ISSN: 2573-9565

Case Report

Journal of Clinical Review & Case Reports

One Case of Anti-Yo Antibody Positive Subacute Cerebellar Degenera

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FUNDING
National Nature Science Foundation of China (81771795).

Submitted:22 Jun 2020; **Accepted**: 02 July 2020; **Published**: 10 July 2020

Abstract

Subacute cerebellar degenera also known as paraneoplastic cerebellar degeneration, is one of the typical neurological lesions caused by paraneoplastic neurological syndrom. It is caused by changes in the immune response. A case of tumor-negative anti-Yo antibody-positive subacute cerebellar degeneration is reported to strengthen clinicians' understanding of the disease. Early diagnosis of subacute cerebellar degeneration is essential to improve patient survival and quality of life.

Keywords: Subacute Cerebellar Degenera; Paraneoplastic Neurological Syndrome; Anti-Yo Antibody

Introduction

Paraneoplastic neurological syndrom (PNS) is a rare paraneoplastic syndrome caused by changes in immune response, which causes damage to peripheral nerves, central nervous, neuromuscular junction and/or muscles due to distant effects of tumors, excluding direct infiltration or compression of tissues by cancer and neurological damage due to radiotherapy, chemotherapy, and immunotherapy in tumor therapy [1, 2]. PNS is more common in middle-aged and elderly patients and presenting subacute progressive course [3]. The results of an epidemiological study conducted by Alberto Vogrig et al. showed that the most common PNS are: limbic encephalitis,subacute cerebellar degenera (SCD), and encephalomyelitis. Anti-Yo antibody is the antibody with the highest positive detection rate, and the report of 89 patients diagnosed with PNS in this study indicated that the positive rate of anti-Yo was 30% [4].

SCD is the PNS that involves the central nerve system and is most harmful and easy to identify [5]. SCD is a neurological syndrome characterized by cerebellar ataxia caused by tumor-induced autoimmunity against cerebellar antigens, which is a rare non-metastatic neurological complication, also known as paraneoplastic cerebellar degeneration (PCD) [6].

SCD mainly leads to acute and subacute cerebellar dysfunction. The disease can deteriorate within a few days or weeks, showing ataxia of limbs and trunk, severe dysarthria, diplopia, nystagmus, nausea, vomiting, etc [7]. It can also be accompanied by cognitive dysfunction and cerebellar cognitive affective syndrome [8]. Psimaras et al. found that 93% of PNS patients had cerebrospinal fluid abnormalities in their study, including cerebrospinal fluid protein elevation, lymphocyte proliferation, oligoclonal bands, etc [9].

SCD is closely related to autoimmunity, and anti-Yo antibody is the most common among nearly 30 different autoantibodies of SCD [10]. Anti-Yo antibody, also referred to as Purkinje cell antigen type 1 antibody, is produced by immune reaction with potential tumor cells, exists in the serum and cerebrospinal fluid, combines with cytoplasm of cerebellar Purkinje cells in the form of particles, and cross-reacts with the antigen of Purkinje cells, resulting in cell death, but the exact pathogenesis is still unclear [11]. Kråkenes et al. confirmed that CDR2L is the main target antigen of Yo antibody in SCD [12].

It has been reported that SCD is often associated with breast cancer, ovarian cancer, lung cancer, and Hodgkin's lymphoma [13]. In the majority of patients, neurological symptoms appear before the discovery of the tumor. The European PNS diagnostic standard suggests that SCD can be confirmed even if no primary tumor lesion is found, with cerebellar syndrome accompanied by characteristic tumor-specific antibodies (anti-Yo, Hu, Ri, CV2, Ma2) [14]. A case of subacute cerebellar degeneration with positive anti-Yo antibody diagnosed and treated in our hospital in November 2019 is summarized and analyzed as follows.

