Approach to a case of myeloneuropathy

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Abstract

Myeloneuropathy is a frequently encountered condition and often poses a diagnostic challenge. A variety of nutritional, toxic, metabolic, infective, inflammatory, and paraneoplastic disorders can present with myeloneuropathy. Deficiencies of vitamin B12, folic acid, copper, and vitamin E may lead to myeloneuropathy with a clinical picture of subacute combined degeneration of the spinal cord. Among infective causes, chikungunya virus has been shown to produce a syndrome similar to myeloneuropathy. Vacuolar myelopathy seen in human immunodeficiency virus (HIV) infection is clinically very similar to subacute combined degeneration. A paraneoplastic myeloneuropathy, an immune-mediated disorder associated with an underlying malignancy, may rarely be seen with breast cancer. Tropical myeloneuropathies are classified into two overlapping clinical entities — tropical ataxic neuropathy and tropical spastic paraparesis. Tropical spastic paraparesis, a chronic noncompressive myelopathy, has frequently been reported from South India. Establishing the correct diagnosis of myeloneuropathy is important because compressive myelopathies may pose diagnostic confusion. Magnetic resonance imaging (MRI) in subacute combined degeneration of the spinal cord typically reveals characteristic signal changes on T2-weighted images of the cervical spinal cord. Once the presence of myeloneuropathy is established, all these patients should be subjected to a battery of tests. Blood levels of vitamin B12, folic acid, vitamins A, D, E, and K, along with levels of iron, methylmalonic acid, homocysteine, and calcium should be assessed. The pattern of neurologic involvement and results obtained from a battery of biochemical tests often help in establishing the correct diagnosis.

Key Words

B12 deficiency, copper deficiency, myelopathy, neuropathy, subacute combined degeneration of the spinal cord

Introduction

Myeloneuropathy is characterized by simultaneous damage of the tracts of the spinal cord and peripheral nerves in the lower limbs. Clinical manifestations of myeloneuropathy include difficulty in walking, weakness of lower limbs, ataxic gait, and sensory manifestations in glove and stocking distribution. On examination, there are myelopathic signs such as hyperreflexia, spasticity, extensor plantar responses, and infrequently, bladder bowel disturbances. Romberg sign indicates involvement of the posterior column. Classical neuropathic signs include glove and stocking sensory loss, absent or diminished ankle jerk, and distal limb atrophy. Cognitive impairment and vision loss, because of optic nerve damage may occasionally dominate the clinical picture in a patient with myeloneuropathy. All of these patients have gait difficulty primarily due to severe sensory ataxia.[1,2]

In classical medicine ward teaching, four causes of an absent reflex and exaggerated knee jerks used to be enumerated; these four causes were taboparesis, subacute combined degeneration, Friedreich's ataxia, and cauda-conus syndrome. Taboparesis is a form of tertiary syphilis, which is characterized by features of both tabes dorsalis and general paralysis of the insane. Patients had upper and lower motor neuron signs in lower limbs, leading to the absence of ankle jerks along with

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extensor planter responses. Taboparesis is a classic example of myeloneuropathy, which is no longer seen. Now, a variety of nutritional, toxic, metabolic, infective, inflammatory, and paraneoplastic conditions are considered in the differential diagnosis of myeloneuropathy.

Nutritional and Metabolic

Nutritional deficiencies lead to myeloneuropathy with a clinical picture of subacute combined degeneration of the spinal cord. In subacute combined degeneration of the spinal cord, there is dysfunction of posterior and lateral columns of the spinal cord along with involvement of peripheral and optic nerves, and to some extent of the brain parenchyma. The earliest clinical feature is usually the presence of paresthesias in extremities; later sensory loss, gait ataxia, lower limb weakness, spasticity, hyperreflexia, and extensor plantar responses may evolve.[3-5] In a very large report that included 143 patients (153 episodes of cobalamin deficiency), paresthesia or ataxia were the initial symptoms of vitamin B12 deficiency. In this cohort, diminished vibration and proprioception in the lower limbs were the most common neurological findings. Other frequent neurologic signs were ataxia, loss of sensation, motor weakness, diminished deep tendon jerks, spasticity, urinary or fecal disturbances, postural hypotension, vision loss, dementia, psychoses, and mood changes. In many patients with subacute combined degeneration, Lhermitte's sign is present.[6] Vitamin B12 deficiency is particularly common in the elderly and after gastric surgery. Many patients with vitamin B12 deficiency have intrinsic factor-related malabsorption similar to that seen in patients with pernicious anemia. Vitamin B12 deficiency results in the failure of conversion of methyl malonyl coenzyme A to succinyl-CoA, resulting in the accumulation of methylmalonic acid. Methylmalonic acid is a neurotoxic substance that produces myelin damage in the posterior columns of the spinal cord. Lesions of the spinal cord are predominately present in the lower cervical and upper thoracic regions. The diagnosis of B12 deficiency is made in the presence of a low serum B12 level. If the blood B12 level is borderline low, increased levels of homocysteine and methylmalonic acid help in confirming the presence of B12 deficiency. Vitamin B12 deficiency is the most frequently reported cause of myeloneuropathy in India.

