Published in final edited form as:

Semin Arthritis Rheum. 2016 February ; 45(4): 475–482. doi:10.1016/j.semarthrit.2015.07.006.

Vasculitis in patients with inflammatory bowel diseases: A study of 32 patients and systematic review of the literature

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Abstract

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Background—Published small case series suggest that inflammatory bowel disease [IBD; Crohn's disease (CD) or ulcerative colitis (UC)] and vasculitis co-occur more frequently than would be expected by chance.

Objectives—To describe this association by an analysis of a large cohort of carefully studied patients and through a systematic literature review.

Methods—Patients with both IBD and vasculitis enrolled in the Vasculitis Clinical Research Consortium (VCRC) Longitudinal Studies, followed in Canadian Vasculitis research network (CanVasc) centers and/or in the University of Toronto's IBD clinic were included in this case series. A systematic literature review of patients with IBD and vasculitis involved a PubMed search through February 2014. The main characteristics of patients with Takayasu arteritis (TAK) and IBD were compared to those in patients with TAK without IBD followed in the VCRC.

Results—The study identified 32 patients with IBD and vasculitis: 13 with large-vessel vasculitis [LVV; 12 with TAK, 1 with giant cell arteritis (GCA); 8 with CD, 5 with UC]; 8 with ANCA-associated vasculitis [AAV; 6 granulomatosis with polyangiitis (GPA), 2 with eosinophilic granulomatosis with polyangiitis (EGPA)]; 5 with isolated cutaneous vasculitis; and 6 with other vasculitides. Patients with LVV and AAV were mostly female (18/21). The diagnosis of IBD preceded that of vasculitis in 12/13 patients with LVV and 8/8 patients with AAV. The review of the literature identified 306 patients with IBD and vasculitis: 144 with LVV (133 TAK; 87 with IBD preceding LVV), 19 with AAV [14 GPA, 1 EGPA, 4 microscopic polyangiitis (MPA)], 66 with isolated cutaneous vasculitis, and 77 with other vasculitides. Patients with IBD and TAK were younger and had more frequent headaches, constitutional symptoms, or gastrointestinal symptoms compared to those patients in the VCRC who had TAK without IBD.

Conclusions—These findings highlight the risk of vasculitis, especially TAK, in patients with IBD (both CD and UC).

Keywords

Vasculitis; Takayasu arteritis; Inflammatory bowel disease; Crohn's disease; Ulcerative colitis

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Vasculitis comprises a group of rare and potentially life-threatening diseases typically classified by the size of the vessels predominantly affected [1]. Primary large-vessel vasculitides (LVV) affect the aorta and its branches and include Takayasu arteritis (TAK) and giant cell arteritis (GCA). Medium vessel vasculitides affect the main visceral arteries and their branches and include polyarteritis nodosa (PAN) and Kawasaki disease. Small-vessel vasculitides affect arterioles and/or capillaries and include anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides [AAV, including granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA) and microscopic polyangiitis (MPA)] and immune-complex-mediated vasculitides [1]. Gastrointestinal tract manifestations can occur in these vasculitides [2,3] due to involvement of the mesenteric arteries or smaller vessels, potentially leading to bowel ischemia. Granulomatous inflammation of the bowel mucosa can develop in GPA and EGPA and occasionally mimics inflammatory bowel diseases [IBD; Crohn's disease (CD) or ulcerative colitis (UC)] [3–5].

The literature on vasculitis in patients with IBD is quite limited. The current understanding of this rare association stems predominantly from case reports and small case series with not more than 10 patients. Various vasculitides have been associated with IBD, especially TAK [6–8] but also GPA [9], isolated cutaneous vasculitis [10], and central nervous system vasculitis [11].

The first objective of this study was to describe the different types of vasculitis that can occur in association with IBD, the temporal relationships of these diagnoses, and the management and clinical outcomes of patients with these 2 diseases. The second objective was to conduct a comprehensive review of the literature on the association of vasculitis and IBD. Additionally, the clinical characteristics of patients with IBD and TAK were compared to those with TAK without IBD.

Material and methods

Patients

Patients were included in the study if they had vasculitis and IBD. IBD could have developed either before or after the former. Only patients with Behçet's disease or with AAV diagnosed within the same year as IBD were excluded, because inflammatory colitis due to these vasculitides can be misdiagnosed as IBD [12,13].

