Myeloradiculoneuropathy due to vitamin B_{12} deficiency: an unusual clinical and radiological presentation

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SUMMARY

A 42-year-old man from rural India presented with asymmetric progressive paraparesis mimicking compressive dorsal myelopathy, followed by distal upper limb, truncal and neck-flexor weakness, further complicated by acute urinary retention. His sensory deficits were marked by loss of joint position sense (JPS) and graded loss of vibration sense, along with a definite sensory level. Deep tendon jerks were hypo-to-areflexic, plantar was bilaterally extensor. He had become less attentive and occasionally failed to keep track with conversations. A syndromic diagnosis of myeloradiculoneuropathy with cognitive impairments was made. Further tailored investigations revealed vitamin B_{12} deficiency with positive anti-parietal cell antibody. Diagnosis of subacute combined cord degeneration (SACD) was confirmed. Neuro-imaging revealed intramedullary intensity changes only along lateral aspect of spinal cord instead of characteristic posterior involvement. Following parenteral vitamin B_{12} supplementation, patient started showing improvement in motor power and subjective sensory symptoms. His bladder symptoms persisted initially, however recovered finally after 6 months.

BACKGROUND

The prevalence of vitamin B_{12} deficiency is worldwide, estimating 10.6% in USA, higher in other parts of the world, with studies from India revealing vitamin B_{12} deficiency in up to 47% of Indian population.[1 2] Vitamin B_{12} deficiency is usually associated with various haematological, gastrointestinal and neuropsychiatric disorders. Neurological symptoms are often considered to be late manifestations, can be seen in approximately 40% of patients with vitamin B_{12} deficiency and usually occur after the onset of anaemia. SACD is the most frequent neurological manifestation of vitamin B_{12} deficiency, and can have diverse clinical presentation.[3 4] However presentation of SACD mimicking compressive myelopathy and acute onset autonomic disturbance in form of bladder involvement with atypical spinal cord lesion instead of typical posterior predominant involvement is exceedingly rare, which make this index case unique and worthy reporting.

CASE PRESENTATION

A 42-year-old non-diabetic, non-hypertensive man, without any history of (H/O) addiction, tailor by occupation, presented to us with insidious onset, gradually progressive asymmetric paraparesis involving both proximal and distal muscles for last 1 year. The weakness started in the right lower limb, initially distal, gradually involving the proximal muscle groups, followed by left lower limb weakness in the next 6 to 7 months. He denied any H/O upper limb or truncal weakness. For the last 4 to 5 months, the patient started having symmetrical onset tingling paresthesia in both lower limbs, distal to begin with, gradually ascending upwards, later involving the distal upper limbs also, associated with diminished sensation in the corresponding areas over the next 1 to 1.5 month. On further probing, he recounted that his sensations had markedly diminished below the nipple level for the last 1 month. Following this, the patient had an acute retention of urine about 20 days ago, which had to be relieved with urinary catheterisation in a local hospital. There was a preceding history of low back pain for the last 1.5 months. Pain was localised, not associated with any local tenderness, swelling and deformity. There was no associated girdle-like-sensation, zone of hyperesthesia or root pain. There was no H/O seizure, altered sensorium, cranial nerve symptoms, headache or vomiting, chronic diarrhoea, weight loss, fever, joint pain or skin rashes.

Physical examination revealed oral ulcers, presence of glossitis and smooth, beefy red tongue. The patient had mild pallor. Assessment of higher mental function was done. MMSE (Mini-Mental State Examination) score was 23/30, with impairment in registration, recall and three steps command. Detailed cognitive assessment revealed errors in A-vigil test and trail making test, forward digit span was 4 and backward digit span was 3. All adding up to predominant deficits in attention and working memory. There was no problem in conceptualisation, abstract thinking, similarities and dissimilarities or any behavioural problems. Pupils were normal size, reactive to direct and consensual light, fundoscopic examination were normal, visual acuity was 6/9 in both the eyes. There was significant asymmetric atrophy predominantly in the lower limbs both proximally and distally, upper limbs also had evidence of early atrophy distally. Tone was decreased in all four limbs. Antigravity actions were lost in the lower limbs (Medical Research Council grading, proximally 1/5 in right limb and 2/5 in left limb, distally 2/5 in both lower limbs). Motor power in upper limbs were preserved proximally, however distally it was 4+/5. There was associated truncal and neck flexor weakness.

