Neurodegenerative Diseases

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Neurodegenerative diseases are characterized by the gradual loss of selectively vulnerable neuronal populations, in contrast to selected static neuronal loss due to metabolic or toxic diseases. Neurodegenerative diseases can be classified according to major clinical features (such as dementia, Parkinson's disease, or motor neuron diseases), anatomical distribution of neurodegenerative diseases (such as anterior temporal lobe degeneration, extrapyramidal disease, or spinocerebellar degeneration), or major molecular abnormalities. The common neurodegenerative diseases in adults such as Alzheimer's disease, frontotemporal lobe degeneration, Parkinson's disease, and multiple system atrophy are really rare in children. The childhood neurogenerative diseases of as yet unclear pathophysiology are sometimes categorized based on whether they affect the brain homogenously (diffuse encephalopathies) or preferentially affecting the cerebral cortex (poliodystrophies), the cerebral white matter (leukodystrophies), the basal ganglia (corencephalopathies), or the cerebellum, brainstem, and spinal cord (spinocerebellar diseases). In this chapter, we only introduce two relatively common neurodegenerative diseases in children and hope to contribute to a more comprehensive and detailed study of childhood neurogenerative diseases in the future.

Case 8.1 Olivopontocerebellar Atrophy

Clinical Presentation

A 9-month-old girl presented to unresponsiveness, weakness in the limbs, and limbs irregular shaking. There was no history of genetic, infectious, or similar cerebral palsy in the family.

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Imaging Findings

A. Axial T2-weighted image passing through mid-pons demonstrates the "hot cross bun" sign typically (arrow) (Fig. 8.1a).
B. Midline sagittal Ti-weighted image shows moderate atrophy in the cerebellum and in the pons, with flattening of its inferior part. The atrophy is severe and involves the whole pons (arrow) (Fig. 8.1b).
C-D. Axial T1-weighted and T2-FLAIR images show the "hot cross bun" sign atypically (arrow). Note the atrophy in the cerebellum (Fig. 8.1c–d).

Discussion

The term "olivopontocerebellar atrophy" was introduced by Dejerine and Thomas [1] in 1900 to designate the pathological presentation in a patient with sporadic adult-onset progressive cerebellar ataxia, and it has survived the test of time and enjoys widespread recognition in either the full expression or its acronym OPCA [2]. In general, OPCA is a slowly progressive neurodegenerative disease of unknown cause, which can be divided into genetic and sporadic types. In genetic OPCA group, the onset age was early. Cerebellar sign was obvious, and it was the most common first symptom, accompanied by dementia, extraocular muscle paralysis, pyramidal fascicle sign, and bulbar paralysis. In sporadic type, frequent urination, urination urgency, and unstable standing were seen in the early stage, followed by common relief disorder, dysarthria, and so on. A small number of patients can also be complicated with bilateral vertebral tract signs, limb muscle atrophy, nystagmus or extraocular muscle paralysis, and other symptoms.

The pathological changes of OPCA were cerebellum, pons, olivary nucleus atrophy, neuronal loss with glial hyperplasia, and also involved red nucleus, nigra, basal ganglia, and cerebral cortex. At present, the pathogenesis of the disease is not clear, which may be related to heredity, immunity, virus infection, free radical damage, biochemical abnormalities, and so on. Up to now, there is no effective therapeutic method. Therefore, early detection and timely treatment can delay the

