Subacute Combined Degeneration of spinal cord with megaloblastic anemia secondary to vitamin B12 deficiency in a 17-year female

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ABSTRACT

Sub acute combined degeneration of spinal cord (SCD), a treatable non-compressive myelopathy, is a rare cause of demyelination of the dorsal and lateral columns of the spinal cord. Megaloblastic anemia is a disorder caused by impaired DNA synthesis and is characterised by a distinctive abnormality in the hematopoietic precursors in the bone marrow in which the maturation of the nucleus is delayed relative to that of the cytoplasm.Both this condition are complication of vitamin B12 deficiency, which is reversible if diagnosed and treated early. We present a case of a 17- year-female patient with symptoms of tingling and numbness in both lower limbs and MRI showing relative thinning of dorsal cord from D4 to D10 level with areas of hyperintensity along posterior surface.A diagnosis of sub acute combined degeneration of the spinal cord was considered and confirmed by laboratory findings especially by blood peripheral smear findings, RBCs indices,bone marrow aspiration cytology and serum vitamin B12. The patient showed complete recovery on B12 therapy. This case is interesting as Vitamin B12 deficiency & neurological presentation in a 17-year young female is uncommon.

Keywords: SCD;Megaloblastic anemia;Vitamin B12deficiency.

INTRODUCTION

Sub acute combined degeneration of spinal cord is a potentially reversible cause of myelopathy, if diagnosed and treated early. This specific type of neuronal degeneration results from Vitamin B12 deficiency. It usually involves the dorsal columns, lateral corticospinal and lateral spinothalamic tracts of spinal cord. Patients usually complain of insidious onset of sensory symptoms followed by motor involvement which may progress to paraplegia in neglected cases. Magnetic Resonance Imaging (MRI) shows hyper intense signal intensity in the posterior and lateral part of spinal cord. Cervical spinal cord involvement usually more common than thoracic spinal cord [1].

Megaloblastic anemias are a subgroup of macrocytic anemias caused by impaired DNA synthesis that results in macrocytic red blood cells, abnormalities in leukocytes and platelets and epithelial changes, particularly in the rapidly dividing epithelial cells of the mouth and gastrointestinal tract[2].

Vitamin B12 deficiency is a well-described disorder with a spectrum of manifestations ranging from macrocytic anemia to neuropsychiatric disorders including depression,dementia, and subacute combined degeneration of the spinal cord. In western countries, pernicious anemia is the most common cause of its deficiency, however, alcoholism, malnutrition and ileocecal tuberculosis are the common causes in India[3]. At risk populations include the elderly, alcoholics, strict vegetarians, as well as patients with intestinal inflammatory diseases, autoimmune conditions, post-bariatric surgery, and users of certain medications including proton pump inhibitors, histamine receptor antagonists, and biguanides [4].

Megaloblastic anaemia due specifically to vitamin B12 deficiency, in which there is also spinal cord degeneration, leading to peripheral neuropathy. It is a disease of later life;only about 10% of patients are aged ,40 years; by the ageof 60 years about 1% of the population are affected, rising to 2–5% of people aged 65 years, as a result of atrophic gastritis (commonly due to autoimmune disease) and hence impaired secretion of intrinsic factor, which is required for the absorption of vitamin B12 [5].

CASE REPORT

A 17-years-female, pure vegetarian by diet since birth, who presented to the hospital with chief complaint of numbness & weakness of both lower limbs,more on right lower limb than left lower limb,lower backache and easy fatiguability for one & half months.These symptoms were slow in onset and progressively worsened so that feelings of instability and decreased strength both lower limbs.Before going to the hospital, she presented total inability to move the lower extremities and numbness in both the legs.

At the hospital, we observed patient had pallor, blood pressure of 110/70 mmHg and heart rate 88 bpm. The neurological examination showed absence of deep sensitivity (positional and vibratory), absence of the sense of touch in the lower limbs, motor deficit of 2/5 in the right leg and 1/5 in the left leg, patellar and Achilles tendon reflexes absent, and left extensor Babinski reflex present.

