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Case Report

Paraneoplastic Neurologic Syndrome Associated with Fallopian Tube Cancer: A Case Report

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Keywords

Paraneoplastic neurological syndromes · Paraneoplastic cerebellar degeneration · Fallopian tube cancer

Abstract

Introduction: Paraneoplastic neurological syndrome (PNS) was identified as a rare and unique clinical complication of primary tumors. Paraneoplastic cerebellar degeneration, a subtype of PNS, involved an immune-mediated attack on cerebellar Purkinje cells, resulting in a series of cerebellar symptoms. ***Case Presentation:*** We report a case of an elderly female patient who presented with subacute cerebellar symptoms, positive anti-YO antibody, and elevated CA-125 levels. Further examination revealed a fallopian tube malignancy. After surgery, intravenous immunoglobulin and glucocorticoid treatment, the oncological response was satisfactory, but the neurological symptoms did not improve. ***Conclusion:*** This case illustrates the importance of considering a paraneoplastic etiology in patients with unexplained neurological manifestations and emphasized the necessity of appropriate management and early treatment of the primary malignancy.

Introduction

Paraneoplastic neurological syndromes (PNSs) were defined as the pathologic involvement of the nervous system in the course of malignancy [1]. In approximately 60% of patients, the onset of neurologic symptoms preceded the diagnosis of cancer [2]. PNS was a

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rare condition, with an incidence of 3 cases per million person-years and a prevalence of 4/100,000 person-years reported in recent studies [3].The most common PNS was limbic encephalitis (31%), followed by paraneoplastic cerebellar degeneration (PCD) (28%) and encephalomyelitis (20%) [4]. Anti-Yo, anti-Hu, anti-Tr, anti-Ri, anti-Ma2, anti-VGCC, anti-mGluR1, and numerous other anti-neuronal antibodies were linked to PCD [5, 6], with a median age of onset around 60 years [7]. Yo-PCD was most commonly associated with high-grade serous ovarian cancer [8]. At the time of diagnosis, most patients have advanced, widespread metastasis (stage III or IV).

The diagnostic criteria for PCD, defined in 2004 [1]and updated in 2021 [9], involve three steps: first, recognition that paraneoplastic disease was likely to be present, with as much clarity as possible about the nature of central nervous system involvement; second, detection of neuronal antibodies in serum and cerebrospinal fluid (CSF); and third, identification of the underlying malignancy. Although these immune-mediated diseases had been recognized for many years, the pathogenesis remains unclear. Due to the rarity of the disease, optimal therapies had not been established and successful treatment of this type of disease remained elusive.

Case Presentation

A 65-year-old female patient was admitted to the Department of Neurology with symptoms of headache, vertigo, dizziness, postural imbalance, gait instability with a tendency to fall, and slurred speech. Physical examination showed blood pressure of 147/95 mm Hg, pulse of 75 beats/min, and temperature of 36.5°C. Her reproductive history included menarche at age 12, G1P1, and menopause at age 45.

Neurological examination revealed clear consciousness, unclear speech, basic answers to questions, equal round and large bilateral pupils, sensitive light reflex, normal eye movement, normal symmetry of bilateral nasolabial fold, central tongue extension, normal pharyngeal reflex, normal muscle strength and muscle tension in limbs, and normal bilateral deep and superficial sensory symmetry. Tests for bilateral finger-to-nose, rotation, heel-to-knee, and tibial functions were inaccurate. The lying-up test was positive. Tendon reflexes were symmetrical and normal, and pathological signs in the lower extremities were negative. The meningeal irritation was negative. The patient was unable to complete gait and standing tests with eyes closed due to difficulty in standing.

Laboratory tests showed albumin was 29.7 g/L (normal range: 35–50 g/L). Routine blood tests, liver function tests, renal function tests, coagulation tests, infectious disease tests, and rheumatic tests were all normal. Electrocardiogram, chest CT, head CT, and head magnetic resonance diffusion-weighted imaging showed no obvious abnormalities (shown in Fig. 1).

CSF analysis: routine analysis was within normal limits. Metagenomic next-generation sequencing of CSF showed that a positive anti-Yo antibody. Tumor markers for ovarian malignancy indicated elevated CA-125 levels at 533 U/mL (normal <35 U/mL).

Further transvaginal sonography revealed a right ovarian mass, possibly a teratoma (O-RADS2 class), with no significant mass echo in the left adnexa (shown in Fig. 2). Considering the abnormal elevation of tumor markers, further positron emission tomography (PET) scan showed multiple nodules in the pelvic and abdominal cavity with active metabolism. A malignant tumor was suspected, with the uterus or ovary as possible origins (shown in Fig. 3).

