Autoimmune haemolytic anaemia in ulcerative colitis

Introduction

This article presents a case of a patient with undiagnosed ulcerative colitis who presented with autoimmune haemolytic anaemia. An admission blood film to investigate a haemoglobin level of 3.6 g/dl was consistent with haemolytic anaemia and crossmatch analysis confirmed autoantibodies. Ulcerative colitis was diagnosed endoscopically following radiological evidence on computed tomography. Treatment with high-dose prednisolone 60 mg and oral mesalazine, in addition to the transfusion of packed red cells, resulted in symptomatic improvement. This is an unusual initial presentation of ulcerative colitis whereby the diagnosis of autoimmune haemolytic anaemia preceded the diagnosis of colitis.

Discussion

This patient presented with a clinical picture more typical of occult malignancy or small bowel pathology and had a diagnosis of ulcerative colitis secondary to that of his autoimmune haemolytic anaemia. This article highlights the varying presentations and clarifies any consensus on long-term management.

Autoimmune haemolytic anaemia is an uncommon but recognized complication of ulcerative colitis. Whereas anaemia arising from haemorrhage or impaired haemopoiesis is relatively anticipated in ulcerative colitis, there have only been approximately 55 case reports of secondary autoimmune haemolytic anaemia to date following the original report by Lorber et al in 1955 (Valderrama Rojas et al, 2003; Yu et al, 2010). These have typically coincided with a flare of existing colitis.

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The prevalence of autoimmune haemolytic anaemia in ulcerative colitis varies between 1.7%, in a study on 302 patients (Giannadakis et al, 1997), and 0.7% in the largest series on 1150 patients (Gumaste et al, 1989). In these case series, the onset of identifiable autoimmune haemolytic anaemia occurred some years after any diagnosis of ulcerative colitis. In Giannadakis et al's (1997) series, the mean interval was 17 months, and later case reports have cited this interval as between 2 and 8 years.

An explanation for the pathogenesis of autoimmune haemolytic anaemia in ulcerative colitis has been inconclusive to date. Abnormal red cell autoantibody production from colonic mononuclear cells has been postulated from a study on mice models (Yates et al, 1992). There is suggested temporal association of autoimmune haemolytic anaemia deterioration with concurrent colonic inflammation (Giannadakis et al, 1997) and this may link to theories of cross-reactivity of non-self red cell antigens with self red cell antigens through the diseased colon.

Management has centred on corticosteroid therapy, followed by immunomodulators as steroid-sparing agents or newer monoclonal antibody therapies. Surgery is generally considered when these medical approaches fail. Of the surgical options, there is no clear evidence for the efficacy of splenectomy *vs* bowel resection. In a number of cases colectomy without splenectomy has led to control of autoimmune haemolytic anaemia (Gumaste et al, 1989). Two cases describe a lack of success with splenectomy and advise against it (Basista and Roe, 1986; Martinez et al, 1991). In contrast, two of the eight cases also in Gumaste et al's (1989) series describe successful remission and use of splenectomy in the event of failed steroid therapy. For bowel resections, the need for panproctocolectomy over limited colectomy is proposed to ensure effective autoimmune haemolytic anaemia remission (Murphy et al, 1996) which adds some weight to the suggestion that inflamed colonic tissue is the source of autoantibodies. BJHM

Case Report

A 49-year-old man presented with a 3-day history of increased lethargy, jaundice and oedema. This had been preceded by a 2-month history of intermittent increases in bowel frequency to three or four non-bloody motions/day, anorexia and marked weight loss of 13 kg, with patient-initiated dietary exclusion of gluten not improving symptoms. He had been otherwise well with no systemic symptoms of infection.

