CASE REPORTS

Crohn's colitis and idiopathic thrombocytopenic purpura

Michael S Boyne, Kevin R Dye

Abstract

A 17 year old girl with active Crohn's colitis developed idiopathic thrombocytopenic purpura that was managed with intravenous immune globulins and cyclosporin A. The possible association between Crohn's disease and immune thrombocytopenia is explored.

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Keywords: Crohn's disease; colitis; thrombocytopenia

Various autoimmune diseases have been associated with inflammatory bowel disease, with the majority of reports describing clustering of autoimmune haemolytic anaemia[1] with ulcerative colitis. An unusual case of Crohn's colitis with the subsequent development of idiopathic thrombocytopenic purpura (ITP) is described.

Case report

A 17 year old girl with a history of Crohn's pancolitis without ileal involvement since age 8, was relatively well until the age of 16, when she had several hospitalisations for exacerbations of her Crohn's disease. This necessitated a medical regimen of prednisone (30 mg/day), azathioprine (100 mg/day), metronidazole, and mesalamine but the symptoms of colitis persisted.

Apart from an anaemia of chronic disease (packed cell volume 0.247), her blood counts were normal until May 1996 when her platelet count was 3×10^9/l, haemoglobin 85 g/l, packed cell volume 0.258, and leucocyte count 9.2×10^9/l. She was also experiencing epistaxis and bloody diarrhoea. She had no history of recent viral infections, immunisations, recent blood transfusions, or use of recreational drugs. Physical examination revealed only mild cushingoid facies and there was no hepatosplenomegaly. Erythrocyte sedimentation rate was 60 mm/hour. Antinuclear antibodies, anti-HIV, Coombs' tests, platelet associated IgG, white cell differential, partial thromboplastin time, and prothrombin time were unremarkable. A peripheral blood smear showed marked thrombocytopenia with occasional giant platelets and no evidence of microangiopathic haemolytic anaemia. A bone marrow biopsy specimen revealed normocellularity with megakaryocytic hyperplasia compatible with peripheral platelet destruction.

The patient's medications were discontinued and she was managed initially with methylprednisone (2 mg/kg/day) and platelet transfusions but without effect. She was then treated with intravenous gammaglobulin (1 g/kg/day) which raised her platelet count to 45 $\times 10^9$/l and maintained on cyclosporin A (5 mg/kg/day) and prednisone (60 mg/day) as an outpatient. Her platelet counts remained between 400 and 680 $\times 10^9$/l. A colonoscopy, one month after discharge, revealed no active Crohn's disease. However, two months later, the return of active colitis prompted the addition of mesalamine to her regimen. One month later, she developed an inflammatory colonic mass necessitating left hemicolectomy. Histology of the mass was consistent with severely active Crohn's colitis. She remained asymptomatic, with normal platelet counts and did not require immunosuppressive medication.

Discussion

There are multiple case reports in the literature describing the association of inflammatory bowel disease with extraintestinal autoimmune disorders. The actual prevalence of these associations is not known, as no controlled population studies, to date, have been performed. However, in the case-control study by Snook *et al*, there was a clustering of autoimmune disorders (including primary sclerosing cholangitis) with ulcerative colitis, with a prevalence of 8.2%–10.5%.[1] The study showed little evidence of an association with

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Table 1 Reported cases of Crohn's disease and idiopathic thrombocytopenic purpura (ITP)

Reference	*Age*	*Sex*	*Duration between Crohn's disease and ITP*	*Location of Crohn's disease*	*Response to glucocorticoids*	*Platelet antibodies*	*Treatment of ITP*
4	65	F	(+) 28 years	Colon	Transient	Yes	Splenectomy, colectomy
5	19	F	On presentation	Colon, distal ileum	Transient	No	Splenectomy, LTF
6	43	M	(−) 2 months	Colon	Yes	?	Glucocorticoids
7	54	M	(−) 7 months	Colon, distal ileum	Yes	Yes	Glucocorticoids
8	22	F	(+) 6 weeks	Colon	Yes	?	Glucocorticoids, 6MP
Present case	17	F	(+) 9 years	Colon	No	No	IV IgG

Key: 6MP = 6-mercaptopurine; LTF = lost to follow-up; (+) = Crohn's disease occurred before ITP; (−) = ITP occurred before Crohn's disease; IV IgG = intravenous gammaglobulins.