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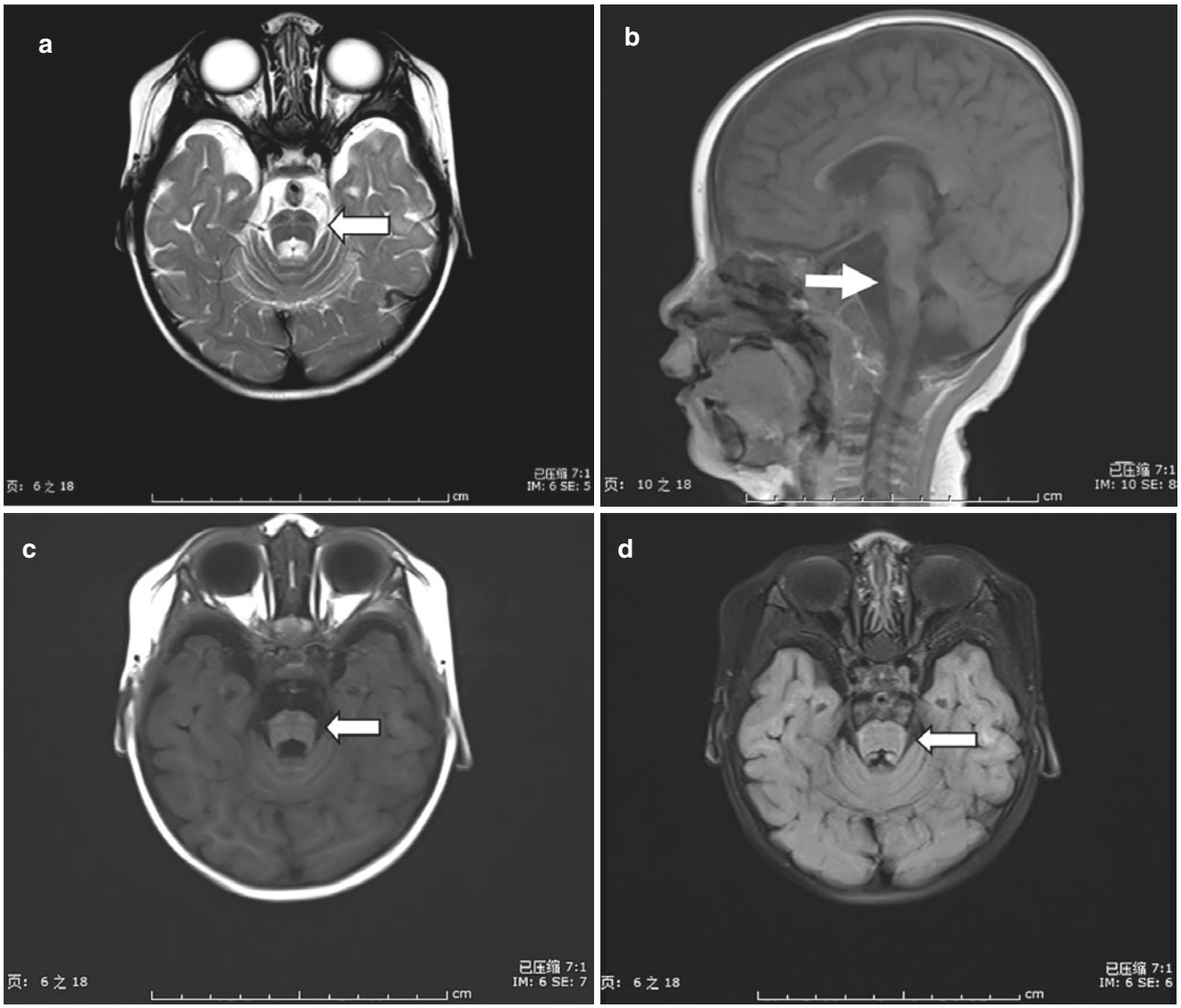

Fig. 8.1 Olivopontocerebellar atrophy (OPCA)

development of the disease, and also improve the clinical symptoms and improve the quality of life of the patients.

CT or MRI examination is a necessary technique to characterize the brain stem and cerebellar atrophy of OPCA in clinical practice [3]. MRI is crucial for the diagnosis of OPCA. The morphological characteristics of MRI in patients with OPCA were atrophy and thinning of brain stem, narrowing of anteroposterior diameter of pons, symmetrical or asymmetrical changes of cerebellar volume, widening and deepening of cerebellar sulcus, enlargement of cistern and ventricle, mild atrophy of frontal and parietal lobe. And the brain parenchyma generally has no abnormal signal. If cerebellopontine foot atrophy occurs, the transverse and longitudinal fibers of pontine are involved, T2WI shows high signal intensity and pons "cross sign," which is of great value in the diagnosis of OPCA. The more serious pons atrophy are, the more obvious the "cross sign" of OPCA are. However, not all OPCA patients were positive for MRI, especially the MRI signs of OPCA patients in the early stage of onset were not canonical. And DWI made up for it in this respect. DWI can quantitatively analyze the early neurodegeneration of OPCA patients by ADC value, and it is not necessary to wait until the late morphological manifestation of the lesion is abnormal. In addition, PET scans of OPCA patients showed significant decreases in local cerebral metabolic rates of lumbrical, cerebellar, and brain stem glucose (LCMRgluc), as compared with those of normal control subjects [4].

