Case report

Polymyalgia rheumatica as presenting manifestation of vasculitis involving the lower extremities in a patient with ulcerative colitis

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ABSTRACT

Extraintestinal features may be observed in patients with ulcerative colitis (UC). We describe a 69-year-old woman who was initially diagnosed as having polymyalgia rheumatica (PMR). Prednisone was progressively tapered to complete discontinuation a year and a half after PMR diagnosis. However, at that time, she started to complain of asthenia, abdominal cramping and pain on the left side, weight loss and bloody diarrhoea. A colonoscopy confirmed a diagnosis of left-sided UC. She experienced several flares of the disease that required admission and treatment with high-dose corticosteroids and azathioprine. Colectomy was performed as the disease became refractory to these therapies. Four months after surgery, when the patient was not receiving any corticosteroid therapy, she started to feel dull and achy pain in the thighs along with claudication of the lower limbs. An 18F-fluorodeoxyglucosepositron emission tomography with CT (FDG PET/CT) disclosed an inflammatory process with mild-moderate diffuse increased metabolism in the thoracic aorta and markedly increased FDG uptake in the in the femoral and posterior tibial arteries on both sides. Treatment with the anti-TNF-alpha monoclonal antibody-adalimumab (40 mg every 2 weeks subcutaneously) along with prednisone (initial dose 15 mg/day) yielded rapid improvement of symptoms. Also, a new FDG PET/CT performed 4 months later disclosed marked decrease of FDG uptake in the involved arteries. This report emphasises the importance of suspecting the presence of large-and medium-vessel vasculitis in a patient with UC presenting with musculoskeletal features. It also highlights the beneficial effect of TNF-antagonists in vasculitis associated to UC.

Introduction

The most characteristic features of ulcerative colitis (UC), a form of inflammatory bowel disease (IBD), are the result of gastrointestinal manifestations, mainly diarrhoea with blood and mucus.

Extraintestinal features may be observed in patients with UC. However, polymyalgia rheumatica (PMR) has not been described to precede a diagnosis of this condition. Also, although aortitis in patients with Crohn's disease has been reported (1-3), to the best of our knowledge, large- and medium-vessel involvement in the setting of UC is exceptional. In this regard, there are only a few cases of large-vessel vasculitis in patients with UC (4-6). Moreover, these cases involved young individuals that fulfilled definitions for Takayasu's disease (4-6).

In the present report we describe a patient initially diagnosed with PMR in her late sixties. Afterwards, she was also diagnosed with UC. Large- and medium-vessel involvement was suspected because of the development of an atypical flare of PMR consisting of severe inflammatory pain and claudication of the lower limbs without elevation of erythrocyte sedimentation rate (ESR). An 18F-fluorodeoxyglucose-positron emission tomography with CT (FDG PET/CT) disclosed the presence of vasculitis involving the aorta and the arteries of the lower extremities.