Based on these antibodies, the characteristic cerebellar symptoms, and her known oncological disease, we diagnosed the patient with PCD secondary to a gynecologic carcinoma. Prior to surgery, the patient was started on steroids, receiving intravenous methylprednisolone

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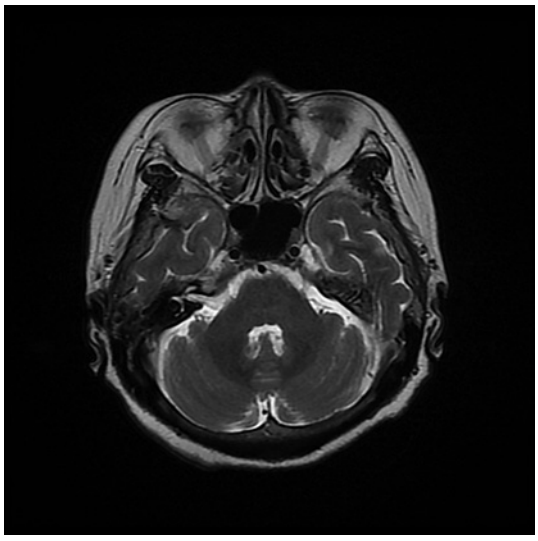

Fig. 1. Head MRI diffusion-weighted imaging.

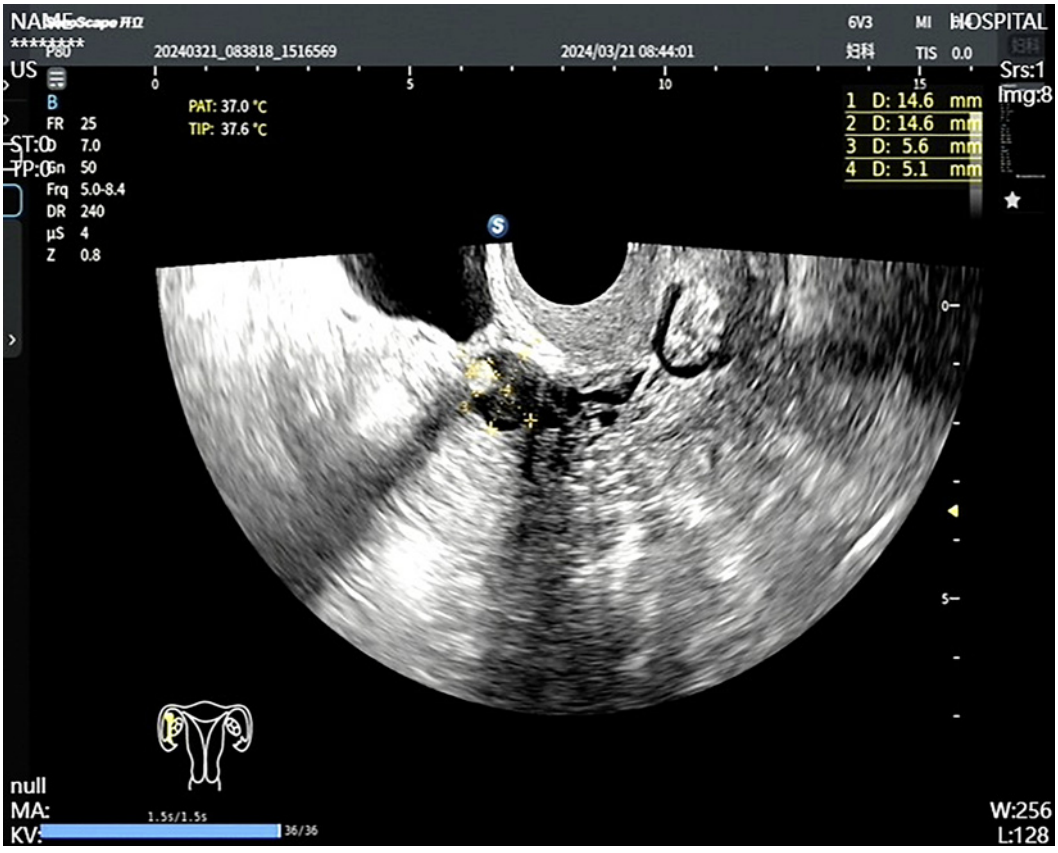

Fig. 2. Transvaginal sonography of right ovarian mass.

