Clinical Reports

Immunoglobulin deficiency responding to vitamin B₁₂ in two elderly patients with megaloblastic anaemia

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Summary: Two elderly patients with vitamin B₁₂ deficiency were found to have low immunoglobulin levels. These returned to normal on treatment with vitamin B₁₂.

Introduction

In younger patients vitamin B₁₂ deficiency may be associated with immunoglobulin deficiency, but the immunoglobulins do not rise when vitamin B₁₂ is given (Conn *et al.*, 1968). In older patients with vitamin B₁₂ deficiency serum immunoglobulins are usually within the normal range (Odgers & Wangel, 1968) and do not change with treatment (Hippe & Jensen, 1969; Selroos & von Knorring, 1973). This report describes two elderly patients with immunoglobulin deficiency associated with megaloblastic anaemia due to vitamin B₁₂ deficiency, whose immunoglobulins rose to normal when vitamin B₁₂ was administered.

Case reports

Case 1

A 79 year old man presented with a 4 year history of weight loss (17 kg) and increasing oedema and lethargy. Investigations showed a macrocytic and megaloblastic anaemia due to vitamin B₁₂ deficiency. Haemoglobin was 7.2 g/dl, mean corpuscular volume (MCV) was 128 fl, serum vitamin B₁₂ was 20 ng/l (normal range 160–975 ng/l) and bone marrow examination showed megaloblastic changes. This was caused by malabsorption due to bacterial contamination of jejunal diverticula, as shown on barium studies, a raised serum folate (36.0 µg/l, normal range 6–21) and no absorption of radio-labelled vitamin B₁₂ without and with intrinsic factor (Chanarin, 1979). A ¹⁴C glycocholate breath test was grossly abnormal. Both the vitamin B₁₂ absorption and the glycocholate

breath test improved towards normal after treatment with erythromycin for 2 months.

Before B₁₂ was given, serum protein levels were low. Total protein was 39 g/l, albumin was 23 g/l; IgG was 5.8 g/l (normal range 5–16 g/l), IgA was 0.75 g/l (1.25–4.25) and IgM was 0.30 g/l (0.5–1.8). Chromium 51 studies showed no evidence of protein-losing enteropathy. After vitamin B₁₂ therapy, and before erythromycin, IgG had risen to 7.2 g/l, IgA to 4.25 g/l and IgM to 0.95 g/l. Concurrently, haemoglobin rose to 11.4 g/dl with an MCV of 92 fl. Albumin was unchanged and only rose after antibiotic therapy. Therefore the rise in immunoglobulins was related to the vitamin B₁₂ therapy, and not to alteration of the bowel flora by antibiotics.

Case 2

An 81 year old woman presented with a 6 week history of vomiting and diarrhoea. Investigations showed a macrocytic and megaloblastic anaemia due to vitamin B₁₂ deficiency. Haemoglobin was 6.0 g/dl, MCV was 108 fl, serum vitamin B₁₂ was 60 ng/l, serum folate was 19.0 µg/l. Examination of the bone marrow showed megaloblastic changes. This was caused by intrinsic factor deficiency shown by very little absorption of radio-labelled B₁₂ alone, but normal absorption of vitamin B₁₂ when given with intrinsic factor (Chanarin, 1979). There was no clinical or biochemical evidence of any other form of malabsorption. Before vitamin B₁₂ administration, total protein was 47 g/l, albumin was 34 g/l, IgG was 4.0 g/l, IgA was 0.6 g/l and IgM was less than 0.25 g/l. Serum transferrin was within the normal range. After vitamin B₁₂, albumin was unchanged, IgG rose to 7.7 g/l, IgA to 1.0 g/l and IgM to 0.65 g/l. Concurrently, haemoglobin rose to 11.4 g/dl with an MCV of 69 fl.

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Discussion

The hypogammaglobulinaemia in these patients was mild and was of no obvious clinical significance. Low immunoglobulins in a patient with vitamin B₁₂ deficiency, rising after vitamin B₁₂ therapy, have only been described once before in an infant with congenital transcobalamin II deficiency (Hitzig & Kenny, 1975). The first patient may have had such a deficiency in view of the abnormality of liver synthesized proteins suggested by the low serum albumin. However, the second patient had a relatively normal serum albumin and also a normal transferrin level suggesting no disturbance in liver protein synthesis. Furthermore, an adult case of transcobalamin II deficiency had normal gammaglobulins (Lawrence, 1966).

References

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Vitamin B₁₂ does seem to be necessary for immunoglobulin synthesis by lymphocytes (Hitzig & Kenny, 1975). This is not surprising in view of the importance of vitamin B₁₂ to metabolic events within the cell. However, low immunoglobulin levels are rare in such patients, so in these patients the lymphocytes may have been unusually sensitive to vitamin B₁₂ deficiency.

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