Psychosis as an initial symptom of autoimmune encephalitis with negative antibodies☆

Psicosis como síntoma inicial de encefalitis autoinmune con anticuerpos negativos

Dear Editor,

Autoimmune encephalitides form part of the inflammatory neurological syndromes of the central nervous system. They are measured by a inflammatory cross-over reaction to intracellular antigens (Hu, Yo, Ri, Ma2, CV2/CRMP5, amphiphysin) or the neuronal surface (NMDA, AMPA, GABAb, glycin, VGKC complex) and are associated in some cases with oncological diseases.[1,2] They usually present in the form of cognitive disorders, epileptic seizures, mood disorders and/or psychotic disorders. Symptoms vary depending on the antibodies involved[3] and non presentation of all the symptoms is common.[4] Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT) is another neurological disorder where an encephalopathy and an autoimmune thyroiditis present together. SREAT may present with or without involvement of thyroid hormones and is associated with epileptic seizures, disorientation, myoclonus, ataxia, cognitive impairment and psychosis.[5] It is an interesting fact that in 10% of cases, symptomatology is reduced exclusively to affective disorders[6] or psychotic disorders.[7,8] Autoimmune encephalitis and encephalopathies such as SREAT are neurological pathologies, which may imitate psychiatric syndromes, but unlike these, they present with changes in cerebral nuclear magnetic resonance (NMR), in cerebrospinal fluid and/or in the electroencephalogram.

We present the case of a 29-year-old patient diagnosed with autoimmune encephalitis with negative antibodies. He did not consume toxic substances nor was there any history of other psychiatric disorders in the family. The start of the disease began when he was 20 years of age with a psychotic episode characterised by paranoid delusional ideation, auditory and visual hallucinatory symptoms and conciliation and maintenance-sleep insomnia. The patient was admitted to the acute psychiatric unit, where in the analysis on entry positive anti-thyroid antibodies were observed (MAK-TPO > 1.300 UI/ml, TAK > 175 UI/ml) with no alteration to thyroid hormones. After starting antipsychotic treatment with olanzapine at 20 mg/day, the patient was referred to the neuro-rehabilitation unit. A brain NMR scan was performed there which was normal. Lumbar puncture showed intrathecal IgG synthesis rate of 11%. Antineuronal antibodies and neuronal surface antibodies tested negative in serum and in cerebrospinal fluid. In the electroencephaologram a general slowing down of moderate severity was observed without potential epileptiforms. On suspicion of a SREAT, treatment was initiated with 100 mg/day prednisone, but the psychotic symptoms severely worsened and treatment had to be suspended 4 days later. After 72 h symptoms remitted and the patient was discharged with a diagnosis of unspecified psychotic disorder and Hashimoto thyroidism in treatment with 20 mg/day olanzapine. Two years later, the patient ceased antipsychotic medication and was asymptomatic up to 27 years of age, when he was admitted to the acute neurological unit with consistent symptoms of intense headache, delusional ideation of prejudice against his mother, psychomotor restlessness and conciliation and sleep-maintenance insomnia. Cerebral NMR was normal. Lumbar puncture again showed intrathecal IgG synthesis of 10.7% and negative antineuronal cell antibodies and neuronal cell surface antibodies.

The electroencephalogram showed a general moderate/serious slowing down without potential epileptiforms. In the Dem-Tect (cognitive Test) the patient obtained 5/18 points (indicator of a severe cognitive impairment). On suspicion of autoimmune encephalitis, treatment was initiative with immunoglobulins (3×10 g) for 5 days together with antipsychotic treatment with 20 mg/day olanzapine. As no improvement was observed, treatment with plasmapherisis was initiated (5 cycles) combined with 150 mg/day azathioprine which was effective and it was possible to reduce the olanzapine dose to 5 mg/day. Following absolute resolution of symptoms and with an *ad integrum* (Dem-Tect 18/18) cognitive recovery, the patient was discharged and sent home. At present, the patient is symptom-free and has been 24 months without any pharmacological treatment.