Patients were identified from 3 different sources: the Vasculitis Clinical Research Consortium (VCRC) Longitudinal Studies cohorts, the Canadian Vasculitis research network (CanVasc) centers, and the Mount Sinai Hospital–University of Toronto referral center for IBD (UoT-IBD). The VCRC Longitudinal Studies prospectively collect data in patients with TAK, GCA, PAN, EGPA, GPA, or microscopic polyangiitis (MPA), all satisfying the 1990 American College of Rheumatology (ACR) modified criteria [14,15], from 7 referral centers in the United States and 2 in Canada (<http://www.rarediseasesnetwork.org/VCRC>). The CanVasc is a Canadian network for research on vasculitis involving clinics in 18 cities (<http://www.canvasc.ca>), including the 2 centers also in the VCRC. In the VCRC database, IBD is systematically recorded as a comorbid illness when present, either at baseline or during follow-up visits. For the 2 other sources, the participating physicians identified patients followed in their clinics who met the inclusion criteria.

Because it was expected that TAK would be the main type of vasculitis associated with IBD, the characteristics of patients with TAK and IBD were compared to those of patients with TAK without IBD from the VCRC cohort.

The protocol was reviewed and approved by the VCRC Steering Committee and by the local research ethics boards at all participating centers.

Literature search and study selection

Two authors (A.S. and C.P.) conducted a systemic literature review to identify published cases of patients with IBD and vasculitis. MEDLINE was searched via PubMed for reports published from 1964 to February 2014, without a language restriction, with the following keywords: Takayasu arteritis, aortitis, giant cell arteritis, large-vessel vasculitis, anti-

neutrophil cytoplasmic antibody-associated vasculitis, Wegener's granulomatosis, Churg–Strauss syndrome, small-vessel vasculitis, retinal vasculitis, systemic vasculitis, central nervous system vasculitis, cerebral vasculitis, cutaneous vasculitis, or angiitis in combination with inflammatory bowel disease, ulcerative colitis, or Crohn's disease. Retrieved and relevant papers were manually searched for additional references.

Studied parameters

The following information, when available, was collected for each patient, directly from patient charts or from retrieved articles, by using a standardized data collection form: age at diagnosis, sex, comorbidities, timing of the diagnoses of IBD and vasculitis, main clinical manifestations of vasculitis, routine laboratory results, medications, and follow-up outcomes (survival and disease status). Physicians within the VCRC, CanVasc, and UoT-IBD were contacted directly to provide information on any missing data.

Statistical analysis

Categorical variables are expressed with number (percentage) and comparisons using the chi-square test or, when appropriate, Fisher's exact test. For continuous variables, median (range) are provided, and means were compared by Student's *t* test. A $p < 0.05$ was considered significant.

Results

Patients from the VCRC, CanVasc, and UoT-IBD

Overall, 43 patients (21 from the VCRC and 22 from CanVasc, including 2 co-managed with the UoT-IBD) with IBD and vasculitis diagnosed between 1986 and 2013 were identified. In all, 4 patients from the VCRC (2 EGPA and 2 GPA) and 5 from CanVasc (4 GPA and 1 EGPA) were excluded because IBD and vasculitis were diagnosed within 1 year of each other. A patient with GCA and another with EGPA were excluded because a definitive diagnosis for colitis could not be established. The demographics and clinical characteristics of the final 32 patients (17 from the VCRC and 15 from CanVasc) are summarized in Table 1. Patient 5 from Table 1 had been reported in a separate case report (also included in the literature review) but follow-up is now longer [16].

The most common group of vasculitides with IBD identified was LVV ($n = 13$), consisting of 12 cases of TAK and 1 case of GCA (8 with CD and 5 with UC). Other cases included 8 cases of ANCA-associated vasculitis (6 GPA with anti-proteinase 3 ANCA and 2 EGPA), 5 with isolated cutaneous vasculitis, and 6 with other vasculitides. Most patients with LVV and ANCA-associated vasculitis were female [median age 27 (range: 17–58) years and 20 (range: 8–52) years at the time of diagnosis of vasculitis and IBD, respectively]. The diagnosis of IBD preceded that of LVV for 12/13 patients and for all 8 patients with ANCA-associated vasculitis. The median intervals between the diagnoses of vasculitis and IBD was 10 years (2 months to 27 years) for LVV and 11 years (2–44 years) for ANCA-associated vasculitis.