Copper deficiency is the next common differential diagnosis in patients with posterolateral involvement of the spinal cord presenting with myeloneuropathy. The predisposing factors for copper deficiency include enteral feeding, gastrectomy, usage of copper-chelating agents, and excessive zinc administration. Copper deficiency is treated with oral or intravenous supplementation of copper. Serum levels of copper and zinc need to be closely followed when oral replacement of copper is used, especially in patients who are also receiving supplemental zinc because zinc and copper compete for intestinal absorption. Excessive oral intake of zinc leads to copper deficiency. Zinc interferes with the absorption of copper in enterocytes of the small intestine. Additionally, excess zinc induces the synthesis of the intracellular ligand metallothionein in enterocytes, which then binds zinc. The excess zinc bound to metallothionein is then excreted in the feces through enterocyte shedding. Copper, given its higher affinity for metallothionein, displaces zinc and is also excreted excessively, leading to copper deficiency.[7-12]

Folic acid deficiency can also produce a clinical picture similar to that of subacute combined degeneration of the spinal cord. Many other deficiencies such as vitamin B12 deficiency are concomitantly present. Folic acid deficiency is usually caused by dietary deficiency, malabsorption syndromes, pregnancy and lactation, usage of anticancer, antiepileptic, or oral contraceptive drugs, and long-term alcoholism. Folic acid deficiency-associated myeloneuropathy partially responds to folic acid supplementation.[12,13]

Vitamin E deficiency is classically characterized with a spinocerebellar syndrome; however, it can also present with myeloneuropathy. Ataxia with vitamin E deficiency is an autosomal recessive disorder. The clinical features of vitamin E deficiency are similar to Friedreich's ataxia. Patients present with cerebellar ataxia, loss of deep jerks, loss of vibration sense, dysarthria, and Babinski sign. Head titubation, retinopathy and dystonia are more common in these patients. Early diagnosis is crucial for successful treatment.[12-14]

Toxic

Nitrous oxide-associated vitamin B12 deficiency can cause subacute combined degeneration of the spinal cord following nitrous oxide anesthesia. Nitrous oxide is a commonly used inhalational aesthetic agent. It is highly lipid soluble and rapidly crosses the blood–brain barrier. Nitrous oxide, in fact, aggravates the manifestations of vitamin B12 deficiency because it impairs the function of methylcobalamin-dependent methionine synthetase enzyme. Nitrous oxide denatures B12 molecule, making it inactive. In patients with preexisting vitamin B12 deficiency, even a single dose of nitrous oxide can produce florid neurological manifestations of vitamin B12 deficiency. High doses of vitamin B12 need to be administered to counteract the inactivating effects of the nitrous oxide. Clinical improvement is usually dramatic.[15,16]

Chlorpyrifos is an organophosphate insecticide, which can cause delayed neurological toxicity following a high dose exposure. A delayed myeloneuropathy following chlorpyrifos poisoning has been reported in an isolated case.[17]

Infective

Among infective causes, chikungunya virus in India has been shown to produce a syndrome similar to myeloneuropathy. A study during a chikungunya epidemic noted that among 90 laboratory-confirmed cases, 12 patients had myeloneuropathy, with or without encephalitis. The outcome of the neurological complications was good. In an another report of 300 patients with chikungunya, in 2006, 14% (7/49) patients had myeloneuropathy.[18,19]

Vacuolar myelopathy in HIV infection is clinically very similar to subacute combined degeneration. Vacuolar myelopathy manifests with a posterolateral spinal cord syndrome with bladder and bowel disturbances. HIV myelopathy appears in the late stages of HIV infection when CD4+ cell counts are very low. Most of these patients concomitantly have other complications of HIV infection such as encephalopathy, opportunistic infections, or malignancies. Spinal cord

pathology, including vacuolar myelopathy, has rarely been reported in Indian HIV-infected patients.[20,21]