Al-Diwani et al.[9] (2019), in their systematic review with 1,100 patients on psychiatric symptoms in the population with encephalitis NMDA-R, observed that the most common psychiatric symptoms were affective and psychotic disorders. The clinical case we present shows the importance of carrying out an appropriate neurological screening in psychiatric patients, and the diagnostic difficulty between the SREAT and autoimmune encephalitis in a patient with Hashimoto thyroiditis. In our case, good response to plasmapheresis with azathioprine and the worsening of symptoms observed with corticoids suggested that this was an autoimmune encephalitis. Early treatment in autoimmune encephalitis with immunosuppressants, immunoglobulin or plasmapheresis is effective,[10] although specific relapses may appear in the future.[4]

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Thyroid alterations in bipolar patients on treatment with lithium☆

Alteraciones tiroideas en pacientes bipolares a tratamiento con litio

Dear Editor,

Lithium salts are considered to be the gold standard for the prophylaxis and treatment of bipolar disorders. Despite their toxicity and potential side effects, they are perhaps the only treatment capable of preventing episode recurrence and reducing the excessive mortality associated with affective disorders.[1]

The diverse changes on an endocrinological level which lithium may produce are well known, with thyroid alterations standing out, together with nephrogenic diabetes insipidus and hyperparathyroidism. Therefore, given their frequency in daily clinical practice, it is important to be aware of these situations and thus avoid treatment failure, false diagnoses and unnecessary therapy.

The main clinical effects of lithium on the thyroids are the appearance of goitre, with a presentation of between 40%–50%,[2,3] although these rates are variable, depending on the population sample studied, the duration of therapy and the diagnostic method used. The increase in the size of the thyroid gland is approximately double and diffuse, although it may also present as multinodular,[4] generally in the first 2 years of treatment.

Hypothyroidism is also a common entity in patients treated with lithium, in the presence or absence of goitre, and is generally subclinical, with an elevation in TSH levels $\geq$5 mU/L, with free T4 levels within the normal range (.7–1.4 ng/dL) and often in the absence of symptoms. Clinically significant hypothyroidism is uncommon.

Its prevalence widely varies from 3.4% up to rates of 6% to 52%,[3,5] depending on the population studied, age, sex, geographic origin and definition of hypothyroidism used.

Most patients are diagnosed during the first years after treatment initiation with lithium, with the mean time being 18 months,[6] although it may also develop during the first few months of therapy.

There is a series of risk factors for the development of lithium-induced hypothyroidism to take into account prior to the initiation of treatment. These include the presence of a family history of thyroid disease, being female, mean age (40–59 years), the presence of autoimmune thyroid disease (defined by positivity of antithyroid antibodies), a diet poor in iodine, raised levels of lithemia and rapid cyclers.[7]

Lithium-associated hyperthyroidism is relatively and most cases present after many years of treatment. The symptoms of thyroid hyperfuncion may be due to autoimmune thyroid disease (Graves' disease), toxic nodular goitre or silent thyroiditis, with the most common thyrotoxicosis aetiology in patients treated with lithium being temporary granulomatous thyroiditis.

Due to the high incidence of endocrinologic alterations in general and of the thyroid in particular, which occur during treatment with lithium, it is recommended that prior to treatment a thyroid examination and biochemical tests be performed, to include the determination of urea, keratinise, calcium, total proteins, plasmatic levels of SH, free T4 and antithyroid antibodies. Several authors recommend performing a thyroid ultrasound at the beginning, since it has been demonstrated to be a simple and inexpensive[8] screening method for goitre and thyroid alterations. Patients with normal thyroid function will be reassessed at 6 months and then annually.

When there is subclinical hypothyroidism (TSH $\geq$ 5 mU/L and $\leq$10 mU/L with normal free T4 l) is recommended at shorter intervals, every 4–6 months.[9]

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