The most common clinical findings in patients with TAK and IBD were constitutional symptoms (in 12/12 patients), vascular signs or symptoms (in 10/12 patients), including limb claudication, decreased peripheral pulse, blood pressure differences between arms, and bruits. Detailed results of computerized tomographic or magnetic resonance arteriography findings were available for 9/12 patients: 5 showed an aneurysm or dilation of at least a portion of the aorta; 7 had stenosis involving the branches of the thoracic aortic artery, 6 showed renal/suprarenal artery involvement, 4 had celiac, superior or inferior mesenteric artery involvement, and 2 had vertebral artery involvement.

The following medications were used in isolation or combination to treat the majority of the patients with IBD: 5-aminosalicylates (5-ASA), glucocorticoids, methotrexate, azathioprine, or an anti-tumor necrosis factor (TNF) alpha agent; 12/32 patients (38%) received at least 1 biologic, most commonly infliximab. A total of 4 patients had also undergone large bowel surgery; 2 patients had previously received infliximab. In 5 patients with CD, TAK developed despite infliximab, but in none of the other 11 patients did the vasculitis develop while receiving a biologic for their IBD.

Of the 29 patients with information on their initial treatment regimen for the vasculitis, 27 (93%) received intravenous or oral glucocorticoids, 23 (79%) received another immunosuppressant such as azathioprine, methotrexate or cyclophosphamide, and 1 (3%) underwent plasma exchange. Overall, 6 (21%) patients received biologics, including infliximab, adalimumab, or abatacept.

Follow-up information was available for 28/32 patients (88%). In all, 3 patients were newly diagnosed with vasculitis and 1 from the VCRC had no documented follow-up visit after the diagnosis of vasculitis at the time of this analysis. After a median follow-up of 5.4 years (range: 3 months–28 years) after the diagnosis of vasculitis, 17 patients (61%) had achieved remission of the vasculitis and 11 (39%) had persistent disease activity or experienced vasculitis flare(s). In 5/9 patients (56%) who received biologic therapy for either vasculitis or IBD and for which follow-up data were available, the vasculitis was in remission at the last follow-up appointment.

Literature review

From the literature review (Fig. and Appendix 1), 306 patients with IBD and vasculitis were identified, within the same 4 main disease categories (LVV, ANCA-associated vasculitides, cutaneous vasculitis, and other vasculitides; Table 2).

Patients with IBD and LVV

The 144 cases of LVV included 70 cases of CD and 74 cases of UC. Most patients (82%) were female; 133 (92%) were reported as having TAK and 11 (8%) patients as having non-TAK LVV (GCA or other LVV). Of the 127 cases with data on the temporal relationship between the 2 diagnoses, the diagnosis of IBD preceded that of vasculitis in 87 (69%) by a median of 4 years (range: 0.5–31 years), including 1 case of LVV with UC and 3 with CD that were reported as possibly drug-induced. In 22 patients, LVV preceded IBD by a median of 6 years (range: 3 months–36 years); vasculitis and IBD were diagnosed concurrently in the remaining 18 patients.

Fewer than 10% of the reported cases with CD and TAK but 66% of those with LVV and UC were from Japan. There were no other significant differences between patients with LVV with UC or CD.

Most patients received a combination of 5-ASA, glucocorticoids, and other immunosuppressive drugs. Overall, 20 patients (16 with CD and 4 with UC) received biologics (16 infliximab, 2 infliximab then adalimumab, 1 adalimumab, and 1 tocilizumab). Good clinical response with biologics was noted for 11/20 patients (55%), which allowed for tapering or discontinuation of the glucocorticoids. In all, 2 of the remaining 9 patients experienced severe allergic reactions to infliximab and 1 patient each had persistently active CD and required hemicolectomy, experienced recurrent infections, or developed aortic arch aneurysm despite infliximab treatment. In the 4 remaining patients, TAK developed while receiving anti-tumor necrosis factor (TNF)-alpha agents, which were later stopped, and all patients showed improvement after receiving high-dose glucocorticoids alone. In all, 9 of the 70 patients (13%) with CD and TAK and 7 of the 73 patients (10%) with TAK and UC required a bowel resection for their IBD.

The median follow-up of patients with CD and LVV was 0.7 years (range: 1 week–20 years) and 0.2 years (range: 1 week–13 years) for patients with UC and LVV. Among these patients, 2 with CD died (myocardial infarction and non-specified cause), as did 4 with UC (one each from cerebral vascular event, aneurysm rupture, respiratory failure, and non-specified cause).