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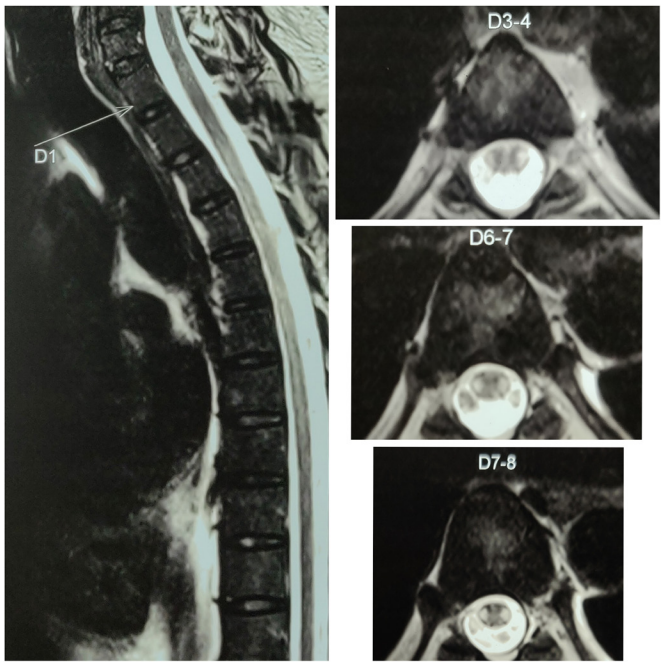

Figure 1 MRI spinal cord at presentation: (sagittal) T2 signal changes extending longitudinally from D3 to D9 and dorsal cord (axial) T2 sequence showing intensity changes predominantly in the bilateral lateral column.

The patient had hyporeflexia (1+) in upper limbs, areflexia was seen in lower limbs. Plantar showed bilateral extensor response. Sensory examination revealed decreased sensation of all modalities until below the nipple area. Besides, fine touch was found to be decreased in upper limb also until mid elbow. JPS was impaired until ankle, graded loss of vibration sense was seen in the lower limbs, entire spine and up to the wrist in upper limb. Cerebellar function was normal in upper limb. Lower limb cerebellar function and Romberg's testing could not be tested because of the existing motor deficits.

INVESTIGATIONS

Complete blood count revealed decreased haemoglobin levels of 11.3 gm% with mean corpuscular volume of 124 fL (normal: 80 to 100). Metabolic parameters and chest radiography were normal. HIV antibody test, hepatitis B and C screening were negative. Nerve conduction study was suggestive of acquired sensori-motor axonal polyradiculoneuropathy. Electromyography (EMG) showed neurogenic denervation pattern. Visual-evoked potential was normal. Cerebrospinal fluid (CSF) analysis was unrevealing, no cells, protein 35 mg/dL (normal: 10 to 50 mg/dL); glucose 64 mg/dL (corresponding serum glucose: 86 mg/dL). Autoimmune (antinuclear antibody (ANA), ANA profile, anti-Sjogren syndrome related antigen A autoantibody (SS-A), anti-Sjogren syndrome related antigen B autoantibody (SS-B)) and paraneoplastic profile came to be negative, serum angiotensin converting enzyme (SACE) were normal. MRI of the brain revealed no significant abnormality. MRI of the spine revealed an intramedullary signal changes in the dorsal cord from D3 until D10 predominantly involving the lateral column (figure 1). Serum vitamin B_{12} levels were done and came to be 140 pg/mL (normal: 197 to 771 pg/mL). Subsequent testing revealed the presence of anti-parietal cell antibody. Upper gastrointestinal endoscopy was normal. Serum homocysteine levels were 60 micromol/L (normal: 5.46 to 16.2) and methylmalonic acid levels were 2248 nmol/L (normal: 50 to 440).