Inflammatory

A paraneoplastic myeloneuropathy is an infrequent immune-mediated disorder that is associated with an underlying malignancy. In some case reports, paraneoplastic myeloneuropathy has been reported with carcinoma of the breast. Antineuronal nuclear antibody 1 (anti-Hu) is frequently positive in these patients and they respond well to corticosteroids.[22,23] Reports on paraneoplastic myelopathies have demonstrated a characteristic magnetic resonance imaging (MRI) pattern of longitudinally extensive signal changes in the spinal cord.

Another inflammatory condition, Sjögren's syndrome, can manifest with myeloneuropathy. Sjögren's syndrome is an autoimmune disorder characterized by decreased secretions of lacrimal and salivary glands (sicca symptoms). The central and peripheral nervous systems' involvement in Sjögren's syndrome is a result of vasculitis as well as direct immunological injury to neurons. Clinical spectrum of Sjögren's syndrome-associated neuropathy includes sensory ataxic neuropathy, trigeminal neuropathy, multiple mononeuropathy, radiculoneuropathy, painful sensory neuropathy without sensory ataxia, autonomic neuropathy with anhidrosis, and multiple cranial neuropathy. Neurological symptoms occur in approximately 20% of patients with Sjögren's syndrome, and may be the presenting manifestations of the disease.[24]

In Hashimoto's disease, antithyroid antibodies can also be associated with acute myeloneuropathy or myelopathy. The exact role of antithyroid antibodies in the pathogenesis of the myelopathy is not precisely clear; however, a vasculitic process has been suggested. There is often a good response to corticosteroids.[25,26]

Sarcoidosis is a granulomatous disorder that can affect virtually any organ of the human body and nearly any component of the nervous system. A variety of neurological manifestations are possible including myelopathic signs and symptoms, and signs of segmental radiculopathy at the affected levels. Polyradiculopathy, including cauda equina syndrome and peripheral neuropathy, may accompany myelopathic finding. The diagnosis of sarcoidosis is quite challenging in such patients.

Tropical Myeloneuropathies

Tropical myeloneuropathies are classified into two overlapping clinical entities — tropical spastic paraparesis and tropical ataxic neuropathy. Tropical spastic paraparesis, a chronic cause of myeloneuropathy, has frequently been reported from South India. It is caused by an infection with human T-cell lymphotropic virus-1. Tropical ataxic neuropathy is a slowly progressive cause of myeloneuropathy seen in cassava-eating countries. This disease characteristically occurs in an endemic form and is clinically characterized by sensory polyneuropathy, gait ataxia, optic atrophy, and nerve deafness. Tropical ataxic neuropathy often starts with dysesthesias in the lower limbs followed by unsteadiness of the gait. Romberg test is

characteristically present. Reflexes in the lower limbs are either diminished or absent. Plantar response is usually flexor. Tropical ataxic neuropathy is seen in populations that use large quantities of cassava in their diets for very long periods. This syndrome has not been reported from India.[27,28]

Hereditary

A variety of hereditary myeloneuropathies have been described. Adrenomyeloneuropathy, a variant of adrenoleukodystrophy, is a noninflammatory involvement of the spinal cord that involves the descending corticospinal tracts, dominantly in the thoracic and lumbosacral regions, and the posterior columns, in the cervical spinal segments. The clinical features of adrenomyeloneuropathy include a slowly progressive spastic paraparesis and mild polyneuropathy in adult men, with or without sensory manifestations and sphincter disturbances.[29]

Recently, Motley *et al.* from Belgium described five siblings in a family with dominantly inherited myeloneuropathy. All affected family members had a mild axonal neuropathy and three out of four family members had lower extremity hyperreflexia, suggestive of a superimposed myelopathy. A nerve biopsy showed evidence of chronic axonal loss. All affected family members had a heterozygous missense mutation in the alanyl-tRNA synthetase gene.[30]