On the basis of the classification of genetic and sporadic types, some authors have further classified according to genetic, clinical, biochemical, and pathological characteristics [5]. The numerous and complex manifestations of OPCA not only lead to confusion in classification, but also bring difficulties to clinical work. A growing number of researchers believe that OPCA may be one of the pathological

features of other diseases, such as multiple system atrophy(MSA), mitochondrial encephalopathy, hexosamine deficiency, adrenal leukodystrophy, or spongiform encephalopathy [6]. In addition, familial OPCA is often misdiagnosed as familial prion disorder (Gerstmann-scheinker Syndrome) or familial insomnia. Therefore, in addition to relying on the typical MRI manifestations ("cross sign"), the differential diagnosis of OPCA should be based on the characteristic clinical symptoms.

In summary, OPCA is a pathological marker that is often associated with lesions at all levels of the central nervous system, essentially presenting as a variable progressive cerebellar-plus syndrome.

Case 8.2 Wallerian Degeneration

Clinical Presentation

A 3-year-old girl had a cerebral hemorrhage in the right frontal temporal-parietal lobe 2 years ago. She was delivered naturally at term and had asphyxia history. Her past surgical and family histories were negative.

Imaging Findings

A. Axial T2-weighted image demonstrates a large area of high signal in the right frontal parietal lobe (arrow), which was the formation of softening focus (Fig. 8.2a).

B-C. The volume of the right pons was smaller than that of the contralateral, while he signal had no significant change (arrow) (Fig. 8.2b–c).

Discussion

Animal experiments and neuroimaging studies had ever shown that there was secondary degeneration in fiber pathways in addition to the primary focus [7, 8], which was called Wallerian degeneration (WD). It means that retrograde and anterograde axonal degeneration secondary damage would occur in distal axon and myelin sheath after neuronal cell or proximal axonal injury [9], and this phenomenon existed widely in the whole nervous system. However, it is most common in the pyramidal tract. In contrast to the WD of the peripheral nerves, the central nervous system develops more slowly.

Combining with pathological and MRI manifestations, Kuhn et al. [10] used the appearance of primary lesions as the starting points and classified WD into the following stages: (1) Within 4 weeks, the axons of the affected nerve fibers begin to degenerate, but the biochemical changes are slight; (2) At 4–10 weeks, the myelin protein of nerve fibers is destroyed, but the lipid in myelin is relatively intact. And the hydrophilicity of degenerated tissues begins to increase; (3) At 10–14 weeks, the myelin lipids of the nerve fibers are destroyed and glial hyperplasia occurs. Then, the hydrophilicity of the degenerated tissue is significantly increased; (4) After several months to several years, the nerve fiber bundle completely disintegrates, the destruction, the local atrophy is obvious.

In terms of different imaging methods, WD presents different image features. CT has hysteresis for MRI examination