Case report

We report the case of a 69-year-old woman who had been initially diag-

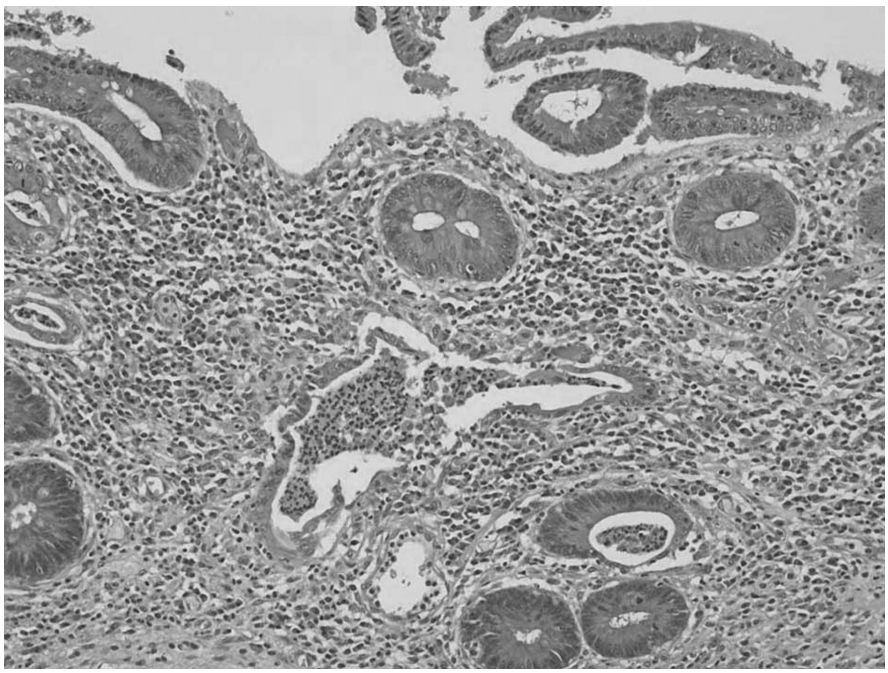


Fig. 1. Diffuse inflammatory infiltrate of the mucosa with crypt abscess and irregular surface.