DIFFERENTIAL DIAGNOSIS

A 42-year-old male patient presented with progressive asymmetric quadriparesis bilateral lower limb weakness (proximal and distal) more than bilateral upper limb weakness (restricted distally) along with truncal and neck flexor weakness associated with marked lower limb predominant wasting coupled with areflexia in lower limbs and hyporeflexia in upper limbs. Deciphering the pattern of motor involvement in terms of progressive asymmetric paraparesis and extensor plantar response gives clue to involvement of pyramidal tract in dorsal cord. However, presence of marked wasting, areflexia and later sequential involvement of upper limb distal muscles, trunk and neck flexors point towards contribution of motor peripheral nerve and multiple radicles by the same underlying pathological process. Considering motor deficits, spinal cord, motor nerves and radicles have to be simultaneously held responsible, which endorsed the syndromic approach to myeloradiculoneuropathy.

Analysing and keeping track with temporal sequencing of sensory involvement, history and clinical examination, it is evident that pattern of sensory involvement started in the distribution of sensory nerve followed by diminution of all modalities of sensation below the nipple line which is indicative of sensory localisation in dorsal cord also. Impairments in JPS, loss of vibration in graded way indicates either large fibre sensory or posterior column involvement inside into the cord. Thus considering the sensory deficits, it is obvious again that peripheral nerve and cord were involved simultaneously in underlying same pathological process.

Regarding higher mental function, in form of attention and working memory deficit, among which attention deficit may be attributed to fronto-parietal attentional network dysfunction and working memory circuit impairments points towards dysfunction either in visuospatial sketchpad, phonological loop or in central executive or coordination failure in the aforementioned loops.

Acute onset urinary retention may be attributed to either descending autonomic tract involvement inside into cord or peripheral autonomic nerve dysfunction.

Thus, combining motor, sensory and autonomic deficits along with higher mental function abnormality and rational analysis to search for underlying anatomical substrate/s involved, give rise to syndromic diagnosis of myeloradiculoneuropathy with subtle cognitive impairment.

Myeloradiculoneuropathy is a frequently encountered clinical scenario with wide array of clinical differentials often sharing overlapping clinical features, thus posing a diagnostic challenge. Handful of aetiologies like,

1. Nutritional: Vitamin B_{12} deficiency, folate deficiency and vitamin E deficiency (red blood cell folate and serum vitamin E level came normal).
2. Drug induced (no significant history).
3. Toxic: Organophosphorus poisoning (chlorpyrifos) and nitrous oxide (no history of exposure).
4. Metabolic: Copper deficiency (no history of exposure to excessive zinc and copper level in blood came normal).
5. Infection: HIV, chikungunya and Lyme disease (HIV antibody was negative, IgM for chikungunya came negative and IgM and IgG for Lyme disease were non-contributory).
6. Inflammatory (Sjogren, sarcoidosis), (ANA profile including SS-A and SS-B, Schirmer's test were negative, SACE was

