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Morvan Syndrome: A Case Report With Patient Narrative and Video

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Abstract

A 74-year-old gentleman was admitted to the regional neurosciences center with encephalopathy, myokymia, and dysautonomia. Chest imaging had previously identified an incidental mass in the anterior mediastinum, consistent with a primary thymic tumor. Antivoltage-gated potassium channel (anti-VGKC) antibodies were positive (titer 1273 pmol/L) and he was hypokalemic. Electromyogram and nerve conduction studies were in keeping with peripheral nerve hyperexcitability syndrome, and an electroencephalogram was consistent with encephalopathy. A diagnosis of Morvan syndrome was made, for which he was initially treated with high-dose steroids, followed by a 5-day course of intravenous immunoglobulin (IVIG) therapy. He also underwent thymectomy, followed by a postexcision flare of his symptoms requiring intensive care management. Further steroids, plasmapheresis, and IVIG achieved stabilization of his clinical condition, enabling transfer for inpatient neurorehabilitation. He was commenced on azathioprine and a prolonged oral steroid taper. A subsequent presumed incipient relapse responded well to further IVIG treatment. This case report documents a thymoma-associated presentation of anti-VGKC-positive Morvan syndrome supplemented by patient and carer narrative and video, both of which provide valuable further insights into this rare disorder. There are a limited number of publications surrounding this rare condition available in the English literature. This, combined with the heterogenous presentation, association with underlying malignancy, response to treatment, and prognosis, provides a diagnostic challenge. However, the association with anti-VGKC antibody-associated complexes and 2 recent case series have provided some scope for both accurate diagnosis and management.

Keywords

general neurology, electromyogram/nerve conduction studies, neurooncology

Introduction

Neuromyotonia is a rare neurological condition, which is characterized by peripheral nerve hyperexcitability.[1] Augustine Marie Morvan was the first to report neuromyotonia alongside autonomic and central nervous system dysfunction in 1890. We present a case of Morvan syndrome accompanied by patient narrative.

Case Description

A 74-year-old gentleman was transferred to the regional neurosciences center in autumn 2013. He presented with encephalopathy and a 7-week history of cold sweats, loss of appetite, daytime somnolence, and nocturnal insomnia. He had been investigated extensively prior to arrival but no final diagnosis had been made.

His symptoms initially commenced on holiday, feeling cold, despite warm weather. These episodes continued and within 2 weeks he developed insomnia, loss of appetite, and profuse sweating. One week later, with the onset of diarrhea, he presented to hospital with weakness in his legs and breathlessness on exertion.

His wife recorded his decline in cognition during his admission. To begin with "he lay awake all night and talked continuously in a calm, quiet voice about people who appeared at the bottom of the bed. He moved his hands as if operating a machine or turning switches on and off." "It was

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as if he didn't know I was there, but he was talking to people he could actually see." He soon became anxious and afraid of his surroundings. "He thought that we were being chased by the police and had to get away in two Transit vans . . . some people were trying to catch us."

He would vividly describe his surroundings to his wife. "He thought he was . . . organising lots of functions. They were all taking place in a very large rectangular building and there were lots of waiters and waitresses coming in and out, but, when he opened the door they all turned into nurses. This hospital turned back into a hotel. When he was in the hotel he had to raise a large sum of money and when it was a hospital he knew he was on a wheel and if he didn't eat [the] food he was given then the wheel spun faster and faster. He knew that if he spun off, he would die."

One particular image has resonated with his wife since, he told her "all of the patients were in drawers and all the doctors and nurses were above them, and looking down on them."

His wife recalls her frustration at this time. Her husband was, 5 weeks previously, living independently—able to drive, walk unaided in the home, and used a walking stick outdoors.

Transfer was arranged to the regional neurosciences center. He was autonomically unstable, with diaphoresis, hypotension, diarrhea, and hypersalivation. He was clinically encephalopathic and, when roused from sleep, he ruminated about spies and computers. Widespread distribution of muscle twitching was noted, consistent with myokymia (video), particularly prominent in the legs. He had some loss of muscle bulk, with bilateral weakness of hip flexion accompanied by unilateral weakness of left ankle dorsiflexion and plantarflexion. Lower limb deep tendon reflexes were depressed.

Past medical history included benign prostatic hyperplasia, aortic stenosis, repair of abdominal aortic aneurysm, and hypertension. Alteration in bowel habit had previously prompted abdominal computed tomography (CT) and whole body positron emission tomography CT imaging, which identified two 18F-fluorodeoxyglucose (FDG) avid lesions in the sigmoid colon and heterogeneous FDG uptake in the thymus gland. Subsequent endoscopy revealed a benign stricture in the sigmoid colon and in view of the thymic lesion, testing for serum acetylcholine receptor antibodies was negative. He was awaiting follow-up for this thymic lesion.

Blood tests at presentation revealed hypokalemia, attributed to diarrhea, requiring ongoing treatment during his admission. Antivoltage-gated potassium channel (anti-VGKC) complex antibodies were positive, with a titer of 1273 pmol/L (subtype unknown). A recent magnetic resonance imaging (MRI) brain showed evidence of cerebral small vessel disease and a repeat CT thorax confirmed an anterior mediastinal mass of $29 \times 25 \times 46$ mm^3 consistent with a thymoma. Nerve conduction studies and electromyogram revealed both neuromyotonic and myokymic discharges alongside fasciculation potentials throughout both the upper and the lower limbs. An electroencephalogram (EEG) showed findings in keeping with encephalopathy. The presence of thymoma, anti-VGKC antibodies, generalized peripheral nerve hyperexcitability syndrome, dysautonomia, encephalopathy, and sleep disturbance was consistent with Morvan syndrome. High-dose corticosteroids had been commenced prior to transfer (1 g/d for 3 days), and he subsequently responded well to a 5-day course of intravenous immunoglobulin (IVIG), with substantial improvement noted in his encephalopathy and myokymia.

