CASE REPORT

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Delayed Diagnosis of Anti-GABA-B Antibody Paraneoplastic Limbic Encephalitis Characterized by Persecutory Delusions: A Case Report

Persekütif Sanrılarla Karakterize Anti-GABA-B Antikoru Paraneoplastik Limbik Ensefalitin Gecikmiş Tanısı: Bir Olgu Sunumu

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ABSTRACT

Limbic encephalitis (LE) is a rare clinical syndrome characterized by subacute limbic dysfunction, including seizures, memory impairment, and behavioral changes, often linked to autoimmune or paraneoplastic causes. Anti-gamma aminobutyric acid-B (anti-GABA-B) receptor-associated LE, frequently related to small cell lung cancer (SCLC), typically presents with neurological symptoms such as seizures and cognitive decline. However, prominent psychiatric symptoms, including psychosis, are rarely reported, posing diagnostic challenges. We report a 56-year-old woman presenting with acute disorganized behavior, paranoid delusions, and cognitive impairment, accompanied by status epilepticus. Initial investigations, including magnetic resonance imaging and cerebrospinal fluid (CSF) analysis, were inconclusive. While levetiracetam-induced psychosis and Hashimoto encephalitis were considered, her persistent symptoms prompted further evaluation. Thoracic imaging detected a lung mass confirmed as SCLC by biopsy; CSF analysis identified positive anti-GABA-B receptor antibodies. This confirmed a diagnosis of paraneoplastic LE. Treatment included pulse steroids, antipsychotics, and chemotherapy, leading to significant symptom improvement. This case emphasizes the importance of considering paraneoplastic autoimmune encephalitis in patients with prominent psychiatric symptoms and seizures. The identification of a lung mass during psychiatric evaluation was pivotal in diagnosing anti-GABA-B receptor LE. Early recognition and multidisciplinary management are essential to improve outcomes in such complex presentations.

Keywords: Limbic encephalitis, anti-GABA-B receptor, paraneoplastic syndrome, psychosis, stereotypic movements.

ÖZ

Limbik ensefalit (LE), nöbetler, hafıza bozukluğu ve davranış değişiklikleri gibi subakut limbik disfonksiyonla karakterize, nadir görülen bir klinik sendromdur ve genellikle otoimmün veya paraneoplastik nedenlerle ilişkilidir. Küçük hücreli akciğer kanseri (KHAK) ile sıkça ilişkili olan anti-gamma aminobutirik asit-B (anti-GABA-B) reseptörle ilişkili LE, genellikle nöbetler ve bilişsel gerileme gibi nörolojik semptomlarla ortaya çıkar. Ancak psikoz gibi belirgin psikiyatrik semptomlar nadiren bildirilmiş olup tanı zorluklarına yol açmaktadır. Bu makalede, akut dezorganize davranış, paranoid hezeyanlar ve bilişsel bozukluk ile birlikte status epileptikus tablosu sergileyen 56 yaşında bir kadın hasta sunulmaktadır. İlk tetkikler, dahil olmak üzere manyetik rezonans görüntüleme ve beyin omurilik sıvısı (BOS) analizi sonuçsuz kalmıştır. Levetirasetam kaynaklı psikoz ve Hashimoto ensefaliti düşünülmüşse de, kalıcı semptomlar ileri değerlendirmeyi gerekli kılmıştır. Torasik görüntüleme bir akciğer kitlesi ortaya koymuş ve biyopsi ile KHAK olarak doğrulanmıştır. BOS analizi ise pozitif anti-GABA-B reseptör antikorları tespit etmiş ve bu durum paraneoplastik LE tanısını doğrulamıştır. Tedavi; yüksek doz steroidler, antipsikotikler ve kemoterapiyi içermiş ve belirgin semptom iyileşmesi sağlanmıştır. Bu olgu, belirgin psikiyatrik semptomlar ve nöbetler sergileyen hastalarda paraneoplastik otoimmün ensefalitin dikkate alınmasının önemini vurgulamaktadır. Psikiyatrik değerlendirme sırasında bir akciğer kitlesinin tespiti, anti-GABA-B reseptör LE tanısında kilit rol oynamıştır. Erken tanı ve multidisipliner yaklaşım, bu tür karmaşık klinik tabloların sonuçlarını iyileştirmek için esastır.