Crohn's disease, irrespective of the extent of colonic involvement.

The association between ITP and ulcerative colitis has been well described,[2] with an estimated prevalence of 0.1%–0.48%.[1 3] However, there are only five other reported cases involving ITP and Crohn's disease as summarised in table 1.[4–8] The most notable common factor is the extensive colonic involvement in all the cases with active colitis being present during the development of the thrombocytopenia. The resolution of ITP, only after colectomy in the case by Kosmo *et al*,[4] also lends some credence to the idea of the colon being involved in the pathogenesis. Hypothetically, during severe colitis, antigens of the colonic lumen (such as bacterial antigens) could generate a humoral response, leading to antibodies that cross react with platelet surface antigens, thus resulting in ITP. An alternative mechanism could be that severe colonic inflammation leads to local destruction and/or sequestration of platelets in the colonic vasculature, which could result in the absence of circulating platelet antibodies and resistance to glucocorticoids. Of course, one cannot totally dismiss a fortuitous association between Crohn's colitis and a self limiting ITP in these cases.

This patient, notably, despite having Crohn's colitis for nine years, did not develop ITP until she had severe flaring of her colitis, raising the possibility of a temporal association. Also, her ITP developed while on glucocorticoids, and once established, the ITP remained steroid resistant. This steroid resistance was also noted in two of the other cases[4 5] and has occurred in some cases of ITP associated with ulcerative colitis.[2 8] The possibility of a drug induced mechanism seems unlikely. Azathioprine, in one series, caused the sudden onset of isolated thrombocytopenia in 1.4% of treated patients with Crohn's disease, but the mechanism is related to bone marrow suppression and there are no reported cases of an immunological mechanism.[9] Unlike sulfasalazine, which can cause immunological destruction of platelets, mesalamine causes thrombocytopenia through non-immunological mechanisms, that is, bone marrow suppression with hypocellularity.[10] Also, this patient was rechallenged with mesalamine without recurrence of thrombocytopenia. There are no reported cases of ITP associated with metronidazole.

The patient was treated with immune globulins, which stimulated partial recovery of her platelet counts, and then continued on maintenance therapy with cyclosporin A in an attempt to maintain her platelet counts[11] and induce remission of the Crohn's colitis. The cyclosporin did induce remission of her colitis as shown by colonoscopy, but this effect was not sustainable, which is consistent with previous observations of similar low dose regimens.[12] Partial colectomy ultimately enabled treatment of the underlying Crohn's colitis, discontinuation of the cyclosporin and there was no recurrence of thrombocytopenia. In the cases of ulcerative colitis and ITP, the thrombocytopenia resolved with glucocorticoids or immune globulins, although it was necessary to perform splenectomies in the steroid resistant patients.[2 8] In three cases of Crohn's colitis, glucocorticoids were therapeutic,[6–8] but the other cases had only transient responses.[4 5] These cases did not respond to splenectomy but one eventually responded to colectomy.[4] Consequently, it would seem reasonable that Crohn's associated ITP should be treated first with glucocorticoids and in resistant or severe cases immune globulins may be tried, which is similar to recognised consensus guidelines on the management of ITP.[13] The efficacy of cyclosporin is questionable in this case and cannot be recommended at present. The present data in refractory cases seem to indicate that splenectomy may not be a successful therapeutic modality, but it is too early to routinely recommend colectomy as an alternative.

Learning points

- Idiopathic thrombocytopenic purpura can be an extraintestinal autoimmune manifestation of ulcerative colitis and less commonly, Crohn's colitis.
- Medications used to control Crohn's disease may cause drug induced thrombocytopenia and should be excluded as a potential aetiology of the thrombocytopenia.
- Crohn's associated thrombocytopenia should be managed like other cases of ITP, but high dose glucocorticoids may not be effective.

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Osteomyelitis and possible endocarditis secondary to *Lactococcus garvieae*: a first case report

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Abstract

Although osteomyelitis is commonly caused by staphylococcal infection, the first case of a lumbar osteomyelitis secondary to *Lactococcus garvieae* is reported. The case was complicated by possible endocarditis of an aortic valve prosthesis.