Neuroimaging

MRI in subacute combined degeneration of the spinal cord usually reveals signal changes on T2-weighted images of the cervical spinal cord. Classically, there are symmetric bilateral hyperintense signals in the posterior and lateral columns. Imaging findings may involve the posterior column of thoracic segments as well. Some amount of cord expansion and enhancement may be present. On sagittal images, longitudinal signal changes are noted along the dorsal columns of the spinal cord. A characteristic pattern of symmetric bilateral hyperintense signals in the dorsal columns has been described as "inverted V" or "inverted rabbit ears" appearance. These changes are partially or completely reversible following treatment[31] [Figure 1].
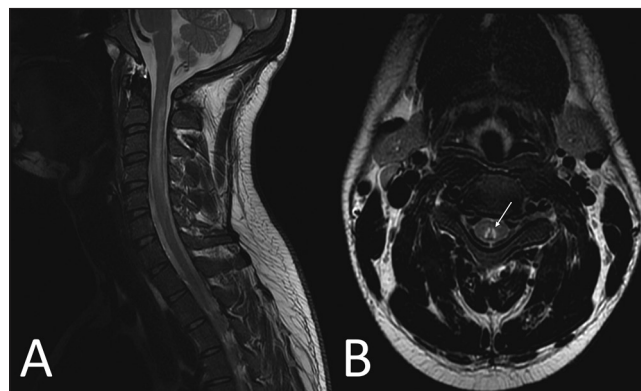

Figure 1: MRI of a patient presenting with subacute combined degeneration secondary to vitamin B12 deficiency depicts hyperintensity involving the posterior part of the cervical spinal cord on T2-W sagittal (A) image and inverted "V" sign on T2-W axial section (B, arrow)

GROUPS	ETIOLOGY	SYNDROME/ KEY POINTERS	LABORATORY PARAMETERS (SPECIFIC)	LABORATORY PARAMETERS (ANCILLARY)	LABORATORY PARAMETERS (NEUROELECTROPHYSIOLOGY)	IMAGING OF THE SPINAL CORD
METABOLIC	Vit. B12 deficiency	Subacute combined degeneration, neuropathy, neurocognitive changes	S.B12 ↓ S.Holotranscobalamin ↓	CBC, S.Homocysteine ↑, Bone marrow S.Methylmalonic Acid ↑; ± S.Copper ↓	ABNL SSEPs, Axonal	Hyperintense posterolateral columns of the spinal cord
	Vit. E deficiency	Spinocerebellar syndrome, sensory deafferentation, neuropathy, retinopathy	S.Vitamin E ↓	CBC, Lipid profile	ABNL SSEPs	Hyperintense posterior columns of the spinal cord
	Copper deficiency	Subacute combined degeneration, sensory deafferentation, neuropathy	S.Copper ↓	CBC, U.Copper, S.Ceruloplasmin, S.Zinc and Iron profile must be done	Axonal	Hyperintense posterior columns of the spinal cord
	Folate deficiency	Subacute combined degeneration, neuropathy, neurocognitive changes	S.Folate ↓	CBC, S.B12, S.Homocysteine	Axonal	Not well characterized
TOXIC	Organophosphates (Chlorpyrifos)	H/o exposure, delayed toxicity	None	RBC cholinesterase activity	ABNL SSEPs, Axonal	Not well characterized
INFECTIVE	HIV	Posterolateral cord syndrome, sphincter abnormalities	HIV testing by ELISA; Antigen testing & viral load assessment	CD4, CD8 counts S.B12 & Folate may be assessed	Demyelination	Vacuolar myelopathy, posterolateral cord involvement
	HTLV	Posterolateral cord syndrome, radiculoneuropathy	HTLV antibody testing	Non-specific	Demyelination	Cord atrophy
	Chikungunya virus	H/o exposure/ epidemic, fever, joint pain, myalgia	Reverse-transcription PCR	Non-specific	Demyelination	Non-specific
AUTOIMMUNE/ INFLAMMATORY	Sarcoidosis	Recurrent or progressive myelopathy, radiculoneuropathy	S. ACE, Bronchoalveolar lavage, Gallium scan, tissue biopsy	Renal ultrasound, ophthalmoscopy, skin biopsy	Axonal, small–fiber neuropathy, mononeuropathy multiplex	Focal or widespread signal intensity changes in the cord and vertebrae
	Sjogren	Mimics neuromyelitis optica, subclinical neuropathy (sensory/motor/mixed)	SS–A, SS–B autoantigens, labial biopsy, Schirmer's test, Rose Bengal score	ANA, Rheumatoid factor, Renal ultrasound, Hepatitis C virus detection	Axonal, small–fiber neuropathy, mononeuropathy multiplex	Hyperintense posterior columns of the spinal cord
MALIGNANT/ PARANEOPLASTIC	Lymphomas; Other malignancies	Varied combinations of myelopathy, neuronopathy, and neuropathy	Flow cytometry FNAC or Histopathology	CBC/ Bone marrow examination Assessment for onconeural antigens	Axonal versus demyelination, depends on the underlying etiology	Cord and meningeal signal intensity variations
HEREDITARY	**Leukodystrophic** · Adrenomyeloneuropathy	*Salient features of the parent syndrome along with an high index of suspicion help in pruning the differential diagnoses*	S.VLCFA, ABCD1 gene (Xq28) testing	Non-specific	ABNL SSEPs, demyelination	Hyperintense posterolateral columns
	· Metachromatic leukodystrophy		Leucocyte aryl-sulfatase	Non-specific	ABNL SSEPs, demyelination	Lumbosacral/cauda equina involvement
	· Krabbe disease		Leucocyte β–galactosidase	Non-specific	Demyelination	Lumbosacral/cauda equina involvement
	· Pelizaeus-Merzbacher disease		Proteolipid protein gene testing	Non-specific	ABNL SSEPs, demyelination	Not well characterized
	Non-leukodystrophic · Hereditary spastic paraparesis		Genetic testing	Depends on the type	Depends on the type	Cord atrophy
	· Cerebrotendinous xanthomatosis		›/↓ Cholesterol, ↑ Cholestanol	Slit lamp examination	Demyelination	Hyperintense posterolateral columns
	· Mitochondrial cytopathies		Mitochondrial genome analysis	S.Lactate, S.Pyruvate, Muscle biopsy	Axonal > Demyelination	Depends on the subtype
	· Friedreich's Ataxia		Trinucleotide repeat (GAA) study	Blood sugar, Vitamin E	Demyelination	Spinal cord atrophy
MEDICATION INDUCED/ DRUG ABUSE	Clioquinol	Subacute myelo-optic neuropathy	None	S.Copper ↓	Axonal	Hyperintense posterior columns
	Nitrous oxide	Subacute combined degeneration, neuropathy, neurocognitive changes	None	S.B12 ↓	Axonal	Hyperintense posterolateral columns
	Anti-cancer drugs	H/o chemotherapy, may overlap with features of radiation myelopathy	Estimation of drug levels, if available	Immunodeficiency or reactive leucocytosis /thrombocytosis	Depends on the agent	Not well characterized