500 mg once daily for 5 days, followed by oral methylprednisolone 24 mg once daily. Intravenous immunoglobulin at 20 g per day was administered for 5 days. After Multidisciplinary treatment consultation, a surgery plan was formulated. The patient was transferred to the Department of Gynecological Ward for further radical surgery, including total hysterectomy,

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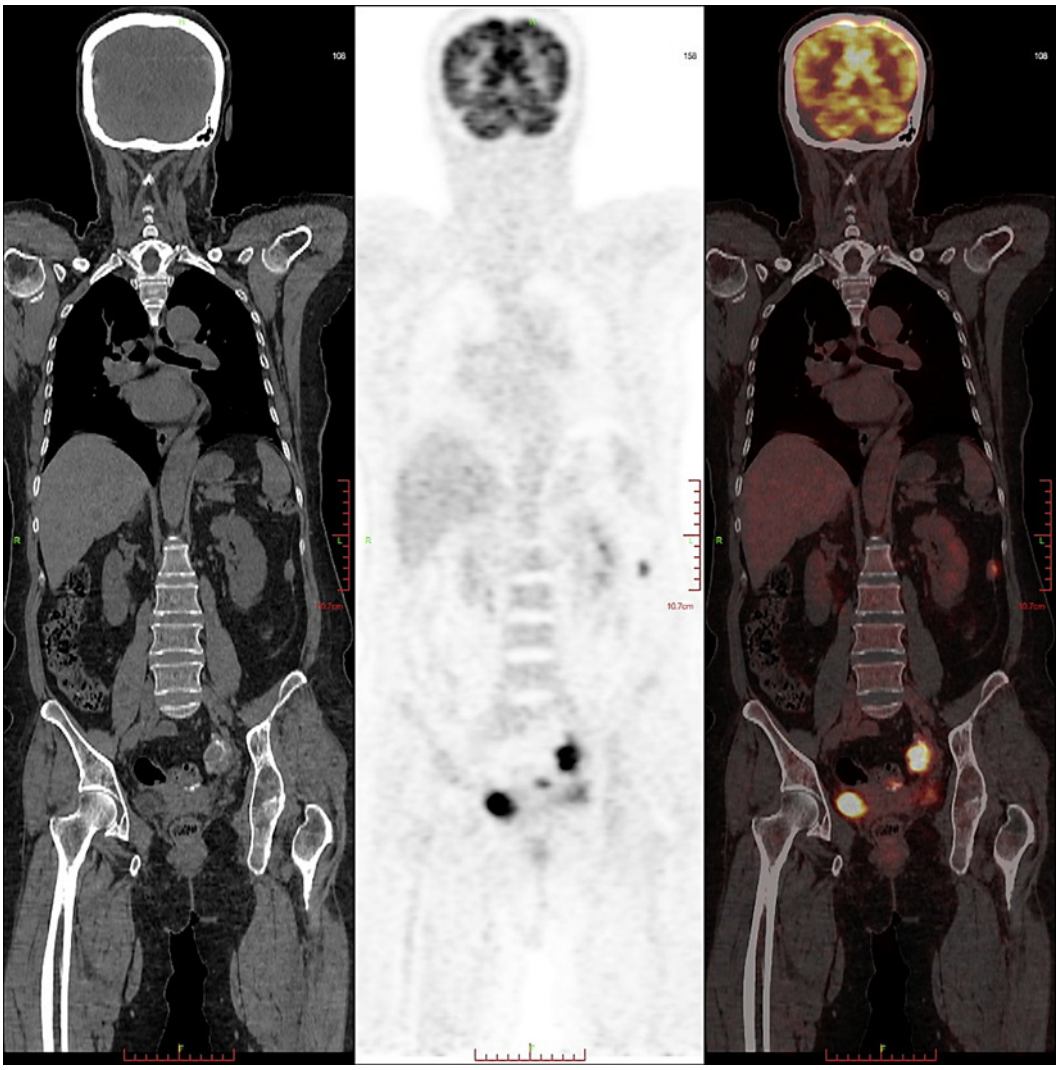

Fig. 3. PET scan showed multiple nodules in the pelvic and abdominal cavity with active metabolism.

bilateral salpingo-oophorectomy, pelvic lymph node dissection, para-aortic lymph node dissection, and omentum resection. During the operation, the tumor grew from the left fallopian tube and a teratoma was found in the right ovary. The operation process was satisfactory and achieved RO status. Postoperative pathology revealed high-grade serous carcinoma of the fallopian tube (stage IIIC). After informed consent was obtained, chemotherapy with Taxol-carboplatin every 3 weeks was administered. Following the first chemotherapy cycle, the CA-125 value decreased significantly (CA-125 = 64 U/mL), but the neurological dysfunction did not improve. The results of genetic testing showed that the patient was positive for BRCA2 germline mutation (Fig. 4).

