Lhermitte-Duclos Disease With Cervical Paraspinal Arteriovenous Fistula

—Case Report—

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Abstract

A 38-year-old man presented with a dysplastic cerebellar gangliocytoma associated with a paraspinal arteriovenous fistula (AVF) at the upper cervical portion. Neuroimaging examination indicated the diagnosis of Lhermitte-Duclos disease. The patient was treated by embolization of the AVF followed by partial resection of the cerebellar tumor. Genetic examination showed a mutation of the phosphatase and tensin homolog deleted on chromosome ten (PTEN) gene. Histological examination confirmed the diagnosis. Lhermitte-Duclos disease is a rare dysplastic gangliocytoma manifesting as a slowly growing mass in the cerebellum and is usually asymptomatic. This case of Lhermitte-Duclos disease associated with paraspinal AVF and mutation of the PTEN gene suggests a relationship between Lhermitte-Duclos disease and Cowden disease.

Key words: Lhermitte-Duclos disease, Cowden disease, arteriovenous fistula, PTEN

Introduction

Lhermitte-Duclos disease is a rare type of dysplastic gangliocytoma in the cerebellum, first described in 1920. Whether the cerebellar lesion is neoplastic, hamartomatous, or has another character remains controversial. There may be an association between Lhermitte-Duclos disease and Cowden disease, which is an autosomal disorder caused by mutation of the phosphatase and tensin homolog deleted on chromosome ten (PTEN) gene.^{1,12,13)} Cowden disease is characterized by mucocutaneous lesions, including facial papules, gingival papillomas, and acral keratoses. PTEN gene mutation may result in Cowden disease, Bannayan-Riley-Ruvalcaba syndrome, and Proteus syndrome, which are all hereditary hamartoma syndromes. These syndromes can be grouped as the PTEN hamartoma-tumor syndrome and may be associated with vascular malformations.^{7,15)}

Here we describe the first case of Lhermitte-

Duclos disease associated with paraspinal arteriovenous fistula (AVF).

Case Report

A 38-year-old male had a 6-month history of occipital headache, hoarseness, and acute progressive left facial sensory disturbance beginning a few days earlier. Neurological examination revealed no cerebellar sign, but found gait disturbance due to vertigo. The patient had no thyroid, cutaneous, or genitourinary symptoms. Further screening revealed no malignant lesion in his body. The patient's family history revealed that his mother had had multiple gastrointestinal polyps, breast cancer, and subcutaneous angiolipomas, with a diagnosis of Cowden disease, and his brother had had a brain tumor but had refused treatment.

Magnetic resonance (MR) imaging showed a high intensity area with the characteristic parallel striation in the cerebellar hemisphere on T₂-weight-

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Fig. 1 A: Preoperative T₁-weighted (fat suppression) magnetic resonance image demonstrating a mass lesion in the right cerebellar hemisphere as a low intensity area with striped enhancement by gadolinium called the tiger-stripe appearance. B: Diffusion-weighted magnetic resonance image showing a high intensity area with the characteristic parallel striation. C: Right vertebral angiogram (anteroposterior projection) revealing a paraspinal arteriovenous fistula (AVF) supplied by two enlarged feeding arteries from the vertebral artery. D: Right vertebral angiogram (lateral projection) showing the AVF draining into the internal jugular vein and paravertebral plexus.

ed imaging and diffusion-weighted imaging, and a low intensity area on T₁-weighted imaging with slight enhancement by gadolinium in the lesion zone causing the characteristic striated appearance called the “tiger-stripe appearance” (Fig. 1A, B). Computed tomography (CT) showed a low density mass lesion. MR imaging and CT also indicated noncommunicating hydrocephalus. MR spectroscopy showed elevated levels of lactate, myo-inositol, and creatine, and decreased level of choline-containing compounds. Single photon emission computed tomography (SPECT) showed a slight increase in thallium-201 uptake in the lesion zone (tumor-to-

Fig. 2 A, B: Photomicrographs demonstrating destruction of the middle Purkinje cell layer and accumulation of dysplastic ganglion cells in the inner granular cell layer. Hematoxylin-eosin stain, original magnification A: $\times 100$ and B: $\times 200$. C, D: Photomicrographs of immunohistochemical staining showing many ganglion-like cells positive for neuron-specific enolase (C) and synaptophysin (D). Original magnification $\times 200$.

normal brain tissue ratio of 1.59:1).

