

## Relapse and Remission of Paraneoplastic Neurologic Syndromes: One Case Report and Literature Review

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### Abstract

Paraneoplastic neurologic syndromes (PNS) is a group of heterogeneous diseases that occurs in tumor patients and can affect the central nervous, peripheral nerve, neuromuscular junction and muscle. The diagnosis should exclude tumor metastasis, infection, metabolic and nutritional defects and side effects of tumor treatment. The cause of PNS is believed to be related to immune factors, such as anti-nervous system antigen antibodies and T-cell immune response. PNS can appear 5 years before the tumor appears, which has an important role in suggesting the occurrence of tumor. We report a PNS case which imaging improves but symptoms become volatile.

**Keywords:** Paraneoplastic Neurologic Syndromes; Relapse-Remission; Sigmoid Colon Tubular Adenoma; Autoantibodies

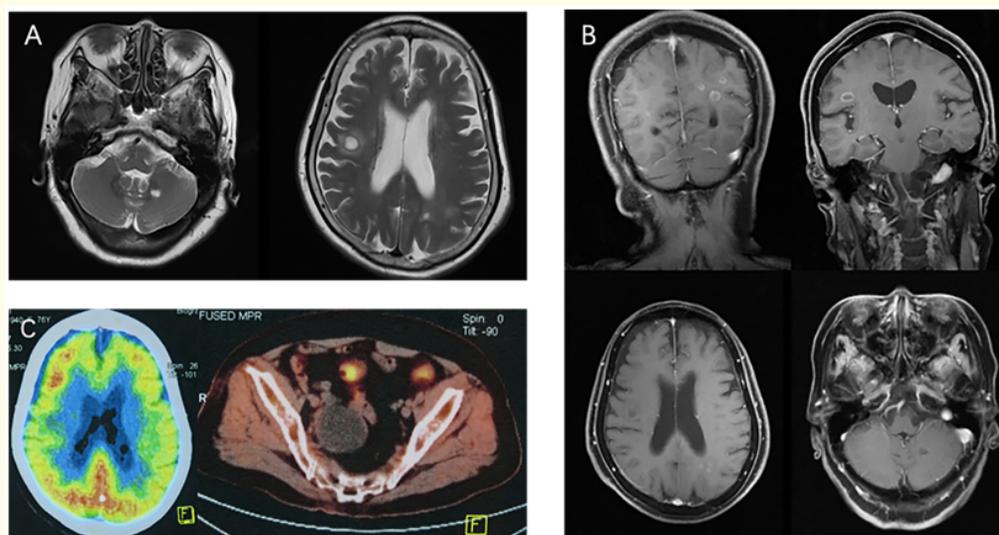
### Introduction

The predominant neurological syndromes of patients with PNS were sensory neuropathy, motor neuropathy, cerebellar ataxia and limbic encephalitis [1]. There are many onconeural antibodies associated with PNS, such as anti-Hu, anti-Yo, anti-CV2, anti-Ri [2], the percent of positive can reach to 80% [3]. Those onconeural antibodies suggest that some PNS may be immune mediated [4]. In the present study, we report a patient with symptoms of neurological defects as the main complaint who finally diagnosed sigmoid adenocarcinoma. We describe the characteristics of the patient's head MRI, PET-CT, CSF tests and autoimmune antibodies. After treatment, those auxiliary examinations turn to normal but the patient's clinical symptoms relapse. This patient has classical syndromes and cancer, it can help us better understand this disease.

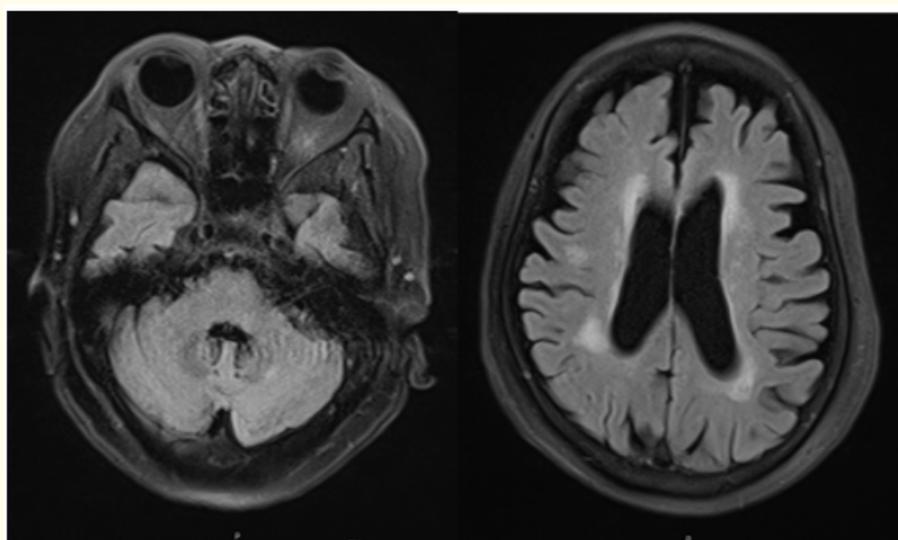
### Case Presentation

A seventy-nine years old female presented in neurology department with the relapse of limbs weakness and numbness. At first, she got a dizziness with occasional headache and both limbs weakness without obvious cause two years ago. The symptoms aggravated at night and the weakness on the right lower extremity was obvious. Patient had no nausea, vomiting, shortness of breath and other discomfort. She entered to our outpatient and did an enhanced head magnetic resonance imaging (MRI) (2017-01-22) showing multiple ring-reinforced focuses were in cerebrum with the possibility of infectious lesions or metastatic tumor. And then she got a positron emission tomography-computed tomography (PET-CT) examination reporting a sigmoid colon occupancy with an abnormal metabolism increase of <sup>18</sup>F-deoxyglucose (FDG), but no metabolic abnormality was found in central nervous system (CNS) (Figure 1). After assessing the disease condition, she finished the tumor surgery smoothly and the pathology diagnosis was sigmoid adenocarcinoma (T2N0M0, phase 1). She

