Paraneoplastic cerebellar degeneration (PCD) is a rare neurological complication in cancer, characterized by the rapid development of cerebellar ataxia resulting from tumor-induced autoimmunity against cerebellar Purkinje cells. It is mostly seen in gynecological cancers, breast cancer, and small cell lung cancer. Here, we present a case of anti-Yo-associated PCD in an ovarian cancer patient. A recurrence in ovarian cancer was observed in this patient after the diagnosis of PCD. Keywords: Paraneoplastic cerebellar degeneration; anti-Yo; ovarian cancer; relapse disease

Paraneoplastic cerebellar degeneration (PCD) is a rare neurological complication in cancer, characterized by the rapid development of cerebellar ataxia resulting from tumor-induced autoimmunity against cerebellar Purkinje cells. It is mostly seen in gynecological cancers, breast cancer, and small cell lung cancer. Anti-Yo antibody, also known as anti-Purkinje cell cytoplasmic antibody type-1 is highly specific and the most frequently found antibody in patients with PCD. Other antibodies associated with PCD are anti-Hu, anti-Tr, anti-Ri, and anti-mGluR1. However, no antibodies are identified in nearly 40% of PCD patients.1-4

PCD occurs in about 0.2% of patients with malignant tumors and is characterized by cerebellar symptoms such as ataxia, vertigo, and dysarthria.5

Here, we present a case of anti-Yo-associated PCD in an ovarian cancer patient.

CASE REPORT

A 54-year-old female patient was followed up after remission of ovarian cancer and was presented to the medical oncology clinic with a 6-month history of a progressively worsening condition of tingling and unsteadiness while walking. She was diagnosed with ovarian cancer in November 2016 and was also operated on, which was followed by six cycles of carboplatin plus paclitaxel adjuvant treatment. She had no dizziness, dysphagia, diplopia, ptosis, urinary or gait incontinence, and retention. Considering a diagnosis of peripheral neuropathy due to chemotherapy in another center nearly three months ago, pregabalin was administered to the patient for these symptoms. However, it did not benefit the patient. Later, physical therapy and rehabilitation program was implemented, but even that did not benefit enough. Due to these symptoms, a brain MRI was performed and was reported as normal. She did not have any other disease or history of drug use. Also, there was no history of alcohol, smoking, and substance abuse nor any neurological disease, and malignancy was observed in her family.

On physical examination, her speech was found to be dysarthric, with hypoesthesia detected in the left lower extremity. Also, ataxia was observed in her walking. However, she had no motor deficits and...
dysdiadochokinesis. Other examinations were also normal. Muscle enzymes, thyroid function tests, vitamin D, and vitamin B12 levels were found normal. The CA-125 values showed an increase compared to the values observed three months ago (23â53 U/mL) (Normal range 0-30 U/mL). Due to the increasing level of CA-125, computer tomography and PET-CT scan were performed. A 1.5 cm diameter hypermetabolic nodular soft tissue lesion was found in the lateral pelvic approach of the left psoas muscle (SUVmax: 13.6). Brain MRI and EMG were planned to detect the cause of walking and balance disorders. No pathology was observed in the MRI and EMG, nor anything was found in the examinations and tests to explain the current condition of the patient. The paraneoplastic panel was taken from the blood, and cerebrospinal fluid (CSF) samples, and the anti-Yo antibodies were (++) found in both of them. Hence, the patient was diagnosed with PCD due to the clinical findings and positive anti-Yo in both samples.

Since the main treatment of paraneoplastic syndrome is the excision of the primary lesion, the gynecological oncology department was consulted further to seek permission for the excision of the recurrent mass. However, the patient was not eligible for surgery due to a history of multiple operations in the abdomen. Therefore, carboplatin, gemcitabine, plus bevacizumab treatment regimen was initiated for recurrent ovarian cancer. For effective treatment of PCD, plasmapheresis was performed two days before chemotherapy administration. It was also performed 5 times every other day. A significant improvement in walking and balance was achieved in the patient when she was admitted to the medical oncology outpatient clinic for the second cycle of chemotherapy after two weeks of discharge.

