Paraneoplastic Cerebellar Degeneration: A Dilemma Resolved with Positron Emission Tomography/Computed Tomography

Abstract

The case of a 39-year-old woman presented with symptoms of progressive cerebellar degeneration for few months preceding by the diagnosis and treatment of breast cancer. The causative association was revealed with the strong positivity of antineuronal antibody. Because of the multidisciplinary team approach with surgery and adjuvant endocrine treatment, the patient did improve symptomatically and she is alive without any evidence of disease after 22 months following the initial diagnosis of the neurological disorder. Interestingly, neurological symptoms regressed partially after surgery. Early recognition and appropriate combined modality treatment of this rare presentation of breast cancer are imperative as it may be crucial for the disease outcome.

Keywords: *Antineuronal antibody, breast cancer, cerebellar atrophy, paraneoplastic*

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A 39-year-old premenopausal woman came to the neurology clinic with abnormal uncoordinated movement and slurred speech for 4 months. Gait ataxia was subacute in onset and rapidly progressive in nature. For walking, she needed the support of 2 people. Dysarthria was associated with nasal regurgitation and truncal ataxia. She had a family history of breast cancer in a paternal cousin. On neurological examination, bulk and power in all 4 limbs were normal, but the tone was decreased in all of them. Titubation was present. Finger-nose test and heel-knee test were impaired. Meningeal signs were negative. Cerebrospinal fluid studies including routine microscopy, Gram stain, culture sensitivity, tuberculosis polymerase chain reaction, Gene Xpert, India ink, and venereal disease research laboratory test were negative. In paraneoplastic profiles, the antiPurkinje cell (anti-Yo) antibody was strongly positive, whereas Ant-Hu, Anti-Ri, and PNMA 2 were negative. Whole-body positron emission tomography-computed tomography (PET-CT) was advised for identifying the primary lesion, as there was no clinically palpable abdominal or breast lump. PET-CT was suggestive of well-defined metabolically active soft tissue nodule lesion of size 1.6 cm × 1.9 cm in upper outer quadrant of the right breast and mildly avid right axillary node with cerebellar atrophy [Figure 1]. There was no disease elsewhere. Bilateral mammography was suggestive of right breast irregular mass in upper outer quadrant at 10 o'clock with 16 mm size in long-axis diameter, breast imaging reporting, and data system (BI-RADS) 4 with no significant axillary lymphadenopathy. Core biopsy of right breast lesion was suggestive of invasive ductal carcinoma, luminal B molecular subtype. After A multidisciplinary tumor board discussion, she was planned for upfront modified radical mastectomy (MRM) with adjuvant endocrine treatment because of poor performance status due to cerebellar ataxia and economical constraint condition for targeted therapy. She underwent the right MRM with uneventful postoperative recovery. Histopathological examination revealed a 1.5 cm × 1.5 cm × 1.2 cm gray white tumor in the upper outer quadrant with features suggestive of invasive carcinoma, nonspecific type, grade 2 with no positive margins, and lymphovascular or perineural invasion, pathologically P T1c N0 cM0 [Figure 2]. All 27 axillary nodes were negative for malignancy. She is taking adjuvant endocrine treatment (Tamoxifen, 20 mg daily). The patient is under regular follow-up with disease-free status after 18 months of index surgery. The paraneoplastic

