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A Case Report on 28 Year Old Male with Morvan Syndrome

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Abstract

Morvan Syndrome (ChoréeFibrillaire) It is characterized by continuous muscle fiber activity sometimes referred to as "neuromyotonia". It is a syndrome that might involve both central and peripheral nervous system, mediated by antibodies against VGKC. This is a case of a 28 year old male who presented with peripheral nerve hyperexcitability, neuropathic and cramping pain and neuropsychiatric manifestations.

Keywords: Morvan Syndrome, Neuromyotonia, Hyperexcitability, Cramp-Fasciculation Syndrome, Hyponatremia.

Introduction

Neuromyotonia is a major feature of several autoimmune neurological syndromes characterized by PNH with or without central neurological system involvement. Experimental and clinical evidence suggest that anti-CASPR2 antibodies are directly pathogenic in autoimmune neuromyotonia patients. Neuromyotonia, a form of PNH, is a major feature in several syndromes associated with anti-CASPR2 antibodies, including cramp-fasciculation syndrome, Isaacs syndrome, Morvan syndrome, and autoimmune limbic encephalitis. Diagnosis relies on the identification of motor, sensory, and autonomic signs of PNH along with other

neurological symptoms, anti-CASPR2 antibody-positivity, and of characteristic electroneuromyographic abnormalities. Paraneoplastic associations with thymoma are possible, especially in Morvan syndrome.[1]

The cramp-fasciculation syndrome is a rare clinical entity in comparison with the frequency of cramps and isolated fasciculations in the general population. It is recognized as a benign syndrome without weakness and atrophy, however a few reports suggest that it may precede the occurrence of a motor neuron disease. Most often, the cramp-fasciculation syndrome is idiopathic and may be a component of a hyperexcitable peripheral nerve syndrome including other activities such as myokymia and neuromyotonia where antibodies to voltage-gated potassium channels (VGKCs) appear to be one of the effector mechanisms. The most complete form of this hyperexcitable peripheral nerve syndrome is Isaacs' syndrome. The central nervous system is also concerned with anti-VGKC antibodies found in Morvan's disease and limbic encephalitis.[2]

Morvan syndrome is characterised by peripheral nerve hyperexcitability (fasciculations, painful cramps, myokimia, neuropathic pain), dysautonomia (hyperhidrosis, tachycardia, arrhythmias, varying blood pressures, urinary disturbances, constipation) and central nervous system involvement(encephalopathy).[3,4] Since first described in 1890, less than 100 cases have been described in literature.[6] This disorder is associated with antibodies against voltage gated potassium channels(VGKC). VGKC are transmembrane channels complexed with various proteins, such as leucine-rich glioma in activated protein 1 (LGI1), contact in-associated protein 2 (CASPR2) and contactin-2. The association with a certain type of protein leads yo a specific clinical presentation. . In brain tissue regions including the hypothalamus, raphe, and locus ceruleus, antibodies to LGI1 bind to neuronal cell bodies including the antidiuretic hormone-secreting and orexin-secreting hypothalamic neurons, whereas CASPR2 antibodies bind more often to the neuropil.[4]

There are some antibody specific features seen in different subset of patients. Patients with LGI1-antibodies have a limbic encephalitis, often with hyponatremia, and about half of the patients have typical faciobrachial dystonic seizures. Caspr2-antibodies cause a more variable syndrome of peripheral or central nervous system symptoms, almost exclusively affecting older males. Immunotherapy seems to be beneficial in patients with antibodies to LGI1 or Caspr2, stressing the need for early diagnosis.[8]

Neurophysiologic studies on patients with morvan syndrome show the following observations. Autonomic testing demonstrated peripheral autonomic neuropathy in addition to autonomic hyperactivity. Polysomnography showed complete absence of sleep. Neuroimaging study findings were largely normal. Morvan syndrome is an autoimmune disorder affecting both the peripheral and central nervous system. Neurophysiologic studies demonstrate hyperexcitability of peripheral nerves, autonomic dysfunction, and severe insomnia.[5]

The most commonly used treatment regimen consists of progressive escalation of immunotherapy using first a combination of glucocorticoids, IVIg, and plasma exchange, and then, if there is no response, rituximab or cyclophosphamide. Phenytoin and carbamazepine have been seen to improve the symptoms occurring as a result of peripheral nerve hyperexcitability.[7]

Case Report

A 28-year old man presented with the complaints of fasciculations in both upper and lower limbs,

predominantly in bilateral calves that was associated with intense cramping pain; insomnia (sleep of 3-4 hours/night with multiple awakening); irritability and anxiety.

There was no significant past history to the best of his understanding. He did not have fever, any seizure like episodes, focal neurological deficit or impairment of sensorium. Neurological examination revealed brisk deep tendon reflexes in lower limbs. Routine investigations revealed no abnormality of the patient's thyroid profile and serum electrolytes. Psychiatric consultation was taken to rule out a concomitant anxiety disorder.

Nerve conduction study was inconclusive.

MRI showed T2/FLAIR hyperintensity in cortical/subcortical region of left occipital lobe. Electromyographic studies revealed abnormal spontaneous motor activities in form of fasciculation potential, myokimic discharges and neuromyotonia, all pointing towards peripheral nerve hyperexcitability and Cramps-Fasciculation disorder spectrum. The patient was, in the meanwhile started on Tab Carbamazepine in increasing doses which showed minimal, if any, resolution of symptoms.

A Neurology consultation pointed out to the possible autoimmune etiology for the patient's symptoms. Peripheral Nerve Hyperexcitability a major feature of Morvan Syndrome. An autoimmune encephalitis panel, including antibodies against NMDA, AMPA and VGKC (CASPR2, LGI1) which was positive for antiCASPR2 and anti LGI1. The combination of the above finding led to a diagnosis of Morvan Syndrome.

Treatment given consisted of a combination of Methylprednisolone pulse therapy in a dose of 1g/day for 5 days and IVI g at a dose of 400mg/kg/day for 5 days and showed notable improvement in symptoms.

Discussion

Morvan Syndrome is a rare disease, very few cases of which have been described in literature. The timely diagnosis, however, is beneficial as patients have shown response to a combination of immunomodulatory therapy.

Our patient presented with a combination of peripheral nerve hyperexcitability and neuropsychiatric manifestations. In cases of certain clinical diagnosis, a trial of treatment might be taken because of a report of seronegative Morvan's in a patient with an association of myasthenia gravis and thymoma in the past; who showed undetectable levels of VGKC Antibodies but nevertheless a good response to corticosteroid therapy.9

About 20% of patients with Caspr2 antibody–associated syndromes have thymoma; this percentage is higher (~40%) in patients with Morvan's syndrome.[7] This warrant ruling out a paraneoplatic association of the disease.

A multi departmental approach is advocated considering autonomic involvement that might lead to life threatening arrhythmias.

Treatment includes an escalation of immunotherapy with many cases responding to oral corticosteroids. Our patient responded to a combination of intravenous pulse steroid therapy and IVIg.

Conclusion

Morvan's syndrome ia rare clinical entity consisting of both central and peripheral nervous system involvement. A careful history and clinical examination, along with a multidisciplinary approach aids in the diagnosis. The diagnosis relies on demonstration of anti VGKC antibodies in the patient's serum and CSF. Timely

diagnosis is crucial because of the promising results of early immunomodulatory intervention.

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