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REVIEW ARTICLE

Limbic Encephalitis: A Narrative Literature Review

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ABSTRACT

Limbic encephalitis is a disease included in the group of autoimmune encephalitis triggered by different factors, including paraneoplastic, infectious, and pharmacological, among others. The main symptoms are memory impairment, seizures, and psychiatric symptoms. This disease can cause severe neuropsychiatric and cognitive sequelae if not treated in a timely manner, and, if underdiagnosed, it can worsen the prognosis when an underlying unidentified tumor exists. Given the importance of this condition, we wrote this article to provide an update on the diagnostic and therapeutic approach for these patients, according to possible findings in imaging, serum, and cerebrospinal fluid studies. Antibody detection tests can be used to identify, according to the location of the antigen (cellular surface, intracellular or synaptic), the relationship with tumors, response to treatment and prognosis. In case of paraneoplastic encephalitis, the therapeutic approach includes specific oncological treatment, immunotherapy, and symptom management, generally simultaneously.

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Encefalitis límbica: una revisión narrativa de la literatura

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RESUMEN

La encefalitis límbica es una enfermedad incluida en el grupo de encefalitis autoinmunes desencadenada por diferentes causas incluidas paraneoplásicas, infecciosas, farmacológicas, entre otras. Los síntomas principales son alteraciones de la memoria, convulsiones y síntomas psiquiátricos. Esta enfermedad puede provocar secuelas neuropsiquiátricas y cognitivas graves si no se hace un tratamiento oportuno y si se subdiagnostica puede empeorar el pronóstico cuando existe un tumor subyacente no identificado. Dada la importancia de esta condición, desarrollamos este artículo para proporcionar una actualización sobre el enfoque diagnóstico y terapéutico de estos pacientes, de acuerdo con los posibles hallazgos en estudios de imágenes, de suero y de líquido cefalorraquídeo. Las pruebas de detección de anticuerpos permiten identificar, según la ubicación del antígeno (superficie celular, intracelular o sináptico), la relación con tumores, la respuesta al tratamiento y el pronóstico; en caso de que se trate de una encefalitis paraneoplásica, el abordaje terapéutico incluye el tratamiento oncológico específico, la inmunoterapia y el manejo para control de los síntomas, generalmente de forma simultánea.

INTRODUCTION

The limbic system is composed of cortical and subcortical structures that connect visceral and emotional states to cognitive and behavioral processes (1). Initially, the term *limbic* was used by Thomas Willis in 1664 to designate a cortical region located around the brain stem, but this concept has changed (1). In 1878, Paul Broca spoke of "le grand lobe limbique" referring to an olfactory structure common to all mammalian brains, but which could also have an effect on the control of social interactions, memory consolidation and emotion formation (1-2). Subsequently, Christfried Jakob in 1906 and James Papez in 1937 formulated the first unified network model for connecting actions and perceptions to emotions in humans (1-2). In 1948, Yakovlev suggested a new conformation of such a network. In two essays in 1949 and 1952, Paul MacLean incorporated the work of Papez and Yakovlev to propose the structure of the limbic system, which has remained virtually unchanged to the present day (1-2).

In the 1990s, the use of functional neuroimaging and diffusion tractography made it possible to study the anatomy of the limbic system in the living human being. Different structures belonging to that system were identified, including the amygdala, the hippocampus, the fornix, the mammillary bodies of the hypothalamus, the mediodorsal and anterior nuclei of the thalamus, the cingulate cortex, and the prefrontal cortex (1,3-4). The functions of the limbic system are multiple, as it is responsible for memory processes, spatial orientation, behavioral inhibition, visceral sensory integration, association learning through reward circuits, pain perception, empathy, attention, and self-recognition, among others. Thus, alterations in this system can trigger diseases with different clinical patterns (1-4).