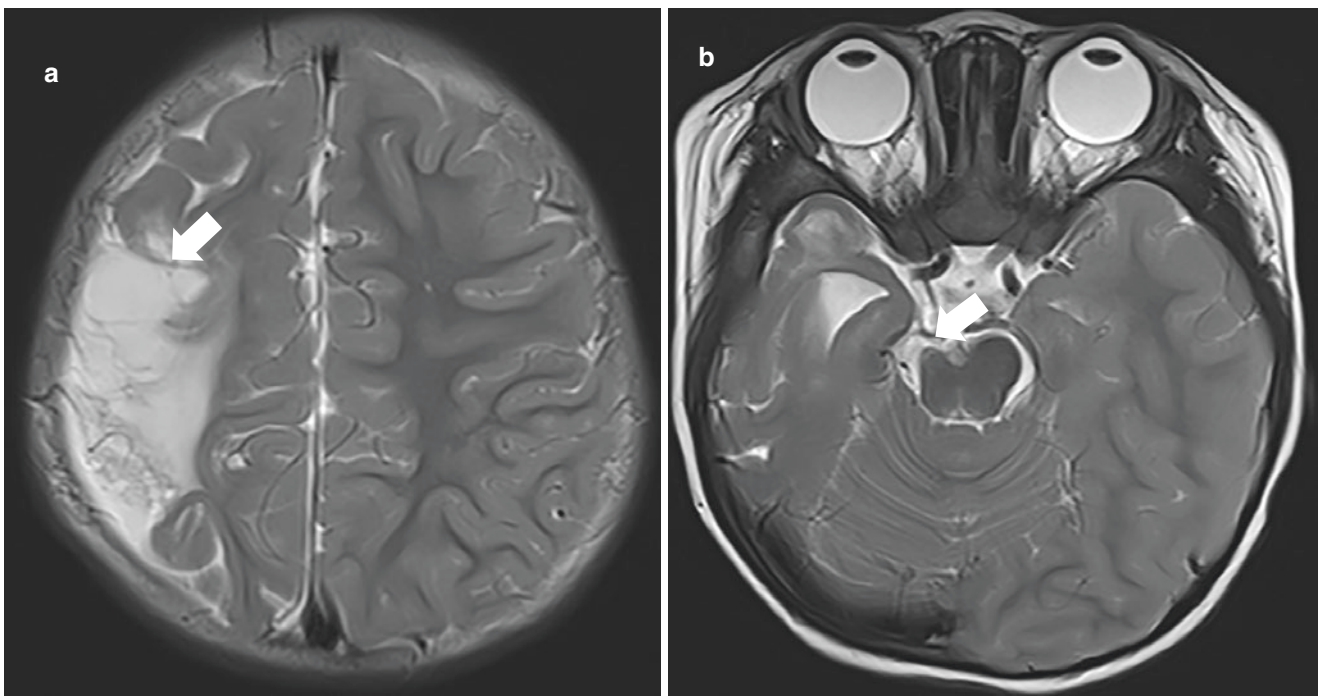

Fig. 8.2 Wallerian degeneration

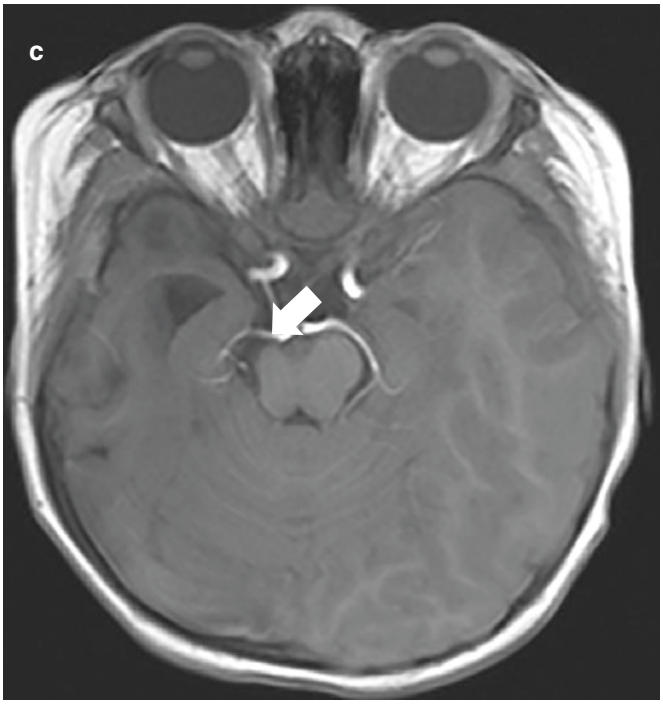

Fig. 8.2 (continued)

and can only detect brain tissue atrophy at the later stage of WD. MRI can initially detect the high signal of WD region in T1WI and low signal of T2WI in the fourth week after brain injury.

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