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## Subacute combined degeneration of the spinal cord in a Nigerian child: a need for a high index of suspicion

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**Abstract:** *Background:* Vitamin B12 deficiency has been reported to be associated with a spectrum of neurological disorders among which is subacute combined degeneration of the spinal cord.

*Method:* We report a case of subacute combined degeneration of the spinal cord secondary to vitamin B12 deficiency and discussed the clinical presentation and management challenge.

*Result:* The diagnosis was made through a high index of suspicion when the clinical presentation ranked highly with the mode of presentation of Vitamin B12 deficiency. Patient responded well to parenteral vitamin B12 preparation but subsequently defaulted

from follow up for 8 years after which he represented with paraparesis and urinary incontinence. He was managed again with parenteral vitamin B12 preparations with good outcome and total resolution of symptoms at discharge.

*Conclusion:* A high index of suspicion is needed in identifying vitamin B12 deficiency related paraparesis in paediatric practice while the need for indefinite treatment and follow up is hereby emphasized.

**Key words:** *Vitamin B12 deficiency; myelinopathy; paraparesis; subacute combined degeneration*

### Introduction

Vitamin B12 (Cobalamin) deficiency results in a wide range of haematological and gastrointestinal disorders. It is well known to be associated with myelinopathy, peripheral neuropathy, optic neuropathy, memory loss, neuropsychiatry disorders and subacute combined degeneration of the spinal cord<sup>(1-4)</sup>. It is a condition that is relatively commoner in adult than in the paediatric age group<sup>5</sup>.

The most frequent causes of Cobalamin deficiency are malabsorption which may follow pernicious anaemia, gastrectomy, intestinal infections, tropical sprue and pancreatic exocrine insufficiency<sup>1,5</sup>. Inadequate absorption can also result from deficiency of intrinsic factor, a glycoprotein responsible for enhancing the absorption of Vitamin B12 from the terminal ileum<sup>6</sup> and hereditary partial transcobalamin II deficiency<sup>7</sup>. Inadequate intake of vitamin B12 has also been implicated as a major cause of its deficiency especially in vegetarians, simply because vitamin B12 is mainly sourced from animal products<sup>1,5,8-10</sup>. Other recognized causes include side effect of Nitric Oxide, an inhalational general anaesthetic agent, usage of which can precipitate Vitamin B12 deficiency post operatively with its attendant sequelae or when employed in substance abuse by adolescents<sup>2,5,11</sup>.

Subacute Combined Degeneration of the Spinal Cord (SCDSC), a condition which could result from vitamin B12 deficiency can present with varying degree of impairment of spinal cord functions, often heralded by posterior column dysfunctions which could manifest as impairment of joint position and vibration sense, ataxia and paraesthesia all of which could be accompanied by varying degree of paresis, increased deep tendon reflexes, urinary incontinence and urinary tract infections<sup>2,3,5,9,12</sup>.

In the nervous system, Vitamin B12 acts as a co-enzyme in the methyl-malonyl-CoA mutase pathway necessary for myelin synthesis. Hence, its deficiency results in defective myelin synthesis resulting in central and peripheral nervous system dysfunction<sup>4</sup>. Normal plasma concentration of vitamin B12 does not exclude the diagnosis of vitamin B12 deficiency<sup>13</sup>. Hence, there is need for a high index of suspicion in diagnosing Vitamin B12 associated SCDSC, especially in paediatric age group where it is relatively rarer compared to the adult population.

The most consistent Magnetic Resonance Imaging (MRI) finding in SCDSC is a symmetrical abnormally increased T2 signal intensity confined to the posterior or

postero-lateral column<sup>4,14</sup> while some pathological findings could be multifocal and vacuolated lesions<sup>9</sup>. Early diagnosis and treatment of Subacute Combined Degeneration of the Spinal Cord is important in reversibility of neuro-deficits and prevention of permanent neurological damage<sup>9</sup>. Promptly diagnosed patients respond dramatically to parenteral Vitamin B12 preparations with improvement in neurological functions and prevention of irreversible neuro disabilities.