Limbic encephalitis (LE) is a disease of relatively recent description. It was first documented by Brierly *et al.* in 1960 when they wrote about three cases of "subacute encephalitis in late adulthood with limbic involvement", two of them with associated neoplasms. At that time, however, they did not consider that there was a relationship between the two conditions. Years later, around 1968, Corsellis *et al.* used the term *limbic encephalitis* to describe a patient with severe short-term memory loss and two patients with equal amnesic impairment but who also had a dementia syndrome associated with bronchial carcinoma. The authors decided to review 8 other reports and subsequently concluded that there was an association between LE and systemic cancer (5,6).

By the 1980s and 1990s, the disease was associated with some antibodies against neuronal surface antigens in patients without evidence of oncologic diagnoses, and reports were made of LE in patients with 'atypical' neoplasms, either because they had not been previously described (such as thymomas or teratomas) or because of their occurrence in the presence of benign tumors. Later on, specific diagnostic criteria were developed and cases were found for causes other than a neoplasm *per se* (5-7). Due to the clinical importance of this disease and the need for a systematic approach to these patients, we decided to perform a narrative literature review to update the existing information as regards clinical presentation, patient management, differential diagnoses and current evidence regarding treatment.

METHODS

To carry out this narrative review, a search was conducted for articles published in the last 10 years using the following MeSH and DeCS terms: "limbic encephalitis", "autoimmune limbic encephalitis",

"paraneoplastic limbic encephalitis", "limbic system", "treatment", "diagnosis", "encefalitis límbica", "encefalitis límbica paraneoplásica". The following search string was used in the NCBI PubMed database: (limbic encephalitis[MeSH Major Topic] AND ((autoimmune[Text Word]) OR (paraneoplastic[Text Word]) AND (diagnosis[Text Word])) OR (management[Text Word])) OR (treatment[Text Word])) AND (encephalitis[Text Word])) AND (limbic[Text Word]). It retrieved 314 documents. In addition, a search was performed in Google Scholar with the following string in Spanish: allintitle: (encefalitis límbica AND autoinmune AND paraneoplásica AND diagnóstico AND tratamiento). It retrieved 269 results. The inclusion criteria for both searches were all those articles in which the topic of limbic encephalitis was updated from 2012 onwards, whether in Spanish or English.

DEVELOPMENT OF THE TOPIC

Definition and diagnosis

LE is a relatively rare inflammatory disease affecting the limbic system. Autoimmune in origin, it is associated with serum and intrathecal antibodies against intracellular and synaptic surface antigens of neuronal cells, and thus it belongs to the category of autoimmune encephalitis (AE) (7-9). Historically, the most commonly related triggers include tumors, in which case it is referred to as paraneoplastic limbic encephalitis (PLE); also, there are other factors such as viral infections or immune checkpoint inhibitor (ICI) drugs (9). LE occurs most often in adults older than 45 years but can affect people of all ages, while gender predominance varies with antibody type (9-10).

Clinically, it is characterized by acute or subacute onset of various neuropsychiatric disturbances, such as short-term memory loss, which is distinctive of this condition and may be its first clinical manifestation (11-12); autobiographical memory is preserved; and in untreated cases cognitive impairment may lead to the development of dementia (7). In addition, seizures and psychiatric symptoms such as depression, anxiety, confusion, irritability, and sensory-perceptual disturbances may occur. Delusional ideas are not common but, when present, may cause agitation. Other symptoms may include, among others, movement disorders, such as ataxia, dystonia or myoclonus; sleep disorders; and autonomic disorders (13-16).

Diagnosis is based on the combination of clinical symptoms and magnetic resonance imaging (MRI), an electroencephalogram (EEG) and cerebrospinal fluid (CSF) studies, as well as on the possible detection of a specific antibody. Sometimes, however, clinical manifestations do not include alterations in neuroimaging or CSF; or, on the contrary, damage is observed in the MRI without the associated typical clinical presentation (9,11,17-18). Table 1 shows the diagnostic criteria proposed by Graus *et al.* (19).