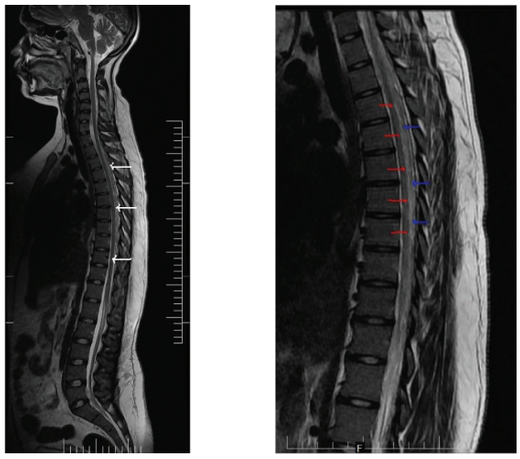

Figure:1 a, b Sag T2 sections of thoracic spine showing thining of cord from D4 to D10 levels (red arrows) with posterior column hyperintensities (blue arrow) suggestive of SCD.

The initial MRI examination of the cervical and dorsal spine was performed using a 1.5-T unit and showed Relative thinning of dorsal cord from D4 to D10 level with areas of hyperintensity along posterior surface suggestive of subacutecombined degeneration of cord (Figure 1). Among the analytical parameters, the following were observed (normal values are in brackets): hemoglobin: 8.9 g/dl (12-18); hematocrit: 25% (37-52); erythrocytes:2.51 millions/cumm (4.2-5.5); mean corpuscular volume: 125fl (76-96); mean corpuscular hemoglobin: 41 pg (27-32); red cell distribution width: 19.8% (11.5 to 14.5); reticulocytes: 2.5% (0.5-2); leukocytes: 8200 cell/mm3 (400-11000), platelets: 200 cell/mm3 (150,000-450,000).Peripheral blood smear reveal predominantly macrocytic RBCs,moderate anisopoikilocytosis, presence of macrovalocytes and hypersegmented neutrophils (Figure 2).

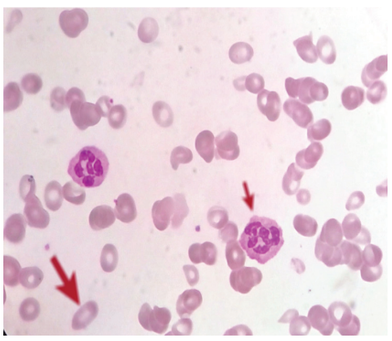

Figure:2 Leishman stained peripheral smear show macrovalocytes and hypersegmented neutrophils.

Liver function test showed indirect bilirubin: 3.5 mg/dl (< 0.7) and lactic dehydrogenase: 4150U/l (160-480). Advised further to do serum Vitamin B12, serum folic acid & bone marrow cytology. Serum Vitamin B12 value was low 63pg/ml(211-616) & folic acid was normal. Bone marrow aspiration done which showed marrow is hypercellular, showing evidence of abnormal proliferation and maturation of erythroid cells. These abnormalities are most evident in the erythroid precursors with large megaloblastic erythroblasts present in increased numbers throughout the marrow. These megaloblasts are abnormal, large, nucleated erythroid precursors, having nuclear- cytoplasmic asynchrony (Figure 3). Few giant metamyelocytes and stab forms seen.

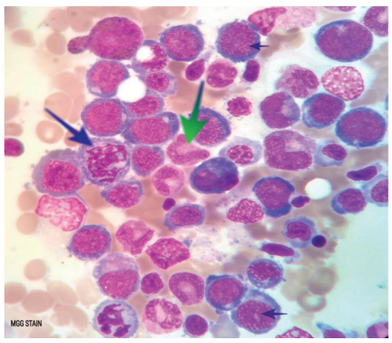

Figure:3 Bone marrow aspirate (MGG stain) Megaloblastic erythropoiesis; Megaloblast with stippled chromatin(blue arrow) giant stab forms (green arrow)

Finally based on radiological and lab findings, Patient was diagnosed with sub-acute combined degeneration of spinal cord due to Vitamin B12 deficiency and was treated with Injection Cyanocobalamine 1000mcg I/M daily for 7 days followed by weekly injection for 1 month. After 1 week her symptoms started improving and she was completely relieved of her symptoms by the end of 1 month.

