

An emerging problem in clinical practice: how to approach acute psychosis

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Abstract

Limbic encephalitis (LE) is rare, presents with memory impairment, seizures and behavioral disorder. We present a 44-year-old female with an agitation-depressive disorder associated with delusions and hallucinations, admitted to our hospital with the diagnosis of psychosis. A computed tomography (CT) scan of the brain and lumbar puncture on admission were normal. Because of clinical deterioration and addition of seizures in the clinical picture, further workup with serum and repeat cerebrospinal fluid studies, magnetic resonance imaging (MRI), and electroencephalogram disclosed a lesion in the left medial temporal lobe consistent with LE. The patient was treated symptomatically with antidepressive, antipsychotic and anticonvulsant drugs. Aggressive diagnostic tests for the presence of an occult cancer were negative. An 8-year follow up has not revealed a tumor to support a paraneoplastic origin of LE. This case, initially diagnosed and treated as psychosis, is a case of non-paraneoplastic, non-infective LE, probably caused by an autoimmune mechanism.

Introduction

Limbic encephalitis has a subacute onset of memory impairment, disorientation, seizures, hallucinations and changes in behavior.^{1,2} Men are more often affected than women, and temporal lobes and hippocampi are usually involved. Magnetic resonance imaging (MRI) is useful for the detection of these morphological abnormalities.

In most cases, LE is of paraneoplastic origin and LE symptoms may precede the diagnosis of cancer for a period of months to many years.^{3,4} LE may also be due to viral infections^{5,6} or, in rare cases, may be a manifestation of an immune-mediated reaction of unknown origin.^{1,7}

We present the clinical features, MRI, laboratory findings and outcome of a patient with

subacute non-paraneoplastic, non-infective LE, presenting as psychosis.

Case Report

A 44-year-old woman was admitted to our hospital with a 4-week history of progressive behavioral-affective disorder, consisting of agitation, general anxiety, insomnia, attention deficit, labile mood and depression. A computed tomography (CT) scan of the brain performed on admission was negative and the cerebrospinal fluid (CSF) was normal. The diagnosis of psychosis was made, and antipsychotic and antidepressive drugs were initiated. Over the following days, the patient developed hallucinations and delusional ideas, severe short-term memory impairment, and mild retrograde amnesia. Some episodes with fear, nausea, atypical abdominal sensation and depersonalization were considered to be complex partial seizures. An MRI scan of the brain was performed and showed a high signal intensity lesion in the left medial temporal lobe on T2-weighted images (Figure 1). An electroencephalogram (EEG) demonstrated paroxysmal sharp theta and delta waves in both temporofrontal regions. Anticonvulsants (oxcarbamazepin) were added to her treatment. Despite numerous cultures and serological examinations of blood and CSF, no infectious agent was detected. Sensitive PCR and hybridization showed neither HSV type 1 nor 2 DNA genomes in the CSF.

Given these findings, the diagnosis of limbic encephalitis (LE) was made, considered to be a possible paraneoplastic manifestation. Extended workup was negative for the presence of tumor, and the sera and CSF anti-Hu antibody was negative. Sera were tested for autoimmunity, thyroid and coagulation disorder and all values were normal. The patient was discharged 20 days after her admission without seizures, but with severe memory and behavioral abnormalities.

Ten months later, a new follow-up MRI showed a decrease in those lesions already identified and bilateral atrophy of the medial temporal horn.

At the most recent follow up, eight years after the onset of LE, the patient's mood was quite stable, memory impairment had improved and hallucinations were absent. The etiology of LE in our patient remained unclear.

Discussion

Limbic encephalitis is usually a paraneoplastic manifestation. Small cell lung cancer (SCLC) is the most common type of cancer

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involved.⁸ Other forms of cancer are testicular,⁹ ovarian,^{4,10} breast cancer,¹¹ thymoma,¹² bladder, colon or kidney cancer, Hodgkin's disease⁸ and epidermoid lung cancer.¹³ In LE, antigens located on tumor cells or capsid of a virus may trigger mechanisms of autoimmune response, so various antibodies have been related with LE. Anti-Hu antibodies are related with SCLC^{3,8,14} and anti-Ma2 antibodies have been found in association with breast¹¹ and testicular⁹ cancer.