Table 1. Diagnostic criteria for definite autoimmune limbic encephalitis

The diagnosis can be made when four of the following criteria are met:

1. Subacute onset (rapid progression in less than 3 months) of recent or working memory deficits, seizures, or psychiatric symptoms.
2. T2-weighted fluid-attenuated inversion recovery (FLAIR) MRI findings revealing bilateral brain abnormalities highly restricted to the medial temporal lobes. FDG-PET may be used to meet this criterion.
3. At least one of the following:
   - CSF pleocytosis (white blood cell count >5 cells per mm^3).
   - Electroencephalogram (EEG) with epileptic or slow wave activity involving the temporal lobes.
4. Reasonable exclusion of alternative causes.

If one of the first three criteria is not met, a diagnosis of definite limbic encephalitis can only be made with the detection of antibodies against cell surface, synaptic, or onconeural proteins.

MRI: magnetic resonance imaging; FLAIR: fluid-attenuated inversion recovery; FDG-PET: fluorodeoxyglucose positron emission tomography; CSF: cerebrospinal fluid

Source: adapted from Graus *et al.* (19)

Specific findings on brain MRI include hyperintensities indicating inflammation in the medial regions of the temporal lobes on FLAIR and T2 signal sequences. This is estimated to occur in approximately 50% of cases (5,20-21). The use of fluorodeoxyglucose positron emission tomography (FDG-PET) is useful when EEG and MRI are negative; several recent studies suggest that PET would have greater diagnostic sensitivity for LE (9,19-20). A lumbar puncture is performed for CSF analysis, in which general inflammatory signs of AE may be found, such as moderate lymphocytic pleocytosis (<100 cells per mm^3), increased proteins and immunoglobulin synthesis with oligoclonal bands (which increase sensitivity for LE); however, in early stages of the disease, CSF results may be normal, and neuronal autoantibodies are detected in the CSF of most LE patients (7,9-10,22). The EEG is altered in about 50% of cases, and epileptic foci or activity may be found in one or both temporal lobes, in addition to focal or generalized slow activity (10,17,23).

Differential diagnoses

Differential diagnoses to consider include Hashimoto's encephalopathy, systemic lupus erythematosus (SLE), Sjögren's syndrome, polychondritis, and Behçet's disease, among others. In these conditions, the damage is usually more generalized at the cortical level and not so circumscribed to the limbic system (7,20,24). Infectious encephalitides, which usually present with fever, seizures, and more extensive imaging changes than AE, should also be ruled out; these include syphilis, tuberculosis, Lyme disease, and human immunodeficiency virus (HIV) infection (7,24-25). Nutritional deficits such as Wernicke's encephalopathy, which may present without ocular motility disturbances, must be considered; also, recreational and pharmaceutical drug use should be ruled out. Due to affective, behavioral, sensory-perceptual and thought content symptoms, mental illnesses should be evaluated as such (7,24).

Patient management

Below, in Figure 1, adapted from reference (9), we present a recommended algorithm for diagnosing patients with possible LE.

