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CASE REPORT

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Laparoscopic management of fallopian tube carcinoma with paraneoplastic cerebellar degeneration

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Abstract An asymptomatic tumor of the fallopian tube with elevation of serum CA125 concentration was found in a 75-year-old woman during a search for primary malignancy that was causing paraneoplastic cerebellar degeneration with a positive anti-Yo antibody. Since there were no apparent metastatic lesions detected by image diagnostic procedures, a diagnosis of early fallopian tube carcinoma was made preoperatively. After confirmation of the presence of a left tubal tumor without apparent invasion to the adjacent organs and peritoneal metastasis, laparoscopic salpingo-oophorectomy was subsequently performed. The histopathological diagnosis was of moderately differentiated serous adenocarcinoma of the fallopian tube with marked plasma cell infiltration. After surgery, the CA125 value immediately decreased, and there was no evidence of tumor recurrence noted thereafter. The patient died 51 months after surgery due to progression of neurological symptoms.

Keywords Fallopian tube carcinoma · Paraneoplastic cerebellar degeneration · Laparoscopy

Primary fallopian tube carcinoma is an uncommon malignancy that accounts for approximately 0.3% of all gynecological cancers and typically affects postmenopausal women [1]. Furthermore, on extremely rare occasions [2–4], fallopian tube carcinoma is known to associate with paraneoplastic cerebellar degeneration (PCD), which is a remote complication of malignant tumor without any relation to metastasis, malnutrition or damage due to chemotherapy [5, 6]. This disorder evolves clinically as progressive ataxia, dysarthria, and nystagmus, and pathologically as extensive loss of cerebellar Purkinje cells [6]. The presence of anti-Yo antibody directed against Yo antigens shared by Purkinje cells and tumor cells in serum and cerebrospinal fluid of the patients suggests an autoimmune mechanism for this disorder [7]. Since the onset of cerebellar dysfunction usually precedes the manifestation of cancer-related symptoms by many months [5], extensive search for occult primary malignancy is essentially important for early diagnosis and treatment of cancer in cases of PCD.

In this paper, we present a rare case of anti-Yo antibody-positive PCD with asymptomatic fallopian tube carcinoma that was successfully diagnosed and managed by laparoscopy.

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Case report

A 75-year-old, gravida 4, para 3, woman with a disease history of hypertension and osteoporosis noticed gait disturbance. Since speech disturbance appeared 3 months later and progressively worsened, she was referred to the Neurology Department of Gifu Prefectural Tajimi Hospital 6 months later. Neurological examination showed saccadic eye movement, downbeat nystagmus, slurred and unclear speech, mild weakness of the proximal limb muscles, and marked limb and truncal ataxia. Cranial MRI showed marked cerebellar atrophy without involvement of the brain stem (Fig. 1a). Since a positive serum titer for anti-Yo antibody that recognizes 58 kDa Yo antigen was identified by Western blotting [2] (Fig. 1b), PCD was strongly suspected, and the search for primary malignancy was initiated. Although the patient did not show any specific cancer-related symptoms, whole-body CT scan showed the presence of pelvic tumor. She was referred to our outpatient clinic for gynecological examination. Pelvic examination indicated the presence of a tumor in the left adnexal region. Transvaginal ultrasonographic examination (Fig. 2a) and MRI scan (Fig. 2b) showed the presence of an adnexal tumor measuring 60 mm×37 mm, with a solid/cystic mixed pattern. There were no apparent metastatic lesions. Serum

