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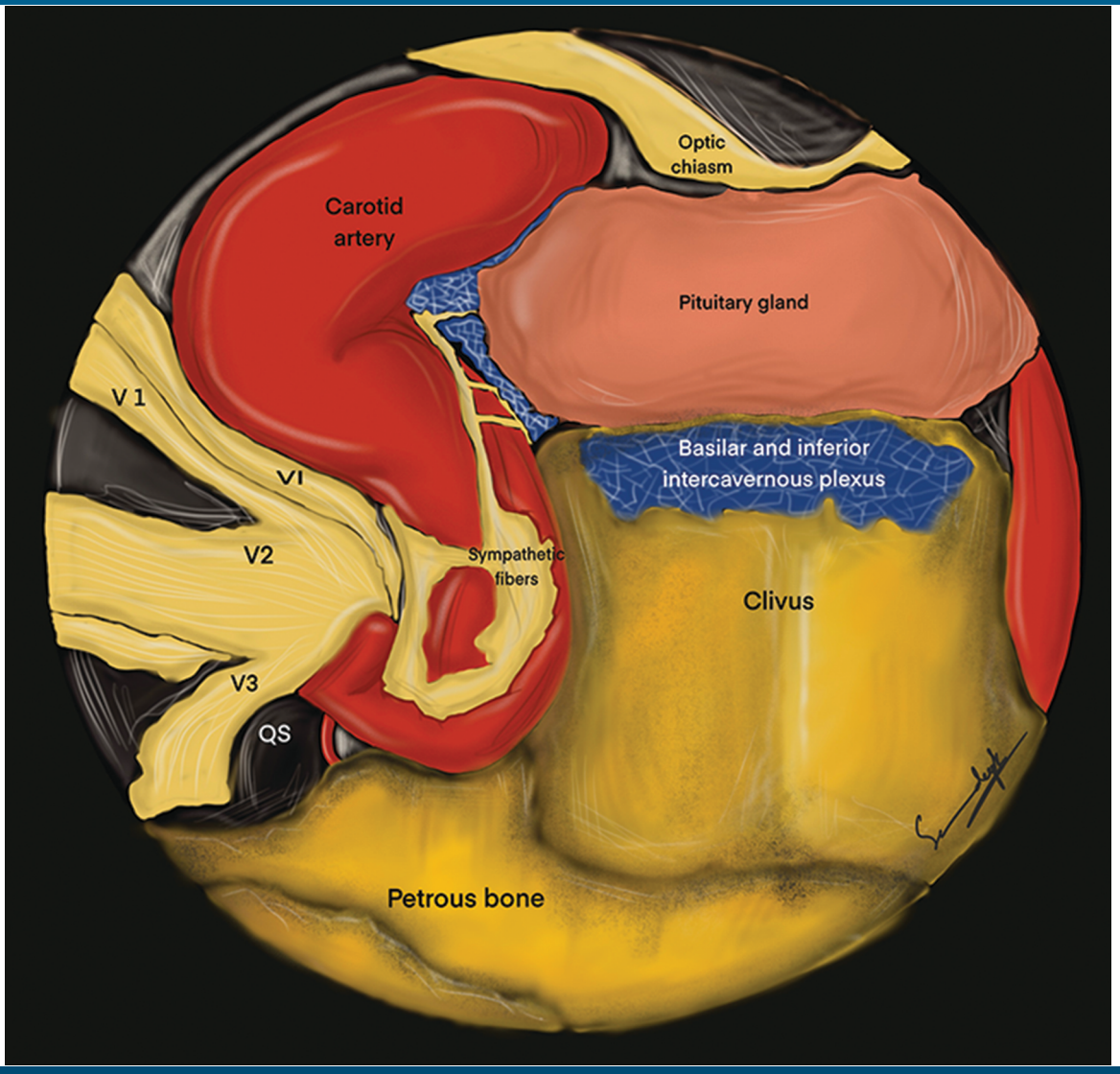

