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Granulomatous gastritis, iron deficiency, vitamin B₁₂ malabsorption and immunoglobulin deficiency

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Summary

A 24-year-old male with recurrent iron deficiency anaemia was found to have a generalized reduction in his immunoglobulin levels, granulomatous gastritis and impaired vitamin B₁₂ absorption corrected by Intrinsic Factor.

There is discussion of the possibility that cell mediated mechanisms may have been involved in the cause of the vitamin B₁₂ malabsorption.

Introduction

Granulomatous gastritis is generally considered to be a rare condition and the usual clinical presentation is with signs of pyloric obstruction (Fahimi *et al.*, 1963). With the advent of fibre-optic endoscopy and associated biopsy techniques it is possible that in the future it may be recognized with greater frequency. A patient is described who presented initially with evidence of iron deficiency, who was found to have achlorhydria and vitamin B₁₂ malabsorption and in whom the histological appearances were highly unusual, showing atrophic gastritis and accompanying granulomata in all areas of the stomach. Further

investigations revealed the additional feature of an immunoglobulin deficiency involving all immunoglobulin classes.

Case report

The patient, a 24-year-old male, presented initially with a complaint of lethargy. Although routine physical examination revealed no abnormality, he was found to be mildly anaemic with a blood film suggesting iron deficiency. Eleven years previously he had been investigated for a similar hypochromic anaemia associated with diarrhoea, but the investigations had been inconclusive and the symptoms had remitted spontaneously. Shortly after being seen he developed upper abdominal pain and vomiting and was admitted for investigation. The haemoglobin was 12.6 g% with hypochromia and microcytosis on the film. The white cell count and platelet count were normal. The bone marrow aspirate showed normoblasts and micronormoblasts with no stainable iron. The serum iron was 35 and TIBC 444 µg%. The serum B₁₂ was 285 pg/ml and serum folate 4.7 ng/ml. Two of six stool samples were positive for occult blood and the faecal fat excretion was 2.7 g/day. The serum globulin was low at 1.8 g% with an IgG of 355 mg% (normal 800–1600 mg%),

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FIG. 1. Gastric mucosal biopsy showing granulomata; (a) H and E $\times 40$; (b) H and E $\times 250$.

IgA of 75 mg% (normal 120–400 mg%) and an IgM of 29 mg% (normal 50–160 mg%). Other biochemical tests were normal. A barium meal and follow-through was normal apart from a reduction of gastric mucosal folds and at gastroscopy a mild gastritis involving the entire stomach was detected. This was confirmed by multiple mucosal biopsies taken from both the body and the antrum. In both areas there was a diffuse cellular infiltration with lymphocytes, histiocytes, polymorphonuclear cells and some plasma cells. In addition non-caseating granulomata were present in all the biopsy specimens (Fig. 1).

Evidence of a generalized granulomatous process was sought but not found. A Mantoux test was positive at 1/10,000 which made a diagnosis of sarcoidosis unlikely. The chest X-ray was normal and examination of sputum, gastric aspirates, urine and bone marrow revealed no evidence of tuberculosis. A barium enema showed no signs of Crohn's disease.

A Schilling test revealed malabsorption of vitamin B₁₂ correctable by intrinsic factor. A pentagastrin-fast achlorhydria was present and no intrinsic factor was detectable in the gastric juice. Intrinsic factor antibodies were found in the serum in low titre (1/16) but no parietal cell antibodies were demonstrable. The fasting plasma gastrin was 181 pg/ml which is in the normal range.

During his period of investigation, the patient's abdominal symptoms remitted spontaneously. He was treated with a total dose infusion of iron and has subsequently maintained a normal haemoglobin, serum iron and TIBC. He has remained well for the past 2 years.

Comment

The association of granulomatous gastritis with achlorhydria and malabsorption of vitamin B₁₂ is one that has not been previously described and this is only one of several interesting features in this case.

In classical pernicious anaemia the histological appearances are characteristic and the gastric antrum is not involved (Magnus and Ungley, 1938). The fasting plasma gastrin is invariably elevated (Ganguli, Cullen and Irvine, 1971). Antral gastritis, however, may lead to impaired gastrin release (Strickland *et al.*, 1971) and involvement of the gastric antrum in our patient presumably accounts for the absence of an increased plasma gastrin level. Another unusual feature was the association of iron deficiency with achlorhydria and vitamin B₁₂ malabsorption in the absence of detectable parietal cell antibodies (Dagg *et al.*, 1966).

Patients with primary acquired immunoglobulin deficiency may exhibit achlorhydria and malabsorption of vitamin B₁₂ (Twomey *et al.*, 1970). These patients, too, differ from those with classical pernicious anaemia, presenting at an earlier age and without detectable humoral antibodies against gastric parietal cells. They do not, however, display granulomata on gastric biopsy.

It is widely accepted that parietal cell antibodies may be involved in the initiation of the process of gastric atrophy in pernicious anaemia (Taylor *et al.*, 1962; Tanaka and Glass, 1970). However, the importance of cell mediated immunity to intrinsic factor is now becoming recognized (Chanarin and James, 1974). The immunoglobulin deficiency, the lack of parietal cell antibodies and the presence of gastric granulomata in our patient, all suggest that cell mediated mechanisms might have been playing a major role in the pathogenesis of the vitamin B₁₂ malabsorption.

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Combination antifungal therapy for cryptococcal meningitis

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Summary

Two patients with Hodgkin's disease and cryptococcal meningitis are described. Both patients were treated with a combination of the two antifungal agents, amphotericin B and flucytosine. Nephrotoxicity was

easily reversible in both patients and clinical improvement was seen with this combination therapy. Intrathecal therapy with amphotericin B was used in both patients. The optimal treatment of this disease may prove to be a combination of oral flucytosine, with amphotericin B given by intrathecal injection as well as rapid low dose intravenous injection.

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