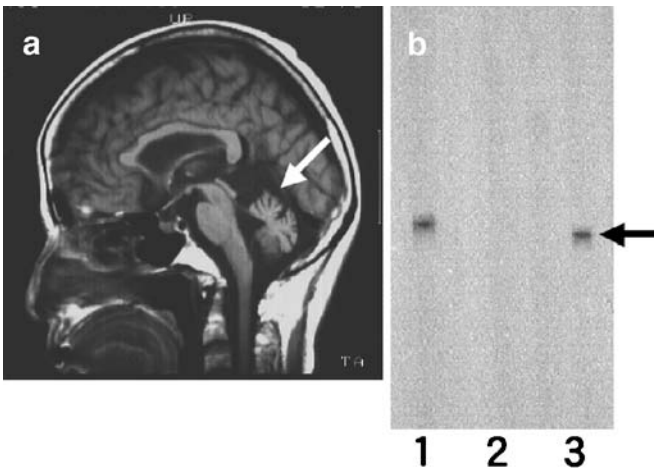

Fig. 1 **a** Sagittal sectional view of cranial MRI demonstrated marked cerebellar atrophy (*arrow*) without involvement of the brain stem. **b** Western blot analysis of the patient's serum for the presence of anti-Yo antibody detected a 58 kDa Yo antigen (*arrow*). *Lane 1* positive control, *lane 2* negative control, *lane 3* patient's serum

CA125 value showed a slight elevation (58 U/ml), but other tumor markers (alpha-fetoprotein 4.3 ng/ml, carcinoembryonic antigen 2.3 ng/ml, CA19-9 5.8 U/ml) were within normal ranges. Based on these findings [8, 9], a diagnosis of early fallopian tube carcinoma was made and surgical intervention was recommended. However, the patient declined surgery at that time due to a lack of cancer-related symptoms, and observation of the disease condition was chosen. Then, CA125 value gradually increased. When the CA125 value reached 149 U/ml, 2 months after the initial gynecological examination and 10 months after the first manifestation of neurological symptoms, the patient's family requested surgical consultation regarding the pelvic tumor. After informed consent, based on the understanding that surgical intervention might not cure either the cancer or the PCD, had been carefully obtained from the patient and family, laparoscopic surgery was chosen as a less invasive treatment.

Gasless laparoscopic surgery was performed as previously described [10]. Under laparoscopic observation, the left tube was enlarged due to hydrosalpinx (Fig. 3a), and a solid mass was noted in the fimbrial portion. However, there was no apparent invasion to the adjacent organs or peritoneal metastasis. Abnormal findings were not noted in the uterus and right adnexal tissue. A small amount of peritoneal fluid was present, but rapid cytological examination for presence of malignant cells gave negative results. The left adnexal tissue was carefully excised by EndoGIA (Tyco Healthcare Japan, Tokyo, Japan). The unruptured tumor was placed in an Endocatch (Tyco Healthcare Japan, Tokyo, Japan) and removed from the body through a 12-mm port. Duration of surgery was 58 min, and intraoperative blood loss was less than 50 ml. After surgery, the patient was admitted to the intensive care unit for immediate postoperative management of her general condition overnight then transferred to the gynecology ward the next day. There were no intraoperative or postoperative complications. The patient was moved to the neurology ward for rehabilitation 3 days after surgery. Adjuvant chemotherapy was not considered because of the patient's neurological condition.

The excised specimen was histopathologically examined. The main solid tumor was at the distal portion of the tube, while the proximal portion of the tube showed hydrosalpinx containing dark red fluid (Fig. 3b). Ovarian tissue was atrophic, and there were no malignant findings. The tumor in the fallopian tube was diagnosed as a moderately differentiated serous adenocarcinoma with marked plasma cell infiltration, which is a frequently observed phenomenon in PCD-related tumor tissue [5] (Fig. 3c). Although the tumor extended into the muscularis, there was no invasion to the serosal surface.