recovered well and those symptoms such as dizziness, headache and limbs weakness gradually improved without any radiotherapy and chemotherapy. She got another head MRI with the report saying: the intracranial multiple abnormal signal shadows and the suspicious ring-reinforced focuses were smaller than before. The further lumbar puncture examinations showed the cerebrospinal fluid pressure was 150 mmH<sub>2</sub>O and the biochemistry laboratory and clinical routine were normal. The cerebrospinal fluid myelin-related proteins, IgG index and OB were not significantly abnormal. Autoimmune indicators: ANA 1: 320 positive, cytoplasmic granular type. In the following year, she appeared many symptoms just like last year and she finished many examinations which were almost normal. After symptomatic treatment, her symptoms lifted. In the last month, she re-emerged limbs weakness without obvious causes, sometimes could not walk without others' help. She presented in our department due to symptoms persisting. Physical examination suggested that the left limb muscle strength was level IV, the right lower limb muscle strength was level II, the right upper limb muscle strength was level III. Abdominal CT did not see the recurrence of tumor and head MRI did not see significant new lesions (Figure 2). Tumor markers, autoimmune antibodies and other blood tests were normal. We used some drugs to nourish the nervous system and to improve circulation. Her symptoms gradually alleviated. Her left limb and right upper limb muscle strength increased to level IV, right lower limb muscle strength to level III.



**Figure 1:** Head MRI and PET-CT. (A) Axial T2 weighted magnetic resonance image (MRI) scan showing high signal in the left cerebellar hemisphere and right medial temporal lobe. (B) T1 contrast enhancement MRI scan showing multiple ring-reinforced focuses. (C) Positron emission tomography-computed tomography (PET-CT) examination reporting a sigmoid colon occupancy with an abnormal metabolism increase of 18F-deoxyglucose (FDG), but no metabolic abnormality was found in CNS.



**Figure 2:** Follow-up head MRI in April 2019, no significant new lesions, but some myelin changes beside the ventricle, and obvious brain tissue atrophy.

### Discussion and Conclusion

The time from the patient's initial symptoms (October 2016) to the tumor being confirmed (March 2017) took a total of 5 months, in line with the report that PNS predates the diagnosis of the tumor by about 7 months [5]. The lumbar puncture examinations suggested that the patient's cerebrospinal fluid para-tumor related protein test is negative, but antibody being negative cannot rule out the diagnosis of PNS [6]. The negative results may be related to the long course of the disease and tumor cure. The incidence of PNS in solid tumors is less than 1% [5], but it may be underestimated. With studies showing that, about 3% of patients with small cell lung cancer will develop to Lambert-Eaton syndrome, about 15% of thymoma patients to severe muscle weakness, and up to 9% of non-small cell lung cancer patients will appear one or more neuropathies [7,8]. However, at the same time, some researches suggest that the patients with non-small cell lung cancer accompanied with PNS will have less metastasis and better clinical results [9].

Imaging examination is propitious to diagnosis, but the sensitivity and specificity are not very high. Head MRI helps to eliminate cerebrovascular accidents and metastasis lesions. The subcutaneous tissue and cerebellum are sometimes affected. Characteristic MRI performance is high signal on FLAIR or T2WI. The contrast enhancement MRI performance is various, sometimes it can indicate characteristic symptoms [10], but elderly patients are usually difficult to present the MRI changes [11]. A study of 104 patients shows that the sensitivity and specificity of 18FDG-PET are 80% and 67%, while CT are 30% and 71% [12]. Another study shows that the combination of 18FDG-PET and CT can improve sensitivity and specificity of tumor diagnosis in PNS patients [13]. A small number of patients experience a second time of PNS after the first PNS remission or recovery. A retrospective study of eight patients shows that five relapsed patients have recurrence of primary tumors and one relapsed patient develops a new tumor [14]. In our case, the clinical symptoms of this patient have the tendency to elapse and relieve, but no new lesions appear in imaging examination, and no evidence of tumor recurrence is found. During two years' follow-up, the patient's brain atrophy can be seen worsen, consistent with previous studies [15].

At present, the treatment of PNS is mainly focused on the treatment of primary tumors and immunotherapy (including immunomodulation and immune-suppression), such as chemotherapy, tumor removal, intravenous immunoglobulin and so on. Those therapies can achieve good results, but some patients with poor outcomes may have caused irreparable damage before starting treatment [16-18]. The prognosis of patients still requires long-term dynamic follow-up.

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### Conflict of Interest

The authors declare that they have no conflict of interest.

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