Cut-offs/Range (May vary with different laboratories and methodology) –
S.B12: <200pg/mL, S.Ceruloplasmin 250-630mg/L, S.Copper: 11-22 µmol/L (70-140 µgm/dL), Vitamin E: 12-42 µmol/L (5-18 µgram/mL), S.Folate: 12.2-40.8 nmol/L (5.4-18.0 ng/ml), S.Homocysteine: 4.4-10.8 µmol/L, S.Zinc: 0.66-1.1 µg/ml

Abbreviations –
ABNL: Abnormal, ACE: Angiotensin-converting enzyme, ANA: Antinuclear antibody, CBC: Complete Blood Count (with quantitative meas ures), ELISA: Enzyme-linked Immunosorbent Assay, HIV: Human Immunodeficiency Virus, HTLV: Human T-lymphotropic Virus, PCR: Polymerase Chain Reaction, S: Serum, SSEPs: Somatosensory evoked potentials, SS-A: Anti-Ro, SS-B: Anti-La, U: Urinary, Vit: Vitamin, VLCFA: Very long chain fatty acids,

Figure 2: Summary of the important clinical, laboratory, and imaging details of various etiologies associated with myeloneuropathy

Table 1: Common nutritional, metabolic, and toxic causes of myeloneuropathy: Etiology, diagnosis, and treatment

Disease	Common causes	Imaging	Diagnosis	Treatment
Vitamin B 12 deficiency	Dietary deficiency, pernicious anemia, atrophic gastritis, gastric bypass surgery	Signal changes in the posterior and lateral columns	Low serum vitamin B 12 assay (<200 pg per milliliter) Elevated levels of methylmalonic acid and homocysteine	Intramuscular B 12 1,000 µg for 5 days followed by monthly injections
Copper deficiency	Dietary deficiency, malabsorption, bariatric surgery, excess zinc ingestion	T2 signal-intensity in the dorsal columns	Low serum and urinary copper and a low ceruloplasmin level	Oral copper (2-4 mg/d) for 6 days for 4-12 weeks
Folate deficiency	Dietary deficiency, malabsorption, bariatric surgery	T2-increased signal intensity involving the dorsal columns	Predominantly sensory axonal neuropathy Low red-cell folate and high homocysteine	1 mg of folic acid daily
Vitamin E deficiency	Genetic in origin or malabsorption syndrome	Spinocerebellar atrophy and dorsal column disease hyperintensity	Serum α-tocopherol levels	200 mg to 600 mg per day orally
Nitrous oxide	Exposure to nitrous oxide	Signal changes in the posterior and lateral columns	Normal serum vitamin B 12	Discontinue exposure and intramuscular B 12