Case Presentasion

History of Present illness: a 64-year-old female patient was admitted to our hospital on November 20, 2019 due to "paroxysmal dizziness for more than 1 month and progressive aggravation for 17 days". The patient had sudden dizziness during activities more than 1 month before admission, manifested as paroxysmal head drowsiness, once every several days, without nausea, vomiting, etc, without any attention or treatment. At about 13:00 on November 3, 2019 (17 days before admission), the patient suddenly developed persistent dizziness, which was a whirlwind sensation with paroxysmal double vision, without nausea or vomiting, and the symptoms were not relieved. On November 5, 2019, the patient experienced nausea without vomiting, and felt unstable walking, generalized weakness, and no significant limb immobility. Cranial CT in a hospital in Zhejiang Province showed no significant abnormalities. The patient was given "Ginkgo Biloba Extract" and "Betahistine Mesylate" orally, but the symptoms were not relieved. On November 9, 2019, the patient suddenly experienced vomiting during activities. The vomitus was gastric contents without bloody material. The patient had poor food intake, and then had recurrent dizziness, nausea and vomiting without remission. On November 11, 2019, the patient was hospitalized in another hospital in Mudanjiang City, and was diagnosed with "posterior circulation ischemia". The patient was given anti-platelet aggregation, circulation improvement and cerebral protection treatment, but the symptoms were not relieved. For further diagnosis and treatment, the patient came to our hospital, and was admitted due to "dizziness of unknown origin". During the course of the disease, the patient had poor mental status, poor diet, normal urination and dry stool.

Past history: the patient had a history of hypertension for 5 years, with the maximum blood pressure of 180/110 mmHg, intermittently orally took "Captopril Tablets 12.5 mg bid", and the blood pressure control was unknown; had a history of paroxysmal atrial fibrillation for more than 10 years, without any treatment; had a history of congestive heart failure and constrictive pericarditis for 48 years; denied a history of diabetes, hepatitis, tuberculosis, food and drug allergy, poison exposure and trauma, vaccination was performed as planned.

Personal history and family history: the patient was born in Heilongjiang Province, with no history of long-term out-of-town residence and no history of exposure to epidemic water. She had a regular diet, no history of smoking or alcohol consumption, and no family history of genetic diseases.

Admission physical examination: the patient appeared in poor general condition, thin stature, had a temperature of 36.5^{0C}, blood pressure of 163/94 mmHg, heart rate of 98/min, pulse rate of 76/min, the heart had an absolutely irregular rate and rhythm on auscultation, unequal intensity of the first heart sound, lungs were clear to auscultation and percussion without rales, rhonchi or wheezes, enlarged lymph node palpable on the left supraclavicular region about 1.0 by 1.5 cm, hard texture, poor activity, negative tenderness, no palpable mass in the breast and armpit. Her abdomen was soft but distended, and there was evidence of ascites, tenderness to palpation but no masses are felt, and no edema in both lower limbs. On neurologic examination, clear consciousness, fluent speech, memory and numeracy have decreased, the cranial-nerve examination revealed full visual fields with no extinction; pupils were 3mm, equal, round, and reactive to light, extraocular movements intact with continuous vertical gross nystagmus, no facial paralysis or lingual paralysis. Motor power was 5/5 in all the muscle groups, normal bulk of muscles, without atrophy, hypertrophy or fasciculations, and tone was normal in upper and lower extremities. She had clumsiness in her both upper and lower limbs when performing finger-to-nose, rapid alternating movements and heel-to-shin testing, and had a positive Romberg test. Sensory examination: Intact to pinprick, temperature, light touch, vibration and proprioception in the extremities bilaterally. The deep-tendon reflexes were ++ and symmetric, negative Babinski. The neck was rigid, but Brudzinski's and Kernig's sign were negative.

Laboratory and imaging data: serum multiple tumor markers: CA125 > 1000.0U/ml (reference range 0-35U/ml), CA153: 135.000U/ml (normal value 0-31.3U/ml), serum ferritin 453.59ng/ml (normal value 4.63-204U/ml), carcinoembryonic antigen, alpha-fetoprotein, CA199, squamous cell carcinoma associated antigen were normal. Combined analysis of ascites: Rivalta test was positive, cell count was 2400 × 10 ^ 6/L (normal value ≤ 100/L), glucose was 17.70mmol/L (normal value 4.3–5.9mmol/L), and CA125 > 1000.0U/mL. Exfoliative cell examination of ascites revealed cancer cells. A lumbar puncture yielded clear, colorless cerebrospinal fluid and cerebrospinal fluid examination showed the following: intracranial pressure: 110 mmH2O, exfoliated cells showed no cancer cells. Cerebrospinal fluid paraneoplastic syndrome antibody showed anti-Yo antibody IgG positive. Cranial CT showed: cerebellar hemispheric sulci slightly widened. Ultrasonographic examination of the right and left carotid arteries showed plaque formation. Cardiac ultrasonographic examination showed: 1. after operation of constrictive pericarditis; 2. left ventricular wall motion and systolic function decreased; 3. pleural effusion (a small amount). Electrocardiogram revealed: 1. ectopic rhythm; 2. atrial fibrillation; 3. ST-T changes. Lung CT and enhanced CT of liver, gallbladder, pancreas and spleen showed: 1. localized pulmonary emphysema; 2. bullae in the right lower lobe; 3. enlarged left lung; 4. pericardial thickening with calcification; 5. liver cirrhosis and ascites; 6. multiple hemangiomas of liver; 7. multiple cyst of liver and kidney. A positron emission computed tomography (PET-CT) examination showed that: 1. multiple enlarged lymph nodes in the supraclavicular lymph node area and posterior cervical triangle lymph node area, PET showed multiple nodular radioactive concentration, which was considered as metastatic tumor; 2. multiple lymph nodes in the right upper paratracheal, right lower paratracheal and the trachea carina, PET showed multiple nodular radioactive concentration, not excluding the possibility of metastatic tumor.

