CASE REPORT

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A Case of Paraneoplastic Cerebellar Degeneration with Anti-Yo Positivity

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ABSTRACT Paraneoplastic neurological syndrome (PNS) is a neurological picture that occurs in patients with cancer, does not occur with the direct effects of the underlying tumor, cannot be explained by metastasis and side effects of cancer treatment, and is accepted to occur by mechanisms of autoimmune origin. The most common PNS, paraneoplastic cerebellar degeneration (PCD) is a neurological picture that occurs due to autoimmune causes related to breast or gynecological cancers. Before the diagnosis of cancer, the patient may apply with cerebellar complaints and the diagnosis can be reached through autoantibodies such as anti-Yo. Here, a case that presented with PCD before being diagnosed with malignancy and had much better surveillance than known cases in terms of prognosis is presented.

Keywords: Paraneoplastic cerebellar degeneration; anti-Yo antibodies

Paraneoplastic neurological syndrome (PNS) is a neurological picture that occurs in patients with cancer, does not occur with the direct effects of the underlying tumor, cannot be explained by metastasis and side effects of cancer treatment, and is accepted to occur by mechanisms of autoimmune origin.[1] The most common PNS, paraneoplastic cerebellar degeneration (PCD) is associated with pancerebellar syndrome with the acute or subacute course due to widespread cerebellar Purkinje cell death.[2] Pancerebellar syndrome is seen with trunk and side ataxia, dysarthria, horizontal and vertical nystagmus and progresses within weeks to months. Computerized tomography (CT)/magnetic resonance imaging (MRI) is normal in the early period; in the late period, cerebellar atrophy and sometimes hyperintensity in the white matter of the cerebellum can be seen. Anti-Yo antibodies are most commonly detected in cerebellar degeneration. This antibody is almost always associated with breast, ovarian, and other gynecological cancers. Here is a case presented with a positive anti-Yo antibody and subacute cerebellar degeneration clinic.

CASE REPORT

A 38-year-old female patient was admitted to our clinic after an increase in complaints of dizziness, nausea, vomiting, imbalance that has existed for several months. There were no specialty features on her resume. About a month ago, cranial CT and MRI performed in the outpatient diagnostic center with complaints of dizziness and diplopia were found to be normal. At the neurological examination of the woman, she was conscious, orientated and coopera-

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tive. There was no restriction on the movement of the globe of eyes, yet horizontal and vertical nystagmus was present. Cranial nerves were normal. Her speech was dysarthric, explosive, and hypophonic, titubation and truncal ataxia were present. Bilateral pronounced dysmetria, dysdiadochokinesia, intensional tremors were present in the upper extremities. Bilateral heel-shin tests in lower extremities were broken, sitting supported in bed, unable to stand due to pronounced ataxia. Muscle strength examination could not be performed objectively because of prominent cerebellar findings. Deep tendon reflexes were decreased. Deep and superficial sensory examinations were normal. There were no pathological reflexes.

With the preliminary diagnosis of pancerebellar syndrome, the patient underwent cranial MRI with and without contrast, lumbar puncture, and screening tests for oncology.

Hemogram, biochemistry, tumor markers, and peripheral smear were normal. There was no pathology except degenerative lymphocytes in the cerebrospinal fluid (CSF). On MRI examination; on axial and sagittal T1 weighted images, linear leptomeningeal enhancement of contrast was seen in post-contrast series and on coronal T2-flair images, cerebellum had a diffuse hyperintense appearance (Figure 1a, Figure 1b, Figure 1c). Oncological screening tests were normal for lung, gastrointestinal system, and genitourinary system malignancies.