DISCUSSION

Vitamin B12 deficiency is a systemic disease that often affects the nervous and hematological system.Megaloblastic anemia is a common early manifestation pointing to an underlying vitamin B12 deficiency, although neurological symptoms may occur in the absence of hematological abnormalities[6].

In our case, patient had marked increased MCV,MCH and peripheral smear finding of macrovaloytes with presence of hypersegmented neutrophils was diagnostic clue for underlying Vitamin B 12 deficiency & MRI findings play major role to explain clinical symtoms and diagnosis.

Vitamin B12 (cyanocobalamin) is found essentially in all meat and dairy products. It is an essential vitamin for DNA and fatty acid synthesis, including myelin synthesis. Vitamin B12 deficiency can be caused by gastro-intestinal malabsorption, poor nourishment of food or genetic deficiency of methylmalonyl-CoA mutase. Vitamin B12 is a cofactor for only two enzymes: methionine synthase and l-methylmalonyl–

coenzyme A mutase. The interaction between folate and B12 is responsible for the megaloblastic anemia seen in both vitamin deficiencies.Dyssynchrony between the maturation of cytoplasm and that of nuclei leads to macrocytosis, immature nuclei, and hypersegmentation in granulocytes in the peripheral blood.

Neurologic symptoms of vitamin B12 deficiency are paresthesias, diminished proprioception and vibration sensation, motor weakness, clonus or hyperreflexia, areflexia, autonomic dysfunction, gait disturbance,intellectual or behavioral impairment, and impaired visual acuity .The most frequent neurologic manifestations are the SCD of the spinal cord and polyneuropathy . SCD affects the posterior columns and the corticospinal tracts and is characterized by swelling of the myelin sheaths and a patchy myelopathic spongy vacuolation of the affected regions of the cord [7]. Decreased B12 levels impair function of Methionine Synthetase and Methylmalonyl CoA mutase. This leads to production of abnormal fatty acids and elevated levels of Methylmalonic acid, which are toxic to myelin. Swelling of myelin sheaths is followed by astrocytic gliosis. Similar impairment of Methionine synthetase is also seen in cases where Nitrous Oxide has been used for anesthesia, possible cause being preexisting subclinical B12 deficiency [8]. The myelopathy of vitamin B12 deficiency (or SCD) is characterized neuropathologically by degeneration of myelin and axonal loss . It is clear now that the neuropathological lesions in SCD are due to overproduction of myelinolytic tumor necrosis factor a (TNF-a) and to the reduced synthesis of the two neurotrophic agents epidermal growth factor (EGF) and interleukin-6. This deregulation of the balance between TNF-a and EGF synthesis is induced by cobalamin deficiency [9]. MRI findings in SCD can be diagnostically extremely helpful. MRI shows a very typical pattern with T2 hyperintense signal alterations usually confined to the posterior columns, which may involve the lateral columns and rarely brainstem [10]. MRI seems to be a good diagnostic tool for the follow-up evaluation. Vasconcelos et al. Concluded that the absence of sensory dermatomal deficit, Romberg, Babinski signs,MRI lesions in =7 segments, and age younger than 50 were associated with a higher complete resolution rate[11]. vitamin B12 supplementation may begin with daily injections of cyanocobalamin at a dose of 1000 µg for the first week, followed by weekly injections for the first month, and maintenance monthly injections thereafter. Oral dosing is acceptable in patients with intact gastrointestinal absorption and absence of severe neurologic manifestations[12]. Treatment response should occur with reticulocytosis within one week as well as eventual reduction in MCV and resolution in the anemia within 1-2 months.

CONCLUSION

Subacute combined degeneration of the spinal cord is a recognized complication of vitamin B12 deficiency. Such myelopathy is reversible, as shown in our case; therefore a prompt recognition of this disorder by MRI,simple peripheral blood smear finding and serum Vit B12 can greatly ameliorate the patients prognosis & avoid irreversible neurological impairment.

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