Discussion

According to the diagnostic criteria for PNS, this case was considered a definite diagnosis. The etiology of PCD is thought to be a cross-reactive immune response in which antibodies against antigens in tumor cells attack the same antigens present in the

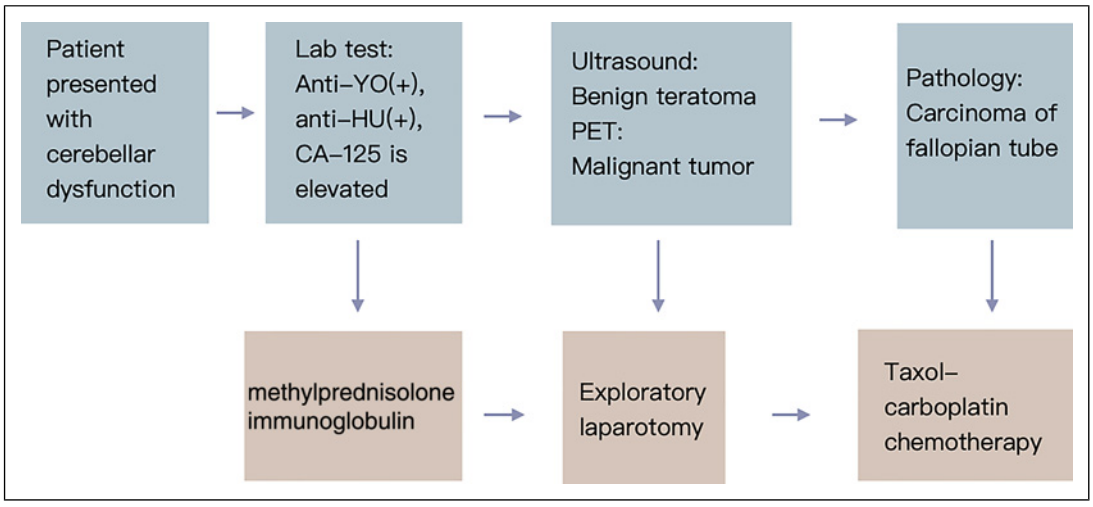

Fig. 4. Timeline of important events.

cerebellum. PCD typically progressed rapidly, causing irreversible damage and poor prognosis due to tumor neural antibodies causing neuronal damage and Purkinje cell loss via cytotoxic T cells, leading to pan-cerebellar dysfunction. Given the limited number of published cases of PCD associated with tumor worldwide, no definitive treatment regimen for PCD has been established. Current treatment modalities for PCD focus on inducing tumor remission (e.g., surgery, radiotherapy, and chemotherapy) and immunosuppression against abnormal immune responses. In the treatment of paraneoplastic neurological disorders, treatment of the tumor is essential, as successful tumor remission can clear the foci of persistent immune activation and may lead to stabilization or improvement of the neurological syndrome [10]. Glucocorticoids and intravenous immunoglobulin were used, and these treatments must be individualized by a multidisciplinary team including neurologists and physicians treating the primary tumor.

Relatively, patients with anti-Yo, anti-Hu, and anti-CV2/CRMP5 were the most difficult to treat and had the worst prognosis [4]. Crucially, all features of this disease involve the death of target neurons, and neurological symptoms developing with depletion of neuronal reserves. Since neurons do not regenerate, the typical course of these diseases is neurological decline ending in a fixed manner, with neurological deficits. Therefore, the timing of treatment initiation was critical to prevent irreversible neurological damage. This suggested that earlier diagnosis of gynecologic tumors could lead to better neurological prognosis and longer survival times.

Paraneoplastic symptoms, although rare, are an important part of the clinical manifestations of malignant tumors. In many cases, PNS symptoms precede the actual cancer diagnosis. Thus, awareness of this association is important in early diagnosis, which can significantly affect patient outcomes [11].

In addition, this patient showed no evidence of malignancy on ultrasound, PET-CT, and tumor markers indicated malignancy, and finally, surgery confirmed fallopian tube cancer. Gynecologic tumors associated with PNS are rare. All the cases reported so far have been primary ovarian cancer, whereas here, the patient had primary fallopian tube cancer. Therefore, it reminds us that even though vaginal ultrasound plays an important role in the discrimination of gynecological lesions, the missed diagnosis of fallopian tube cancer by ultrasound cannot be ignored, and attention should be paid to it.

Conclusion

PNSs and PCD coexisting gynecologic tumors are rare. Earlier diagnosis of gynecologic tumors could lead to better neurological prognosis and longer survival times. If the patient has elevated tumor markers, gynecological ultrasound and PET are necessary in clinical practice.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request. Ethical approval is not required for this study in accordance with local or national guidelines. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000542885).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Y.W. and H.W. were responsible for data acquisition; J.G. was responsible for wrote the first draft of the manuscript; and J.W. assisted and guided the reviewed data extraction. All authors critically revised the protocol and manuscript. J.W. was responsible for the final approval of the manuscript.

Data Availability Statement

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from the corresponding author (wangj425@mail.sysu.edu.cn).

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