The myelopathies that often need to be considered in the differential diagnosis of subacute combined degeneration of the spinal cord include spondylotic myelopathy, infectious or postinfectious myelitis, multiple sclerosis, vascular malformations of the spinal cord, spinal cord infarction, and many connective tissue diseases such as systemic lupus erythematosus. In most of these conditions, MRI reveals T2 hyperintensity in the dorsal columns.

Approach to a Case of Myeloneuropathy

Establishing the correct diagnosis of myeloneuropathy is important because compressive myelopathies may pose diagnostic confusion. An asymmetrical onset of neurological manifestations and progression, a definite upper level of involvement, Brown-Séquard syndrome like picture, or early bladder and bowel involvement, indicate a possible compressive cause for myelopathy [Figure 2].

Once the presence of myeloneuropathy is established, all these patients should be subjected to a battery of tests. Blood levels of vitamin B12, folic acid, methylmalonic acid, homocysteine, vitamins A, D, E, and K, iron, and calcium should be assessed to detect other nutritional deficiencies. Imaging of the brain and spinal cord, with contrast, is always needed. Electromyography and nerve conduction study results are often consistent with

axonal sensorimotor polyneuropathy in the legs; somatosensory evoked potentials may provide an electrophysiological evidence of dysfunction in the central pathways.

Various conditions causing dietary and nutritional deficiencies should be recognized early. A history of malabsorption, gastrointestinal surgery, pregnancy and lactation, usage of anticancer, antiepileptic, or oral contraceptive drugs and long-term alcoholism hold the key to a proper diagnosis of nutritional deficiency myeloneuropathies [Table 1].

Conclusion

A correct diagnosis of myeloneuropathy is often challenging. Vitamin B12, folate, copper, and vitamin E deficiencies lead to myeloneuropathy. The clinical picture in all these conditions is similar to that of mimics subacute combined degeneration of the spinal cord. The pattern of neurologic involvement and results obtained from a battery of biochemical tests help in establishing the correct diagnosis.

Conflicts of interest
There are no conflicts of interest.