Following thymectomy, histology confirmed a thymoma, type AB, with infiltrative growth pattern. Postoperatively, he developed hypotension secondary to hemorrhage and type I respiratory failure necessitating mechanical ventilation for 48 hours. Within 1 week, he experienced a postexcision flare of his previous symptoms, redeveloping encephalopathy, myokymia, and diarrhea. He again improved with immunomodulatory therapy, receiving plasma exchange (PE), a second course of IVIG, initiation of azathioprine (titrated to 150 mg/d), and a prolonged oral prednisolone taper. Four months following initial onset of symptoms, he was transferred for inpatient neurorehabilitation. He remained here for approximately 3 months prior to discharge home with a walking frame.

Eight months after symptom onset, he was found to be making excellent progress and complained only of some variable color changes in his hands and distal paresthesiae. Five weeks later, during outpatient review, he was using a wheelchair more frequently and was complaining of intermittent coldness of the hands and further episodes of diaphoresis. Elective readmission was arranged for repeat IVIG treatment, in addition to an increase in his oral prednisolone dose, for a presumed incipient relapse of Morvan syndrome. Subtle myokymia was once again noted at this time. Repeat testing of anti-VGKC antibodies was, however, negative. He showed a good response to treatment and was discharged home, with further outpatient review planned.

Discussion

There have been few reported cases of Morvan syndrome in the English literature since its initial description in 1890.[2,3] Although the immune-mediated pathophysiology is uncertain,[2] it is thought to be part of the spectrum of anti-VGKC complex-associated conditions.[4] This patient classically demonstrated a strongly positive serum anti-VGKC titer; however, this is not a requirement for the diagnosis of Morvan syndrome.[2,5-9]

The increasing spectrum of diseases associated with anti-VGKC complex antibodies has recently been summarized.[10,11] These conditions initially included disorders of the peripheral nervous system such as acquired neuromyotonia or Isaacs syndrome, and cramp-fasciculation syndrome. Involvement of the central nervous system (CNS) was subsequently described in Morvan syndrome. Anti-VGKC antibody titer levels are usually higher (>1000 pmol/L) in patients with CNS involvement than in those with peripheral nerve hyperexcitability. Subsequently, anti-VGKC antibodies were reported

in patients with limbic encephalitis (LE), which may be associated with tumors such as thymoma or lung cancer or may be nonparaneoplastic. Other clinical features have also been reported in association with anti-VGKC antibodies such as chorea and chronic pain. Anti-VGKC antibodies have also been described in some patients with refractory focal epilepsy.

Research into specific antigenic components of the anti-VGKC antibody complexes, such as contactin-associated protein 2, leucine-rich glioma inactivated 1, and most recently contactin-2, has demonstrated some correlation between clinical manifestation and topographical distribution of these antibodies within the CNS.[5] Although anti-VGKC antibody negative cases of Morvan syndrome have been reported in the literature, it is possible that, in these cases, the antigenic components are yet to be formally identified.

The principal differential diagnoses were LE and neuromyotonia.[5] By comparison with LE, neuropsychiatric manifestations of Morvan syndrome show significantly less amnesia and confusion/disorientation, fewer seizures, and more hallucinations/agitation. Dysautonomia, features of peripheral neuropathy, insomnia, and tumors are found in some patients with neuromyotonia but are significantly more common in Morvan syndrome and occur infrequent in LE.

The MRI brain scan in our patient showed only evidence of small vessel disease. Brain MRI was normal in 92% of patients with Morvan syndrome.[5] Limited EEG data have been reported in Morvan syndrome, but in 1 investigation of neurophysiological studies, EEG showed diffuse slow wave abnormalities in 1 patient and was normal in another, with a literature review showing generalized slowing as the principal EEG finding,[12] in keeping with the nonspecific encephalopathic changes seen in our patient.

Diagnosis of Morvan syndrome should prompt investigation for an underlying antigenic source, particularly thymoma.[8] Our patient's relapse of symptoms postthymectomy has been documented, presumed to be associated with intraoperative release of anti-VGKC antibodies into the serum.[3] Similarly, while the long-term clinical course is incompletely understood, symptom relapse without anti-VGKC antibody increase has been reported.[13]

Immunosuppressive therapies, encompassing corticosteroids, azathioprine, methotrexate and more recently, rituximab, are the mainstay of therapy.[14] Other treatments include PE, IVIG, and thymectomy. Antiepileptics can be used for symptomatic relief of peripheral nerve hyperexcitability. Patients reportedly exhibited a heterogenous response to immunomodulation. Indeed, some patients have exhibited a spontaneous remission of symptoms. Prognosis is inherently clouded; however, current analysis suggests that those associated with thymoma, benign or malignant, show a less favorable prognosis.[5] This case provides unique patient narrative of Morvan syndrome, coupled with video recording of associated myokymia.

Authors' Note

MM substantially contributed to the conception and design, literature review, drafting of the manuscript, and approved the final version to be published. SC and RD substantially contributed to the conception and design, critically revised the report for important intellectual content, and approved the final version to be published. CG was responsible for the clinical management of the patient, contributed substantially to the conception and design, critically revised the report for important intellectual content, and approved the final version to be published. HE was responsible for the clinical management of the patient, contributed substantially to the conception and design, critically revised the report for important intellectual content, approved the final version to be published, and was the lead for this study. This article has previously been submitted to the *Journal of Neurology, Neurosurgery and Psychiatry* but was declined due to case reports only being published rarely.

Declaration of Conflicting Interests

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