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Case Reports

A REVERSIBLE RAPIDLY PROGRESSIVE COGNITIVE DISORDER: LIMBIC ENCEPHALITIS WITH LEUCINE-RICH GLIOMA INACTIVATED-1 PROTEIN ANTIBODY AND AN ECTOPIC ADRENOCORTICOTROPIC HORMONE SYNDROME

To the Editor: We report a case of a 75-year-old woman who developed acute limbic encephalitis with leucine-rich glioma inactivated-1 protein (LGI-1) antibody[1] associated with syndrome of inappropriate secretion of antidiuretic hormone (SIADH) and ectopic adrenocorticotropic hormone (ACTH) syndrome (EAS).[2]

CASE REPORT

A 75-year-old woman was hospitalized for treatment and etiological diagnosis of two generalized tonic–clonic seizures. Her medical history showed complex partial epilepsy (dystonia of the right upper limb and automatic gesture) and rapidly progressive cognitive disorder (designation trouble, executive disorder, anterograde amnesia) for 3 months. Clinical examination was normal. Laboratory tests found SIADH (serum sodium 119 mmol/L, natriuresis 60 mmol/L, urine osmolarity 468 mosm/L, plasmatic osmolarity 267 mosm/L) and ACTH-dependent hypercortisolism (high ACTH and urinary free cortisol levels, abnormal circadian pattern of cortisol secretion, nonsuppressibility to low-dose dexamethasone tests) without other pituitary involvement. Lumbar puncture showed a discrete intrathecal immunoglobulin G synthesis and positive anti LGI-1 antibodies. Further examinations were performed to investigate the etiology of these disorders. Brain and pituitary magnetic resonance imaging (MRI) showed aspecific isolated periventricular leukoencephalopathy. Electroencephalography found some nonspecific focal discharges, more prevalent in the left cerebral hemisphere, without clinical seizures. Computed tomography of the thorax, abdomen, and pelvis; positron emission tomography; and octreoscan (positive uptake on the right colon with normal colonoscopy) were normal. Diagnosis of limbic encephalitis with LGI-1 antibodies associated with SIADH and EAS was made. Cancer was not found, nor was the source of the endocrine disorders. The woman evolved favorably after intravenous corticosteroids and two intravenous immunoglobulin treatments and then an oral corticosteroid, azathioprine, and levetiracetam; her cognitive disorders, epilepsy, and endocrine disorders were corrected in 9 months.

DISCUSSION

Limbic encephalitis (LE) was originally described as a rare paraneoplastic cliniconeuropathological entity involving amnesia, seizures, and psychological disturbance.[3] Over the past 15 years, some individuals without detectable tumors were described and considered to have autoimmune LE, as LE with autoantibodies directed against voltage-gated potassium channel (VGKC).[1] Sometimes, the antibodies target not the VGKC itself but the LGI-1 protein complexed with it.[4]

In a U.K. study, 3% of 203 individuals with encephalitis had LE with VGKC antibodies.[5] As in the current case, previous reports showed that the clinical features of LGI-1 encephalitis are progressive memory loss, hyponatremia, epileptic seizures characterized as faciobrachial dystonic, and electroencephalographic abnormalities.[1,6] As in the current case, approximately 45% of individuals do not have MRI evidence of medial temporal lobe inflammation.[7] Moreover, in this case, there were cerebrospinal fluid changes with oligoclonal bands, which is not usual.[4,8]

To the knowledge of the authors, this is the first description of EAS associated with LE. It was surprising that no cancer was diagnosed, which may have been for two main reasons. First, because of a low prevalence of LE and EAS, their association may be rarely described.[1,2] Second, even if these disorders were corrected and no cancer was found in the current case, an "occult" tumor may be found years after diagnosis of EAS, so long-term follow-up will be necessary.[2]

A suggested treatment for LE is high doses of corticosteroids, intravenous immunoglobulin, and possibly plasmapheresis as first-line therapy, adding rituximab or cyclophosphamide as second-line therapies in refractory cases.[7] A few people have shown spontaneous improvement without treatment.[9] Despite broad cognitive dysfunction in the acute phase, as in the current case, individuals with VGKC LE can make substantial or full recovery with immunotherapy (75–80%), but it may take time.[1]

Finally, because LE may be reversible and treatable, it should be thought of when rapidly progressive cognitive disorder is associated with epileptic seizure, as can be seen in Creutzfeldt-Jakob disease, the main differential diagnostic.[3,10]

Guillaume Chapelet, MD
Centre Hospitalier Universitaire de Nantes, Pole de Gérontologie Clinique, Hôpital Bellier, Nantes, France

Catherine Baguenier-Desormeaux, MD
Pascal Lejeune, MD
Centre Hospitalier Départemental Vendée site de le Roche-sur-Yon, Service de Neurologie, La Roche sur Yon, France

Anne Sophie Boureau, MD
Gilles Berrut, MD, PhD
Laure de Decker, MD, PhD
Centre Hospitalier Universitaire de Nantes, Pole de Gérontologie Clinique, Hôpital Bellier, Nantes, France

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AN UNUSUAL CAUSE OF A HIGH CARBONHYDRATE ANTIGEN 19–9 LEVEL IN AN ELDERLY INDIVIDUAL: POLYCYSTIC LIVER DISEASE

To the Editor: Carbonhydrate antigen 19–9 (CA19–9) is used as a biomarker that has been found to be correlated with high levels with tumor progression and prognosis of several types of gastrointestinal malignancies such as pancreatic, biliary tract, gastric, and colorectal carcinoma, although markedly high CA19–9 levels can also be seen in nonmalignant gastrointestinal conditions such as biliopancreatic diseases, steatohepatitis, acute liver failure, and chronic hepatitis.[1,2] Single hepatic cysts are common in the general population, but benign polycystic liver disease is uncommon. An individual with a polycystic liver with high serum CA 19–9 levels is described.

A 77-year-old woman was admitted for follow-up of liver cysts that been diagnosed 4 years before. Her past medical history and physical examination were unremarkable. Hematological and all routine biochemical tests were normal except for high serum CA 19–9 (261 U/mL; reference <35 U/mL). Other serious neoplasmatic markers, including alpha-fetoprotein, CA 125, and carcinoembryonic antigen, were normal. Enhanced abdominal magnetic resonance imaging demonstrated multiple liver cysts (maximum diameter 3 cm) (Figure 1). Upper gastrointestinal endoscopy, colonoscopy, and pelvic computed tomography performed to exclude possible causes of high CA 19–9 were all normal. Three months later, at the outpatient clinic, she was free of symptoms yet still had a high serum CA 19–9 level.

High serum CA19–9 levels have been described in several benign digestive diseases, including acute cholangitis with bile duct lithiasis, Mirizzi's syndrome, and liver pseudotumor.[3] A high CA 19–9 level has also been found with autoimmune biliary diseases such as primary sclerosing cholangitis and autoimmune cholangitis, with normalization of levels after corticosteroid therapy.[4] Serum CA19–9 was also reported to be significantly high in individuals with simple hepatic cysts or intracystic hemorrhage.[5] High serum CA19–9 levels in individuals with liver cysts is due to the production and secretion of this compound by local cyst epithelia and its leakage into the circulation. Therefore, CA 19–9 may also be high in individuals with benign biliary cysts but has never been reported.

Polycystic liver disease should be considered in the differential diagnosis of high CA19–9 levels to prevent unnecessary tests.