Pediatric Neurocutaneous Syndromes with Cerebellar Involvement

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KEYWORDS

• Neurocutaneous syndromes • Cerebellum • Intracranial • Children • MR imaging

KEY POINTS

- Neurocutaneous syndromes are associated with widespread cerebellar involvement.
- Cerebellar involvement in certain types of neurocutaneous syndromes may cause neurocognitive deficits, in particular with regard to language and visuospatial abilities in children.
- Accurate characterization of cerebellar involvement may help in the diagnosis and influences long-term neurocognitive prognosis of children with neurocutaneous syndromes.
- In neurocutaneous disorder, cerebellar tumors such as medulloblastoma in basal cell nevus syndrome have a significantly different management regime compared with sporadic medulloblastoma.

INTRODUCTION

Neurocutaneous syndromes (NCS) are a group of congenital disorders of histogenesis in which the overall brain structure may be normal but anomalous cells persist and continue to differentiate. NCS primarily involves structures derived from the neuroectoderm and, consequently, typically affect the skin and central and/or peripheral nervous system. Most textbooks and reviews focus on the description of the typical supratentorial findings in NCS, with few focusing on the coexisting infratentorial lesions. Neuroimaging has proven to play a key role in the characterization, definition, and diagnosis of NCS. The cerebellum is, however, involved in various types of NCS and its careful evaluation should be part of every neuroimaging study in children with NCS. Cerebellar involvement may (1) be helpful or needed for the diagnosis of certain types of NCS and (2) explain the cognitive and behavioral phenotype (eg, impaired visuospatial ability, impaired language, or abnormal social behavior) of children with some NCS.

This article describes various types of NCS with cerebellar involvement. For each disease or syndrome, clinical features, genetic, neuroimaging findings, and the potential role of the cerebellar involvement is discussed.

NEUROFIBROMATOSIS TYPE 1

Neurofibromatosis type 1 (NF1; Online Mendelian Inheritance in Man [OMIM] entry 162200) is the most common NCS with a prevalence of 1 in 2500 to 3000 individuals.[1] It is an autosomal dominant disorder caused by heterozygous mutation in the neurofibromin gene on chromosome 17q11.2.

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Neurofibromin is widely expressed with high levels in the nervous system and acts as a tumor suppressor. Neurofibromin reduces cell growth and proliferation by negative regulation of the cellular proto-oncogene p21RAS and by control of the serine threonine kinase mammalian target of rapamycin (mTOR).[2] Impaired neurofibromin function predisposes to benign and malignant tumor formation.

The principal clinical manifestations of NF1 involve the skin and the nervous system, but the complications are variable and may involve most of the body systems.[3]

Neuroimaging abnormalities in NF1 include intracranial neoplasms, parenchymal T2-hyperintense lesions, cerebral vasculopathy, and sphenoid wing dysplasia. Intracranial neoplasms include glioma, cranial nerve schwannoma, and plexiform neurofibroma.[4] Gliomas generally develop in the optic pathways, brainstem, and, rarely, cerebellum. Optic pathway gliomas are the most frequent neoplasms seen in about 15% of children with NF1 and are typically low-grade pilocytic astrocytomas. Parenchymal T2-hyperintense lesions, also referred to as unidentified bright objects, can be seen in up to 75% of pediatric patients with NF1 and tend to decrease in prevalence with advancing age (**Fig. 1**A).[4] These lesions are not space occupying, do not or very rarely show contrast enhancement, and are typically located in the basal ganglia, internal capsule, brainstem, and cerebellum. Increased apparent diffusion coefficient (ADC) values in unidentified bright objects match the histopathological finding of myelin vacuolation and spongiotic changes attributed to increased water accumulation.[5]

Primary cerebellar tumors are a rare presentation in NF1. In a series of 600 NF1 subjects, only 2 children had low-grade astrocytomas arising primarily from the cerebellar hemisphere (**Fig. 1**B).[6] Vinchon and colleagues[7] showed an overall better outcome for cerebellar gliomas

