

## Case Report

# A Case of Morvan's Syndrome Associated with Heavy Metal Poisoning after Ayurvedic Drug Intake

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ABSTRACT

Morvan's syndrome is an autoimmune disorder of peripheral and central nervous system mediated by VGKC antibody. Here we report a case of Morvan's syndrome who presented 1 month after ayurvedic drug intake. She presented with symptoms of peripheral nerve hyperexcitability and autoimmune testing revealed positive result for VGKC antibody. Heavy metals level was also significantly raised. She improved after a course of steroids. This case report tries to highlight the association of VGKC mediated Morvan's syndrome with heavy metal poisoning and its incidental occurrence after Ayurvedic drug intake.

**KEYWORDS:** *Ayurvedic drug intake, heavy metal poisoning, Morvan's syndrome, peripheral nerve hyperexcitability*

## INTRODUCTION

The first description of Morvan's syndrome was in 1890 by Augustin Marie Morvan, a French physician, who reported five patients with irregular myokymia without movement across a joint space, cramps, hyperhidrosis, delirium, and hallucinations as well as insomnia.<sup>[1]</sup> It is now well established that Morvan's syndrome is associated with voltage-gated potassium channel (VGKC) antibody. There are several reports that associate ayurvedic drug intake with heavy metal toxicity.<sup>[2,3]</sup> Here, we report a patient who consumed ayurvedic medicine and presented 1 month later with Morvan's syndrome (myokymia, insomnia, burning pain of feet, and dysautonomia).

## CASE REPORT

A 55-year-old female presented to our department with complaints of pins and needles sensation over both feet for 2 weeks duration. On eliciting further history, it came to light that she was suffering from fever associated with chills and sweating for previous 1 month and was extensively evaluated for pyrexia of unknown origin elsewhere. She had also been suffering from insomnia for the past 3 weeks. She also complained of giddiness whenever she stood up from lying position. Examination revealed a moderately built female whose blood pressure was 130/90 on lying position with

significant postural fall to 100/80 on standing. Her pulse rate was 80/min. Temperature measured was normal even when the patient was complaining of feeling of warmth. Her Mini-Mental State Examination was 30/30. Inspection revealed myokymic rippling over her left arm, periorbital area, and fasciculations over tongue. Motor examination was normal. She had hyperalgesia over both feet. Investigations done outside were essentially normal except for mildly elevated transaminases. Further probing revealed that the patient had taken ayurvedic medicine 2 months prior for a duration of 10 days for complaints of bleeding per rectum, before the onset of her present symptoms. The patient had not taken any ayurvedic medications previously. Sympathetic skin response showed absent waveform. Electromyography (EMG) showed persistent doublets, triplets and neuromyotonic discharges in deltoid, biceps, and quadriceps. A heavy metal screen by urine toxicology was sent and it revealed elevated levels of heavy metals such as lead 162 µg/l (normal <80 mcg/l), mercury 53.37 µg/l (normal <10 µg/l), manganese

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38.31 µg/l (normal <2 µg/l), and nickel 18 µg/l (normal <5.2 µg/l). Electroencephalogram done was normal. In view of the presence of peripheral nerve symptoms like myokymia, burning sensation of feet, and central nervous system symptoms like insomnia, autonomic dysfunction, Morvan's syndrome was thought of and test for VGKC antibody was done. CASPR2 antibody turned to be positive in high titer and LGI1 antibody was positive in low titer. Hence, an association between the ayurvedic drug intake and Morvan's syndrome was considered in view of them being temporally related to each other. The Naranjo drug reaction scale was used and it was indicative of a probable adverse drug reaction (actual score being 6).<sup>[4]</sup> Computed tomography (CT) chest and CT abdomen were done and it ruled out malignancy. She was treated with pulse IV methylprednisolone for 5 days followed by slow steroid taper over 3 months. Patient's symptoms resolved completely and she is doing well at 2 months of follow up after gradual taper of steroids Repeat sympathetic skin response was normal after 2 months. Repeat EMG did not show any neuromyotonic discharges. A repeat VGKC titer and urine heavy metal screening was planned but could not be done due to financial constraints.

## DISCUSSION

Morvan's syndrome is thought of as an autoimmune disorder because of its association with VGKC antibodies in a significant percentage of patients. VGKC antibodies are believed to play a key role in peripheral as well as the central manifestations of Morvan's syndrome.<sup>[5]</sup> Morvan's syndrome is associated with high-titer CASPR2 antibodies, often accompanied by low-titer LGI1 antibodies. CASPR2 and LGI1 antibodies bind to multiple brain regions, which help to explain the multifocal clinical features of this disease.<sup>[6]</sup> Morvan's syndrome is clinically characterized by neuromyotonia, neuropsychiatric features, neuropathic pain, and dysautonomia. The main neuropsychiatric features noted were insomnia, confusion, hallucinations, and amnesia.<sup>[6]</sup> Our patient had all the above features with insomnia as the main neuropsychiatric feature. Her symptoms of feeling of warmth with chills and sweating were attributed to a possible autonomic dysfunction (thermal dysregulation). The clinical features of our patient with the classical EMG findings clinically made us to suspect Morvan's syndrome. The diagnostic dilemma arose whether the acquired neuromyotonic syndrome was due to heavy metal toxicity or due to autoimmune etiology as suggested by the presence of CASPR2 and LGI1 antibodies. Another thought was whether heavy metal intake had triggered an autoimmune response that led to

this acquired neuromyotonic syndrome. Ayurvedic drug treatment is used by 18.7% of Indian population for common ailments and 5.02% for serious ailments.<sup>[7]</sup> The temporal association with ayurvedic drug intake made us suspect a causal association between toxin exposure and the peripheral nerve hyperexcitability syndrome. There has so far been only one study from Indian subcontinent with twenty patients which has shown an association between toxins exposure in the form of heavy metals' intake in "Ayurvedic drug" and to peripheral nerve hyperexcitability, but the toxin levels were not measured.<sup>[8]</sup> There have been case reports where gold, lead, silver, and mercury have been associated with peripheral nerve hyperexcitability,<sup>[9,10]</sup> the exact mechanism by which these drugs and toxins lead to hyperactivity of the peripheral nerves in continuous muscle fiber activity is not clear and is yet to be determined.<sup>[9]</sup> There are not many case reports highlighting autoimmune diseases triggered by ayurvedic drugs, but the role of gold and mercury in inducing autoantibodies and immune complexes, thereby inducing renal pathology, is well known. Genetic factors may play a role in mouse and rat models of metal-induced autoimmunity.<sup>[11]</sup> This case report highlights the occurrence of VGKC antibody-mediated Morvan's syndrome in a patient with ayurvedic drug intake 1 month before occurrence of symptoms with proven elevated heavy metal levels and antibody positivity. In a country like India where ayurvedic drugs are abundantly used, such a treatable entity should not go unrecognized when a patient with similar phenotype presents to the physician or general practitioner.

## 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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## Conflicts of interest

There are no conflicts of interest.

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