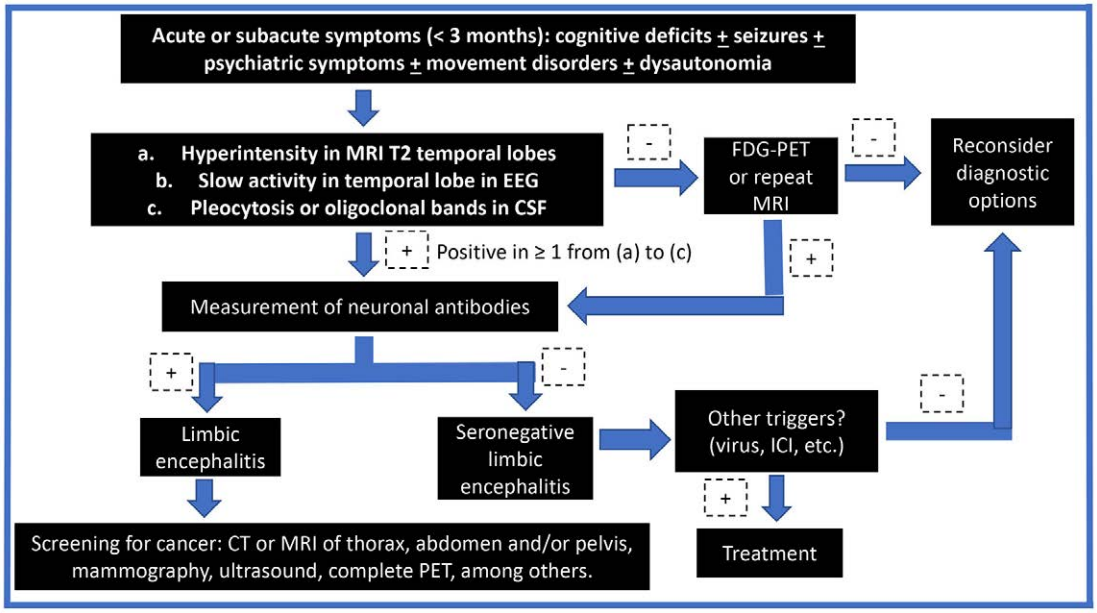

Figure 1. An approach to the diagnosis of limbic encephalitis

MRI: magnetic resonance imaging; FDG-PET: fluorodeoxyglucose positron emission tomography; ICI: immune checkpoint inhibitors; CT: computed axial tomography
Source: adapted from reference (9)

Antibody determination

The presence of antineuronal autoantibodies in serum or CSF is one of the most specific findings for the diagnosis of LE and occurs in more than 80% of patients (7). It is essential to determine the antibodies and their specific targets, whether intracellular proteins, neuronal cell surface antigens (directed to receptors or membrane ion channels), or synaptic antigens, because those acting at the extracellular level respond normally when the immune response or the tumor are targeted, whereas intracellular ones do not respond well to such therapies (except for anti-Ma2, associated with testicular tumor) (7,26-29).

Ectopic expression of a neuronal protein in a tumor appears to trigger the antitumor immune response; onconeuronal antibodies thus arise as part of the antitumor immune response against different intracellular proteins; the injury is mediated by cytotoxic T lymphocytes, whereas antibodies directed against membrane antigens exhibit cytotoxicity due to complement-mediated humoral immune mechanisms (7,26-29). It should be noted that a positive antibody detection result is not mandatory for the diagnosis of limbic encephalitis, since in about 7% to 26% of cases no antibodies were found, which is termed seronegative LE (9,30) (Table 2).

Table 2. Classification of the main antibodies associated with limbic encephalitis

Antibodies against neuronal surface antigens	Antibodies against intracellular antigens	Other antibodies
Anti-LGI1 It could be associated with thymoma, SCLC and others, such as breast, thyroid, colon, and pancreatic cancer, among others, but it is usually the Ab least associated with malignancy, with a frequency of less than 10%.	**Anti-Hu/ANNA-1** SCLC. With a frequency of association with malignancy greater than 90%.	**Anti-GAD65** (It is a synaptic and/or intracellular Ab). SCLC, thymoma. With a frequency of association with malignancy of about 25%.
Anti-AMPAR SCLC, thymoma or breast cancer, with a frequency of association with malignancy of about 60%.	**Anti-Ma2** Testicular cancer. With a frequency of association with malignancy greater than 90%.	**Anti-NMDAR** (It is an Ab against a membrane and/or synaptic antigen). Ovarian tumor in women younger than 45 years, with a frequency of association with malignancy of about 40%. Also testicular tumor.
Anti-GABA BR SCLC. With a frequency of association with malignancy of about 50%.	**Anti-CRMP5/CV2** SCLC, thymoma, NSCLC. With a frequency of association with malignancy greater than 90%.	**Anti-D2R (dopamine-2 receptor)** Not associated with LE or tumors but with other types of AE such as basal ganglia encephalitis. Parkinsonism.
Anti-CASPR2 It could be associated with thymoma but usually has a low association with malignancy, with a frequency of about 20%. Morvan's syndrome.	**Anti-Amphiphysin** SCLC, breast cancer. With a frequency of association with malignancy greater than 90%. It is associated with several neurological disorders such as paraneoplastic stiff-person syndrome.	**/**
Anti-VGKC It could be detected in thymomas but is not usually associated with malignancy. It has been associated with Morvan's syndrome.	/	/
Anti-mGluR5 Hodgkin lymphoma. With a frequency of association with malignancy of about 50%. Ophelia syndrome.	/	/
Anti-GlyR Its association with tumors is uncommon. It may present with stiff-person syndrome.	/	/

