (thick arrows) with grey matter in periventricular white matter areas in the right basal ganglia-corona radiata plane and dilatation of the lateral ventricle (arrowheads)

oedema. In addition, accelerated myelination may be responsible for the mechanism of brain damage in patients with hemimegalencephaly and West syndrome [8]. The second patient had disease of hypomelanosis of Ito (Incontinentia pigmenti achromians). Multiple neurologic manifestations are present in 57% and macrocephaly in 16% of patients with hypomelanosis of Ito. Hemimegalencephaly is rare in hypomelanosis of Ito disease, but a few cases have been reported in the literature [2]. Hemimegalencephaly can be detected on the ipsilateral or contralateral side with skin lesions, while somatic hemihypertrophy is often ipsilateral to hypomelanotic lesions in hypomelanosis of Ito disease. In the present case, while hemimegalencephaly is on the same side as the skin lesions, compatible with the previous reports, hemihypertrophy is on the opposite side of the skin lesions [9].

Santos et al. [6] reported that 5 of 13 hemimegalencephaly cases were syndromic. One of the syndromes was hypomelanosis of Ito, one was epidermal nevus, one was cutaneous keratosis, one was tuberous sclerosis, and another one was incontinent pigmenti syndrome. In addition, focal cortical dysplasia was observed in 8 of 13 hemimegalencephaly patients. Hemimegalencephaly might affect a whole hemisphere, or sometimes only a part of hemisphere may be involved, which is called Hemi-hemimegalencephaly. They reported that the entire hemisphere was affected in 10 of 13 hemimegalencephaly

patients. The posterior part of the temporal and parietal lobes and the entire occipital lobe (posterior brain regions) were partially involved in the remaining three patients.

Recent studies have identified abnormalities such as cerebral hypometabolism, hyperperfusion, or hemimicrocephaly, which may project common pathologies of neural migration on the contralateral hemisphere. In contrast, the contralateral hemisphere is generally considered normal [1, 10–12]. In the study conducted by Jeon et al. [1], including 20 children with hemimegalencephaly, the dysplastic cortex was observed on the ipsilateral side in all patients and on the contralateral side in 10% of them. In addition, 10 (91%) of 11 patients aged 18 months or younger had accelerated myelination in the affected hemisphere. Furthermore, they also detected diffuse microstructural changes in the affected and contralateral hemispheres in their tract-based spatial statistics analysis on diffusion tensor imaging in hemimegalencephaly patients. Moreover, based on this result, they reported that hemimegalencephaly might contain wider abnormalities than predicted in neuronal networks.

Early and accurate diagnosis of hemimegalencephaly is crucial because it can sometimes be confused with obstructive hydrocephalus or cerebral neoplasia and result in unnecessary surgery [2]. Magnetic resonance imaging is the best imaging method to observe structural alterations in the brain regarding hemimegalencephaly, and provides high-resolution images allowing symmetry and volume comparisons. The magnetic resonance imaging of the patients with hemimegalencephaly showed increased thickness areas and uniform abnormality in cortical grey matter, abnormal gyral patterns, increased signal intensity in subcortical white matter, atrophy or hemispheric hypertrophy, blurred grey matter–white matter transition, and demyelination on T2-weighted images. White matter significantly increases in volume and generally includes tissue isointense to cortical grey matter, coherent with grey matter heterotopia. The change of white matter signal may be related to either dysmyelination or advanced myelination. The ipsilateral ventricle is generally engorged and dysmorphic, along with the occipital horn of the lateral ventricle across the midline [12].

The limitation of the study is that advanced magnetic resonance imaging techniques such as spectroscopy and diffusion tensor imaging were not applied to the patients in these case reports.

Conclusions

Hemimegalencephaly findings may accompany syndromic diseases such as West syndrome with epilepsy and hypomelanosis of Ito disease with cutaneous findings. In these patients, a brain magnetic resonance imaging should be performed to establish an accurate diagnosis, determine the severity of cerebral involvement and prevent unnecessary treatment procedures. However, in these syndromic patients, besides the brain parenchyma findings, hemihypertrophy can rarely be detected on the opposite side of the skin pigmentations, as in hypomelanosis of Ito disease.

Abbreviations

EEG: Electroencephalogram; MRI: Magnetic resonance imaging; SPGR: Spoiled gradient-recalled; TR: Repetition time; TE: Echo time; TI: Inversion time; FLAIR: Fluid-attenuated inversion recovery.

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Author contributions

All authors have read and approved the manuscript, and data of the cases are shared and ensured by them.

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Availability of data and materials

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Declarations

Ethics approval and informed consent to participate

Not applicable.

Consent for publication

Formal informed consent was obtained from the patient's parent via telephone. Written consent could not be obtained as the patient's parents did not want to return for follow-up due to concern for COVID and associated restrictions.

Competing interests

The authors declare that they have no competing interests.

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