Paraneoplastic LE has a subacute presentation whereas non-paraneoplastic, viral LE usually has an acute onset. Herpes simplex viruses, type-2-adenovirus⁵ and enterovirus⁶ have been accused of causing acute non-paraneoplastic LE. There are also rare cases of non-paraneoplastic LE that seem to be idiopathic, possibly due to autoimmune failure.¹ Reports associating LE with changes in immunity focus on either immunodeficiency or autoimmunity disorders. More specifically, there is one report where authors reported coexistence of common variable immunodeficiency and limbic encephalitis in a 16-year old female patient.¹⁵ Other authors reported limbic encephalitis related to lupus erythematosus,^{16,17} while there is a report of Vogt-Koyanagi-Harada disease associated with non-herpetic acute limbic encephalitis,¹⁸ suggesting a possible link between autoimmunity disorders and LE.

Short memory impairment, seizures and confusion are among the most common symptoms of LE. Psychiatric disturbances include affective and personality changes.^{4,5,14} There are cases which present only psychiatric symptoms, such as anxiety, confusion and hallucinations, leading to incorrect diagnosis of schizophrenia or other psychotic disorders.^{3,8,19,20} A normal CT scan and subacute onset of the symptoms increase the possibility

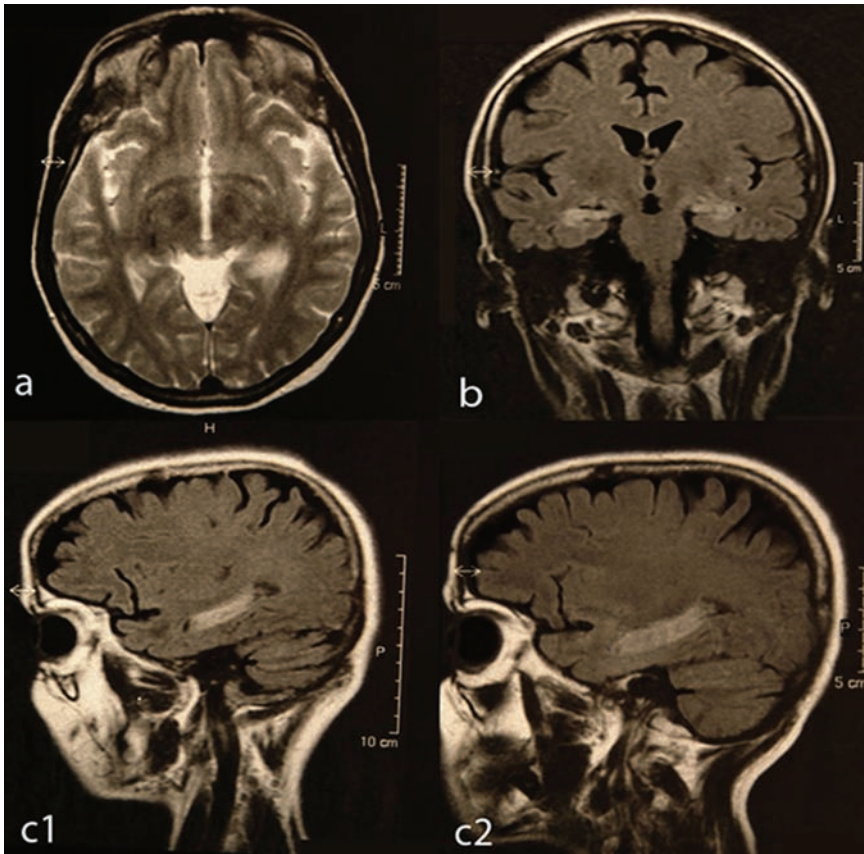


Figure 1. Admission magnetic resonance imaging scan of the patient's brain showing a high signal intensity lesion in the left and right medial temporal lobe on T2-weighted images. (A) Transverse; (B) Coronal; (c1) Sagittal right; (c2) Sagittal left.

of misdiagnosis. In these cases, an MRI scan can reveal the cerebral abnormalities of LE.^{7,8} EEG may also be indicative of encephalitis, showing epileptiform activity and diffuse slow waves or discharges of sharp waves in temporal lobes.^{3,8,14} Analysis of CSF may demonstrate inflammatory changes, including mild pleocytosis and increased proteins.¹⁴

Since paraneoplastic LE is much more common than non-paraneoplastic, extensive diagnostic tests should be performed to rule out cancer at an early stage. Follow up is necessary to exclude late onset of a tumor, since this may appear as long as six years later.⁴ In our patient, an 8-year follow up did not reveal any occult cancer, suggesting autoimmune LE to be the most probable cause. There is little likelihood that the patient will develop a malignant condition in the next years.

In conclusion, a psychotic event can sometimes conceal the diagnosis of LE. Thus, in suspected cases a normal CT does not exclude LE, and an MRI is warranted. An intensive diagnostic intervention is necessary in order to exclude a possible occult cancer. Patients without occult cancer, and without laboratory findings of viral encephalitis, should be followed up for a period of many years, since LE may precede the development of cancer.

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