Frequency of association with tumors adapted from references (10,20). Ab: Antibody; LE: limbic encephalitis, AE: autoimmune encephalitis; SCLC: small cell lung cancer. NSCLC: non-small cell lung cancer; LGI1: leucine-rich glioma inactivated protein 1; AMPAR: α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor; GABA BR: γ-aminobutyric acid receptor B; CASPR2: contactin-associated protein-like 2; VGKC: voltage-gated potassium channels; mGluR5: metabotropic glutamate receptor subtype 5; GlyR: glycine receptor; ANNA-1: antinuclear neuronal antibody type 1; CRMP5: collapsin response mediator protein 5; GAD: glutamic acid decarboxylase; NMDAR: N-methyl-D-aspartate receptor.

Source: adapted from references (9,10,31)

The following are some clinical features of the most important antibodies:

Cell surface antibodies

- Anti LGI1 (Leucine-rich1 glioma-inactivated protein): Encephalitis due to these antibodies is included in VGKC-associated diseases (voltage-gated potassium channels) (32-34). Its clinical manifestations include faciobrachial dystonic seizures, which are very specific to this encephalitis and are found in 47% to 72% of patients (32), hyponatremia, and amnesia (in most patients); it is also more common in persons over 50 years of age. The prognosis, in general, is good (32-34).
- Anti-AMPAR (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionate receptor): Patients may present with confusion, amnesia (in 52% of cases), psychiatric symptoms (in many cases, psychotic) and seizures (20); less frequent symptoms are hemiparesis, nystagmus and ataxia (35).
- Anti-GABA BR (γ-aminobutyric acid-B receptor): The main symptom is epileptic seizures; these seizures are usually refractory to drugs but respond well to immunotherapy; other symptoms are cognitive impairment (memory loss) and mental (may be psychotic) and behavioral disorders (9,36,37).
- Anti-VGKC: The two main antigens in this complex are LGI1 and CASPR2 (32). A study of 96 patients with VGKC antibodies showed that 57% had antibodies to LGI1, 20% had antibodies to CASPR2, and 3% were specific to the channel itself. LGI1 is more specific to limbic encephalitis; in contrast, CASPR2 is more specific to neuromyotonia but may also present LE (20). It is associated with subacute amnestic syndrome, partial seizures, REM sleep disturbances and hyponatremia (20,38,39).

Intracellular antibodies

- Anti-Hu/ANNA 1 (neuronal antinuclear antibody type 1): Hu is a protein that binds RNA located in the nuclei of neurons and plays an important role in neural development (20). LE occurs in 10% to 20% of patients; other manifestations include subacute cerebellar degeneration, sensory and/or motor neuropathy, brain stem encephalitis, cerebellar ataxia, autonomic neuropathy, and symptoms of multifocal cortical disease, such as epilepsy, aphasia, and alterations in visual fields (14,20,38).
- Anti-Ma2 antibody: These proteins have a role in mRNA biogenesis and are expressed in neurons (19,38). LE is observed in 20% of patients; brain stem and hypothalamic dysfunction and cerebellar alterations may also be present (19,20,38).

Other antibodies

- Anti-GAD65 (glutamic acid decarboxylase 65): Its antibodies are associated with several neurological syndromes such as LE, stiff-person syndrome, cerebellar ataxia and progressive encephalomyelitis with rigidity and myoclonus (PERM) (40).
- Anti-NMDAR (N-methyl-D-aspartate receptor): It is a membrane receptor but also belongs to the group of encephalitides due to antibodies against synaptic proteins (41). It is a potentially lethal disorder. Its clinical manifestation is characterized by prodromal flu-like symptoms and then progresses to acute delusions and hallucinations, agitation, confusion, epilepsy, movement disorders, dystonia and catatonia, and even hypoventilation. Herpes simplex virus (HSV) has been described as one of the triggers of this encephalitis (41-43).