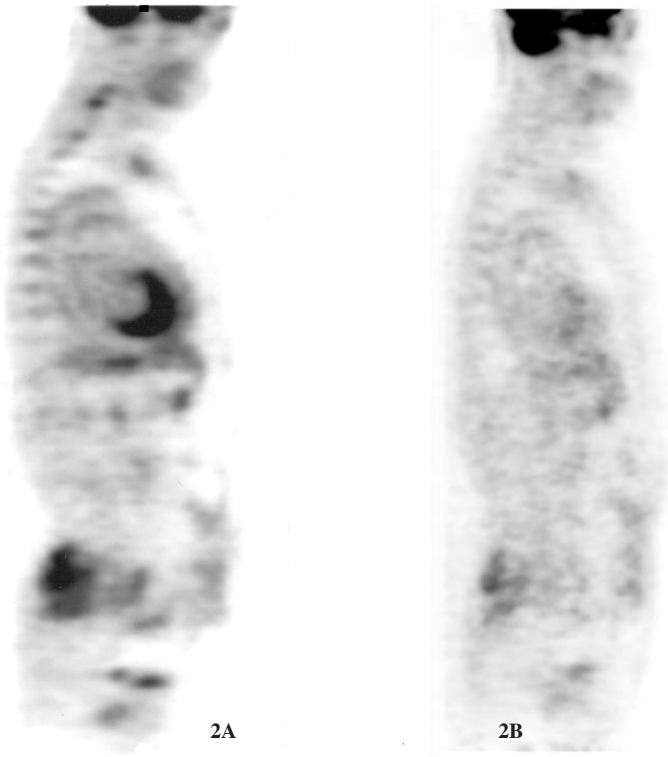


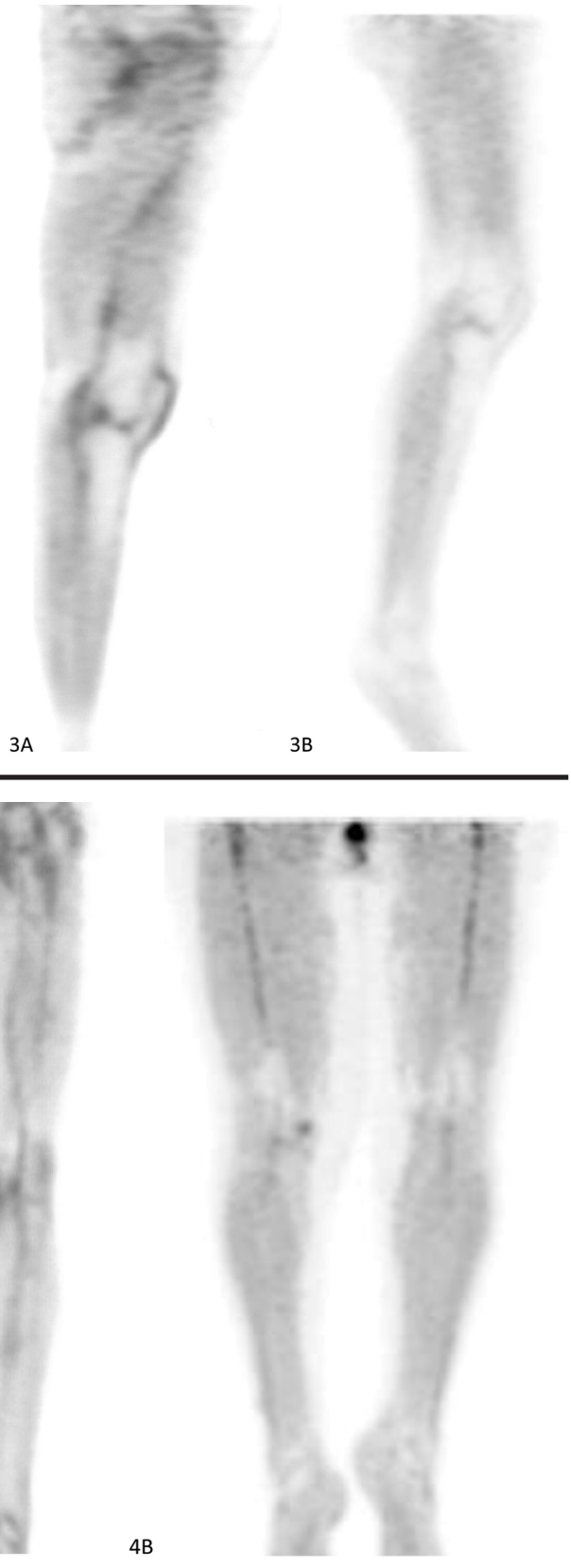
Fig. 2A. Moderate diffuse FDG uptake in the thoracic aorta.
Fig. 2B. Mild vascular FDG uptake in the thoracic aorta following anti-TNF-alpha therapy

nosed as having PMR because of pain and aching involving mainly the neck, the shoulder girdle and proximal aspects of the arms and in a less severe way the pelvic girdle and proximal aspects of the thighs associated to morning stiffness of more than 1 hour duration and an ESR greater than 50 mm/1st hour. At that time her past medical history was unremarkable. Treatment with prednisone 10 mg/day was started with rapid improvement of symptoms and normalisation of acute phase reactants. Prednisone dose was progressively tapered to complete discontinuation a year and a half later. However, at that time, she started to complain of asthenia, abdominal cramping and pain on the left side, weight loss and bloody diarrhoea. A colonoscopy revealed a diffuse pattern of erythema, superficial ulceration, friability, and mucopus extending in a continuous pattern on the left side of the colon. Tissue biopsies from the macroscopically involved areas disclosed continuous crypt architectural distortion with crypt abscesses and expanded acute and chronic inflammatory cells in the lamina propria (Fig. 1) confirming a diagnosis of left-sided UC. Regrettably, the patient experienced several flares of the disease that required admission and treatment with high-dose corticosteroids and azathioprine. Colectomy was performed as the disease became refractory to these medical therapies. Four months after surgery, when the patient was not receiving any corticosteroid therapy, she started to feel dull and achy pain in the thighs along with claudication of the lower limbs. However, typical symptoms of PMR such as pain and aching in the arms and shoulder girdle were mild at that time. She denied headache or other cranial features of giant cell arteritis. In addition, the ESR was only 12 mm/1st hour. Blood cell count, serum chemistry and urine analyses only disclosed slight microcytic anaemia. Antinuclear antibodies, antineutrophil cytoplasmic antibodies, antisaccharomyces cerevisiae antibody (ASCA), rheumatoid factor**,** anti-CCP antibodies, serum complement C3 and C4 levels were negative or normal. Likewise, screening for coeliac disease, serological tests for hepatitis B and C, HIV, cytomegalovirus, parvovirus B19, mononucleosis, borrelia, and brucella, and skin tuberculin test were negative. Also, a chest x-ray was normal.