Haemoglobin on admission was 3.6 g/dl and C-reactive protein was 76 mg/litre, with a normal biochemical profile except for an albumin level of 24 g/litre. Blood film revealed spherocytes, macrocytes, polychromasia and nucleated red blood cells consistent with autoimmune haemolytic anaemia. The patient required five units of blood transfusing with a crossmatch Coombs' analysis indicating positive markers for anti-IgG, IgA, IgM and C3d (*Table 1*). High-dose prednisolone (60 mg) was started following haematology review with infection the presumptive cause of his autoimmune haemolytic anaemia. The differential diagnoses of acquired autoimmune haemolytic anaemia are shown in *Table 2*.

In view of the marked weight loss a full body computed tomography scan was performed to exclude occult malignancy. This instead revealed colorectal mural thickening, consistent with proctocolitis, and incidental bilateral subsegmental pulmonary emboli. An upper gastrointestinal endoscopy and biopsies from the second part of the duodenum were normal. Subsequent colonoscopy to the terminal ileum revealed severe extensive pancolitis consistent with ulcerative colitis with a macroscopically normal terminal ileum. The colonic biopsies confirmed the diagnosis of ulcerative colitis.

The patient made a good recovery on a reducing course of prednisolone and maximal oral mesalazine, resulting in gradual improvement of the anaemia and normalization of bowel frequency. He did not require any other immediate immunosuppression or surgery but was anticoagulated in view of the pulmonary emboli, corroborated on computed tomography pulmonary angiography. Haematology and gastroenterology follow up have noted that both autoimmune haemolytic anaemia and ulcerative colitis are currently in remission, without the need for any further immunosuppression.

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Table 1. Admission laboratory findings

Blood findings	Haemoglobin	3.6 g/dl
	Platelets	512
	International normalized ratio	1.1
	Mean corpuscular volume	125.8 fl
	Reticulocytes	370.9x10^9/litre
	Lactate dehydrogenase	646 IU/litre
	Haptoglobin	<0.06 g/litre
	Iron	4.8 umol/litre
	Transferrin saturations	13.2%
	Folate	8.1 ug/litre
	Vitamin B_{12}	295 ng/litre
	Immunoglobulin A tissue transglutaminase antibody	1.0 U/ml
	25OH vitamin D	7 ug/litre
Crossmatch analysis	Anti-C3d	3+
	Anti-immunoglobulin G	5+
	Anti-immunoglobulin A	4+
	Anti-immunoglobulin M	2+
	No atypical alloantibodies	
Infective screen	Stool (Bristol stool type 5)	Negative culture
	Urine	Negative culture
	Hepatitis B and C	Negative
	Human immunodeficiency virus 1 and 2	Negative
	Syphilis	Negative

Table 2. Causes of acquired autoimmune haemolytic anaemia

Autoimmune disease	Rheumatoid arthritis
	Systemic lupus erythematosus
	Scleroderma
	Chronic active hepatitis
Immune deficiency	Hypogammaglobulinaemia
	AIDS (acquired immunodeficiency syndrome)
Malignancy	Multiple myeloma
	Chronic lymphocytic leukaemia
	Lymphoma
	Thymoma
Infection	Epstein–Barr virus and cytomegalovirus infections
	Mycoplasma pneumoniae

LEARNING POINTS

- This case report highlights the presentation of ulcerative colitis as symptomatic autoimmune haemolytic anaemia.
- Initial treatment with transfusion and high-dose corticosteroids is guided by experience of management of idiopathic autoimmune haemolytic anaemia.
- There is evidence for the efficacy of splenectomy in idiopathic autoimmune haemolytic anaemia but conflicting evidence of its role in ulcerative colitis-mediated autoimmune haemolytic anaemia, and of the extent of colonic resection necessary for total remission.

Forthcoming case reports

An 85-year-old woman with acute back pain
Biliary cystadenocarcinoma complicated by intralesional haemorrhage
Pulmonary embolism and patent foramen ovale causing an ischaemic stroke
Accidental overdose of proprietary branded, combination analgesics available over the counter
Lemierre's syndrome masquerading as necrotizing fasciitis