Macrocytic anemia with Paraplegia due to Tuberculosis - Case Report

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Abstract

Vitamin B12 deficiency can result in macrocytic anemia. There are various neurologic abnormalities associated with vitamin B12 deficiency. Segmental involvement of the distal ileum, like tuberculosis, could cause vitamin B12 deficiency.

Case presentation: A 16-year-old girl had presented with complaints of paraplegia, ataxia, fever and fatigue that had started a few months earlier and which had been getting worse in the last three weeks. Her laboratory results were indicative of macrocytic anemia with a serum vitamin B12 level <90 pg/ml and hyper-segmented neutrophils. Her MRI findings revealed brain atrophy. Her fever eventually led to the diagnosis of tuberculosis which was documented by bone marrow aspiration smear & culture. A small bowel series showed that tuberculosis had typically involved the terminal ileum which had resulted in vitamin B12 deficiency. She was treated for vitamin B12 deficiency and tuberculosis. Her fever ceased and her hemoglobin level returned to normal. Vitamin B12 deficiency should be considered in patients with neurologic features such as paresthesia, sensory deficits, urinary incontinence, dysarthria, and ataxia. The fundamental cause of B12 deficiency should be determined and treated to prevent the patients' need for long term vitamin B12 therapy.

Key words: Macrocytic anemia, Vitamin $B_{12,}$ Tuberculosis

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Introduction: Vitamin B12 deficiency is a major public health problem: however, there is no consensus on how to diagnose this deficiency [1]. This deficiency can result in macrocytic anemia. Neurologic abnormalities of B12 deficiency include paresthesia, sensory deficits, loss of deep tendon reflexes, movement disorders, developmental regression, dementia and neuropsychiatric changes [1, 2]. Magnetic resonance imaging (MRI) has been able to demonstrate brain atrophy and delayed myelination in these cases [3]. B12 deficiency may also cause seizures [4,5]. Possible causes of vitamin B12 deficiency in childhood include decreased intake, abnormal absorption and defects in vitamin B12 transport and metabolism. Segmental involvement of the distal ileum, such as in tuberculosis, can cause macrocytic anemia [6,7]. To our knowledge, macrocytic anemia with unusual neurologic manifestations due to intestinal tuberculosis is rarely reported.

Case presentation

A 16-year-old girl was brought to Medicine department of Santhiram Medical College hospital in 2011 and she presented with complaints of fatigue, inability to walk, urinary incontinence, dysarthria, and ataxia that had worsened in the last three weeks. She also had fever, weight loss and decreased appetite. On physical examination, her blood pressure was 122/60 mmHg and she had a pulse rate of 92/min, a respiratory rate of 16/min and oral temperature of 38.6°C. Her growth and development were normal, reached menarche at the age of 13, followed by regular cycles until two months before admission. Her weight was 51 kg and her height was 157 cm. She had received all vaccinations and had no family history of diabetes, hypertension and metabolic disorders.

Her consciousness level was normal and she had no neck stiffness. In spite of being awake, she could not talk with anyone and only used indistinct words. The pupils were normal in size and her sclera was pale.

On neurological examination, her upper limbs were slightly spastic, and her muscle strength was 3/5 as far as she could cooperate. Her upper limb reflexes and also her sensory examinations were normal.

Her lower limbs were flaccid and mild atrophic and the patellar reflex was absent. She showed an extensor plantar

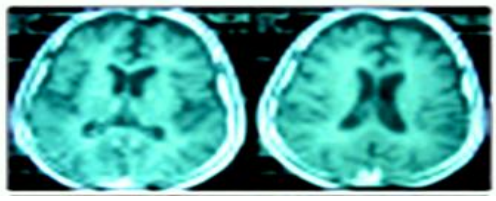
reflex. Her lower limb sensory examination showed lost senses of light touch, pain, temperature, vibration and joint position.

She was unable to stand or walk. Her abdominal, chest and heart examinations were normal. Her hemoglobin was 7.8 gm%. All other blood tests were normal. Her cerebrospinal fluid examination and chest X-ray were also normal.

Serum vitamin B12 level was <90 pg/ml and peripheral blood smear that showed hyper-segmented neutrophils (5 and 7 segments).

The MRI demonstrated senile dilatation in the CSF space and sulci of both hemispheres; a finding compatible with mild atrophic changes (Fig. 1).

Figure 1: Brain MRI shows senile dilatation in the CSF space and sulci of cerebral hemispheres



Treatment was started with vitamin B12 (1mg/IV/day) and folic acid (5 mg/oral/day). After 4 weeks, her symptoms improved and she was able to talk and eat. Her upper limb mobility improved and she began to communicate. However, she was febrile in spite of being treated with Vancomycin (1gm/BID) and Imipenem (500 mg/QID) which were chosen based on the infected bed sore cultures and antibiograms. After one month, her hemoglobin slightly increased and remained in the range of 8–9 gm/dl. Although her serial blood cultures were negative, she remained febrile, and we suspected an unusual source of infection that did not respond to broad spectrum antibiotics. Therefore, a bone marrow aspiration and biopsy was performed three weeks after initiating the treatment, and the specimen was examined for unusual germs such as tuberculosis and brucellosis.

