Case Report

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A Rare Case of Paraneoplastic Limbic Encephalitis leading to Epileptic Seizure in a Patient with Ovarian Carcinoma

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Abstract

Paraneoplastic limbic encephalitis (PLE), a rare and diagnostically-challenging encephalopathy, is frequently associated with an underlying malign neoplastic tumor. Epileptic symptoms are uncommon but can be the first sign of the disease. We present a patient admitted to our intensive care unit (ICU) unit with epileptic seizure and a Glasgow Coma Scale (GCS) of six. All tests and investigations that had been utilized for this patient's diagnosis, including blood tests, serological analyses, magnetic resonance imaging (MRI), electroencephalogram (EEG) and cerebrospinal fluid (CSF) test results were evaluated. The patient had been diagnosed with ovarian carcinoma within the last year. The patient's cancer history, her most recent complaints and MRI results were strongly suspicious for paraneoplastic limbic encephalitis. Her neurological condition improved rapidly in a few days with steroid therapy. This case showed that any neurological deterioration based on an ovarian oncologic disease can bring PLE to mind. The possibility of PLE must be taken into consideration in patients presenting with epileptic seizures after neoplastic diagnoses.

Key Words: paraneoplastic limbic encephalitis, ovarian carcinoma, seizure, epileptic

Introduction

Paraneoplastic limbic encephalitis is a rare condition which is often difficult to diagnose. It is an immune-mediated encephalopathy that is often found in relation with an underlying malign neoplastic tumor. Corsellis and colleagues first described PLE as a clinicopathological entity in 1968[1]. The limbic system is the area that is primarily involved, but other areas of the nervous system, particularly the brain stem may be affected. The diagnosis of PLE is very difficult. Symptoms of this entity are similar to that of various other diseases, such as, brain metastases of primary cancers, toxic and metabolic encephalopathies, hypertensive encephalopathy, side effects of cancer therapy, and viral or bacterial infections of the central nervous system (especially herpes simplex)[2]. Most of the cases are diagnosed by clinical presentation, EEG findings, MRI studies, CSF sampling and neuropathological examination. Specific antineural antibodies have not been investigated for PLE[2,3,4,5,6].

Paraneoplastic limbic encephalitis has increasingly been shown to cause epileptic seizures in patients. These seizures are suggested to occur by autoimmune-mediated mechanisms of antibody-associated limbic encephalitis[7,8]. Epileptic symptoms are uncommon, but may as well be the first symptom of PLE. We present a 73-year-old woman with ovarian cancer who was diagnosed with PLE after presenting with epileptic seizures.

Case Report

A 73-year-old woman was admitted to ICU from another hospital with a preliminary diagnosis of status epilepticus. On the first evaluation, she was unconscious with a Glasgow Coma Scale of six. In her history, she was found to have a mild headache, anxiety and had demonstrated personality changes within the last three weeks. She had been evaluated by a psychiatrist and given risperidone treatment. In spite of the treatment, her complaints and symptoms had progressed. She had short term memory loss, agitation, depressive mood and personality changes. She was admitted to the previous healthcare center with stupor one day before; however, she had an epileptic seizure on the same day even though the patient had no history of epilepsy. Her epileptic seizure was still ongoing. Her MRI report was showing temporal cortical and subcortical, insular and right thalamic regional hyperintensities on T2 and flair sequences (Figure 1 and 2). Afterwards, she was referred to our hospital for further diagnosis and management. While evaluating the medical history of the patient we found that she had ovarian carcinoma which was diagnosed 1 year ago. She had been operated on and had received six cycles of chemotherapy after the operation. She was still attending follow-up studies in oncology.

When she was admitted to the ICU, she was unconscious and intubated. She was under sedation with midazolam. Her physical examination revealed pupillary isocoria, positive