Is it paraneoplastic?

The most common neurologic paraneoplastic syndromes (NPS) are LE and cerebellar degeneration (29). Several diagnostic aids should be requested to rule out neoplastic processes; initially, a CT scan of the chest, abdomen and pelvis, with and without contrast; however, knowledge of the antibody detected helps to guide the search for cancer and order complementary studies-ultrasound, mammography, MRI and total body PET, among others (44). The tumors that most frequently induce PLE are small cell lung carcinoma, testicular tumors, breast and ovarian cancer, thymoma or Hodgkin's disease, among others (44-45).

Other triggers?

Viral encephalitis?

This is a strong diagnostic possibility because herpes simplex virus encephalitis (HSVE) is not that rare and, in fact, it is common to routinely prescribe acyclovir for patients with the characteristic clinical manifestations (46). The CSF analysis may produce false-negative results if obtained within 72 hours of the onset of neurologic symptoms (46-47). It is characterized by a rapid progression with altered consciousness, focalization, edema, and evidence of hemorrhage in CSF and MRI results (46). Human herpesvirus 6 (HHV-6) can cause encephalitis in immunosuppressed individuals following hematopoietic stem cell or bone marrow transplantation (46-47).

It should be noted that several neurological disorders have been associated with the COVID-19 virus, including ischemic strokes, different types of encephalitis (including LE, acute disseminated encephalomyelitis [ADEM], miscellaneous encephalitis, acute hemorrhagic necrotizing encephalopathy, and anti-NMDAR, among others), and leptomeningeal enhancement (48). Clinical symptoms include fever, seizures, headache, behavioral disturbances, altered consciousness, cognitive impairment, aphasia and focal motor deficits (48-50). For this encephalitis, the first line of treatment encompasses corticosteroids and intravenous immunoglobulin; and, in some cases, plasmapheresis (49-52).

Immune checkpoint inhibitor (ICI) drugs?

These are biologic anticancer drugs that can have central nervous system (CNS) and peripheral nervous system (PNS) complications (45). LE is the most frequent CNS complication (53); it has been observed in patients with small cell lung cancer (SCLC) but also in tumors not typically associated with NPS, such as melanoma and myxoid chondrosarcoma, and those receiving this type of drug (45). Most cases with this type of encephalitis showed marked neurologic improvement upon discontinuation of the ICI drug and management with steroids as the first line of treatment (29,45,53).

Treatment

Treatment consists of immunotherapy, tumor management (if present), and symptom control. Determination of antibody type can help predict response to immunotherapy (54). As a general feature, membrane and synaptic antibodies respond better to immunotherapy, since they are associated with fewer inflammatory infiltrates and fewer neoplasms, and, if the latter are present, the response upon tumor removal can be substantial (44,54). Intracellular antibodies, on the other hand, are usually more resistant to immunotherapy; therefore, the most important thing in these cases is to treat the tumor early with surgery, chemotherapy or radiotherapy, and thus have a better response to immunotherapy. Limbic encephalitides even without a well-characterized group of antibodies have an adequate response to immunotherapy (7-8,44,54).

Treatment algorithms are based on case reports and retrospective studies; it is recommended to start treatment as early as possible to avoid hippocampal atrophy and cognitive impairment; the goal is not only recovery but also to avoid relapses and progression (22,55). Table 3 presents the drugs currently used as first-line immunotherapy, which can be used either as monotherapy or combined therapy (24-25,54).

Table 3. First-line immunotherapy in limbic encephalitis

First-line drugs	Dosage
IV methylprednisolone	High-dose pulses. 1 g per day IV for 5 days.
IV immunoglobulin (IV Ig)	0.4 g/kg/day for 5 days or 2 g/kg divided over 3–5 days.
Plasmapheresis (plasma exchange or immunoadsorption)	3 to 5 sessions over 5–10 days.

