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A Case of Anti-Caspr2 Autoimmune Encephalitis Associated with Adenocarcinoma of the Lung

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ABSTRACT

Autoimmune encephalitis (AIE) is an inflammatory brain condition with multiple aetiologies but is mainly associated with paraneoplastic syndromes. Several antibodies described in AIE are being investigated in relation to different cancers, including antibodies against Contactin-associated protein-like 2 (Caspr2), which have been associated with thymoma but very rarely with lung cancer. The authors present the case of a 72-year-old man with cardiovascular risk factors, who presented with a 3-week history of left hemichorea following a first unprovoked seizure the week before, with no other signs or symptoms. The patient was submitted to extensive aetiological investigation, testing positive for anti-Caspr2 antibodies in the cerebrospinal fluid. AIE was diagnosed after other possible causes had been excluded. A PET scan showed signs of abnormal metabolism, with a lung biopsy confirming lung adenocarcinoma. This case highlights a very rare association and the importance of a thorough aetiological investigation for neurological complaints.

LEARNING POINTS

- Neurological complaints require a thorough aetiological investigation, and positive findings on imaging studies must be carefully examined.
- Anti-Caspr2 antibodies are classically associated with Morvan syndrome, but other neurological presentations must also be considered.
- Anti-Caspr2 autoimmune encephalitis may be the primary presentation of lung adenocarcinoma.

KEYWORDS

Autoimmune encephalitis, paraneoplastic syndrome, anti-Caspr2, lung adenocarcinoma

INTRODUCTION

The presence of autoantibodies to Contactin-associated protein-like 2 (Caspr2)—a cell adhesion molecule—can manifest with central and peripheral nervous system symptoms [1]. Depending on the region involved, there can be deficits in motor control, sensation, behaviour, memory, awareness, and cognitive and autonomic function.

The characteristic constellation of symptoms consists of neuromyotonia, encephalitis, dysautonomia and insomnia (Morvan syndrome), but there may be other manifestations [1]. Throughout the course of the disease, cognitive disturbance and epilepsy are present in up to 80% and 50% of patients, respectively [2]. Anti-Caspr2 antibodies are mostly associated with thymoma, but are very rarely associated with other solid tumours, namely lung adenocarcinoma [2–4].

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The diagnosis of autoimmune encephalitis (AIE) is challenging and requires the exclusion of other causes. The presence of anti-neuronal antibodies aids diagnosis and is crucial for determining management and guiding aetiological investigation [5]. Treatment consists of immunosuppression and, when indicated, tumour resection. Without treatment, neurological deterioration and death can occur [6].

CASE DESCRIPTION

A 72-year-old man with a medical history of hypertension, dyslipidaemia, acute myocardial infarction and transitory ischaemic stroke, was admitted to the emergency department with a 3-week history of left hemichorea, preceded a week earlier by a first episode of nocturnal generalized seizure, with no other signs or symptoms.

Computed tomography and magnetic resonance imaging revealed the presence of chronic vascular lesions in the basal ganglia bilaterally, as well as signs of chronic microangiopathic leukoencephalopathy with findings of T2 hyperintensities around the ventricles, in subcortical areas, basal ganglia and brainstem, compatible with enlarged peri-vascular spaces considering attenuation in T2-FLAIR. The electroencephalogram showed slow and abrupt waves in the right temporal lobe. In light of these findings, the diagnosis of epilepsy was assumed and the patient was started on levetiracetam. He was then submitted to a vascular study of the neck, intracranial and supra-aortic vessels and cardiac imaging, with no relevant abnormalities being detected. Blood tests revealed secondary hyperparathyroidism due to vitamin D deficiency and positivity for antiphospholipid antibodies, without other serum autoimmune markers, nutritional imbalances, organ dysfunction or electrolyte disturbances detected. Treatment for vitamin D deficiency was started promptly and the patient was put on anticoagulation with warfarin.

A lumbar puncture was performed and anti-Caspr2 antibodies were seen in both cerebrospinal fluid and serum, confirming the diagnosis of AIE. An investigation for occult primary neoplasm was carried out with a whole-body CT scan and positron emission tomography scan, which showed an area of hypermetabolism within the lung. The patient was then submitted to lung biopsy which confirmed the diagnosis of lung adenocarcinoma. He was treated with chemotherapy and immunotherapy.

DISCUSSION

AIE is an inflammatory brain disease characterized by compromised brain function due to antibodies directed against neuronal cell-surface proteins, ion channels or receptors [7]. Depending on the brain area affected, patients can present with a wide variety of symptoms. Anti-Caspr2 antibody-mediated AIE usually evolves over a period of 4 months, with some cases developing over a year [2]. Our patient's symptoms, which are present in up to a third of cases at first evaluation, prompted several follow-up investigations early in the course of the disease, allowing for a diagnosis approximately 1 month after symptom onset. During the investigation, a diagnosis of idiopathic antiphospholipid syndrome (aPL) was made according to the Sydney Classification Criteria, in light of the presence of brain vascular lesions associated with positive antiphospholipid antibodies. Several neurological disorders have been reported in aPL-positive patients, including epilepsy, psychosis, chorea, hemiballismus, transverse myelopathy, sensorineural hearing loss and migraine. However, a strong association has not been established between these manifestations and aPL [8]. The neuroimaging abnormalities in our patient were not typical for AIE and because the presence of anti-neuronal antibodies alone is not diagnostic of AIE, the positive finding of anti-Caspr2 antibodies was only taken into account because the distribution of the vascular lesions did not fully explain the clinical presentation and because other possible causes had been ruled out, namely neurologically relevant vitamin deficiencies, toxic/metabolic disturbances, infections and other autoimmune and neurodegenerative disorders.

A wide panel of anti-neuronal antibodies should be used in patients with symptoms consistent with AIE which has not yet been definitively diagnosed.

Correlation between AIE and tumours is variable [9]. In patients with lung cancer, most neurological paraneoplastic manifestations occur with small-cell carcinoma, with very few cases reporting an association with lung adenocarcinoma [4, 9]. The diagnosis of lung adenocarcinoma in this patient allowed the underlying condition to be treated, thus improving prognosis. This clinical report highlights the association between non-small-cancer carcinomas and lesser-known antibodies, namely anti-Caspr2, as well as the importance of an extensive search for tumours in patients with antibody-mediated AIE. In view of the clinical variables of this case and the few reports associating anti-Caspr2 with lung adenocarcinoma, further studies are warranted to better clarify these findings.

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