Cerebral angiography showed a slight tumor stain in the right cerebellar hemisphere, and a paraspinal AVF in the right cervical portion. The AVF was supplied by the right vertebral and external carotid arteries (Fig. 1C, D). The symptom of facial sensory disturbance was thought to be caused by the AVF at the cervical portion and not the cerebellar tumor. The diagnosis was Lhermitte-Duclos disease.

The patient was treated by embolization of the AVF followed by partial resection of the cerebellar tumor. The symptom of facial sensory disturbance disappeared after the embolization. Histological examination revealed destruction of the middle Purkinje cell layer and accumulation of dysplastic ganglion cells in the inner granular cell layer. Those dysplastic ganglion cells expressed neuron-specific enolase and synaptophysin, indicating neural cell characteristics (Fig. 2). Constitutive deoxyribonucleic acid was collected from the patient's leukocytes, and polymerase chain reaction-single-strand conformation polymorphism and sequencing analysis for PTEN mutations revealed mobility shift from the normal band of the PTEN gene in exon 5, and base change in codon 130 in exon 5 (CGA(Arg), TGA(STOP)).

After resection of the tumor, the symptoms of

increased intracranial pressure, headache, and nausea disappeared. The patient was discharged home without neurological deficit except slight hoarseness.

Discussion

The present case showed an association between Lhermitte-Duclos disease and vascular malformation in the central nervous system. The cervical paraspinal AVF was identified by MR imaging, MR spectroscopy, SPECT, angiography, and histological examination. Lhermitte-Duclos disease was confirmed by histological examination of the resected sample.

The neuroimaging findings in our case were in accordance with other cases of Lhermitte-Duclos disease,^{5,6,8-10)} except that T₁-weighted imaging with gadolinium showed striated enhancement of the tumor. Lhermitte-Duclos disease may present with atypical MR imaging findings with contrast enhancement.²⁾

The patient's mother had been treated under a diagnosis of Cowden disease, or multiple hamartoma syndrome, which is an autosomal dominant condition with variable expression that results from a mutation in the PTEN tumor suppressor gene (also termed MMAC1 or TEP1) on chromosome arm 10q23. Such PTEN mutations have been detected in autosomal disorders, such as Cowden disease, Bannayan-Riley-Ruvalcaba syndrome, or Proteus syndrome, which are hereditary hamartoma syndromes. Lhermitte-Duclos disease can coexist with systemic arteriovenous malformations.¹¹⁾ These findings suggest that Lhermitte-Duclos disease and Cowden disease can be grouped as the PTEN hamartoma-tumor syndrome, and may coexist with vascular malformations.

In the present case, the paraspinal AVF at the cervical portion may have been coincidental with Lhermitte-Duclos disease, but the AVF could also have been a result of the mutation of the PTEN gene, which is related to cell proliferation and migration, especially in vascular smooth muscle cells.^{3,4,14)} PTEN has protein phosphatase and 3'-phosphoinositol phosphatase activities which regulate numerous cellular processes, including proliferation and migration. In other words, PTEN could regulate angiogenesis by modulating endothelial cellular functions.^{3,4,14)} On the other hand, some brain tumors such as meningioma may coexist with systemic arteriovenous malformation, which suggested that the tumors induced angiogenesis and the formation of the vascular malformations. Although gangliocytoma is not very hypervascular, certain

tumors associated with Lhermitte-Duclos disease showed hypervascularity by SPECT or perfusion MR imaging.²⁾ Therefore, Lhermitte-Duclos disease may induce angiogenesis.

The present case of the Lhermitte-Duclos disease associated with paraspinal AVF indicates a genetic link between Lhermitte-Duclos disease and Cowden disease. We emphasize that patients with Lhermitte-Duclos disease and vascular malformation manifesting as acute progressive symptoms should be screened for vascular information.

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