Taken together all these data along with the presence of atypical features of PMR such as the predominance of symptoms involving the thighs with only mild pain in shoulders and normal ESR, a diagnosis of aortitis with involvement of lower extremity vessels was suspected. Interestingly, FDG PET/CT disclosed an inflammatory process with moderate diffuse increased metabolism in the thoracic aorta (grade 1–2 on a 0–3 scale) and markedly increased

FDG uptake in the femoral and posterior tibial arteries on both sides (grade 3 on a 0–3 scale) consistent with vasculitis of large- and medium-vessels (Figs. 2A, 3A, 4A). Because of the presence of vasculitis and the previous history of UC that had failed to respond to azathioprine therapy, in an attempt to spare high-dose corticosteroids, treatment with the anti-TNF-alpha monoclonal antibody-adalimumab (40 mg every 2 weeks subcutaneously) along with prednisone (initial dose 15 mg/day) was initiated with rapid improvement of symptoms in the lower extremities. Four months later prednisone dose had been reduced to 7.5 mg/day and the patient was free of symptoms. At that time and a new FDG PET/CT showed mild vascular FDG uptake in the thoracic aorta as well as markedly decrease of vascular FDG uptake in the femoral and posterior tibial arteries (grade 1 on a 0–3 scale) (Figs. 2B, 3B, 4B).

Fig. 3A. and **4A.** Markedly increased FDG uptake in the femoral and posterior tibial arteries of the lower limbs.
Fig. 3B. and **4B.** Decrease of vascular FDG uptake following anti-TNF-alpha therapy.



Discussion

This case emphasises the need to keep in mind a large- and medium-vessel vasculitis as a potential extraintestinal manifestation of UC. This may be particularly true in cases presenting with of atypical manifestations of PMR in the setting of this IBD.

There are several considerations that deserve to be taken into account in this singular case. First, the patient was initially diagnosed as having PMR because she fulfilled classification criteria for this condition (7). With respect to this, PMR is relatively common in elderly women from Western countries (8) and its diagnosis is relatively straightforward when typical symptoms are present (9). However, clinical and laboratory findings in PMR are not specific and PMR features have been reported in the setting of different conditions including autoimmune diseases (10, 11). Therefore, in some cases a disease different from "pure" isolated PMR must be searched, in particular when clinical features are not typical or corticosteroid therapy does not yield rapid and dramatic improvement of symptoms (12-14). Although in our case the patient initially presented with typical manifestations of PMR, it is plausible to think that PMR symptoms could have also been manifestations of an IBD whose gastrointestinal manifestation had initially been masked by the corticosteroid therapy. This speculation is supported by the occurrence of digestive symptoms as soon as prednisone was discontinued.

Second, the presence of aortitis and lower extremity vasculitis in the context of UC required further discussion. With respect to this, UC is known to be an uncommon cause of secondary large-vessel vasculitis (4-6). In this regard, unlike most cases reported previously (4-6), our patient did not fulfill definitions for Takayasu's arteritis. We realise that a large- and medium-vessel vasculitis may represent a diagnostic challenge in our case since the only clue for suspecting this complication was the presence of atypical features of PMR. However, as emphasised by Pipitone and Salvarani, FDG PET/CT may be useful to detect large-vessel vasculitis (15). This may be especially true in some patients presenting with PMR features that do not experience adequate response to corticosteroid therapy or exhibit atypical PMR manifestations. By this technique these authors disclosed a vasculitis involving only the lower extremities in a patient presenting with PMR features (16). In our case combined therapy with prednisone (initial dose 15 mg/day) and the fully human anti-TNF-alpha monoclonal antibody-adalimumab yielded a rapid improvement of symptoms. Although the role of PET in the follow-up of large-vessel vasculitis require further elucidation a new FDG PET/CT performed at month 4 after the onset of this combined therapy showed an important decrease of vascular FDG uptake in our patient.

Finally, as described in some corticosteroid-refractory patients with PMR (17), our results highlight the beneficial effect of TNF-alpha antagonist therapy in the management of patients with severe extraintestinal manifestations of UC.

In conclusion, the present report remarks the importance of suspecting the presence of large- and medium-vessel vasculitis in a patient with UC presenting with musculoskeletal features. The spectrum of extraintestinal manifestations of UC may be wider than it was previously considered. Rheumatologists should be aware of the possibility of a silent large and middle blood vessel vasculitis in patients presenting with UC when atypical musculoskeletal manifestations are present.

