Anti-Yo-Associated Paraneoplastic Cerebellar Degeneration Manifesting as Acute Cerebellitis with Posterior Cranial Fossa Hypertension

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Key words
- Breast neoplasms
- Cerebellar diseases
- Intracranial hypertension
- Paraneoplastic cerebellar degeneration

Abbreviations and Acronyms
Ig: Immunoglobulin
MRI: Magnetic resonance imaging
PCD: Paraneoplastic cerebellar degeneration
PNS: Paraneoplastic neurologic syndrome

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Citation: World Neurosurg. (2018) 112:117-122. https://doi.org/10.1016/j.wneu.2018.01.105

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

BACKGROUND: **Paraneoplastic cerebellar degeneration (PCD) is a rare complication of some malignant cancers. It is most commonly described in women with gynecologic or breast malignancies; however, there have been reports in other types of cancers. Symptoms include ataxia, dysarthria, and tremors, which could be the first manifestations of an underlying malignancy.**

CASE DESCRIPTION: **A 50-year-old woman had an acute PCD with anti-Yo antibodies from an underlying breast invasive ductal carcinoma. She presented with intracranial hypertension in the posterior cranial fossa that required an emergent decompressive craniectomy.**

CONCLUSIONS: **PCD is an uncommon disease that may manifest initially as posterior cranial fossa hypertension and subsequent acute hydrocephalus owing to diffuse cerebellar swelling. To our knowledge, this is the first described case of an anti-Yo PCD that has manifested as acute posterior cranial fossa hypertension owing to diffuse cerebellar edema. Early diagnosis and treatment should be pursued to improve long-term outcomes.**

INTRODUCTION

Paraneoplastic neurologic syndromes (PNSs) represent a group of disorders that result in damage to the nervous system in the setting of an underlying cancer and that are not related to metastasis, infection, or metabolic derangements associated with cancer.[1-4] Although PNS may manifest in a patient with diagnosed cancer, most commonly it is the presenting symptom in a previously well individual with a hidden tumor that may be detected only by advanced imaging techniques.[1,5,6] These rare syndromes are estimated to occur in <0.01% of patients with cancer[1,7,8]; however, accurate data regarding their prevalence are still unavailable. The incidence of PNS seems to be increasing owing to both improvements in the recognition of clinical syndromes and technologic advances in diagnostic testing.

One of the most common characterized PNSs includes paraneoplastic cerebellar degeneration (PCD), which is characterized by cerebellar symptoms including truncal and appendicular ataxia, nystagmus, dysarthria, diplopia, dysarthria, dysphagia, and sometimes oscillopsia and transient opsoclonus that begin abruptly and progress over weeks to months and then stabilize by 6 months.[1,6,8-11] We describe an uncommon case of PCD owing to anti-Yo antibodies, which initially manifested as acute cerebellitis and posterior cranial fossa hypertension and required a suboccipital decompressive craniectomy.

CASE DESCRIPTION

A previously healthy, 50-year-old woman presented to the emergency department with vertigo, ataxia, intense occipital headache, and projectile vomiting without preceding nausea that occurred when standing or with Valsalva maneuvers. She denied recent flulike symptoms, and her past medical history was unremarkable. Magnetic resonance imaging (MRI) of the brain performed on admission showed a diffuse cerebellar edema with tonsillar descent and leptomeningeal enhancement (Figure 1). The next day the patient's symptoms progressed despite initial medical therapy, and computed tomography scan of the brain revealed increased cerebellar swelling and fourth ventricle occlusion with enlarged lateral ventricles (Figure 2).

The patient underwent a suboccipital decompressive craniectomy to relieve pressure owing to posterior cranial fossa intracranial hypertension. During the surgical procedure, a cerebellar biopsy specimen was taken (Figure 3A–G), which showed a diffuse inflammatory infiltrate, with immunohistochemistry being negative for herpes simplex virus 1 and 2, *Toxoplasma gondii*, Epstein-Barr virus, and cytomegalovirus. The infiltrate was predominantly of $CD3^+$ lymphocytes, with a slight predominance of $CD4^+$ T lymphocytes over $CD8^+$ T cells. Initial laboratory tests were targeted toward infectious causes of acute cerebellitis, such as immunoglobulin (Ig) M and IgG for cytomegalovirus, *Cryptococcus neoformans* antigen, IgG and IgM for *T. gondii*, IgM for *Leptospira*, rapid plasmin reagin for syphilis, and enzyme-linked immunosorbent