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Keywords: *Lactococcus garvieae*; osteomyelitis

Lactococci are often believed to be of low virulence. We report a first case of osteomyelitis secondary to *Lactococcus garvieae* in a previously well, middle aged woman.

Case report

A 56 year old woman was referred to a rheumatology clinic with a nine week history of lower back pain and a five week history of rigors and night sweats. She was anorexic and had lost approximately 3.5 kg in weight in six weeks. Systems review was unremarkable. Her past medical history included a xenograph aortic valve replacement for aortic stenosis 12 years earlier (Ionesu-Shiley valve) and she was known subsequently to have mild aortic regurgitation. She took no prescribed medication and until this illness had been fit and well. Examination was unremarkable other than tenderness over L5/S1 and a soft early diastolic murmur at the left sternal edge in keeping with the aortic regurgitation. Results of routine tests were as follows: haemoglobin 99 g/l (mean corpuscular volume 92 fl), white cell count 6.1×10^9/l, erythrocyte sedimentation rate 74 mm/hour, and C reactive protein 12.6 mg/l; urea, electrolytes, creatinine, liver function tests, and a bone profile were all normal. The urine culture was negative, the chest radiography was normal, an electrocardiogram showed sinus rhythm with a normal axis and deep T wave inversion in the inferolateral territory. This was unchanged from earlier electrocardiograms (previous history of aortic stenosis). Thoracic and lumbar spine radiographs showed a thoracolumbar scoliosis with loss of disc height at L2/L3 and subchondral bone loss. A bone scan revealed increased tracer activity in the mid-lumbar region (fig 1).

Three days later she was admitted with increasing back pain and spiking temperatures. A diagnosis of presumed osteomyelitis was made and she was treated with analgesics and bed rest, while blood cultures were repeatedly taken during temperature spikes. A computed tomographic guided vertebral biopsy was arranged.

On day 6 after admission, pale splinter haemorrhages were noted in several nails of her hands and toes, not previously documented. There was no splenomegaly or microscopic haematuria and there was no other evidence of embolic phenomena. The murmur of aortic regurgitation was unchanged. A transthoracic echocardiogram revealed a well seated valve replacement in the aortic position, with thin mobile leaflets and mild to moderate transvalvular aortic regurgitation. Other valves appeared normal and no vegetations were identified. In view of the high suspicion of infective endocarditis, a transoesophageal echocardiogram was undertaken. No vegetations or changes consistent with an aortic root abscess were identified. The aortic regurgitation remained unchanged in severity and no further splinter haemorrhages subsequently developed.

All blood cultures, in addition to the biopsied bone, grew Gram positive cocci growing in chains on blood agar. They were identified as *Lactococcus garvieae* and were found to be indistinguishable from one another by API Strep (bioMerieux, Basingstoke, Hants, UK), sensitivity testing and their identity was confirmed by the Streptococcal Reference Laboratory (Respiratory and Systemic Infection Laboratory, London, UK). Vancomycin had been started after the bone biopsy, which was subsequently replaced by teicoplanin to which the organism was sensitive. With antibiotic treatment her clinical course improved and her remaining admission was uneventful. She was discharged after one month of intravenous treatment, with a temperature chart, to complete a further two months of teicoplanin at home via a Hickman line. She has remained well and continues under active follow up.

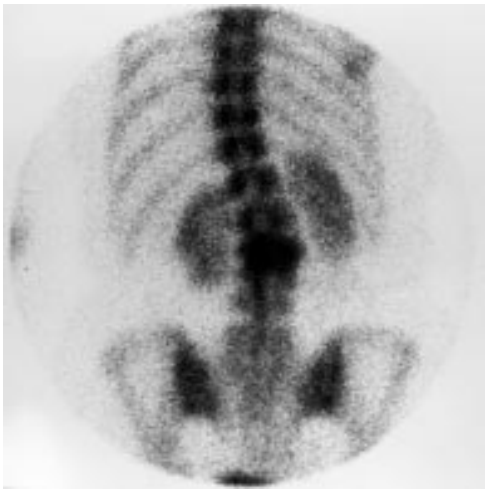

Figure 1 Bone scan showing increased tracer uptake in mid-lumbar region.

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