

A Rare Case of Anti-Yo Antibody Associated Paraneoplastic Sensory Polyganglionopathy in a Patient with Ovarian Cancer

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Abstract

Paraneoplastic cerebellar degeneration is a rare, fatal neuronal syndrome associated with ovarian, breast and lung cancers. Anti-Yo antibody mediated paraneoplastic cerebellar degeneration is known to be associated with gynecological malignancies, especially ovarian cancer. However, there are no reports of anti-Yo antibody associated predominant peripheral mixed sensory and motor neuropathy in patients with ovarian cancer. Hereby, we present a case of a 75-year-old female who predominantly developed peripheral mixed sensory and motor neuropathy after undergoing surgery and adjuvant chemotherapy for FIGO stage 3, high grade serous ovarian carcinoma. She presented approximately 11 months after completion of her chemotherapy with a history of progressive peripheral mixed sensory and motor neuropathy that affected both upper and lower limbs. There was no evidence of recurrent ovarian cancer.

Since paraneoplastic peripheral neuropathy is a rare disorder, timely diagnosis and early therapeutic intervention can achieve a better outcome, although management of paraneoplastic neurological disorders still remains a challenge for clinicians.

Keywords: Ovarian cancer, Paraneoplastic syndrome, Paraneoplastic sensory polyganglionopathy, Anti-yo antibodies, Paraneoplastic cerebellar degeneration

Introduction

Paraneoplastic syndromes are rare disorders triggered by an altered immune system response to a neoplasm. They are defined as clinical syndromes involving non-metastatic systemic effects that accompany malignant disease.¹ Paraneoplastic neurologic disorders are reported in 3%–5% of patients

with small-cell lung cancer, 15%–20% with thymomas, 3%–10% with B-cell or plasma-cell neoplasms and in less than 1% of breast and gynecological cancers.²

Paraneoplastic cerebellar degeneration is a rare, fatal neuronal syndrome associated with ovarian, breast and lung cancer patients. Anti-Yo antibody mediated paraneoplastic

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cerebellar degeneration is known to be associated with gynaecological malignancies, especially ovarian cancer. However there are no reports of anti-Yo antibody associated predominant peripheral mixed sensory and motor neuropathy in patients with ovarian cancer.

Case Presentation

We present a case report for a 75-year old female who predominantly developed peripheral mixed sensory and motor neuropathy. In March 2012, she underwent laproscopic vaginal hysterectomy (LAVH), bilateral salpingo-oophorectomy (BSO) and subtotal omentectomy for FIGO stage 3 high grade serous carcinoma with no residual macroscopic disease. The patient required a splenectomy due to intraoperative splenic injury, which failed to resolve by conservative management. She received an appropriate post-splenectomy immunization.

The patient underwent single agent chemotherapy with carboplatin AUC 5 in view of her co-morbidities that included uncontrolled AF. She completed six cycles of chemotherapy without any complications. Post-treatment CT scan of the chest, abdomen and pelvis showed no radiological evidence of disease progression or recurrence. At that time, the patient was considered disease-free.

She presented approximately 11 months post-completion of chemotherapy with a history of progressive peripheral mixed sensory and motor neuropathy that affected both upper and lower limbs. Her symptoms developed over a period of six months. The patient was hospitalized due to rapid worsening of her mobility. She was also found to have ataxia, binocular multidirectional nystagmus, diplopia and pseudoathetosis at a later stage.

Initial impression of a paraneoplastic sensory neuropathy was made. Investigations included an Electromyography (EMG); MRI head with contrast; MRI spine; CT scan of the chest, abdomen, and pelvis; and a lumbar puncture for cerebrospinal fluid (CSF) analysis. Other investigations included vasculitic screen and

immunology.

Positive findings included an EMG consistent with advanced predominantly sensory polyganglionopathy and positive anti-Yo antibodies. There was no evidence of recurrent ovarian cancer. The final diagnosis of paraneoplastic sensory polyganglionopathy was made. She was initially considered for plasma exchange but her general condition deteriorated and she was not a suitable candidate. The neurologist also considered a course of Intravenous immunoglobulin (IVIG) and steroids.