**DISCUSSION**

Here, we have described a patient who developed ataxia three years after the remission of ovarian cancer and was diagnosed with PCD. The patient’s symptoms had started nearly six months ago and had been worsening. The diagnosis of paraneoplastic syndrome, along with the mild elevation in the CA-125 level leads to the diagnosis of recurrent ovarian cancer. Generally, PCD occurs before the cancer diagnosis. However, in approximately 30% of the patients, the ataxic symptoms occur when the cancer is in its remission stage, as reported in our case. Therefore, when a patient is diagnosed with PCD, a whole-body screening is necessary to reveal the underlying malignancy.

The diagnostic criteria, based on the guidelines of the Paraneoplastic Neurological Syndrome Euronetwork in 2004, requires the development of a severe pancerebellar syndrome in <12 weeks with no MRI evidence of cerebellar atrophy, except in some cases, it is expected considering the patient’s age. In our case, although it took about six months to develop the symptoms, the past three months saw worsening of them. Also, no significant changes were observed in the cerebellum in the MRI scan, which also supported the diagnostic guidelines. Similarities and differences between our case and the Anti-Yo associated PCD characteristics are shown in detail in Table 1. The PCD diagnosis was verified by identifying anti-Yo antibodies in both cerebrospinal fluid and serum.

There is a strong association between PCD and anti-Yo, but its pathological function is still not clear. Some studies suggest that the PCD17/cerebellar degeneration-related protein 2 (cdr2) harboring the leucine zipper motif can function primarily as a transcriptional regulator. Also, the presence of tumor-specific cytotoxic T lymphocytes (CTL) is linked to PCD.

Treatment of PCD is unfavorable, and patients usually have a poor prognosis. Plasmapheresis, intravenous immunoglobulin (IVIG), and cyclophosphamide are the treatment options. Since the effectiveness of plasmapheresis and IVIG treatments are similar, we preferred plasmapheresis over IVIG, and it was also easily accessible in our center. It is very important to treat underlying malignancy with surgery or chemotherapy. We administered chemotherapy in the presented case because the patient was not eligible for re-surgery. Only limited neurological improvements were achieved in the ovarian cancer patients with PCD after following a combination of treatment. The long term survival rates were reported to be less than 25% in PCD patients.

In conclusion, when patients have unexplained neurological symptoms and a history of cancer, a
paraneoplastic syndrome should be considered, along with an investigation of underlying malignancy. Also, the anti-Yo antibody is a very important marker for PCD. Though the prognosis is poor, further research on the pathogenesis of PCD may lead to more effective treatment options.

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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.

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### TABLE 1: Similarities and differences between our case and the anti-Yo associated PCD characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Anti-Yo Mediated PCD Characteristic</th>
<th>Our Case</th>
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<tbody>
<tr>
<td>Duration of Symptoms Development</td>
<td>&lt;12 weeks</td>
<td>6 months</td>
</tr>
<tr>
<td>Diagnosis Time</td>
<td>Preceding the cancer diagnosis</td>
<td>PCD led the diagnosis of recurrence</td>
</tr>
<tr>
<td>Type of Malignancy</td>
<td>Usually pelvic and gynecological cancers</td>
<td>Ovarian cancer</td>
</tr>
<tr>
<td>Gender</td>
<td>Female Predominance</td>
<td>Female</td>
</tr>
<tr>
<td>Laboratory Findings</td>
<td>Non-specific</td>
<td>Non-specific</td>
</tr>
<tr>
<td>MRI Findings</td>
<td>Non-specific</td>
<td>Non-specific</td>
</tr>
<tr>
<td>Treatment Options</td>
<td>Plasmapheresis, IVIG, Cyclophosphamide</td>
<td>Plasmapheresis was preferred.</td>
</tr>
</tbody>
</table>

### Authorship Contributions