Paraneoplastic neuromyelitis optica spectrum disorder associated with breast cancer: a case report and literature review

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Case Report

Keywords: Neuromyelitis optica spectrum disorder, paraneoplastic syndrome, breast cancer

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Abstract

Background: Neuromyelitis optica spectrum disorder (NMOSD) is an astrocytopathy with demyelinating lesions caused by aquaporin 4 (AQP4) antibodies. Although most commonly an idiopathic autoimmune condition, NMOSD may also occur as a paraneoplastic syndrome in rare instances.

Case presentation: Herein, we report a rare case of a 60-year-old woman with paraneoplastic NMOSD associated with breast cancer.

Conclusions: Our findings increase the recognition that NMOSD may present as a paraneoplastic neurological syndrome associated with breast cancer. Our case also raises awareness of an important complication of neurological complications of breast cancer. Early diagnosis of paraneoplastic NMOSD may be imperative for a better prognosis.

Keywords: Neuromyelitis optica spectrum disorder, paraneoplastic syndrome, breast cancer.

Background

Neuromyelitis optica spectrum disorder (NMOSD) is a group of relapsing, inflammatory, demyelinating neurologic disorders involving the central nervous system associated with antibodies against aquaporin-4 (AQP4) [1]. Paraneoplastic syndromes are remote effects of cancer caused by an autoimmune response triggered by tumor cells. However, although most commonly an idiopathic autoimmune condition [1], there were only a few cases of NMOSD presenting paraneoplastic syndromes, such as mature B-cell neoplasm [2], hepatic metastasis from a small-bowel neuroendocrine tumor [3], stomach carcinoid tumor [4], lung carcinoma [5, 6], esophageal cancer [7], adenocarcinoma of the lung and breast [8], squamous cell lung, ovarian carcinoma and adrenocortical carcinoma [9], esophageal Adenocarcinoma [1]. As a result, NMOSD in elderly patients should raise the suspicion of paraneoplastic etiology.

To the best of our knowledge, there were only a few cases of NMOSD occasionally develop carcinomas, however, the underlying mechanism for these rare cases is not well characterized [9]. Herein, we report a case of a 60-year-old woman with paraneoplastic NMOSD associated with breast cancer.

Case Presentation

A 60-year-old woman presented with speech difficulties for 10 days after an upper respiratory infection. She was diagnosed with breast cancer three years ago and was treated with surgery, radiation and chemotherapy. Neurological examinations revealed speech difficulty, slight weakness of both lower limbs, positive Hoffmann sign, hyperactive deep tendon reflexes on both sides. Left ankle clonus was positive.

Brain magnetic resonance imaging (MRI) showed some abnormal signals involving in the splenium and the body of corpus callosum, midbrain, bilateral internal capsule, with slight contrast (Fig. 1). Contrast

enhanced cervical MRI indicated T2 hyperintense lesions involving C3-T5 (Fig. 2). Contrast enhanced thoracic MRI showed T2 hyperintense lesions extending from T7-T12 (Fig. 3). High resolution CT of chest found not any lung cancer. PET-CT found that the right breast cancer.

The antibodies of human immunodeficiency virus and neurosyphilis were negative. The results of cerebrospinal fluid (CSF) were increased leucocyte count (38/?L, reference range 0-8/?L) and protein concentration (189mg/dl, reference range 15-45 mg/dl). CSF IgG was 16.30 mg/dl. The myelin basic protein both in serum and CSF were positive, however, the oligoclonalbands in serum and CSF were negative. The Ig index and blood-brain barrier permeability were both increased. AQP-4 autoantibodies were detected both in serum and in CSF. The inflammatory, immune and infectious biomarkers of both CSF and serum were also unremarkable. The biomarkers of tumor and paraneoplastic syndrome in serum were normal. The The antibodies of anti-ganglioside and autoimmune encephalitis were unremarkable.

The weakness of both lower limbs gradually decreased to I level after her admission. The D-dmmer was 17.83(mg/L FEU), and lower extremity ultrasound showed obvious venous thrombosis in both lower limbs and right peroneal vein. The computed tomography pulmonary angiography found the pulmonary embolism. She was finally diagnosed as paraneoplastic NMOSD. She was treated with intravenous methylprednisolone 1g daily (gradually reduced for 3-5 days) and intravenous immunoglobulin 25g daily for 5 days. After 3 weeks, the patient's speech difficulties were slightly improved. After 3 mouths follow up, the patient made a relatively good recovery with both clinical and radiological improvement.