During the detailed examinations of the patient in terms of breast and gynecological malignancy, lymphadenomegaly was detected in the left axillary region on breast palpation. Mammography showed 4 mm of calcification in the upper outer quadrant of the left breast. The mass lesion did not wash out with 4 mm of suspicious contrast and did not show a malignant curve in the breast MRI. While the tru-cut biopsy performed from the upper outer quadrant of the left breast was normal, the tru-cut biopsy performed from the left axillary lymphadenomegaly was evaluated as compatible with carcinoma metastasis. No pathology was detected in the whole-body positron emission tomography, except for the involvement in the left axillary lymph node.

In the patient who could not find a primary focus, anti-Yo antibody, one of the paraneoplastic autoantibodies, was positive in the serum, and the patient was accepted as PCD. A significant improvement was achieved in the cerebellar findings of the patient, who was treated with 0.4 g/kg/day intravenously immunoglobulin G (IV IG) for 5 days. Post-treatment cranial MRI T1 and post-contrast T1 weighted images were normal (Figure 2a, Figure 2b). The patient, who was able to do her daily work with assistance within six months with physical therapy, has been followed up by oncology for malignancy screenings every 6 months for ten years and the primary cancer focus has not been detected yet. Informed consent was obtained from the patient for the article.

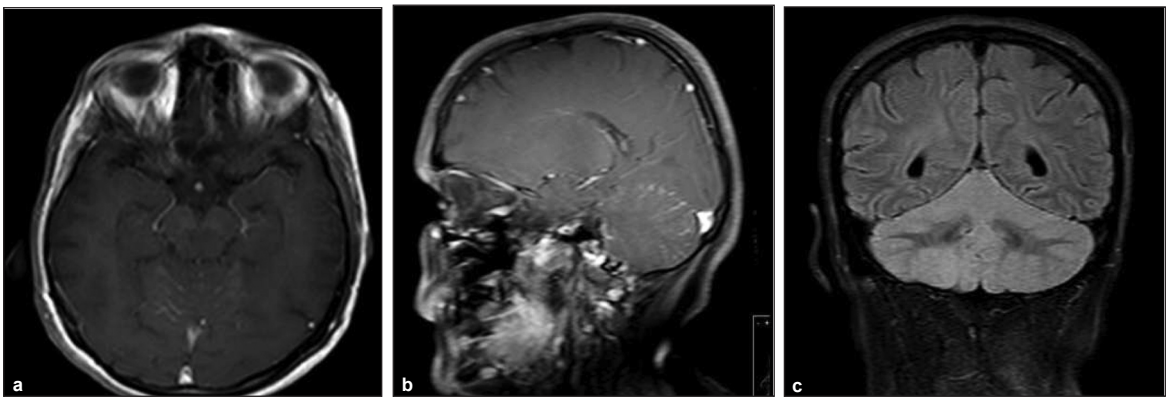

FIGURE 1: a) Linear leptomeningeal enhancement of contrast can be seen in post-contrast series on axial T1-weighted magnetic resonance images, **b)** Linear leptomeningeal enhancement of contrast can be seen in post-contrast series on sagittal T1-weighted magnetic resonance images, **c)** Diffuse hyperintense appearance on coronal T2-flair magnetic resonance images of the cerebellum.

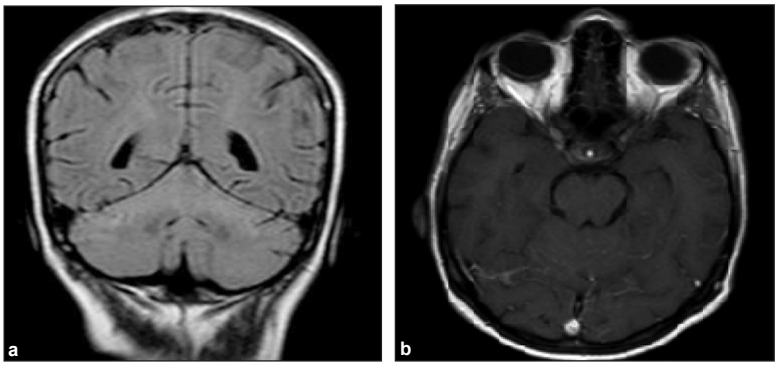

FIGURE 2: a) A month after treatment, T1 weighted images were normal except for mild cerebellar atrophy, **b)** A month after treatment, post-contrast T1 weighted images were normal except for mild cerebellar atrophy.