Bone marrow examination (Figure 2) showed some degree of megaloblastic changes, giant metamyelocytes and cytoplasm dissociation. The laboratory report showed there were acid fast bacilli in her bone marrow aspiration smear. Therefore, we started a six month anti-tuberculosis treatment with Isoniazid- (5mg/kg/day), Rifampin (10 mg/kg/day), Ethambutol (15mg/kg/day), and Pyrazinamide20mg/kg/day.

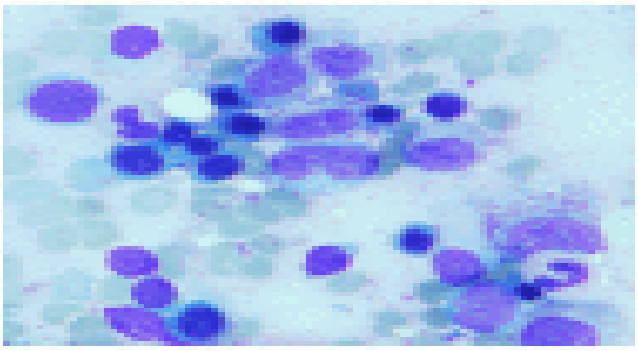


Figure 2: Bone marrow examination showed some degree of Megaloblastic changes, Giant Metemyelocytes with cytoplasm Dissociation

This treatment resulted in the termination of fever on the fourth day, with further increase in hematological parameters. Her upper limb and lower limb reflexes were normal. To find the cause of megaloblastic anemia, we reassessed the case. We concluded that her vitamin B12 deficiency might be of a gastrointestinal origin. A small bowel series by barium examination showed terminal ileum narrowing, irregularity and mucosal ulceration; highly indicative of tuberculosis (Fig. 3).

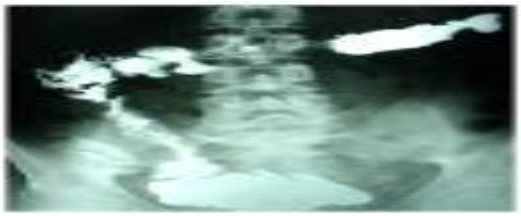


Figure 3: Small bowel series shows narrowing and irregularity of the terminal Ileum

It is proved that M. tuberculosis had caused the terminal ileum disease and possibly vitamin B12 deficiency in this patient. At present, our patient has been treated for vitamin B12 deficiency and M. tuberculosis. After being treated with anti-tuberculosis drugs her fever terminated and her hemoglobin level returned to normal. Her latest tests after 6 months of treatment showed a hemoglobin level of 13.7 gm/dl and hematocrit 39.4 %.

Discussion: The patient symptoms could be attributed to B12 deficiency. In one study on 50 patients with vitamin B12 deficiency and megaloblastic anemia, the commonest finding was peripheral neuropathy, but sub-acute

combined degeneration of the cord was uncommon. About a quarter of these patients had either cognitive impairment or an affective disorder, but a third had no detectable nervous system involvement [8].

The mechanism of neurological effects in cobalamin deficiency is not fully elucidated. Impaired methionine synthesis may lead to depletion of S-adenosyl-methionine which is required for the synthesis of myelin phospholipids. As in this patient, brain atrophy and some delayed myelination are observed on MRI. She also suffered from fever, especially at night, weight loss and reduced appetite. Fever is a strange finding in B12 deficiency unless it is accompanied with another disease. Her fever workup showed there were acid fast bacilli in her bone marrow aspiration smear, further confirmed by a positive culture after 48 days.

After treatment with anti-tuberculosis drugs, her fever terminated her hemoglobin level elevated and her general condition improved. This response to therapy was a good indication confirming the involvement of tuberculosis.

Probable causes of vitamin B12 deficiency in childhood include decreased intake, abnormal absorption and defects in vitamin B12 transport and metabolism [9]. She was subjected to small bowel series which showed terminal ileum involvement. As there was no signs in her barium examination about celiac disease, atrophic gastritis and food cobalamin malabsorption. So we suspected that M. tuberculosis might be the cause of macrocytic anemia. As studies have shown, segmental involvement of the distal ileum, such as seen in tuberculosis, or regional enteritis, can cause macrocytic anemia without any other manifestations of intestinal malabsorption such as steatorrhea [6, 7]. The diagnosis was supported by cleared signs of stricture in the terminal ileum after completion of the anti-tuberculosis treatment.

Conclusion:

Vitamin B12 deficiency should be considered in patients with neurologic features and the underlying cause of B_{12} deficiency, which can include intestinal tuberculosis and other treatable causes, should be determined and treated to obviate the patient's need for long term vitamin B12 therapy.

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