Patients with IBD and other types of vasculitis

In total, 66 patients had IBD and cutaneous vasculitis: 45 had been reported with isolated cutaneous vasculitis (25 with “leukocytoclastic vasculitis” and 20 with cutaneous PAN), 11 with isolated cutaneous granulomatous small-sized vessel vasculitis, 8 with IgA vasculitis (Henoch–Schönlein purpura), and 1 each with nodular vasculitis, urticarial vasculitis, and lymphocytic vasculitis. For 33/56 cases (59%) with cutaneous vasculitis and available information on the intervals between the 2 diagnoses, the vasculitides occurred after the diagnosis of IBD. All but 3 (95%) of these cutaneous vasculitides reportedly resolved after treatment with glucocorticoids, mesalamine, sulfasalazine, azathioprine, methotrexate, or dapsone, but some patients were additionally treated with antibiotics or colectomy when the IBD was active. Overall, 8 cases (including 3 with IgA vasculitis) were reported as secondary to anti-TNF-alpha treatment (infliximab or adalimumab). Cutaneous lesions resolved after treatment with methylprednisolone, diphenhydramine, and ranitidine in 1 patient and, for 6/7 of the remaining patients, after the discontinuation of the anti-TNF-alpha therapy; however, the re-administration of the same anti-TNF-alpha therapy in 2 patients was associated with recurrence of skin lesions.

In all, 19 patients with ANCA-associated vasculitides were reported: 14 with GPA, 1 with EGPA, and 4 with MPA. Of the 16 patients with available information on treatments and outcomes, 9 had received glucocorticoids combined with cyclophosphamide (followed by mycophenolate mofetil, azathioprine, or methotrexate), azathioprine, methotrexate, or infliximab; 11 reportedly entered remission, and “good response” to treatment was obtained in the remaining 5.

A total of 77 other cases of vasculitis were found associated with IBD, including more than 10 cases each of IgA vasculitis with glomerulonephritis, retinal vasculitis, or central nervous system (CNS) vasculitis. Sporadic cases of systemic PAN, anti-glomerular basement membrane (anti-GBM) disease, Kawasaki disease, or isolated vasculitic neuropathy were described associated with IBD.

Characteristics of patients with TAK with or without IBD

Table 3 summarizes the demographic and clinical features of the 12 patients with IBD and TAK in this series (8 from the VCRC cohort), the 132 patients identified in the literature, and the 152 patients from the VCRC with TAK but without IBD. Most patients with IBD and TAK from the literature were Asian and had a much shorter follow-up than those from this series or from the VCRC but without IBD. Patients with IBD and TAK were younger at the time of diagnosis of TAK than those without IBD and had more frequent headaches, constitutional, and gastrointestinal symptoms. At the last follow-up, most patients (63–89%), achieved remission of their vasculitis, with similar rates in all groups. No patients with TAK from the VCRC cohort, with or without IBD, had died at the time of this analysis, as compared with 6 (9%) of those with TAK and IBD in the literature.

Discussion

This case series, one of the largest reported to date, and the systematic literature review emphasize that different types of vasculitis can occur in patients with IBD, including in decreasing order of frequency: LVV, mainly TAK, cutaneous vasculitis, and ANCA-associated vasculitides, mostly GPA. In most cases, the diagnosis of IBD preceded that of vasculitis by years, and IBD was usually not active at the time of the onset of vasculitis.

TAK and ANCA-associated vasculitis are rare and the probability of their coexistence with IBD by chance is minimal, although this occurrence cannot be excluded. The prevalence of CD was as high as 9% in a French series of 44 patients with TAK [6]. In a North American study of 32 patients with TAK, 2 (6%) had CD, as compared to an estimated prevalence of 0.2% of CD in the general population [17]. Of the 160 patients with TAK in the VCRC, 8 (5%) patients with associated IBD were identified. The reasons for the more distinctive association between IBD and TAK or GPA are unclear but may indirectly support some common pathogenic mechanisms [18]. TAK and UC were also found to share a significant proportion of their genetic background, which may contribute to their coexistence [19,20]. A recent genetics study showed that patients with TAK complicated with UC displayed higher positivity for *HLA-B*52:01* than patients without UC [20]. Granulomatous inflammation is a hallmark of both TAK and GPA, as is also a key feature of CD [21,22].

