Case Report

Limbic Encephalopathy Associated with Gaba-B Receptor and N-Type Voltage Gated Calcium Channel Antibodies in A Patient with Small Cell Lung Cancer: A Case Report

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Abstract

Paraneoplastic limbic encephalitis (PLE) from GABA-B receptor or N-type voltage gated calcium channel (VGCC) antibodies is a rare complication of small cell lung cancer. We present the case of an 80-year-old female diagnosed with small cell lung cancer after presenting with neurological symptoms. The patient was admitted with complaints of recurrent syncope, confusion, gait abnormalities and progressive deterioration in mental status. Cerebrospinal fluid analysis was positive for both GABA-B receptor and N-type VGCC antibodies. The discovery of the autoantibodies led to a paraneoplastic workup. Computed tomography of the chest revealed a hilar mass, subsequently confirmed on biopsy to be small cell lung cancer. This case emphasizes the need to pursue primary tumor investigation in patients with positive findings of these autoantibodies that are associated with paraneoplastic syndromes.

Keywords: small cell lung cancer, paraneoplastic encephalitis, limbic encephalopathy, voltage-gated calcium channel, GABA-B receptor

Introduction

Paraneoplastic limbic encephalitis (PLE) is an autoimmune disorder driven by antibodies formed secondary to malignancy that is characterized by memory impairment, bizarre behavior, seizures, and altered mentation [1]. Antibodies against intracellular antigens such as anti-Hu and anti-GAD causing PLE are commonly associated with small cell lung cancer (SCLC) [2]. Antibodies against synaptic and surface receptors, such as voltage-gated calcium channel (VGCC) and GABA-B receptors, have recently been associated with SCLC [3,4]. Here we report a case of a patient who presented with neurological deterioration and was found to have SCLC induced PLE with multiple antibodies present.
Case Report

An 80-year-old female was admitted with progressive deterioration in mental status. She was an active 30-pack year smoker, without any history of alcohol or illicit substance use. Over the past two years she was found on the floor several times, rigid but awake with a blank stare. The episodes were self-limited and improved without treatment. Despite several hospitalizations, neurologic evaluations were inconclusive. She was suspected of having seizures, although none were ever recorded on electroencephalogram. Prior to presentation, she was noted to be more forgetful, walked with a shuffling gait, and often repeated tasks. She was subsequently admitted for further workup after being found on the floor, this time unconscious with upper extremity tremors. She was started empirically on antimicrobial therapy for suspected infectious encephalitis, antiepileptic medications for possible seizures, and intubated for airway protection secondary to continued deterioration of mental status. Cerebrospinal fluid analysis was not consistent with bacterial or viral meningitis. Magnetic Resonance Imaging of the brain with contrast showed increased T2 signal in the limbic region. Electroencephalogram showed evidence of severe left temporal cerebral dysfunction characterized by left temporal slowing and sharp spikes, without evidence of seizures. A cerebrospinal fluid encephalopathy panel was found to be positive for both GABA-B receptor and N-type VGCC antibodies. Due to the fact that these antibodies can be associated with paraneoplastic syndromes, computed tomography imaging was performed revealing a left upper lobe mass. Biopsy of the mass confirmed the presence of SCLC and the patient was diagnosed with PLE. Despite treatment with plasmapheresis and steroids, her mental status never improved, and the family elected to withdraw life support in light of her poor prognosis.

Discussion

Neurologic paraneoplastic manifestations of SCLC are traditionally associated with diagnoses such as Lambert-Eaton Myasthenic syndrome or Paraneoplastic Cerebellar Degeneration [3]. Recently, limbic encephalitis has been recognized as one of these paraneoplastic manifestations. Detectable antibodies can each cause a pattern of presentation characteristic to the location in which the antibody acts. PLE from SCLC is commonly associated with anti-Hu (up to 50%) and anti-GAD antibodies [2]. Other less common antibodies associated with PLE are SOX2, HuD, P/Q VGCC, N-type VGCC, and GABA-B [2,3,5,7]. PLE caused by GABA-B receptor antibodies was first described in literature in 2010 [4] and has emerged as a strong indicator of SCLC in PLE [6]. Multiple antibodies may be present at a time, although less common [4,6]. A 2015 study demonstrated concurrent P/Q VGCC and GABA-B antibodies in 20% of SCLC patients with Lambert-Eaton Myasthenic syndrome [8]. Our patient exhibited aspects of both peripheral and central neurological manifestations, with N-type VGCC and GABA-B antibodies discovered upon testing. A similar 2014 case report showed SCLC with identical antibodies, however dissimilar neurologic patient presentation [9]. This supports the recommendation that discovery of these antibodies should prompt a thorough workup for malignancy irrespective of neurological presentation [10].

PLE is not often included in the initial differential diagnosis due to rarity and nonspecific manifestations. Patients with self-limited or episodic presentations are more likely to be misdiagnosed, particularly those without a known malignancy [5]. As in our case, the patient’s neurological symptoms preceded her diagnosis by approximately 2 years. Prognosis of PLE due to SCLC is poor [8], with treatment of the underlying malignancy pertinent to recovery [11]. Prognosis of GABA-B associated PLE is highly variable even after treatment, ranging from complete or partial neurologic recovery to death [12]. Our patient was not a candidate for treatment of her SCLC, and had little to no improvement with other treatments.
Conclusion

Early recognition of clinical patterns and evidence of limbic encephalopathy on imaging should prompt additional paraneoplastic antibody testing from the cerebrospinal fluid. If present, a guided search for tumors should follow based on the specific types and combinations of antibodies rather than neurological presentation. Limbic encephalopathy of paraneoplastic origin may be treated with some success if the associated malignancy is treated.

References