We report this case to sensitize physicians to a high index of suspicion of this condition while managing children presenting with paraparesis.

### Case report

A 4-year-old boy presented at the Paediatric Neurology Clinic of University College Hospital (UCH), Ibadan on account of poor growth and recurrent fever of three years duration, darkening of the palms and feet of 2 years duration, difficulty with walking of 3 weeks duration and 2 days history of passage of loose stool.

Patient's illness dated back to 3 years before presentation when mother noticed poor weight gain despite good appetite. He had associated recurrent episodes of fever and had been treated on outpatient basis for recurrent acute respiratory tract infections, otitis media and diarrhoea. About 2 years prior to presentation, he was observed to have developed progressive darkening of the palms and soles. There was no associated hyper pigmentation in any other part of the body. He was pale most of the time with associated effort intolerance and inability to play as his peers. His Packed Cell Volume (PCV) ranged from 17%-25% from then till presentation at the neurology clinic. Haemoglobin genotype was AS.

There were associated recurrent episodes of mouth ulcers with redness of the tongue, easy bruising and difficulty with eating in the 10 months preceding presentation; and at about 3 weeks prior to presentation, he developed difficulty with walking. Tremors of the hands were also observed while the patient fed himself. There was no history of seizures.

He started schooling at age 2 1/2 years but has been irregular in school due to recurrent illnesses. Pregnancy, labour and delivery history were not contributory and developmental milestones were essentially within normal limits. He was born into a polygamous setting and there was no history of similar illness in the family.

Findings on examination revealed a male child with sparse depigmented hair. He was a febrile, anicteric with satisfactory hydration status. He weighed 13.5 kg (96% of expected) and had hyper pigmentation of the palms and soles (figures 1 and 2). Grade II digital clubbing were noted. He was conscious and alert with normal speech, occipitofrontal circumference was 50cm which was normal for his age. There was no cranial nerve deficit. He had ataxic gait and was unable to tandem walk. The muscle power was grade 4 in all limbs. The muscle tone was increased in the lower limbs whilst the deep tendon reflexes were exaggerated in all limbs. There was no sustained ankle clonus and joint position and vibra-

tion senses were difficult to assess. Liver was palpable 4cm below the right costal margin, smooth and non-tender. Other systemic findings were within normal limit.

**Fig 1:** Hyperpigmented palms



**Fig 2:** Hyperpigmented soles. The examiner's hand was included for comparison



An assessment of possible Vitamin B12 deficiency with chronic anaemia, spastic paraparesis, recurrent glossitis and recurrent bacterial infections was made. Full Blood Count with Mean Cell Volume (MCV), Mean Corpuscular Haemoglobin Concentration (MCHC) and Mean Corpuscular Haemoglobin were requested all of which were elevated except MCHC. [MCH= 34.7pg (Ref range: 26.5-33.5pg); MCHC = 32.8g/dl (Ref range: 31.5 -35.5g/dl); MCV=106 fl (Ref range: 80-97fl)]. Red cell morphology revealed macrocytosis and hypochromasia. He was forthwith commenced on intramuscular (IM) Vitamin B12 1mg alternate days for 2 weeks, then 1mg weekly for 6 weeks, then 1mg monthly. Two weeks into the therapy, he made a remarkable clinical improvement evident by his ability to walk better and improvement in appetite. PCV then was 35%. He was thereafter scheduled for another follow-up in 6 weeks. However, patient defaulted from clinical care because mother felt it was no longer necessary and was lost to follow-up.

He represented 8 years later on account of difficulty with walking of 3 weeks duration, passage of bloody urine of 1 week duration and urinary incontinence of 3 days duration. Persistence of hyperpigmentation of the palms and soles earlier noted were observed on evaluation. He was unable to walk unaided with grade 4 muscle power in both lower limbs and normal muscle power in both upper limbs. Muscle tone and deep tendon reflexes were increased in both lower limbs with impairment of joint position and vibration sense and bilateral extensor plantar responses. A diagnosis of Vitamin B12 deficiency with SCDSC, spastic paraparesis, impaired joint position and vibration sense and urinary incontinence with Urinary Tract Infection (UTI) were made.

