A 40-year-old woman 'off legs'

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SUMMARY

We present the case of a 40-year-old woman with progressive lower-limb weakness resulting in an inability to mobilise independently. This was associated with a degree of confusion and shortness of breath on exertion. This case illustrates rare and severe complications of vitamin B₁₂ deficiency, namely subacute combined degeneration of the spinal cord, megaloblastic anaemia and impaired cognitive function. The patient's condition improved considerably with adequate early resuscitation, followed by administration of synthetic vitamin B₁₂ analogues and neuro-rehabilitation.

BACKGROUND

Within the emergency department, this is an unusual presentation of severe vitamin B₁₂ deficiency in a young patient. Early recognition of clinical signs enables a prompt diagnosis and instigation of appropriate treatment. There are a number of factors to consider on initiation of treatment, which are outlined in the case.

CASE PRESENTATION

A 40-year-old woman attended our emergency department with an inability to walk independently. Over a 7-week period she had noted a steady deterioration in her ability to mobilise. Initially she noted some minor numbness and tingling of the feet, which progressed to significant weakness in both legs.

These symptoms were associated with lethargy, mild shortness of breath on exertion and some confusion. She had no medical history of note, took no regular medications and had no known allergies.

Routine observations were within normal limits. Examination of her cardiac, respiratory and gastrointestinal systems was unremarkable. Neurological examination of the lower limbs noted no obvious muscle atrophy, although there was increased tone, and power was markedly reduced bilaterally (2/5 Medical Research Council Scale). Further examination highlighted altered proprioception, a positive 'Babinski' sign (up-going plantar) and significant ankle clonus on the right side. Her upper limbs were unaffected and her abbreviated mental test score was 8 of 10.

INVESTIGATIONS

Routine blood results reported a haemoglobin level of 2.3 g/dl (11.5–16.5), mean cell volume of 122 fl (84–102), white cell count of $3.4 \times 10^9/l$ (4–11) and a platelet count of $98 \times 10^9/l$ (150–450).

The significant macrocytic anaemia with clear neurological symptoms and signs led our team to suspect severe vitamin B₁₂ deficiency, causing subacute combined degeneration (SCD) of the spinal

cord. An urgent serum sample was sent for vitamin B₁₂ levels, which confirmed the diagnosis.

MRI spine demonstrated patchy areas of hyper-intensity on diffusion-weighted imaging within the cervical and mid-thoracic spinal cord (figure 1).

TREATMENT

The patient was admitted to a medical ward under the care of our specialist haematology team. First-line treatment included adequate resuscitation involving administration of oxygen and transfusion of packed red cells (2 units). Thereafter, the patient received daily intramuscular hydroxycobalamin injections (1 mg) and oral folic acid (5 mg). As her haemoglobin levels climbed her confusion subsided, and an aggressive neuro-rehabilitation regime was started.

OUTCOME AND FOLLOW-UP

Our patient is undertaking continued rehabilitation and making steady progress. Her shortness of breath and confusion improved after a few hours of resuscitation. As her haemoglobin levels steadily increased, her condition continued to improve. After 4 weeks of therapy in a recognised neuro-rehabilitation unit, the patient can now mobilise with a frame. She attends community rehabilitation although she still suffers from reduced power and altered sensation in the lateral aspects of the lower limbs.

DISCUSSION

Vitamin B₁₂ is an essential factor required in cell division, maturation and myelin synthesis. It cannot be synthesised by the body and thus needs to be ingested. Certain foods are particularly rich in vitamin B₁₂ including seafood, meat, cheese and eggs. Once ingested, gastric acid aids breakdown of food in order to liberate vitamin B₁₂. Vitamin B₁₂ then combines with intrinsic factor, a compound released by parietal cells within the gastric mucosa allowing absorption within the terminal ileum.

Deficiency of vitamin B₁₂ is defined as a serum level <148 pmol/l. The prevalence of vitamin B₁₂ deficiency increases with age. The elderly are less able to absorb vitamin B₁₂ due to gastric atrophy and a subsequent reduction in gastric acid production.

Common causes of vitamin B₁₂ deficiency include dietary insufficiency, intrinsic factor deficiency (pernicious anaemia) and malabsorption.

Vitamin B₁₂ deficiency affects cell division and maturity within the body, in particular affecting normal erythropoiesis. This results in reduced red cell turnover causing anaemia. When in combination with folate deficiency (required for nucleic acid synthesis), large immature and dysfunctional cells are formed (megaloblasts).

Severe deficiency also alters myelin synthesis which may lead to degeneration of the spinal cord. Patches of demyelination along dorsal and lateral

To cite: Mehrotra P, Bhalla A. *BMJ Case Reports* Published online: [please include Day Month Year] doi:10.1136/bcr-2012-007791

Figure 1 Sagittal diffusion-weighted image demonstrating patchy hyperintensity in the cervical and thoracic spinal cord.

columns causes paraesthesia, spastic paresis, loss of deep tendon reflexes and positive pathological reflexes (manifesting as a positive Babinski test).

The mainstay of treatment for vitamin B₁₂ deficiency is with cyanocobalamin (synthetic form of vitamin B₁₂) which can be delivered via intramuscular, sublingual, subcutaneous, oral and intranasal routes with similar effectiveness.

Even patients who are asymptomatic are treated with maintenance cyanocobalamin to prevent the potentially irreversible neurological complications. Symptomatic patients with severe haematological and/or neurological symptoms should be treated urgently.¹ When treatment is urgently administered there is a risk of hypokalaemia as the rapidly dividing cells utilise potassium, depleting circulating stores.² These patients also require folic acid supplements, which are administered after synthetic B₁₂ analogues as the folic acid can drive nucleic acid synthesis, further depleting vitamin B₁₂ stores.

In cases where severe anaemia is present, additional blood transfusions should be used with caution due to risk of fluid overload due to compensatory physiological changes that occur in chronic anaemia.³ A review of 153 patients with neuropathy in vitamin B₁₂ deficiency found that all patients responded to treatment, and in 40% there was complete neurological recovery.⁴ This review also found that the percentage improvement over baseline neurological status after treatment was inversely related to duration of symptoms and serum haematocrit levels.

There are a number of cases reporting SCD of the spinal cord due to vitamin B₁₂ deficiency, as well as a few cases commenting on the cardiovascular effects of B₁₂ deficiency; however, the majority of these cases were in elderly patients. Our literature review was unable to find any such case describing such severe anaemia in conjunction with severe neurological findings in a young adult.

Learning points

- ▶ If anaemia is severe with a high mean cell volume, suspect a chronic, haematological cause rather than an acute cause (such as haemorrhage).
- ▶ When severe chronic anaemia is present, haematology specialists should be consulted early and transfusion of blood products should be administered slowly due to the risk of cardiac failure.
- ▶ Treatment of vitamin B₁₂ deficiency requires the administration of folic acid in conjunction with synthetic B₁₂, although the patient must receive the synthetic B₁₂ first. If folic acid is given first, it may worsen neurology.
- ▶ In treatment of vitamin B₁₂ deficiency the patient must be observed for hypokalaemia, which can cause fatal cardiac arrhythmias.
- ▶ For vitamin B₁₂ deficiency the importance of continuing maintenance treatment in the community and during hospital admissions is imperative.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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