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Case Report
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A Patient with Anti-NMDA Receptor Encephalitis and Thyropathy: A Possible Correlation?

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Introduction

Encephalitis is an inflammatory condition of the brain which has different etiologies. Anti-NMDA Receptor (NMDAR) encephalitis is associated with an immune-mediated mechanism and clinically characterized by a prominent neuropsychiatric syndrome [1]. Other clinical features include sleep dysfunction, agitation, fluctuating catatonia, memory deficit, decrease of verbal output or mutism, seizures, dyskinesia and autonomic instability [1-3]. Psychosis is less common in adults. In children there can be prominent early psychiatric symptoms, but dysautonomia and hypoventilation are less frequent and severe [4,5].

The diagnostic approach is based on neuroimaging, EEG, lumbar puncture (lymphocytic pleocytosis or oligoclonal bands) and antibody testing on serum and cerebrospinal fluid [6].

Another NMDAR encephalitis characteristic is its association with tumors (mostly ovarian teratomas) and herpes simplex infection [7]. There is evidence that tumor identification and treatment and immunotherapy are responsible for stabilizing or slowing disease progression.

Currently, we have not found yet any biomarkers that can be useful to guide therapy or predict outcome.

Case Presentation

A 46-year-old Italian woman was found pathologically excited, anxious, and restless. For this reason, she was admitted to the Psychiatry Department, where it was decided to start an antipsychotic therapy with olanzapine and delorazepam. After two days, she was discharged clinically compensated. Nevertheless, she came back to Psychiatry because she was feeling sick.

During her hospitalization, she underwent brain MRI with contrast that was negative for any findings. Blood tests revealed increased thyroglobulin antibody levels (112 UI/mL). Electroencephalogram showed diffused slow and sharp waves, while lumbar puncture demonstrated lymphocytic pleocytosis (72 cells). Thus, it was decided to transfer the patient to neurology.

Principal viral and bacterial meningoencephalitis were excluded, and anti-NMDA receptor antibodies were detected in the cerebrospinal fluid and serum. A full body CT scan was performed, that showed left thyroid lobe inhomogeneity and tracheal deviation. Furthermore, total body PET demonstrated left thyroid nodule uptake.

Discussion

At the Neurology Department, she was first treated with a 5-day cycle of high-dose methylprednisolone associated with a 7-day cycle of plasmapheresis. Subsequently, she was given 5-day cycle of immunoglobulins. Her clinical status fluctuated following initiation of treatment, and it was necessary to transfer her to ICU because of important psychomotor agitation and difficulty in carrying out treatments.

Lumbar puncture was repeated, and it showed minimal lymphocytic pleocytosis (5 cells) and anti-NMDA receptor antibodies persistence. Repeat brain MRI were also performed, which underscored right hippocampus and amygdala hyperintensity.

Because of neurological worsening, corticosteroids were again administered, which was accompanied by a progressive reduction in oral dose. Furthermore, the immunoglobulin cycles were repeated monthly.

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Electroencephalograms (EEG) initially showed a slow, continuous, rhythmic activity in the theta range. This pattern is typically associated with the catatonic-like stage [8]. Moreover, diffuse delta brushes, a characteristic EEG pattern of anti-NMDAR encephalitis [9], were evident.

During hospitalization, the patient progressively showed a slight improvement in mental status, self-orientation, disease insight and EEG pattern.

With regard to the association with tumors, after total body TC and PET results, otolaryngologists agreed to recommend thyroidectomy because of the uncertain presence of thyroid cancer and tracheal compression. Actually, we know that the most frequent tumor autoimmune encephalitis-associated is ovarian teratoma, but no one has ever described a correlation with thyroid tumors or thyropathy.

After one month from discharge, although maintaining normal consciousness, motor, and sensory function, she had a small limitation in executive skills (MoCA 25/30) without implications in daily life activities.

Lesson Learned and Recommendations

First of all, we have to remember that NMDAR encephalitis not only is the most common autoimmune syndrome, but also it has to be considered on the differential diagnosis of all patients presenting encephalopathies. This is well represented by a multicenter report from the United Kingdom which found that this condition is responsible 4% of encephalopathies [8].

This case report highlights the importance of considering every imaging result suggestion of probable cancer or thyropathy. From this perspective, it would be interesting to evaluate thyroid function and structure in other patients.

In the end, symptoms presented by these patients are often thought to be purely psychiatric, so these conditions are often misdiagnosed. Unfortunately, a favorable outcome is time dependent. We have to remember that organic causes of psychosis have to be fully evaluated and considering the lack of biomarkers in clinical practice, imaging results, blood test and clinical data have to be integrated as much as possible.

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