Unfortunately the patient experienced a rapid decline in her general condition and was managed conservatively with palliation of symptoms by specialist palliative care input. She died within six months of onset of neurological symptoms with predominately rapid decline in the last few weeks of her life.

Discussion

Paraneoplastic syndromes are rare disorders and are most commonly associated with small cell lung cancer, thymomas, B-cell neoplasm and rarely with gynaecological and breast cancer.

These disorders can affect any part of the nervous system. Different forms of paraneoplastic peripheral neuropathies include autonomic neuropathy, acute sensorimotor neuropathy, chronic sensorimotor neuropathy and vasculitic neuropathy.³

The presenting symptoms and signs of paraneoplastic syndromes are diverse. The neurologic disorder usually appears before the cancer has been identified. In many instances an initial search for cancer is unrewarding; the tumor is found months or even a few years after the appearance of the neurologic syndrome.⁴

Currently, it is thought that most or all paraneoplastic neurologic disorders are immune-mediated. Many patients with paraneoplastic syndromes have antibodies in their serum and cerebrospinal fluid that react with both the nervous system and the underlying cancer. The identification of these antibodies and their target neural antigens has substantially advanced the

ability to make an early diagnosis and contributed to the concept that paraneoplastic neurologic disorders are immune-mediated.⁴

Despite considerable overlap, each of these antibodies is associated with a limited range of clinical syndromes and a restricted sub-group of malignancies. Numerous onconeural antibodies are found to be related to paraneoplastic cerebellar degeneration (PCD). Examples include anti-Yo antibody with cancers of the breast and ovaries, anti-Hu antibody with small cell lung cancer, anti-Ri with breast cancer and anti-Tr antibody with Hodgkin's disease.⁵ In addition to antibody-mediated immune response, cytotoxic T-cell responses also appear to play an important role in the pathogenesis.

Anti-Yo antibody mediated paraneoplastic cerebellar degeneration is known to be associated with gynecological malignancies, especially ovarian cancer.^{6,7} The hallmark of paraneoplastic cerebellar degeneration is an extensive loss of Purkinje cells that might be associated with inflammatory infiltrates in the cerebellar cortex, deep cerebellar nuclei, and inferior olivary nuclei.²

Patients with PCD typically present with frequent, acute nausea, vomiting and dizziness, followed several days later by diplopia, dysarthria, gait instability, both truncal and appendicular ataxia, oscillopsia and dysphagia.⁸ However our patient presented with mainly peripheral mixed sensory and motor neuropathy that affected both upper and lower limbs. She was also found to have ataxia, binocular multidirectional nystagmus, diplopia and pseudoathetosis at a later stage. EMG was consistent with advanced predominantly sensory polyganglionopathy.

Paraneoplastic syndromes are considered to be immune-mediated hence treatment approaches include either removal of the source of the antigen or suppression of the immune response. The combination of either plasma exchange or intravenous immune globulin and immunosuppressive agents such as corticosteroids, cyclophosphamide, or tacrolimus can be used for patients whose conditions worsen.^{9,10,11}

There are no randomized controlled trials of

treatment for paraneoplastic neuropathy. Current evidence comes from case series, case reports or expert opinion.¹² There are isolated case reports of benefit for various immunotherapeutic interventions.^{13,14}

Paraneoplastic cerebellar degeneration is associated with neuronal loss that develops sub-acute, hence treatment is often delayed and ineffective.

Conclusion

Paraneoplastic peripheral neuropathy is a rare disorder. Timely diagnosis and therapeutic intervention can achieve better outcomes. Early identification of symptoms is important to guide appropriate investigations and management. However the rarity of conditions poses difficulties for clinicians. Despite significant advances in treatment of ovarian cancers, management of paraneoplastic neurological disorders remains a challenge for clinicians.

Conflict of Interest

No conflict of interest is declared.

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