Neuromyotonia: A Sequel to Indigenous Medication

Dear Editor,

Mercury toxicity-induced neuromyotonia is reported in India following the rampant use of indigenous medicines for neurological illnesses. Mercury poisoning is associated with CASPR2 antibody-positive neuromyotonia, myokymia, sensory and autonomic dysfunction. This case illustrates the importance of suspecting and diagnosing mercury intoxication in cases of peripheral nerve hyperexcitability with life-threatening complications.

A 40-year-old man, nonsmoker presented with tremulousness and shaking of legs two weeks after taking an over-the-counter health care product from indigenous medicine. A week later, there was burning, tingling, and weakness of both legs causing him to walk with his knees flexed. There were mood swings, irritability, and depression. He had symptoms of autonomic dysfunction with constipation, profuse sweating, palpitation, urinary urgency, and restlessness. As time progressed, he experienced intractable, excruciating, unbearable pain, stiffness of legs, cramps, and writhing movements of leg muscles. His sleep was interrupted by painful cramps of the body and legs, frequent awakenings, night sweats, and urinary symptoms. Clinical examination revealed a middle-aged man who had constant involuntary movements of the muscles of the thighs and calves causing him much discomfort. His skin was cold and clammy with a maculopapular erythematous and blanching rash on the chest. There was an erythematous scaling rash over both hands [Figure 1a]. He was apathetic, irritable, and depressed but he was oriented to time, place, and person. Cranial nerves and cerebellar system examination were normal. There was no focal wasting and tone was normal in all four limbs. There were constant twitching and fasciculations over the arms, thighs, and calves of both legs [Video 1]. Primary sensory modalities, posterior column sensation, and joint position sense were normal. Deep tendon reflexes were brisk and planters were flexor. There was no peripheral nerve thickening or neurocutaneous markers. Routine blood and urine examination were normal except for low serum sodium levels which were corrected. FT3, FT4, Thyroid-stimulating hormone, and thyroid antibody levels were normal. CSF was clear, cells 20 [100% lymphocytes], protein 46.80 mg/dl [normal 20 – 40 mg/dl], sugar 58.00 mg/dl [corresponding blood sugar was 110 mg/dl]. Blood and urine mercury levels were 40.94 µg/l [normal <10 µg/l]. Paraneoplastic screen and serology for herpes virus, cytomegalovirus, Lyme disease were negative. Motor and Sensory nerve conduction study were normal.

EMG was characterized by continuous spontaneous muscle fiber activity with doublets [Figure 1b] and a high irregular intra-burst frequency and large burst duration. [Figures 1c and 1d]. FDG PET – CT of the brain was normal. The patient had elevated CASPR2 antibody levels [VGKC type] in serum and cerebrospinal fluid. Based on the history, clinical characteristics, EMG findings, positive CASPR2 antibody levels, elevated serum, and urinary mercury levels, a diagnosis of neuromyotonia triggered by indigenous drug intake was made. The medication was discontinued, six plasma exchanges were given followed by intravenous immunoglobulin, oxcarbazepine, and phenytoin. He responded to treatment and was discharged a month later.

Morvan's Syndrome, described in 1980, consists of a constellation of symptoms characterized by a sleep disorder, delirium, continuous muscle fiber activity, and autonomic dysfunction.[1,2] Antibodies against contactin-associated protein

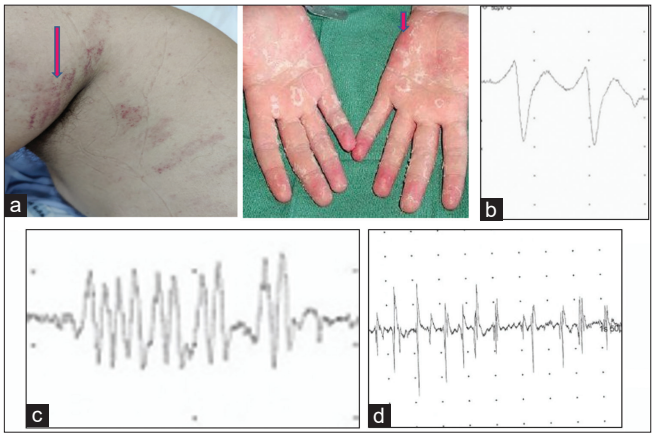

Figure 1: (a) Maculo-papular erythematous and blanching rash on the chest. Erythematous scaling rash over both hands. (b) EMG: Continuous spontaneous muscle fiber activity with doublets. (c) EMG: Neuromyotonia with high irregular intra-burst frequency and large burst duration. (d) EMG: Neuromyotonia with a large burst duration

2 bind to the brain and the peripheral nerve axon causing neuropsychiatric features, neuropathic pain, neuromyotonia, and autonomic dysfunction.[1] Central nervous system involvement is heralded by subtle behavioral changes, agitation, confusion, insomnia, and seizures.[1] Peripheral nervous system involvement presents with a sensory-motor demyelinating or axonal polyneuropathy while autonomic nervous system involvement presents with sweating, palpitation, constipation, itching, urinary incontinence, and fatigue.[2] Neuronal hyperexcitability with the ephaptic transmission of neuronal signals along the peripheral nerves progresses to constant muscle twitching, cramps, paresthesias, weakness, and stiffness.[1]

Neuromyotonia is immune-mediated and triggered by neoplasms, thymomas, lymphomas, insecticides, or heavy metals like gold or mercury in indigenous medication.[2] Siddha medicines containing heavy metals trigger an autoimmune response with positive VGKC – CASPR 2 antibodies.[3] Mercury is used in the liquid form, as red sulfide, perchloride, subchloride, or the red-oxide of mercury.[3] Mercury poisoning can manifest in multifarious ways with direct neurotoxicity of peripheral nerve terminals, autoimmunity against ion channels, motor nerve hyperexcitability, continuous muscle fiber hyperactivity, and encephalopathy.[3] Antibodies to VGKC result in the inadequate opening of the potassium channels, poor repolarization, and prolonged opening of the Voltage-gated Calcium channels resulting in excessive calcium entry in the nerve terminal, excess acetylcholine quanta, and continuous muscle fiber activity.[4,5] These symptoms are reversible on stopping the offending agent.[4]

EMG findings pathognomic of this condition are continuous muscle fiber activity with doublets, triplets, or multiplets with a high intra-burst frequency, large burst duration, and waning character of the amplitude of the discharges [Figure 1b-d].[6] Treatment includes the use of plasma exchange and intravenous immunoglobulins to reduce the antibody levels and membrane-stabilizing agents like carbamazepine to reduce neuronal hyperexcitability.[6] This case highlights the importance of asking history of indigenous medicine intake in patients presenting with neuromyotonia. It brings home the message that proper regulations regarding heavy metal compositions in alternative medicines like Siddha should be implemented by drug regulatory agencies.

Consent for publication

The patient has given his informed consent prior to submitting this manuscript. Patient consent form attached.

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Conflicts of interest

There are no conflicts of interest.

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