After surgery, the CA125 value immediately decreased, indicating successful removal of the fallopian tube carcinoma. There was no evidence to suggest tumor recurrence thereafter. However, anti-Yo antibody persisted and neurological symptoms gradually worsened. Two years

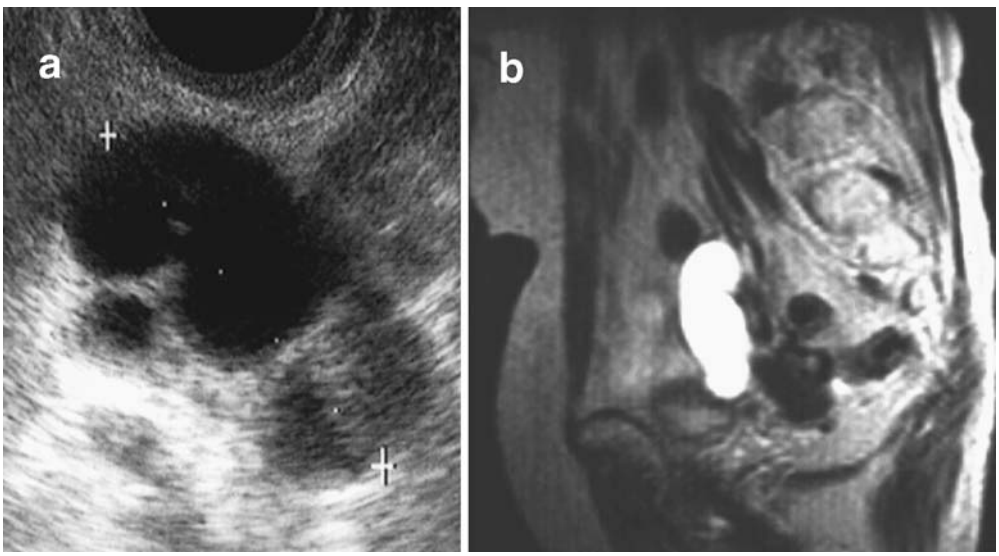

Fig. 2 **a** Transvaginal ultrasonographic image of the left adnexal mass (60 mm×37 mm) showing a solid/cystic mixed internal pattern. **b** Sagittal abdominal MRI showing a tumor with tubular structure with a high signal intensity on T2-weighted image

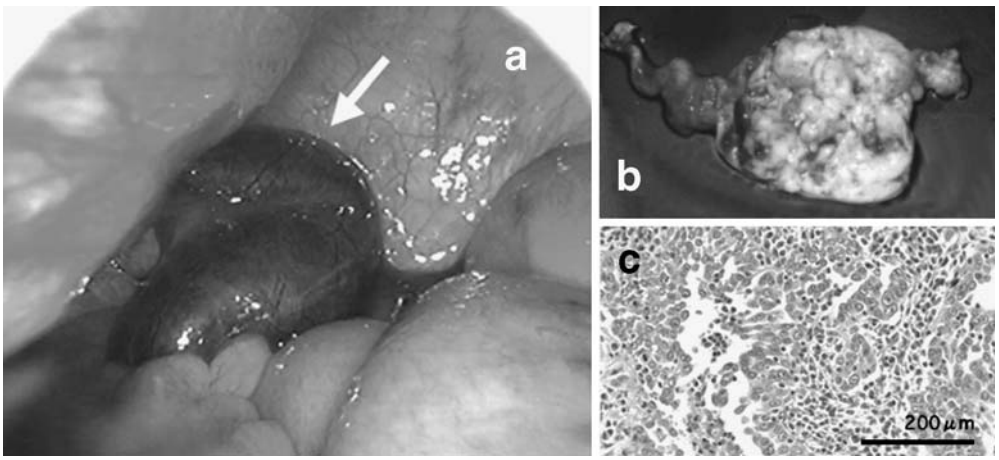

Fig. 3 **a** Laparoscopic view of the left tubal tumor manifesting as hematosalpinx (*arrow*). **b** Gross appearance of the excised tumor showing solid components in the distal portion of tube. **c** Histological findings of the tumor showing marked plasma cell infiltration around tumor cells (hematoxylin–eosin, *scale bar* 200 μm)

after surgery, the patient became bedridden and died 51 months later due to progression of neurological symptoms. Autopsy was not permitted by the family.