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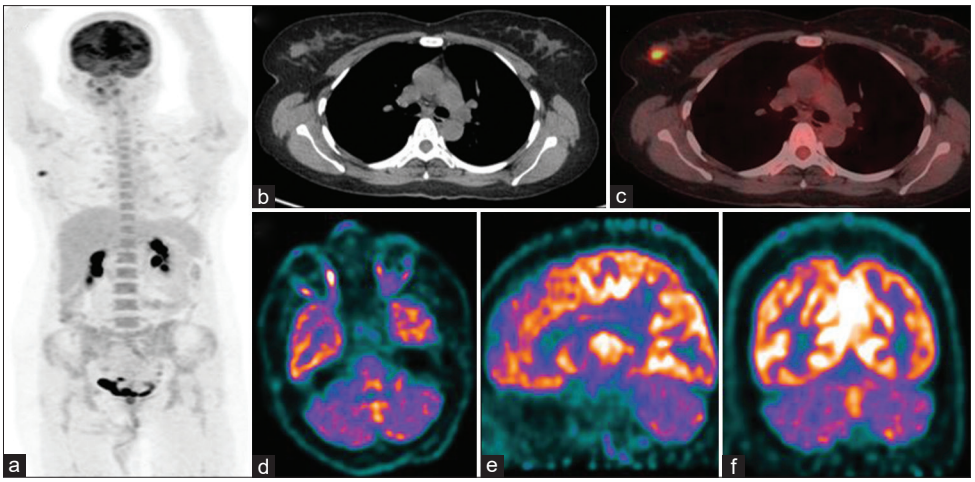

Figure 1: (a) Maximum intensity projection image of fluorodeoxyglucose positron emission tomography-computed tomography showing the focal area of tracer uptake in the right anterolateral chest region corresponding to nodular lesion in the right breast parenchyma in the upper-outer quadrant on axial computed tomography section (b) and showing fluorodeoxyglucose uptake in the fused positron emission tomography-computed tomography image (c). (d), (e and f) – Axial, sagittal, and coronal positron emission tomography only images showing reduced fluorodeoxyglucose uptake in the bilateral cerebellar hemispheres, suggestive of cerebellar atrophy

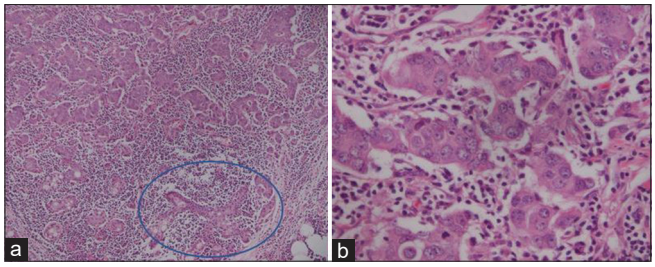

Figure 2: (a) Microphotograph showing invasive ductal carcinoma with dense intratumoral lymphoplasmacytic infiltrate. Normal breast parenchyma can be seen at the encircled lower right corner of the image (H and E, ×100); (b) ×400

symptoms improved gradually and she walked slowly to the outpatient department without any support.

The paraneoplastic disorder is a rare clinical manifestation in breast cancer.[1] The nonspecific symptoms lead to delayed and/or incorrect diagnosis. We are reporting an unusual presentation of breast cancer patients, i.e., gait ataxia with dysarthria due to paraneoplastic cerebellar atrophy, without any symptoms of Parkinsonism, cognitive and behavioral changes, and sensorineural deficits. This was favored with raised serum anti-neuronal antibody (anti-Yo antibody), PET-CT findings of atrophic cerebellum with a metabolically active breast lesion. The latter was confirmed with the histopathological examination and immunohistochemical studies. Paraneoplastic cerebellar degeneration (PCD) is a heterogeneous group of neurological disorders, caused by remote systemic effects of primary cancer or metastasis.[2] The direct involvement by tumor, metastasis, or antitumor treatment effects of systemic therapy should be ruled out before assigning PCD. It is observed in <0.01% of all cancer patients of which the majority are small cell lung cancer, Hodgkin's lymphoma, breast cancer, and gynecologic malignancies.[3,4] Antibody-mediated humoral and cytotoxic T cell immune response causes degeneration of Purkinje cells with minimal inflammatory infiltrates. This may be due to cross-reaction to tumor cells and neuronal antigens by the immune system.[2,5] among the other antineuronal antibodies, the anti-Yo antibody is the main culprit for the development of PCD. In our patient, strong positivity of serum anti-Yo antibody guided for the identification of underlying primary tumor. The prognosis of the disease may be masked by the severity of PCD associated neurological morbidities.[1,6] Diagnosing the patient with such rare manifestation is critical and it needs a multidisciplinary expertized team approach.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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