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Paraneoplastic Choreoathetosis in a Patient with Small Cell Lung Carcinoma and Anti-CRMP5/CV2: A Case Report

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Key Words

Paraneoplastic choreoathetosis · Anti-CRMP5/CV2 antibodies · Small cell lung carcinoma · Movement disorder · Cancer · Nervous system

Abstract

Introduction: The occurrence of more or less monosymptomatic paraneoplastic choreoathetosis associated with anti-CRMP5/CV2 antibodies is rare. Typically, such autoantibodies are associated with a more classical syndrome – paraneoplastic encephalomyelitis. Frequently, small cell lung carcinoma (SCLC) is the related neoplastic finding. ***Case Report:*** We present a 71-year-old woman who developed visual symptoms with papilledema and chorea. Anti-CRMP5/CV2 antibodies were a feature of both the serum and cerebrospinal fluid. Although SCLC was suspected already at the time of the initial examinations, no signs of primary or metastatic tumors were revealed on chest X-ray, MRI or whole-body PET scan. EEG and bronchoscopy were also unremarkable. However, 6 months after the onset, a repeated PET scan and subsequent bronchoscopic biopsy revealed SCLC. In spite of chemotherapy, the SCLC progressed, and the patient died 14 months after the onset of the symptoms. ***Conclusion:*** We report paraneoplastic choreoathetosis associated with anti-CRMP5/CV2 antibodies. Such published case histories are rare. Although expected, we did not find any reduced signal intensity at the basal ganglia on the T1-weighted or increased intensity on the T2-weighted MRI scans.

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Introduction

The occurrence of anti-CRPM5/CV2 antibodies is usually associated with paraneoplastic encephalomyelitis and with chorea as a possible feature, although typically being a multifocal syndrome [1]. On the other hand, paraneoplastic choreoathetosis (PNCA) is defined as a more or less isolated movement disorder as a remote effect of a cancer on the nervous system [1]. In PNCA, the most frequent neoplastic finding is small cell lung carcinoma (SCLC) [1]. We report such a rare case with papilledema as the only additional symptom.

Case Report

A 71-year-old woman presented to a general practitioner with a 5-day history of progressively decreasing left-sided vision. The sequelae of a prior surgery for a right-sided acoustic neuroma had left her with blindness on her right eye, right-sided hearing loss and peripheral facial palsy. She was a smoker with a history of 60 pack-years, and did not use medication daily. No family disposition could be obtained, since the patient was adopted. Over the previous 6 months, there had been an unintended weight loss of 10 kg. An ophthalmological examination revealed ischemic papillary stasis, which was treated with prednisone 80 mg/day. Furthermore, there was a sudden onset of involuntary movements of the upper and lower limbs. She was admitted to a hospital 7 days later. On neurological examination, she was alert and orientated. In addition to the already known features related to the treatment of an acoustic neuroma, there was universal choreoathetosis. The initial workup, including brain MRI (with T1, T2 and FLAIR sequences), and routine chest X-ray were all unremarkable. A whole-body PET scan did not reveal signs of primary or metastatic tumors. Further examinations with EEG and bronchoscopy were unremarkable. The following analyses of serum and cerebrospinal fluid were normal: ANA, ANCA, anti-Hu, anti-Yo, Ri-antibody, amphiphysin-1 antibody and anti-Zic4. However, anti-CRMP5 (alias anti-CV2, method: line-blot from Euroimmun, Lübeck, Germany) was strongly positive in both media – also indicating an occult cancer. She was then treated with immunoglobulin, which improved the choreiform movements. Unfortunately, over the following months, there was increasing weight loss, and the general condition worsened as well. Six months after the onset, a repeated PET scan showed foci suspicious of malignancy in the mediastinal lymph nodes and the right lung hilum. In May 2007, subsequent bronchoscopic biopsy revealed an SCLC. In spite of chemotherapy, repeated lung CT scans showed further progression, and the PNCA did not improve. As a palliative treatment for the SCLC, radiotherapy (10 Gy) was then given. She died 14 months after the onset of the symptoms, and her death was attributed to the SCLC complicated with infection.