DISCUSSION

Cerebellar degeneration is the most common presentation in paraneoplastic syndromes. It is known that the brain stem, basal ganglia, spinal cord, peripheral nervous system, and neocortex are affected.[3] Cerebellar degeneration from autoimmune-caused PNS in about 1% of oncology patients is in combination with gynecological cancers, breast tumors, Hodgkin's lymphoma.[2,4] Anti-Yo, anti-Tr, anti-Ri, and anti-Hu antibodies synthesized against intracellular paraneoplastic onco-neural antigens can be detected.[2,4] About 50% of PCD cases are related to anti-Yo antibodies, also known as CDR2/CDR2L (cerebellar degeneration-related antigen).[5] In anti-Yo antibody is known as the Purkinje cell cytoplasmic antibody Type-1. Anti-Yo-associated PCD, there is a selective loss, especially in Purkinje cells, and it has been reported that axonal destruction and secondary demyelination are observed in Purkinje cells.[6] Antibodies can only be detected in serum or CSF in 60-70% of patients.[1] Most cases of anti-Yo-positive PSD presented in the literature are women over the age of 60.[7] PCD is usually treated in 2 ways: one of them is the treatment of the underlying tumor and the other is general immunosuppressive drugs. Immunotherapies such as IVIG, steroids, plasmapheresis are known to benefit in the treatment of PNS but it is still controversial.[8] In anti-Yo positive PCD cases, it has been reported that corticosteroids are ineffective but partial benefits of rituximab and plasma exchange can be seen.[9-11] Although the efficiency of intravenous immunoglobulins has been demonstrated in small studies.[12] In many studies, it has been shown that the prognosis of anti-Yo-positive PSD cases is worse than other antibodies and they are bed-dependent within three months of diagnosis.[7] Patients are usually lost due to the progression of the primary tumor, not from neurological PCD symptoms.[7]

Here, we presented a female patient with an anti-Yo antibody-positive PSD diagnosis with a subacute course of pancerebellar syndrome. In contrast to the literature, our patient was very young compared to the cases presented, had locally lymph node metastasis, although the primary tumor could not be detected, and responded better to IVIG treatment compared to other patients with serum anti-Yo antibody positivity. We know that paraneoplastic syndromes occur before tumor diagnosis, and these patients need to undergo tumor scans at intervals of 3-6 months for at least 5 years. Although our case was followed by mammograms, pap-smears, and pelvic MRI with contrast, malignancy has not yet been detected for 10 years. So this good prognosis supported that IVIG is the best treatment option for anti-Yo-positive PCD.

PNS cells usually develop in the early stages of cancer and it is often not possible to detect the tumor. Neuronal autoantigens are extremely useful diagnostic biomarkers and have a much more decisive role in early diagnosis and treatment than thought. As seen in our case, anti-Yo antibody focuses on cancer screening, especially on the ovary and breast, and helps patients receive early and effective treatment. With appropriate treatment, the onset of primary cancer may be delayed much longer than is known.

Source of Finance

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Elif Sarıca Darol;* ***Design:*** *Elif Sarıca Darol;* ***Control/Supervision:*** *Hüsnü Efendi;* ***Data Collection and/or Processing:*** *Elif Sarıca Darol;* ***Analysis and/or Interpretation:*** *Elif Sarıca Darol;* ***Literature Review:*** *Elif Sarıca Darol;* ***Writing the Article:*** *Elif Sarıca Darol;* ***Critical Review:*** *Elif Sarıca Darol;* ***References and Fundings:*** *Elif Sarıca Darol;* ***Materials:*** *Elif Sarıca Darol.*

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