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Morvan's syndrome Presenting with Psychiatric Manifestations - A Case Report and Review of the Literature

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Abstract:

The term "la chorıe fibrillare" was used by the French physician Augustine Marie Morvan to describe a syndrome showing hyperactivity features involving the central, autonomic, and peripheral nervous system. The central hyperactivity symptoms are confusion, behavioral problems, hallucinations, myoclonus, and insomnia; the autonomic hyperactivity symptoms are hyperhidrosis and variations in blood pressure; and peripheral hyperexcitability is characterized by painful cramps, myokymia, and neuromyotonia. Here, we present a case that has typical features of Morvan's syndrome and provides a brief description based on available literature.

Key Words:

Hallucination, Morvan's syndrome, myokymia, voltage-gated potassium channel antibodies

Key Message:

Morvan's syndrome is a mimicker of many diseases considering its clinical features, including psychiatric disorders. A high index of suspicion is needed for the right diagnosis and proper management of this condition.

Morvan's syndrome is an autoimmune disease with symptoms of hyperexcitability of peripheral nerves and dysfunction of the autonomic and central nervous system (CNS). Augustin-Marie Morvan, a French physician, had described it in 1890 for the first time. Irregular small muscle contractions, painful muscle cramps, itching, hyperhidrosis, delirium, hallucinations, and severe sleep disturbances were reported in his case. There are only a few published reports of this condition.[1] Morvan's syndrome shows voltage-gated potassium channel (VGKC) antibodies in most of the patients, and among VGKC antibodies, Contactin-associated protein-like 2 (CASPR-2) antibodies are the important ones, which play a key role in peripheral and CNS manifestations.[2] Here, we report a patient with all the features of this syndrome with VGKC antibodies.

Case Report

A 23-year-old male, presented with painful cramps and twitching of calf, thigh, and shoulder muscles for 21 days, followed by decreased sleep and behavioral disturbances for 10 days. The pain was precipitated by exertion and relieved by gentle pressing. There was no numbness, tingling, or weakness of any limbs.

Gradually, he developed decreased sleep with behavioral changes like abusive talk, irritability, visual and auditory hallucinations, day time drowsiness, and confusion. He also had profuse sweating, constipation, and polydipsia. Mr. Z had a history of weight loss of around 10 kg. Past medical and family history was insignificant. The nervous system examination was unremarkable.

For pain relief, he was earlier prescribed pregabalin, but he took it in excess quantity. Due to behavioral issues, he was admitted in our hospital and started on risperidone 4 mg, trihexyphenidyl 4 mg, clonazepam 1 mg, and lorazepam on SOS basis. During the inpatient stay, he had severe insomnia, auditory and visual hallucinations, multifocal myoclonic jerks, and myokymia. As the condition was deteriorating, neurology opinion was sought.

All investigations, including creatine phosphokinase, renal function test, thyroid

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profile, antinuclear antibodies, and rheumatology evaluation were negative, except for mild hyponatremia. Magnetic resonance imaging (MRI) of the brain and computed tomography (CT) thorax were normal. Nerve conduction studies (NCS) and electromyography (EMG) studies showed a predominant neurogenic pattern with myokymia. The neuroimmunological study was strongly positive for CASPR 2 antibodies.

On the basis of the clinical and laboratory findings, the patient was diagnosed with Morvan's syndrome and was started on methylprednisolone and phenytoin, along with psychiatric medications. The patient started showing improvement in pain, sleep, and spontaneous muscle activity. After 10 days, his abnormal behavior disappeared completely, and he was continued on the same drugs for another month. He was free of symptoms on a follow-up visit after 6 weeks.