Discussion

PNCA is an extremely rare disorder [1]. Most likely, it is caused by a damage of the nervous tissue by the remote effects of onconeuronal autoimmune factors including autoantibodies [1]. Associated with autoantibodies against intracellular epitopes, such a disorder is likely to be T cell mediated. It is provoked by cancer located outside the central nervous system and most frequently SCLC. However, based on the underlying pathogenesis, paraneoplastic disorders of the central nervous system can be divided into two categories: group

1 with antibodies against intracellular antigens (e.g. Hu and CRMP5/CV2) and group 2 with antibodies binding to superficial cell membrane structures (e.g. receptors and channels).

The occurrence of papilledema is explicable in terms of ischemic papillary stasis due to inflammation. Choreiform movements in the paraneoplastic syndrome have been reported in case reports of patients with different types of cancer, SCLC being the most frequently reported (table 1). Common for nearly all reported cases of PNCA due to SCLC is the presence of CRPM5/CV2 antibodies (table 1). Additionally, in patients with paraneoplastic chorea, the expected brain MRI finding is reduced signal intensity from the basal ganglia on the T1-weighted and increased intensity on the T2-weighted MRI scans. In the current case, however, such abnormalities were not observed. However, in half of the reported cases of PNCA, the MRI did not show changes in the basal ganglia (table 1). Thus, in patients who present with new-onset and rapidly developing movement disorders and no pathological findings by routine biochemistry or brain MRI, a paraneoplastic origin should be considered. Moreover, paraneoplastic symptoms may occur months before the neoplastic disorder becomes detectable. An adequate diagnosis is a primary task for a neurologist, although a prompt and intensive workup may include an interdisciplinary team (e.g. ophthalmologists, radiologists, pulmonologists and oncologists). The outcome and prognosis depend on an early establishment of the diagnosis and a prompt start of therapy.

Movement disorders, including chorea, are common in the elderly. In view of the extreme scarcity of reported PNCA in contrast to a much more common occurrence of anti-CRMP5/CV2, PNCA may be underdiagnosed.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

There are no conflicts of interest in relation to this publication.

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Table 1. Reported cases of PNCA

First author [Ref.], year	Age, years	Sex	Symptom	Tumor	Antibodies	Reduced intensity on T1- and increased intensity on T2-weighted MRI
Nakae [1], 2014	72	M	hemichorea	thymoma	no anti-CRMP5	no
Jiménez Caballero [2], 2014	69	M	chorea	SCLC	positive anti-CRMP5/CV2	no
Bohrer [3], 2013	7	M	choreo-dystonia	cardiac	no anti-CRMP5/CV2 or anti-NMDA	no
Vick [4], 2012	69	F	chorea	SCLC	positive anti-CRMP5	yes
Saito [5], 2009	63	M	chorea	lung ACA	no anti-CRMP5 or anti-Yo	yes
Martinkova [6], 2009	60	F	chorea	breast	positive anti-Hu and anti-Ri	no
Kleinig [7], 2009	73	F	chorea	SCLC	no anti-Hu, anti-Ri or anti-Yo; anti-CRMP5 not tested	yes
Kellinghaus [8], 2007	40	M	chorea	testicular	positive anti-CRMP5	no
Krolak-Salmon [9], 2006	72	M	chorea	lung ACA	positive anti-Yo	n.a.
Dorban [10], 2004	48	F	chorea	SCLC	positive anti-Hu; no anti-CRMP5/CV2	yes
Kinirons [11], 2003	62	F	chorea	SCLC	positive anti-CRMP5	yes
Tan [12], 2003	62	F	chorea	PCL	n.a.	n.a.
Vernino [13], 2002	69 mean	10 F 6 M	chorea	SCLC 12, renal 1, NHL 1, lung mass 2	positive anti-CRMP5 in all	yes (n = 5), no (3), n.a. (8)
Kujawa [14], 2001	55	M	chorea	renal	n.a.	no
Tani [15], 2000	73	M	chorea	SCLC	positive 68-kDa antibody; no anti-Hu, anti-Yo and anti-Ri	yes
Nuti [16], 2000	70	M	chorea	NHL	no anti-Hu or anti-Yo; anti-CRMP5 not tested	n.a.

ACA = Adenocarcinoma; NHL = non-Hodgkin lymphoma; PCL = primary cerebral lymphoma; n.a. = not assessed.