Discussion

NMOSD is one of demyelinating, autoimmune disease affecting the central nervous system. In most cases, NMOSD is associated with autoantibodies targeting AQP-4. Herein, we reported a rare case of a 60-year-old woman with paraneoplastic NMOSD associated with breast cancer.

Autoimmune diseases are sometimes associated with neoplasms. Patients with NMOSD occasionally develop carcinomas. Several case reports have demonstrated AQP-4 expression in tumor tissue, and the prevalence of cancer in patients with NMOSD associated with positive AQP4-IgG antibodies has been reported incidentally in 0.02% [9]. There are quite rare cases presenting as a paraneoplastic syndrome in association with carcinomas [10], such as carcinoma of lung [5, 6], esophageal [7], small-bowel neuroendocrine tumor [3], carcinoid tumor of the stomach [4], thymoma, breast carcinoma, lymphoma. As a result, the possibility of underlying malignancy should be considered in patients with the diagnosis of NMOSD, especially in the elderly. What triggers the production of AQP4-IgG antibodies in patients with malignancy has been poorly understood, but it has been speculated that such antibody production is triggered by an immune response against a patient's cancer. [1] However, AQP-4 is also expressed in neurologically normal patients' tumors, suggesting additional factors are required for NMOSD induction in patients with cancer [11]. AQP4-IgG may involve in the pathogenesis of paraneoplastic NMOSD, however, its clinical utility and underlying exact mechanism warrant further investigations.

Breast cancer has been proved to be related paraneoplastic endocrine syndromes with neurologic syndromes. As for the breast carcinoma found in NMOSD, there was an observation about 41 patients with positive NMO-IgG, six malignancies were identified in five NMOSD seropositive patients, including breast carcinoma (three cases), lymphoma, cervical carcinoma and leiomyosarcoma (in a patient who also had breast carcinoma) [12]. Furthermore, from another studies of 34 paraneoplastic NMOSD cases, 11 (32%) cases had breast carcinoma [13]. We should attach importance to the detection of paraneoplastic etiology, especially the breast carcinoma in NMOSD cases.

The strengths of our case were showed as follows. Firstly, we reported a rare case of a 60-year-old woman with paraneoplastic NMOSD associated with breast cancer. The final of diagnosis of paraneoplastic NMOSD was performed, which was based on the patient's progressing neurological symptoms, MRI findings both in brain and spine, and breast cancer, the positive AQP-4 autoantibodies, and the effect of treatment. Secondly, our case was finally diagnosed as paraneoplastic NMOSD after the occurrence of breast cancer with the interval of 3 years. As a result, clinical findings suggestive of NMOSD in elderly patients should raise the suspicion of paraneoplastic etiology and warrants thorough investigations for an underlying cancer, with long-term follow-ups, at least for several years. Thirdly, this case was combined with the diagnosis of pulmonary embolism and venous thrombosis in both lower limbs and right peroneal vein, which may be due to the hypercoagulable state from the breast cancer, which could also support the paraneoplastic syndrome may also occur in NMOSD cases.

Conclusion

In summary, we herein reported a rare case of a 60-year-old woman with paraneoplastic NMOSD associated with breast cancer. Our case may extend the context that AQP-4 may have a paraneoplastic basis in some cases. Early diagnosis of paraneoplastic NMOSD is of great importance for a better outcome.

Abbreviations

NMOSD: Neuromyelitis optica spectrum disorder; PS: Paraneoplastic syndrome; AQP4: aquaporin-4; MRI: magnetic resonance imaging; CSF: cerebrospinal fluid.

Declarations

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us data collection, analysis, and interpretation of data.

Availability of Data and Materials

Not applicable

Authors' contributions

JLY, ZJJ and WQ examined, evaluated the patient. JLY and ZJJ drafted and revised the manuscript. WLH participated in the design of the case-report and helped to draft the manuscript. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

The study was approved by the Institutional Ethical Committee of Beijing Chaoyang Hospital, Capital Medical University.

Consent for publication

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 of this journal.

Competing interests

The authors declare that they have no competing interests

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Figures

Figure 1

Brain magnetic resonance imaging (MRI) showed some abnormal signals involving in the splenium and the body of corpus callosum, midbrain, bilateral internal capsule, with slight contrast.

Figure 2

Contrast enhanced cervical MRI indicated T2 hyperintense lesions involving C3-T5.

Figure 3

Contrast enhanced thoracic MRI showed T2 hyperintense lesions extending from T7-T12.

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