



Severe Paraneoplastic Parkinsonism: A Rare Cause Revealing Breast Cancer

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Dear Editor,

We report a case of a 63-year-old woman who presented to our center complaining of gait and balance disturbances that had gradually worsened over a 3-month period. She had no medical history besides arterial hypertension, which had been treated with losartan at 50 mg/day for 4 years. A resting tremor started 6 months before admission, which initially involved the right fingers and wrist and then became bilateral over a few weeks, and was associated with slowness of voluntary movements and some stiffness. She also experienced frequent falling while walking. All of the symptoms progressed rapidly until she needed assistance for performing her activities of daily living. Her family noticed some personality changes, in that she often became isolated and tired when making even the slightest effort. In a neurological examination she did not respond to pull testing. She exhibited marked bradykinesia and axial rigidity, and both resting and action tremors in both upper limbs. There were some pyramidal signs, with hyperreflexia and a positive Babinski sign on the right side. Examination of the oculomotor nerves revealed an inability to direct the gaze of the eyes downwards, slow saccades, and broken pursuits. Cerebellar syndrome was not present. The findings of the Mini Mental State Examination were normal (score of 30 out of 30). She presented new symptoms of dysarthria and swallowing difficulties during the hospitalization, and her postural instability became more severe, eventually resulting in the use of a wheelchair. Brain T2-weighted MRI images showed non-specific white-matter hyperintensities in the caudate and putamen bilaterally without midbrain atrophy (Fig. 1A and B). Cytochemical and bacteriological tests of the cerebrospinal fluid (CSF) produced normal findings. Serum and CSF protein electrophoresis revealed intrathecal synthesis of immunoglobulin G. In view of the rapid progression of symptoms, a paraneoplastic syndrome (PNS) was considered and specific assessments were started. Pending the outcome of ongoing investigations, we tried levodopa therapy as a symptomatic treatment. However, her motor symptoms were refractory even with adequate dosology. Serum and CSF studies showed high concentrations of anti-Ri antibodies, with negativity for anti-Hu, anti-amphiphysin and anti-Yo antibodies. Whole-body positron-emission tomography showed an active lesion on the left breast (Fig. 1C). A biopsy of the suspected lesion revealed a high-grade infiltrating ductal carcinoma (Fig. 1D). There was no local or regional metastasis. Based on the diagnostic criteria for PNS (2004),¹ we diagnosed our patient as definite PNS with nonclassical symptoms, associated with breast cancer (BC) and positive onconeural antibodies. We administered methyl-prednisolone intravenously at 1 g daily for 5 days, but there was no clinical improvement. She was then referred to a specialized center for surgery and oncological treatment, where she received quadrantectomy and ipsilateral axillary lymphadenectomy. She also received adjuvant chemotherapy with paclitaxel, carboplatin, and trastuzumab. Unfortunately the patient died 8 months later.

PNS is often associated with tumors but is not directly caused by the tumor invasion.² Im-