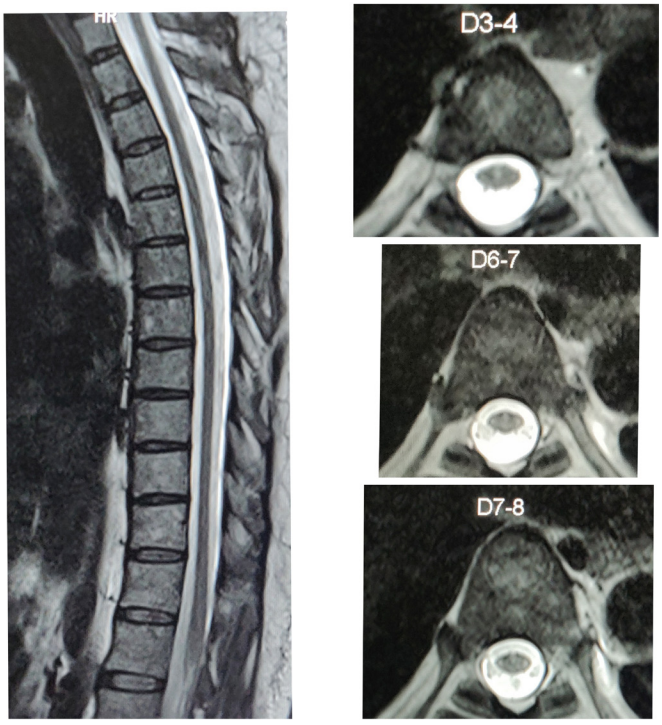

Figure 2 MRI spinal cord following therapy at 6 months follow-up: (sagittal) T2 sequence and dorsal cord (axial) T2 sequence showing resolution of the intramedullary signal changes.

normal and high-resolution CT of the thorax to rule out hilar lymphadenopathy were non-contributory).
7. Paraneoplastic disorders (18FDG positron emission tomography study was screened negative for malignancy).
8. Inherited disorders: In association with leukodystrophies like adrenomyeloneuropathy (MRI of the brain was normal and no evidence of leukodystrophies seen).
9. Tropical ataxic neuropathy (no history of cassava intake).
10. Tropical spastic paraparesis (no evidence of spasticity in lower limbs).
11. Syphilis (tabes dorsalis) (VDRL (Venereal disease research laboratory test) was negative).
12. Cauda-conus syndrome (MRI of the lumbosacral spine noncontributory and CSF study was normal).
13. Friedrich's ataxia (no clinical evidence of ataxia noted).
14. Hashimoto's myeloradiculoneuropathy with cognitive impairments (euthyroid status, anti-thyroid peroxidase was negative and electroencephalogram (EEG) was normal).

can present with myeloneuropathy. The clinical picture in all these conditions is similar and often a battery of test has to be undertaken to reach a correct diagnosis.[5] However a thorough history and clinical examination for possible micronutrient deficiency with a corroborative evidence of megaloblastic picture from simple complete haemogram can greatly aid in directed investigations and can obviate the need for expensive investigations. Dietary modifications and vitamin B_{12} replacement usually herald substantial improvement from this disabling neurological ailment.[6]

TREATMENT

The patient was supplemented with weekly injections of 1000 mcg of methylcobalamin subcutaneously for the next 8 weeks and then once monthly.

OUTCOME AND FOLLOW-UP

There was marked improvement in the motor and sensory symptoms. At the end of 6 months, motor power was 4+/5 in both the lower limbs both proximally and 5/5 distally and 5/5 in the upper limbs, with ability to clear the scapula until inferior angle, along with definite improvement in sensory examination in the areas of previously diminished sensation. The bladder dysfunction though initially persisted and he had to be remained catheterised, has improved subsequently after 6 months. The delayed recovery of bladder may be related to improper bladder training. Repeat MRI showed complete resolution of intramedullary signal changes of the dorsal spinal cord. (figure 2)

DISCUSSION

Vitamin B_{12} deficiency can range from entirely asymptomatic to protean of haematological and neuropsychiatric manifestations. The central nervous system (CNS) involvement may range from psychiatric symptoms of depression, manic, irritability, paranoia, delusion, lability ('megaloblastic madness'), cognitive decline and altered mental state, optic neuropathy and anosmia to myelopathy (SACD). Peripheral nervous system (PNS) may manifest as motor-sensory polyneuropathy or autonomic neuropathy. Combined CNS and PNS involvement in the form of myeloneuropathy is also seen.[4 7]

Myelopathic signs tend to be symmetric and reflect the predominant involvement of posterior and lateral columns of the spinal cord.[3 8] However, the index case presented with asymmetric onset motor weakness involving the right and left lower limb sequentially, mimicking a compressive myelopathic presentation, which was misleading because spinal imaging did not reveal any significant compression. Hence symmetricity may not be the rule always.