Treatment process: After admission, the patient was given symptomatic treatments including improvement of circulation, anticoagulation, adjustment of autonomic nervous system and dehydration, etc, after when the patient's dizziness symptoms were better than that at the time of admission, she required to be discharged from hospital. During the current follow-up (more than half a year), the patient still had dizziness, could not stand and walk, and needed to stay in bed, but the condition was not

aggravated.

Case Analysis

Medical history Characteristics: in our case, the patient is a middle-aged woman with subacute onset, the first symptom was dizziness and progressively worsened, manifesting as symptoms and signs of cerebellar damage: nausea, vomiting, nystagmus, and ataxia. She had a history of hypertension, atrial fibrillation, congestive heart failure, and constrictive pericarditis, no history of exposure to poisons, smoking or alcohol consumption. Positive signs of nervous system examination mainly include: bilateral eyeball continuous vertical gross nystagmus, ataxia. Auxiliary examination showed: cerebrospinal fluid paraneoplastic syndrome antibody showed: anti-Yo antibody IgG positive;combined analysis of ascites: Rivalta test was positive, cell count was 2400 × 10 ^ 6/L, glucose was 17.70mmol/L, and CA125 > 1000.0U/mL; ascites exfoliative cell examination: cancer cells were found. Because the patient had a history of constrictive pericarditis, MRI could not be performed, PET-CT did not find the primary tumor lesion, the remaining laboratory tests and cranial CT showed no obvious special performance.

Diagnosis: cranial CT and lumbar puncture were performed to rule out cerebellar stroke, cerebellar tumor, infection, increased intracranial pressure and toxic cerebellar lesions. Nutritional disorders, degeneration, infection, endocrine glands, genetics, trauma, poisoning and stroke were excluded according to the diagnostic principle of "MIDNIGHTS". The possibility of tumor was considered comprehensively. Combined with the positive antibody anti-Yo antibody IgG (+) in cerebrospinal fluid paraneoplastic syndrome, the final diagnosis was subacute cerebellar degeneration.

Conclusions

The diagnosis of SCD in this case is clear. At present, cases of tumor-negative SCD are rare, and the examination of this case is more comprehensive, with the value of this case lies in improving the physician's understanding of SCD patients with negative tumors in clinical work. Close follow-up is necessary for this type of patients. The treatment of SCD includes the following three aspects: tumor treatment, immunomodulatory treatment and symptomatic treatment [15]. Due to the rarity of the disease in clinical practice and the lack of evidence-based medical guidelines. Optimal treatment strategies have not been developed for SCD patients with negative tumors, further studies are needed to confirm the benefit of drug treatment. The prognosis of SCD is poor, most patients are bedridden due to disability, and the survival of anti-Yo antibody-positive SCD patients is 13 months, of which 67% of patients died from neurological diseases [16].

Since most SCD patients have neurological symptoms earlier than the time of tumor diagnosis, the understanding of the disease should be improved. If the following patient conditions are encountered in clinical practice: middle-aged and elderly patients, with subacute onset, progressive aggravated cerebellar symptoms and signs and inconsistent with pathological features of primary neurological diseases, excluding the following lesions: cerebellar tumor, stroke, inflammation, poisoning, etc. SCD should be considered, and then comprehensive physical examination and imaging examination should be performed to avoid missing the primary tumor lesions. Early diagnosis of SCD and its relationship with specific tumor antibodies can guide the early treatment of tumors, prevent further deterioration of neurological function, and improve the survival rate and quality of life of patients.

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