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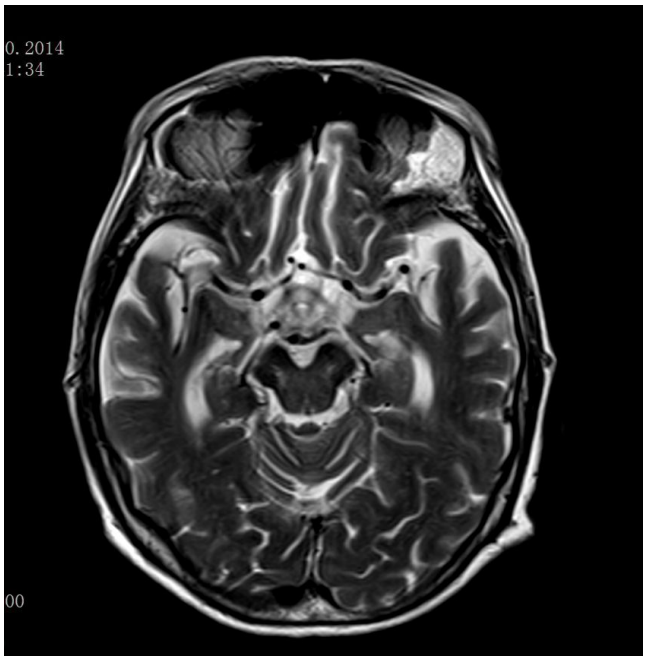

Figure 1. T2 image of first MRI scan presenting intensity changes at temporomesial and limbic areas

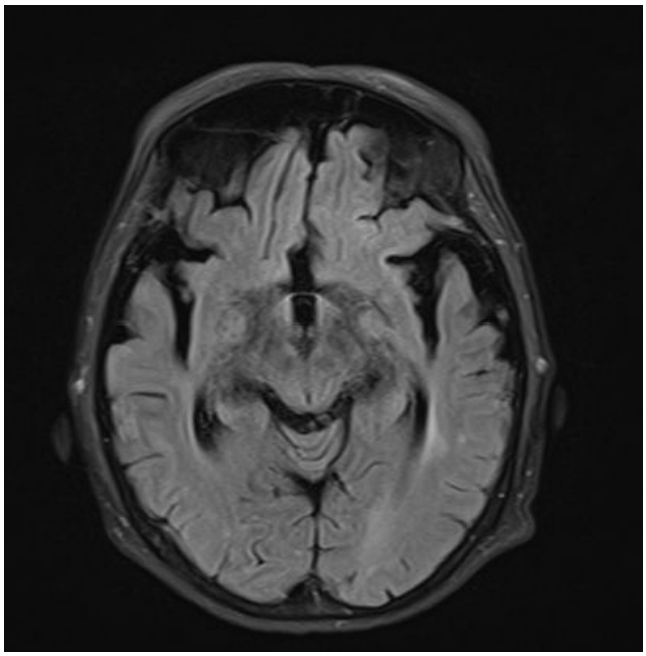

Figure 2. Flair image of first MRI scan presenting intensity changes at temporomesial and limbic areas

light reflex (bilaterally), incomprehensive verbal response and strained arms and legs. In addition to midazolam, we have continued to parenteral levetiracetam for treatment of the status epilepticus. There was no fever. Blood test results, including CBC, sedimentation, CRP and procalcitonin levels, were not signifying an infection. An infectious diseases specialist was consulted and lumbar puncture was performed. The CSF was clear and had unpressurized flow. A sample was sent to the laboratory for further tests. Blood and CSF PCR test results (especially for antineural antibodies) were all uneventful.

The patient's cancer history, her most recent psychiatric complaints and MRI results were strongly suspicious for paraneoplastic limbic encephalitis. The patient was treated at second day of hospitalization with high dose (1000mg / day) intravenous methyl prednisolone additionally to intravenous levetiracetam 1000mg / day for five days. The patient's sedation was stopped on the 3rd day and the seizures were under control. The general condition of the patient improved rapidly. She was extubated on the same day. Despite having mild confusion, she could communicate verbally. All four extremities were moving actively and spontaneously,