Discussion

PCD is a rare remote effect of malignant tumor [5, 6] that is characterized clinically by evolving cerebellar dysfunction and histopathologically by widespread loss of cerebellar Purkinje cells. Evidence is accumulating that patients with PCD have a particular autoantibody referred to as anti-Yo antibody (also known as anti-Purkinje cell antibody) that possesses cross-reactivity to the Yo antigen of tumor cells as well as Purkinje cells [5]. Although the pathogenesis of PCD remains unclear, it has been hypothesized that cerebellar degeneration is a result of an autoimmune-induced destruction of Purkinje cell function by anti-Yo antibody generated against cross-reactive tumor cell Yo antigen [7].

In patients with anti-Yo antibody-positive PCD, gynecological malignancies are known to be frequently associated [5, 6]. The majority of these cases involve ovarian cancer, and, on rare occasions, tubal carcinoma is known to be associated with PCD [2–4]. Two approaches can be used to treat paraneoplastic neurologic syndrome [11]. The first treatment is directed toward the underlying tumor, while the second approach focuses on the autoimmune disease causing the cerebellar dysfunction. For the neurologist, paraneoplastic syndrome is a therapeutic challenge, and medical treatment for paraneoplastic syndrome is generally unsatisfactory [7]. Therefore, early tumor detection and treatment by a gynecologist should be the primary objective in these patients. According to a review [11] of long-term clinical outcomes in cases of anti-Yo antibody-associated PCD, cancer progression was the cause of death in almost half of the patients, including a patient with advanced cancer. Most of these cancer-related deaths were due to the delay in diagnosis of the primary malignancy, and patients with early stage cancer showed a relatively favorable cancer-related prognosis. Manifestation of cerebellar dysfunction usually precedes the onset of symptoms of the primary malignancy by many months [11]. Therefore, early screening of anti-Yo antibody in patients with cerebellar degeneration is an important step before one initiates an extensive search for the primary tumor to achieve improvement of cancer-related prognosis in PCD patients. Further, it is known that the presence of anti-Yo antibody is important to predict the cancer-related prognosis of patients, since tumor progression in PCD patients with anti-Yo antibody is slower than usual [6], probably due to the suppression of tumor growth through antibody-mediated immune mechanisms by massive infiltrating inflammatory cells, as shown in the present case. Thus, the preoperative evaluation of cancer metastasis and invasion to local structures that drastically decreases the possibility of tumor control [11] should be carefully pursued before the treatment strategy for the individual case is developed.

Unfortunately, early detection and even cure of the cancer underlying PCD usually does not affect neurological symptoms in most cases, since cerebellar dysfunction stabilizes in the early stage after symptom onset before the cancer has been diagnosed and treatment initiated [5, 6]. This was also true in our patient, as anti-Yo antibody persisted even after the CA125 level had decreased and, without apparent recurrence of cancer, the neurological symptoms gradually worsened. However, cases in which the symptoms of cerebellar degeneration either improve or stabilize have also been reported [2]. Thus, early detection and treatment of the primary malignancy may contribute to improving the neurological prognosis in some patients as well as decreasing the incidence of cancer-related death.

When PCD-related primary gynecological malignancies are found, exploratory laparotomy has been traditionally chosen for diagnosis and treatment [2, 5, 6]. However, this more invasive treatment may worsen the general condition of a patient with cerebellar dysfunction. Along with advances in operative laparoscopic procedures and surgical equipment, recent advances in image diagnostic procedures [8] have facilitated the accurate evaluation of primary tumor and the presence of metastases. Therefore, if apparent metastatic regions are not recognized and early stage of primary malignancy is assumed preoperatively, as in the present case, a laparoscopic approach could be a less invasive procedure to diagnose and further treat the

primary cancer in a patient showing a relatively poor condition due to cerebellar dysfunction.

Further study is necessary to clarify the indications for laparoscopic treatment of primary malignancy in patients with PCD by accumulating additional cases. Both neurologists and gynecologists need to have sufficient knowledge of this rare disorder in order to improve the prognosis of PCD patients by early detection and treatment of the primary malignancy.

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