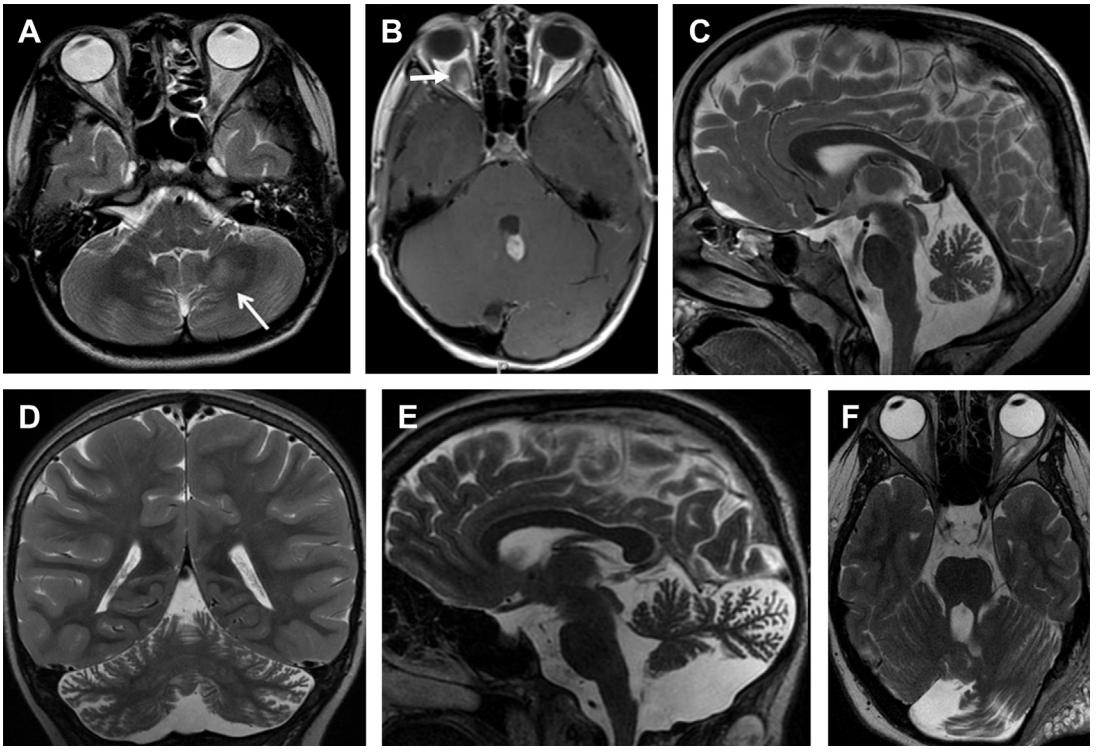

Fig. 1. Neurofibromatosis type 1. (*A*) Axial T2-weighted image showing cerebellar parenchymal T2-hyperintense lesions (*arrow*), also referred to as unidentified bright objects. (*B*) Axial T1 postcontrast image demonstrating an enhancing glioma in the rostral and medial aspect of the cerebellar vermis and optic glioma on the left (*arrow*). (*C*) Sagittal and (*D*) coronal T2-weighted images showing normal size of the cerebellar vermis and hemispheres with stable enlargement of the interfoliar spaces consistent with cerebellar hypoplasia. (*E*) Sagittal and (*F*) axial T2-weighted images showing enlargement of the left cerebellar hemisphere. The posteromedial part of the left cerebellar hemisphere is bulky, crosses the midline, and its interfoliar spaces are enlarged, consistent with cerebellar dysmorphia. (*From* Toelle SP, Poretti A, Weber P, et al. Cerebellar hypoplasia and dysmorphia in neurofibromatosis type 1. Cerebellum 2015;14(6):642–9; with permission.)