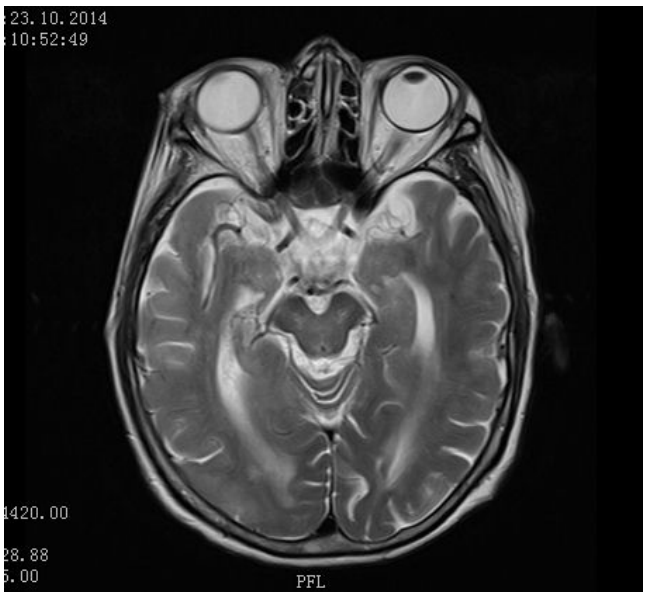

Figure 3. T2 image of control MRI scan presenting regression of intensity changes at first week of the treatment

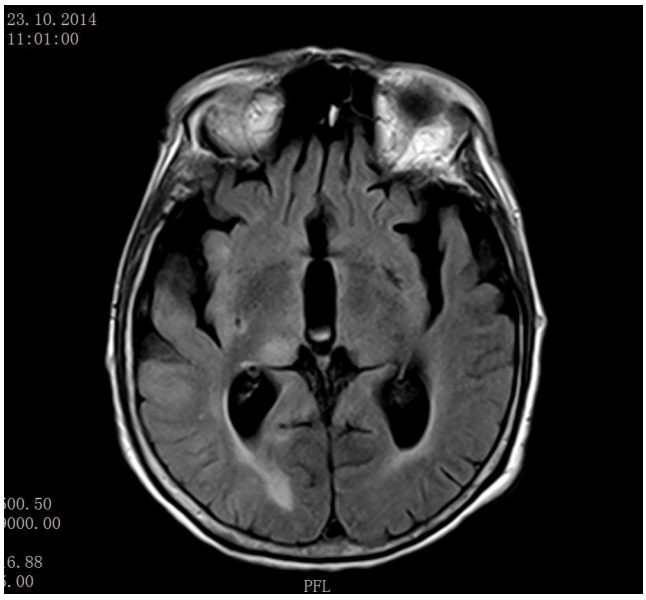

Figure 4. Flair image of control MRI scan presenting regression of intensity changes at first week of the treatment

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and she was responding to commands. Laboratory CSF examination results were negative for CMV IgM, HSV Type 1 IgM, HSV Type 2 IgM, indicating that there was no central nervous system infection. When cranial MRI examination was repeated, lesions in the limbic field were found to be in regression (Figure 3 and 4). After EEG examination, paroxysmal epileptiform activity in both temporal fields (more dominant in the right field) was observed. Following five days with high dose methyl prednisolone and antiepileptic treatment and supportive care, it was observed that the patient's neurological status was recovering swiftly. After she was discharged from the intensive care unit, she was followed in a normal ward and showed dramatic regression of psychiatric symptoms. Unresponsiveness to initial antiepileptic therapy and rapid and good recovery with additional high dose steroid therapy was confirmed our initial diagnosis of PLE. After a few days follow up in the department, her neurological examination was unproblematic and she was discharged with low dose oral prednisolone (2x40mg per a day) and oral levetiracetam (2x500mg) treatment.

Discussion

In the literature, patients with PLE often have an acute or subacute onset of recent memory disorder associated with psychiatric manifestations, including personality changes, depression, hallucination, irritation and agitation[1,3,5]. In our case, headache, personality changes and following agitation, dementia and progressive rapid course that finally led to an epileptic seizure were typical for the diagnosis of limbic encephalitis. Her symptoms and ovarian adenocarcinoma history were the key features. In patients with PLE, tumor detection rate is around 60%. Sometimes, PLE is the first diagnostic sign of a neoplasm. While the most frequent malignancy observed together with PLE is small cell lung cancer, ovarian tumors are not rare. As seen in our case, patients may apply to the hospital with epileptic seizures[7,8]. Treatment of PLE includes steroid therapy, immunosuppression and immunomodulation. Patients with PLE respond often demonstrate dramatic response to therapy. In our case, the patient's epileptic seizure and psychiatric manifestations improved after a 5-days course of glucocorticoid therapy, similar to the results of another study[6].

Conclusion

Our case showed that any neurologic deterioration based on an oncologic disease must bring PLE to mind. It should not be forgotten that, when PLE is diagnosed, a dramatic recovery can be possible with steroids and immune therapy.

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