IV: Intravenous

Source: adapted from references (24,25,54)

In case of failure to respond to first-line treatment within 2 to 3 weeks or worsening of symptoms, second-line immunotherapy is used, mainly with rituximab (intravenous dose of 375 mg/m^2 1 time a week for 4 weeks) or cyclophosphamide (dose of 750 mg/m^2 every month for 3–6 months); mycophenolate mofetil or azathioprine are sometimes used (24-25,54-56). In refractory cases, in which there is no response to first- or second-line therapy or there is a relapse, third-line therapy may be required, which is still experimental, with tocilizumab, bortezomib, and daratumumab, among others; and even low doses of interleukin 2 (IL-2) could be useful. Tocilizumab is a humanized monoclonal antibody directed against the IL-6 receptor to prevent the inflammatory cascade (25,57).

As for symptomatic treatment, many patients require antiepileptics at high doses and with different combinations, as some develop refractory epilepsy (58-61). Sometimes, immunotherapy is more effective against seizures than anticonvulsants; for example, in anti-LGI1 encephalitis (61). Commonly used psychotropic drugs are antidepressants and antipsychotics, among others; it is recommended to be careful with interactions and to monitor the seizure threshold (avoid clozapine and olanzapine, as they can lower this threshold); typical neuroleptics should also be avoided so that the disease is not confused with a neuroleptic malignant syndrome; therefore, quetiapine could be a good option (58-61). If agitation is present, benzodiazepines can be used (58,60-61). In cases of poor response to psychotropic drugs, electroconvulsive therapy with anesthesia and relaxation (ECTAR) has been used; although its mechanism of action is not clear, it is believed that it could be related to the up-regulation of NMDA receptors, since it has worked precisely when there are circulating anti-NMDA antibodies (41,56,61).

It is important to avoid abrupt discontinuation after acute treatment in order to prevent early recurrence; therefore, a bridging strategy for slow discontinuation or initiation of long-term treatments (if prescribed) should be implemented. A common strategy is to start with oral prednisolone at 1 or 2 mg/kg/day immediately after completion of acute therapy and then taper it gradually over weeks to months (61). If there is poor response to first- and second-line therapy or relapse, maintenance therapy with drugs such as azathioprine, mycophenolate mofetil (MMF), or methotrexate is required for at least 1 year after primary therapy is discontinued to avoid the high relapse rate (24,61).

Follow-up and prognosis

The follow-up of patients whose initial screening for tumors was negative should be repeated at least every 6 months for a minimum of 4 years (61). On the other hand, antibody titers are detectable for months or even up to 6 years after clinical remission in LE of intracellular subtype; hence, there is no good clinical correlation for the follow-up, whereas in cases presenting with membrane antigens, these levels decrease as symptomatic improvement occurs (61-62). LE caused by GAD, LGI1 or CASRP2 antibodies showed little improvement in memory even after receiving immunotherapy (9). Follow-up should include neuropsychiatric assessments for several months or years, depending on the individual patient, to assess cognitive recovery and neuropsychiatric symptoms (62).

CONCLUSIONS

Increasing knowledge about LE shows the importance of this disease due to its neurocognitive sequelae, complications, and poor prognosis if not diagnosed and treated early. Medical staff should suspect it whenever a patient presents with psychiatric symptoms, seizures and memory disturbances. The initial diagnosis can be challenging for the physician due to its differential diagnoses and because the results of imaging, serum and cerebrospinal fluid analyses may be normal. Its underlying cause and triggers, including COVID-19 infection, should be found and treated promptly. Antibody detection shows that intracellular antibodies are more closely associated with neoplasms and less responsive to immunotherapy than surface or synaptic antibodies. Tumor resection is essential for the complete recovery process, as well as to avoid relapses and to speed up the resolution of the disease. In general, most patients with LE have an adequate response to immunotherapy. Complementary symptomatic treatments with psychotropic drugs are part of the arsenal for patient management, and, in cases of treatment refractoriness, ECTAR is an option that has shown efficacy in some cases.

CONFLICT OF INTEREST

There are no conflicts of interest to be reported.

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