Bladder symptoms may be seen in about one-third of the patients of SACD, often a late feature, usually seen in moderate-to-severe clinical picture. Neurogenic detrusor overactivity with high pressure voiding and large volume areflexic bladder may be seen due to involvement of the lateral corticospinal and involvement of posterior column with adjacent dorsal root ganglia, respectively.[9] Also, autonomic failure can be associated in vitamin B_{12} deficiency similar to patterns seen in diabetic autonomic neuropathy.[10] However, manifestation of acute urinary retention in vitamin B_{12} deficiency has rarely been reported.

Patient's perspective

I gradually became non-ambulatory due to weakness of both of my lower limbs which was progressive and started almost a year ago from right lower limb. For last 4 to 5 months paresthesia was disabling, first involved the lower limbs and gradually ascended to involve the distal part of upper limbs. I couldn't feel sensations properly below my mid-chest position. I became depressed 20 days before hospital admission as I wasn't able to pass urine voluntarily. I thought I would never be cured. Family members took me to hospital. There, after examinations and investigations, I have been told that all my neurological aliments are due to deficiency of vitamin B_{12}. Injectable medications were started and after 2 months of hospital admission I feel much better as my lower limbs power has started improving and there is significant decrease in paresthesia which was disabling before. And now after 6 months all my disabilities are resolving and I feel very hopeful to be able to lead a near normal life in future.

Learning points

- Wide array of clinical manifestations may occur in vitamin B_{12} deficiency, subacutecombined cord degeneration (SACD) being the most common neurological phenotypic presentation.
- Non-compressive myelopathy may sometimes mimic compressive myelopathy clinically in many senses.
- Bladder involvement in SACD may stem from either descending autonomic tract involvement in spinal cord or from peripheral autonomic involvement. Whatever may be the cause it is uncommon in SACD, but its presence does not exclude clinical diagnosis of SACD.
- Lateral column involvement in MRI of the spinal cord though considered as one of the late imaging findings and is usually preceded by posterior column involvement. However, it must not be considered as a rule.
- Cognitive and behavioural impacts of vitamin B_{12} deficiency range from madness, schizophreniform illness, recent memory dysfunction to attention deficit and working memory dysfunction.

MRI is an important and sensitive tool in diagnosing SACD; affection of posterior column in longitudinally extensive fashion is seen predominantly in the upper and mid thoracic spinal cord, giving rise to 'inverted V' or 'inverted rabbit ears' sign on imaging. The involvement of lateral column occurs in more severe disease.[3 11] However, interestingly our case had predominant lateral cord involvement on imaging with relative sparing of posterior column, a rare occurrence.

In India, vitamin B_{12} deficiency is encountered in vegetarians, due to religious and cultural reasons, food faddism and poor socioeconomic status. Genetic and autoimmune abnormalities may also contribute to vitamin B_{12} deficiency.[9] It can present with myriad of neurological manifestations in various combinations, and can even mimic compressive myelopathy, have acute bladder symptoms. Spinal imaging may also not have classical posterior involvement. However, a detailed bedside evaluation of the patient with the aid of simple and inexpensive testing can often help us to diagnose a vitamin B_{12} deficiency, which on replenishment can pay rich dividends in patient's clinical improvement and decrease the financial burden of investigation equally.

Contributors ShD contributed to conception, literature review and initial drafting of manuscript, carrying out all the necessary investigations, collecting all the relevant data and was directly involved in patient care. SoD was involved in supervision of patient's management, gave expert opinion regarding the case and contributed to editing, critical revision and final approval of the manuscript. He also supervised the entire attempt to report the case. AP gave expert opinion regarding the case, and was involved in critical revision and final approval of the manuscript. BKR contributed to supervision of patient's management, gave expert opinion regarding the case and contributed to critical revision and final approval of the manuscript. All the authors are in agreement to be accountable for all the aspects of the work in ensuring that query related to its authenticity and accuracy are adequately evaluated and settled.

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