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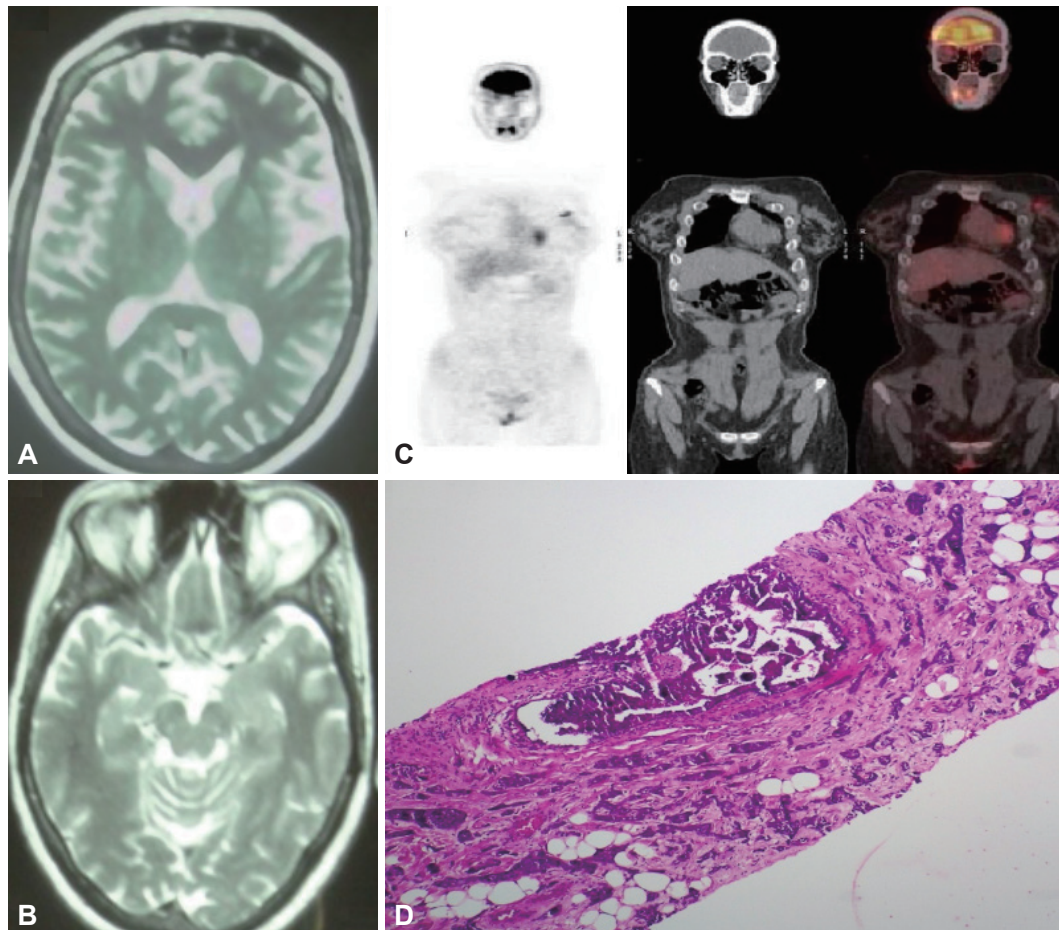


Fig. 1. A: Sequence of axial brain T2-weighted MRI images showing bilateral hyperintensities in the caudate and putamen. B: Sequence of axial brain T2-weighted MRI images showing no midbrain atrophy. C: Coronal views of PET, whole-body CT, and fused images in a patient with an abnormal hot spot in the upper outer quadrant of the left breast. D: Left-breast biopsy sample with hematoxylin-eosin staining (magnification $\times 20$). Image of high-grade tumor cells showing all the attributes of cytological malignancies: mammary parenchyma widely infiltrated by a carcinomatous process whose architecture is trabecular with a few tumor glands associated with intraductal carcinoma *in situ*.

munological factors are believed to be incriminated because of autoantibodies and T-cell response against antigens of the nervous system.¹ BC is not usually associated with paraneoplastic-parkinsonism (PNP).³⁻⁵ Golbe et al.⁵ reported the first case of PNP with metastatic BC in a patient who developed symptoms similar to those observed in our patient, but they did not detect any antibodies. Anti-Ri antibodies are commonly associated with brainstem encephalitis, paraneoplastic cerebellar degeneration, and paraneoplastic encephalomyelitis, and rarely with other syndromes. The brainstem syndrome may include opsoclonus/myoclonus, parkinsonism, cranial nerve palsies (including the oculomotor nerves), and dysphagia.^{2,6} The presence of these antibodies is a predictor of severe neurological impairment, with 60% of patients progressing to wheelchair dependence.⁶ That may explain the severe prognosis of our patient despite her BC being treated at an early stage.

Conflicts of Interest

The authors have no financial conflicts of interest.

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