Anahtar Kelimeler: Limbik ensefalit, anti-GABA-B reseptör, paraneoplastik sendrom, psikoz, stereotipik hareketler

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Introduction

In recent years, the growing recognition and awareness of limbic encephalitis (LE) have underscored its importance as a critical diagnosis in the context of neuropsychiatric symptoms. This increased awareness can profoundly influence both the course of the disease and the treatment strategies. LE is a clinical syndrome characterized by a subacute onset of limbic symptoms, with structural and functional evidence of mesiotemporal damage in the absence of a more plausible explanation than an autoimmune or paraneoplastic cause (1,2). The paraneoplastic form of LE is associated with tumors such as small cell lung cancer (SCLC), germ-cell testicular tumors, breast cancer, Hodgkin's lymphoma, immature teratoma, and thymoma. Among these, SCLC is the most commonly linked with antibodies such as anti-Hu, anti-Ma2, anti-NMDAR, anti-AMPA, and anti-gamma aminobutyric acid-B (anti-GABA-B) often targeting the limbic system. Patients may present with mood and sleep disturbances, seizures, hallucinations, and short-term memory loss, which may progress to dementia (3).

The discovery of newly identified antibodies related to LE has expanded our understanding of the condition's clinical spectrum. Lancaster and colleagues were the first to describe a case series of fifteen patients with LE associated with GABA-B receptor antibodies (4). LE linked to anti-GABA-B antibodies is predominantly characterized by neurological symptoms, including epileptic seizures, status epilepticus, and rapid cognitive decline. However, psychiatric symptoms may include personality changes such as loss of interest, irritability, emotional instability, and increased aggression (e.g., verbal or physical outbursts). Affective symptoms like sadness are relatively common, while psychotic features such as hallucinations and paranoid thoughts are rare but have been documented in the literature (5,6).

Here, we report the case of a 56-year-old woman who presented with persecutory delusions, disorganized behavior, rapidly progressive cognitive impairment, and seizures. She was diagnosed with LE associated with anti-GABA-B receptor antibodies, confirmed by a biopsy revealing SCLC. The patient and her son were informed about the study, and written informed consent was obtained.

Case Report

A 56-year-old housewife living with her two sons was admitted to our psychiatric clinic with acute disorganized behavior, speech disturbances, and paranoid delusions. At admission, she displayed stereotypic hand movements, disorientation to time and place, and disorganized speech.

Her medical history included hypothyroidism, treated tuberculosis, and chronic obstructive pulmonary disease. Five years earlier, she had been treated with fluoxetine for two years for a non-psychotic major depressive episode.

Three months prior to admission, she experienced her first generalized tonic-clonic seizure and visited the emergency department. Brain magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) analyses showed no abnormalities. Scalp interictal electroencephalogram revealed continuous 5-6 Hz theta waves. She was discharged on levetiracetam 1000 mg/day. However, she experienced three additional seizures over the following three months, the last of which evolved into status epilepticus, requiring a 28-day stay in the intensive care unit (ICU). Upon ICU discharge, her levetiracetam dose was increased to 3000 mg/day, and she remained seizure-free for the following month.

Approximately one month after ICU discharge, she began to display increasing behavioral disturbances, including disorganized behavior, speech disturbances, and paranoid delusions. These symptoms progressively worsened and led to her psychiatric admission two months later.

At psychiatric evaluation, she appeared older than her stated age and wore oversized clothing. Her son reported mild weight loss and a decline in personal hygiene. She showed limited cooperation, increased psychomotor activity, and perseverative, disorganized, and incoherent speech. Her thought processes were tangential, with impaired goal-directedness and paranoid ideation, but no hallucinations were noted. Her appetite was decreased, and her sleep was also decreased. She smoked 1.5 packs of cigarettes daily and reported no alcohol or substance use.

Premorbidly, her son described her as anxious and introverted, with normal developmental milestones and motor skills. Family history was notable for epilepsy in all three of her sons: one with absence seizures, and two with generalized tonic-clonic seizures that resolved in adulthood.

Neurological examination revealed impaired orientation to time and place but no cranial nerve, cerebellar, or pyramidal signs. Mental status examination confirmed confusion, disorientation, impaired concentration, and poor cooperation. According to her son, her baseline intellectual functioning had been normal.

During hospitalization, psychosis due to an underlying medical condition was considered the preliminary diagnosis. Differential diagnoses included levetiracetam-induced psychotic disorder, postictal psychosis, Hashimoto's encephalopathy, autoimmune LE, and catatonia. Her vital signs were within normal limits. Neuroimaging and laboratory investigations, including thoracic radiography, thoracoabdominal computed tomography (CT), and lumbar puncture, were performed. Except for thyroid function

tests, hematological and biochemical parameters were within the normal range. Thyroid tests showed TSH: 55.90, Anti-TPO: >600, and free T4: 6.32. Despite these findings, Hashimoto's encephalopathy was ruled out by endocrinology consultation.