References

1. DOMÈNECH E, GARCIA-PLANELLA E, OLAZÁBAL A *et al*.: Abdominal aortitis associated with Crohn's disease. *Dig Dis Sci* 2005; 50: 1122-3.
2. CHEEMA AA, MCNEILL AJ: Images in cardiology. Left main coronary artery stenosis associated with aortitis in a patient with Crohn's disease. *Heart* 2006; 92: 618.
3. KELLERMAYER R, JAIN AK, FERRY G, DEGUZMAN MM, GUILLERMAN RP: Clinical challenges and images in GI. Aortitis as a rare complication of Crohn's disease. *Gastroenterology* 2008; 134: 668-9.
4. SATO R, SATO Y, ISHIKAWA H *et al*.: Takayasu's disease associated with ulcerative colitis. *Internal Medicine* 1994; 33: 759-63.
5. ISHIKAWA H, KONDO Y, YUSA Y *et al*.: An autopsy case of ulcerative colitis associated with Takayasu's disease with a review of 13 Japanese cases. *Gastroenterol Jpn* 1993; 28: 110-7.
6. CALLEJAS-RUBIO JL, LÓPEZ-NEVOT MA, MARTÍN-IBÁÑEZ J, ORTEGO-CENTENO N: Takayasu arteritis associated with ulcerative colitis. *Med Clin* (Barc) 2006; 126: 518.
7. BIRD HA, ESSELINCKX W, DIXON AS, MOWAT AG, WOOD PH: An evaluation of criteria for polymyalgia rheumatica. *Ann Rheum Dis* 1979; 38: 434-9.
8. GONZALEZ-GAY MA, VAZQUEZ-RODRIGUEZ TR, LOPEZ-DIAZ MJ *et al*.: Epidemiology of giant cell arteritis and polymyalgia rheumatica. *Arthritis Rheum* 2009; 61: 1454-61.
9. SALVARANI C, CANTINI F, HUNDER GG: Polymyalgia rheumatica and giant-cell arteritis. *Lancet* 2008; 372: 234-45.
10. GONZALEZ-GAY MA, GARCIA-PORRUA C, SALVARANI C, OLIVIERI I, HUNDER GG: The spectrum of conditions mimicking polymyalgia rheumatica in Northwestern Spain. *J Rheumatol* 2000; 27: 2179-84.
11. GONZÁLEZ-GAY MA, GARCÍA-PORRÚA C, SALVARANI C, OLIVIERI I, HUNDER GG: Polymyalgia manifestations in different conditions mimicking polymyalgia rheumatica. *Clin Exp Rheumatol* 2000; 18: 755-9.
12. GONZALEZ-GAY MA, GARCIA-PORRUA C, SALVARANI C, HUNDER GG: Diagnostic approach in a patient presenting with polymyalgia. *Clin Exp Rheumatol* 1999; 17: 276-8.
13. GONZALEZ-GAY MA, GARCIA-PORRUA C, MIRANDA-FILLOY JA, MARTIN J: Giant cell arteritis and polymyalgia rheumatica: pathophysiology and management. *Drugs Aging* 2006; 23: 627-49.
14. GONZALEZ-GAY MA, AGUDO M, MARTINEZ-DUBOIS C, POMPEI O, BLANCO R: Medical management of polymyalgia rheumatica. *Expert Opin Pharmacother* 2010; 11: 1077-87.
15. PIPITONE N, SALVARANI C: Role of imaging in vasculitis and connective tissue diseases. *Best Pract Res Clin Rheumatol* 2008; 22: 1075-91.
16. GERMANÒ G, VERSARI A, MURATORE F *et al*.: Isolated vasculitis of the lower extremities in a patient with polymyalgia rheumatica and giant cell arteritis. *Clin Exp Rheumatol* 2011; 29 (Suppl. 64): S138-9.
17. SPIES CM, BURMESTER GR, BUTTGEREIT F: Methotrexate treatment in large vessel vasculitis and polymyalgia rheumatica. *Clin Exp Rheumatol* 2010; 28 (Suppl. 61): S172-7.