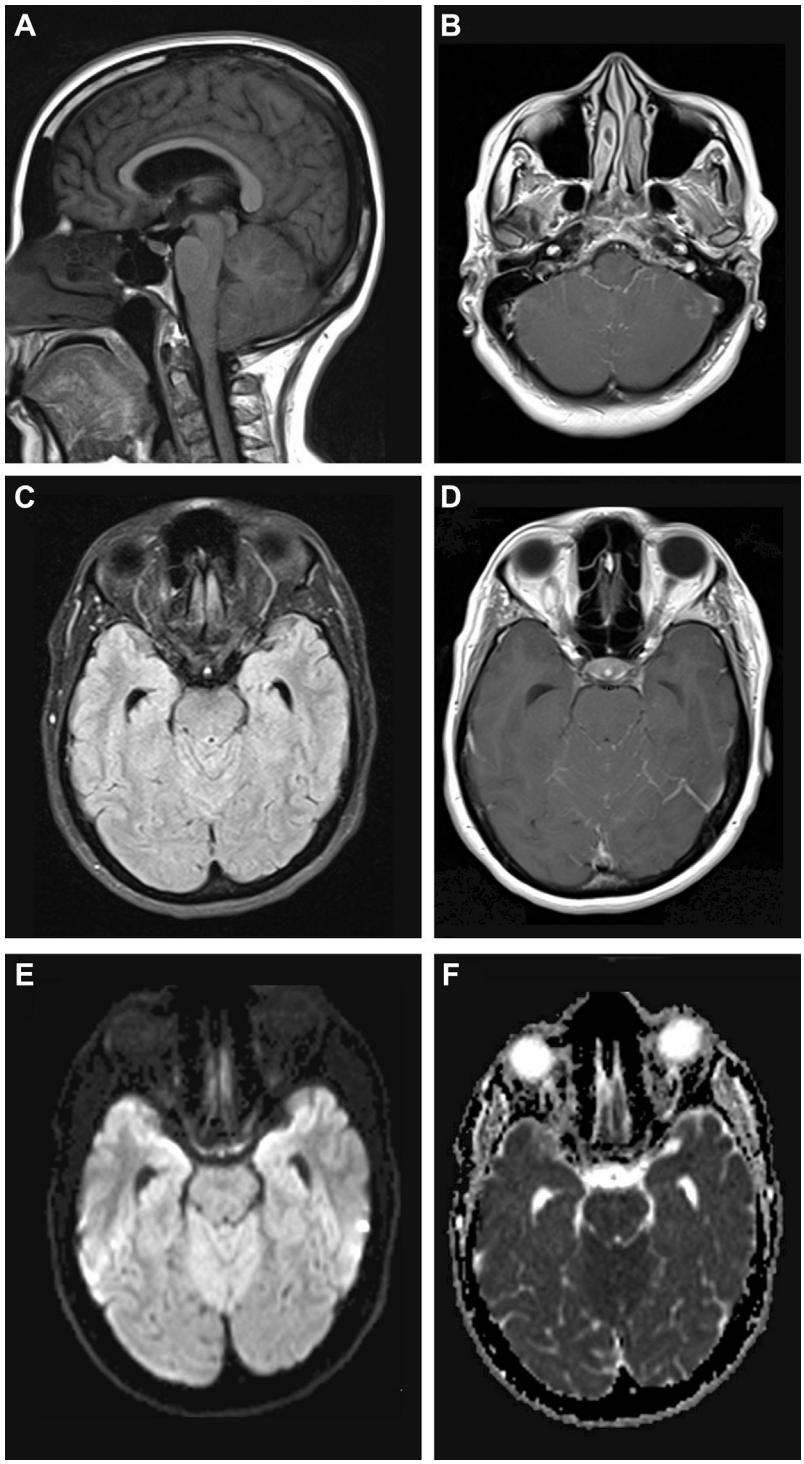

Figure 1. Brain magnetic resonance imaging. (**A**) Sagittal T1-weighted sequence showing diffuse cerebellar swelling with herniation of the cerebellar tonsils through the foramen magnum. (**B**) Axial T1-weighted contrast-enhanced sequence revealing diffuse leptomeningeal smooth enhancement. (**C**) Axial fluid attenuated inversion recovery sequence showing a high-intensity signal in the bilateral cerebellar folia owing to cerebellar edema. (**D**) Axial contrast-enhanced T1-weighted sequence revealing leptomeningeal enhancement in the cerebellar vermis. (**E** and **F**) Axial diffusion-weighted and apparent diffusion coefficient sequence showing diffusion restriction in the cerebellar vermis.

assay for human immunodeficiency virus; these were all negative, however. Initial blood cell count and C-reactive protein were also normal.

As an infectious etiology was ruled out, a paraneoplastic cause from a hidden cancer was considered, and methylprednisolone was initiated with progressive improvement of symptoms. Anti-Yo antibodies were positive, and anti-Hu antibodies were negative. Abdominopelvic MRI and mammography were performed to detect a primary tumor. A mass lesion was identified in the right breast (Figure 3H). A biopsy revealed a ductal carcinoma, estrogen receptor 2%, progesterone receptor <1%, and strong positivity for human epidermal growth factor receptor 2 ($HER2^{+++}$). Staging revealed no lymph node involvement and no metastatic lesions. Chemotherapy with 5-fluorouracil, doxorubicin, cyclophosphamide, paclitaxel, and trastuzumab was initiated.

During ambulatory follow-up at 7 months, the patient presented with persistent unstable gait requiring assistance, dysmetria, and dysarthria. Motor symptoms improved mildly with amantadine. Follow-up brain MRI (Figure 4) showed postoperative changes owing to suboccipital decompressive craniectomy and resolution of cerebellar edema.

DISCUSSION

In PNSs, onconeural antigens are expressed by both tumoral cells and neuronal tissue and are targeted by the immune response.[1,6] This occurs especially in tumors originating from tissues derived from the ectoderm that have the capacity to produce neuronal proteins.[2] The role of onconeural antigens in the pathogenesis of PNSs remains unclear but may relate to humoral versus cellular immunity.[1-3] Certain antibodies may exert direct damage to neural tissue (humoral mechanism) because the targeted antigens are expressed in the cell surface, such as voltage-gated calcium channel antibodies or N-methyl-D-aspartate antibodies, but many other antibodies are directed to antigens expressed intracellularly, which do not produce direct damage or injury. In these instances, a cellular component of the immune attack