References

1. Goodman BP. Diagnostic approach to myeloneuropathy. Continuum (Minneap Minn) 2011;17:744-60.
2. Kumar N. Metabolic and toxic myelopathies. Semin Neurol 2012;32:123-36.
3. Kalita J, Misra UK. Vitamin B12 deficiency neurological syndromes: Correlation of clinical, MRI and cognitive evoked potential. J Neurol 2008;255:353-9.
4. Aaron S, Kumar S, Vijayan J, Jacob J, Alexander M, Gnanamuthu C. Clinical and laboratory features and response to treatment in patients resenting with vitamin B12 deficiency-related neurological syndromes. Neurol India 2005;53:55-9.
5. Puri V, Chaudhry N, Goel S, Gulati P, Nehru R, Chowdhury D. Vitamin B12 deficiency: A clinical and electrophysiological profile. Electromyogr Clin Neurophysiol 2005;45:273-84.
6. Healton EB, Savage DG, Brust JC, Garrett TJ, Lindenbaum J. Neurologic aspects of cobalamin deficiency. Medicine (Baltimore) 1991;70:229-45.
7. Bolamperti L, Leone MA, Stecco A, Reggiani M, Pirisi M, Carriero A, *et al*. Myeloneuropathy due to copper deficiency: Clinical and MRI findings after copper supplementation. Neurol Sci 2009;30:521-4.
8. Spain RI, Leist TP, De Sousa EA. When metals compete: A case of copper-deficiency myeloneuropathy and anemia. Nat Clin Pract Neurol 2009;5:106-11.
9. Schaumburg H, Herskovitz S. Copper deficiency myeloneuropathy: A clue to clioquinol-induced subacute myelo-optic neuropathy? Neurology 2008;71:622-3.
10. Goodman BP, Bosch EP, Ross MA, Hoffman-Snyder C, Dodick DD, Smith BE. Clinical and electrodiagnostic findings in copper deficiency myeloneuropathy. J Neurol Neurosurg Psychiatry 2009;80:524-7.
11. Goodman BP, Chong BW, Patel AC, Fletcher GP, Smith BE. Copper deficiency myeloneuropathy resembling B12 deficiency: Partial resolution of MR imaging findings with copper supplementation. AJNR Am J Neuroradiol 2006;27:2112-4.
12. Goodman BP. Metabolic and toxic causes of myelopathy. Continuum (Minneap Minn) 2015;21:84-99.
13. Román GC. Nutritional disorders in tropical neurology. Handb Clin Neurol 2013;114:381-404.
14. Vorgerd M, Tegenthoff M, Kühne D, Malin JP. Spinal MRI in progressive myeloneuropathy associated with vitamin E deficiency. Neuroradiology 1996;38(Suppl 1):S111-3.
15. Pema PJ, Horak HA, Wyatt RH. Myelopathy caused by nitrous oxide toxicity. AJNR Am J Neuroradiol 1998;19:894-6.
16. Layzer RB. Myeloneuropathy after prolonged exposure to nitrous oxide. Lancet 1978;2:1227-30.
17. Ostwal P, Dabadghao VS, Sharma SK, Dhakane AB. Chlorpyrifos toxicity causing delayed myeloneuropathy. Ann Indian Acad Neurol 2013;16:736.
18. Tandale BV, Sathe PS, Arankalle VA, Wadia RS, Kulkarni R, Shah SV, *et al*. Systemic involvements and fatalities during Chikungunya epidemic in India, 2006. J Clin Virol 2009;46:145-9.
19. Chandak NH, Kashyap RS, Kabra D, Karandikar P, Saha SS, Morey SH, *et al*. Neurological complications of Chikungunya virus infection. Neurol India 2009;57:177-80.
20. Modi G, Ranchhod J, Hari K, Mochan A, Modi M. Non-traumatic myelopathy at the Chris Hani Baragwanath Hospital, South Africa-the influence of HIV. QJM 2011;104:697-703.
21. Shankar SK, Mahadevan A, Satishchandra P, Kumar RU, Yasha TC, Santosh V, *et al*. Neuropathology of HIV/AIDS with an overview of the Indian scene. Indian J Med Res 2005;121:468-88.
22. Alsharabati M, Oh SJ. Paraneoplastic myeloneuropathy in a man with breast cancer. Muscle Nerve 2015;52:685-6.
23. Rajabally YA, Qaddoura B, Abbott RJ. Steroid-responsive paraneoplastic demyelinating neuropathy and myelopathy associated with breast carcinoma. J Clin Neuromuscul Dis 2008;10:65-9.
24. Verma R, Lalla R, Patil TB, Mehta V. Acute myeloneuropathy: An uncommon presentation of Sjögren›s syndrome. Ann Indian Acad Neurol 2013;16:696-8.
25. Kayal AK, Basumatary LJ, Dutta S, Mahanta N, Islam S, Mahanta A. Myeloneuropathy in a case of Hashimoto›s disease. Neurol India 2013;61:426-8.
26. Turkoglu R, Tuzun E. Steroid-responsive myeloneuropathy associated with antithyroid antibodies. J Spinal Cord Med 2010;33:278-80.
27. Oomman A, Madhusoodanan M. Tropical spastic paraparesis in Kerala. Neurol India 2003;51:493-6.
28. Ajdukiewicz A, Yanagihara R, Garruto RM, Gajdusek DC, Alexander SS. HTLV-1 myeloneuropathy in the Solomon Islands. N Engl J Med 1989;321:615-6.
29. Chafale VA, Lahoti SA, Biswas A, Roy A, Senapati AK. Adrenomyeloneuropathy with bulbar palsy: A rare association. Ann Indian Acad Neurol 2014;17:361-3.
30. Motley WW, Griffin LB, Mademan I, Baets J, De Vriendt E, De Jonghe P, *et al*. A novel AARS mutation in a family with dominant myeloneuropathy. Neurology 2015;84:2040-7.
31. Sen A, Chandrasekhar K. Spinal MR imaging in Vitamin B12 deficiency: Case series; differential diagnosis of symmetrical posterior spinal cord lesions. Ann Indian Acad Neurol 2013;16:255-8.