Levetiracetam-induced psychosis was also considered, and her medication was gradually replaced with carbamazepine. However, no improvement in psychiatric symptoms was observed. Repeat brain MRI revealed increased FLAIR signal intensity in the right medial temporal lobe. Thoracic CT revealed a 35 mm mass in the lower lobe of the left lung, obstructing the bronchus. Bronchoscopy and biopsy confirmed stage IV SCLC, which strongly supported the diagnosis of paraneoplastic LE. A subsequent lumbar puncture revealed anti-GABA-B receptor antibody positivity, confirming the diagnosis.

Treatment and Outcome

Initial treatment consisted of carbamazepine, haloperidol, and biperiden, which was later revised to risperidone and quetiapine. Due to persistent psychiatric symptoms and the confirmed diagnosis of LE, the patient received 1 g/day intravenous methylprednisolone for five consecutive days. This resulted in substantial symptom reduction and marked cognitive improvement. Her psychiatric medications were then adjusted to olanzapine 10 mg and quetiapine 100 mg.

She has been followed up for eight months by psychiatry, neurology, and oncology services. During this time, she completed eight cycles of chemotherapy and initiated radiation therapy. In the post-steroid and chemotherapy period, the patient remained seizure-free and showed sustained cognitive improvement. Positron emission tomography imaging revealed regression of SCLC; oncological treatment was completed. However, three months after completing chemotherapy, seizures recurred. Follow-up brain MRI showed increased FLAIR hyperintensity in the right temporal lobe.

Discussion

This case highlights the unique clinical features of GABA-B receptor-associated LE, in which the diagnosis was complicated by the initial neurological presentation, prominent psychiatric symptoms, and rapidly progressive cognitive decline. A key factor was the delayed recognition of encephalitis, despite the occurrence of status epilepticus during the patient's ICU stay. Autoimmune LE often presents with a combination of psychiatric and neurological symptoms, which can obscure the underlying neurological etiology and contribute to diagnostic delays (2).

The patient's prominent psychiatric symptoms including disorganized behavior, paranoid delusions, and stereotypical gestures were particularly noteworthy. Although such motor behaviors are less frequently reported, they have been described in autoimmune encephalitis cases, where stereotyped movements and disorganized thought processes can mimic primary psychiatric disorders (4,6). This underscores the importance of considering autoimmune encephalitis in patients who present primarily with psychiatric manifestations.

The incidental discovery of a lung mass during the psychiatric evaluation was pivotal in narrowing the diagnosis to paraneoplastic GABA-B receptor encephalitis, which is strongly associated with SCLC (7). This link between GABA-B receptor LE and paraneoplastic syndromes is well-established in the literature (2).

GABA-B receptor LE typically presents with seizures, status epilepticus, and rapidly progressing cognitive deterioration. Psychiatric symptoms such as anxiety, mood disturbances, and confusion may accompany these neurological signs but are generally considered secondary to seizure activity (8). The early occurrence of status epilepticus is a hallmark feature of GABA-B receptor LE and can lead to a swift progression of cognitive and behavioral disturbances, including memory impairment and thought disorganization (5).

In the present case, the patient initially experienced generalized tonic-clonic seizures that culminated in status epilepticus, consistent with the classic presentation of GABA-B receptor LE. However, the subsequent emergence of prominent psychiatric symptoms such as disorganized behavior, paranoid ideation, and stereotypic hand movements added diagnostic complexity. Unlike the typical course, in which psychiatric manifestations follow neurological symptoms, this patient's psychiatric features became central to her clinical presentation.

Autoimmune LE was considered the leading diagnosis based on the coexistence of seizures, cognitive decline, and psychiatric symptoms. Levetiracetam-induced psychosis was deemed unlikely due to the persistence of symptoms despite drug discontinuation. Postictal psychosis was ruled out due to the prolonged and progressive nature of the symptoms. Although hypothyroidism was present, it was not considered the primary etiology after the identification of anti-GABA-B antibodies and a confirmed paraneoplastic syndrome. Catatonia, suggested by the presence of disorganized behavior and stereotypies, was also considered as part of the broader autoimmune encephalitis spectrum.

A thorough diagnostic approach is essential in patients presenting with unexplained psychiatric and neurological symptoms, as an underlying malignancy may be a critical clue in identifying paraneoplastic autoimmune conditions (3).

Conclusion

In conclusion, we present a compelling case of GABA-B receptor LE characterized by psychosis, stereotyped movements, and cognitive impairment, with a history of status epilepticus; underscoring the diagnostic challenges posed by overlapping psychiatric and neurological features.

Ethics

Informed Consent: The patient and her son were informed about the study, and written informed consent was obtained.

Footnotes

Authorship Contributions

Surgical and Medical Practies: N.E., E.P.A., T.C.Ş., Ö.A.Ö., Concept: N.E., E.P.A., Design: N.E., E.P.A., T.C.Ş., Data Collection of Processing: N.E., E.P.A., Literature Search: N.E., E.P.A., Writing: N.E., E.P.A., T.C.Ş.

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