Discussion

Morvan's syndrome is a clinical diagnosis. A high index of suspicion is necessary to diagnose this rare condition when a patient presents with a combination of diverse symptoms. This patient had symptoms of hyperexcitability of peripheral, autonomic, and CNS. Confusion, vivid complex hallucinations, insomnia, aggression, constipation, and weight loss were the symptoms of central hyperactivity, and hyperhidrosis was the autonomic one. Peripheral motor hyperexcitability symptom was painful cramps, myokymia demonstrated both clinically and electrophysiologically. And VGKC antibodies were strongly positive.

The most common CNS manifestation—severe insomnia—was reported in 86% of the patients.[3] Here, insomnia was severe and had shown absent or reduced sleep spindles and K complexes. Insomnia occurs because of the dysfunction of the thalamus, hypothalamus, locus coeruleus, and raphe nuclei. Monoaminergic diencephalic and brain stem nuclei are known to be involved in awake and autonomic equilibrium. Disturbance in this homeostasis causes insomnia, dysautonomia, and, less frequently, hyponatremia. In fatal familial insomnia, there is progressive thalamic degeneration, whereas there is reversible dysfunction in Morvan's syndrome, with changes in VGKC antibodies. Hallucinations, delusions, and behavioral problems are because of encephalopathy. Although seizures are uncommon in Morvan's syndrome, they may occur during the early acute phase or a few months before.[3]

The index patient had hyperhidrosis, which is the most common reported feature of enhanced autonomic activity. Hyperhidrosis could be secondary to the hyperexcitability of peripheral sudomotor nerves.[4] VGKC antibodies bind to hypothalamic paraventricular neurons and increase antidiuretic hormone secretion, which leads to water retention and hyponatremia.

The MRIs of the brain (to rule out autoimmune limbic encephalitis [LE]) and thorax (to rule out thymoma) were normal in our patient. The limbic region showing hypermetabolic activity is frequently seen on positron emission tomography (PET) scan in LE.[5] To differentiate LE from Morvan's syndrome, a PET scan is more sensitive than MRI. Morvan's syndrome patients have only rare evidence of inflammation in cerebrospinal fluid (CSF; as opposed to LE). As the MRI brain was normal, we did not proceed with the CSF study.

VGKC antibody alteration shows a wide range of the clinical spectrum, ranging from headache to seizures.[6] These antibodies decrease the membrane density of these channels, resulting in increased resting membrane potential and making it hyperexcitable. Among VGKC antibodies, CASPR-2 or LGI1 antibodies seem to be the important one. In our patient CASPR-2 antibodies titer was very high. The binding of CASPR-2 antibodies leads to the downregulation of CASPR2/VGKC subunit complexes on peripheral nerve axon and results in autonomic dysfunction in Morvan's syndrome.[7]

Our patient had electrophysiological evidence of peripheral nerve hyperexcitability. The evidence of motor hyperactivity was depicted as neuromyotonic and myokymic discharges on EMG and after-discharges on NCS.[8] This emphasizes the role of EMG in proving the peripheral nerve hyperexcitability. The electroencephalogram (EEG) shows a generalized slowing in the majority of Morvan cases, whereas focal abnormalities are seen in LE. As CASPR-2 antibodies were confirmatory, EEG was not done in this patient.

The natural history of Morvan's syndrome shows a wide spectrum ranging from spontaneous remission to a fatal course. In the index case, many of the clinical features were the result of central effects, but we do not know with certainty that the peripheral hyperexcitability and autonomic disturbance are probably entirely peripheral. To date, there is a lack of knowledge of how a very wide range of features is related to the antibodies. Thymoma, a common feature in Morvan's syndrome, was ruled in this case by imaging. Like many other paraneoplastic and autoimmune diseases, Morvan's syndrome response to IV Ig, plasma exchange and immunosuppressants. The prognosis of Morvan's syndrome is poor when associated with thymoma. Our patient showed significant improvement with prednisolone therapy within 2 months. Considering its clinical features, including psychiatric disorders, Morvan's syndrome is a mimicker of many diseases. A high index of suspicion is needed for the right diagnosis and proper management of this condition.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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