He was readmitted and commenced on IM Vitamin B12 1mg alternate days for 2 weeks, then 1 mg weekly for 6 weeks. Urine Microscopy Culture and Sensitivity yielded *E. coli* for which he had oral cefixime for 1 week while Spinal Magnetic Resonance Imaging (MRI) showed essentially normal findings. He was also com-

menced on physiotherapy. MCV, MCHC and MCH values were increased with presence of macrocytes in the peripheral blood film [MCH=35.4 pg (Ref range: 26.5-33.5pg); MCHC=39.8 g/dl. (Ref range:31.5-35.5g/dl); MCV= 98.7 fl (Ref range: 80-97fl)] Serum Vitamin B12 and Folic acid assays were requested but results were still pending as at the last clinic visit. After 2 weeks of his management, he regained both day and night continence and could walk unaided. He was discharged home after 3 weeks on admission and prior to discharge, the patient and his caregivers were counseled on the need to complete the subsequent doses of Vitamin B12 injection on outpatient basis and continue IM Vitamin B12 1mg at least 2 monthly indefinitely. The possibility of irreversible neurological damage which could result from non-compliance was also extensively discussed with them before discharge. Clinical improvement was sustained when he was last reviewed 12 days after discharge. He was subsequently scheduled for another follow-up visit in 4 weeks.

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## Discussion

This report illustrates a classical clinical presentation of SCDS secondary to Vitamin B12 deficiency. The history of difficulty with walking and the physical examination findings of ataxia, paraparesis, increased deep tendon reflexes and impairment of joint position and vibration sense together with the dramatic response to parenteral Vitamin B12 supplements all agree with this assertion as previously reported in the literatures<sup>2,3,8</sup>. The younger age and normal anatomical findings on spinal neuroimaging in this patient likely contributed to the favourable outcome of his management, more-so that previous reports have shown strong correlation between presence of anatomical lesions on spinal neuro imaging of patients with Vitamin B12 deficiency-related SCDS and permanent neurological damage<sup>4,9</sup>.

Although the exact aetiological agent responsible for

Vitamin B12 deficiency in this patient could not be ascertained due to paucity of facilities for diagnosis, a possible postulate is that this might have resulted from malabsorption probably secondary to lack of intrinsic factor as history did not suggest inadequate dietary intake, previous gastric surgery or inflammatory bowel disease. The absence of similar illness in the family also makes the possibility of hereditary transcobalamin II deficiency unlikely<sup>7</sup>. The skewing of haematological parameters (MCV, MCHC, MCH) beyond the upper limit of normal and the presence of macrocytes in the peripheral blood film during the second admission of this patient indicate an evolution of megaloblastic anaemia which is a characteristic haematological manifestation of vitamin B12 deficiency<sup>9</sup>.

It is pertinent to note that SCDS could persist despite Vitamin B12 administration in some patients with clinical and radiological features of SCDS similar to that secondary to Vitamin B12 deficiency<sup>(15)</sup> When this occurs, the possibility of other metabolic problems such as hypocupricemia (Copper deficiency) should be sought. Hypocupric (Copper deficiency) myelopathy is a myelopathy which is clinically and radiologically indistinguishable from SCDS due to Vitamin B12 deficiency<sup>15</sup>.

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## Conclusions

This patient presented with classical clinical picture in keeping with SCDS secondary to Vitamin B12 deficiency. There is need to keep a possibility of Vitamin B12 deficiency in view while evaluating and managing patients with paraparesis, especially when such patients fail to respond to conventional management of common aetiologies of paraparesis in paediatric age group. The recurrence of this condition in this patient further illustrates the consequence of neglecting a cheap and highly effective therapy and the need for an indefinite follow-up and treatment.

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