There were some demographic and clinical characteristics more common among patients with coexisting vasculitis and IBD. Patients with IBD and LVV or ANCA-associated vasculitis were often female. Most patients with IBD and TAK in the literature were Asians but not in the current series, which included patients from North American vasculitis networks. Rény et al. [6] reported that patients with coexistent CD and TAK tended to be younger at the time of diagnosis of TAK and had more frequent constitutional symptoms, including fever, weight loss, or fatigue, than those with TAK without IBD. The current study

replicated these findings. Patients with IBD and TAK from the literature and this series were on average 8–12 years younger at the time of the diagnosis of TAK than those with TAK without IBD. Patients with IBD and TAK were also more likely to have constitutional symptoms, gastrointestinal symptoms, and headache/dizziness but were less likely to experience claudication of the extremities. A recent case series of 11 patients with ANCA-associated vasculitides (7 patients with GPA and CD and 4 with EGPA and UC) suggested that the coexistence of GPA and UC or EGPA and CD was infrequent [22]. We did not observe this exclusive associative pattern in our patients (1 GPA with CD, 3 GPA with UC, 1 EGPA with CD, and 1 EGPA with UC), but our study replicates another important finding—that the diagnosis of IBD most often antedates the diagnosis of ANCA-associated vasculitis.

Cutaneous vasculitis in patients with IBD remains an isolated and less severe complication, which is sometimes seemingly caused by the drugs used to treat IBD. Although less common, IgA vasculitis with or without glomerulonephritis, retinal vasculitis, and central nervous system vasculitis have also been associated with IBD. Some of these diseases could be coincidental and/or drug-induced. Importantly, patients with IBD carry an increased risk of thrombotic events, including strokes and white-matter CNS abnormalities [23,24], which may be mistaken as CNS vasculitis. Therefore, reported cases of CNS vasculitis, including those seen in this series, may be questionable without histological evidence of vasculitis.

Interestingly, the same drugs are often used to treat IBD and vasculitis, especially TAK. Anti-TNF-alpha monoclonal antibodies have been found effective for cases of IBD-associated TAK that did not adequately respond to conventional medical treatment and immunosuppressants [18]. In the current study, vasculitis developed in only 1/12 patients receiving anti-TNF-alpha therapies; however, several cases of new-onset TAK or cutaneous vasculitis have been reported in patients with IBD receiving these drugs [16,25–29].

This study has several strengths, including the relatively large sample size of 32 patients with vasculitis and IBD with substantial time of follow-up, a systematic literature review, and the inclusion of all types of vasculitides. Most previous studies focused on only 1 type of vasculitis [9]. Importantly, patients with a diagnosis of Behçet's disease or a diagnosis of ANCA-associated vasculitis made within the same year were excluded from this study because they represent a different population, with possible initial misdiagnoses. The initial presenting features of IBD and these vasculitides can overlap and delay or confound the diagnosis of one or the other, especially when the gastrointestinal manifestations are isolated [3,6,12]. The comparison of the characteristics of the patients with TAK with or without IBD also adds to the available literature.

This study has some limitations to consider. It is retrospective, and hence certain detailed clinical information such as the initial clinical features that led to a suspicion of vasculitis in a patient with underlying IBD is not always available from the VCRC database. However, a standardized recording form was used and physicians were contacted as needed to obtain the missing information. While the literature review was comprehensive, some cases of patients with IBD and vasculitis that were embedded within general case series of patients with vasculitis may have been missed. However, these cases would have likely lacked detailed clinical information relevant to the study and, therefore, would have had minimal impact on

the findings. In addition, the diagnosis of IBD and vasculitis often relied on authors' statements, rather than strictly using classification criteria [4,5]. Finally, in the absence of a longitudinal multicentric IBD cohort, the exact frequency of vasculitis in patients with IBD could not be determined.

This case series and literature review highlight the likely non-coincidental association of IBD and vasculitis, although the association remains rare. TAK is the most common, but not exclusive type, of vasculitis observed with IBD. The co-occurrence of these diagnoses most often arises in young patients with already established IBD and at a time when the IBD is usually not active. Clinicians treating IBD should have a high index of suspicion for vasculitis in patients with unusual symptoms and should have a low threshold to screen patients for the possibility of vasculitis.

The treatment and outcomes of patients with vasculitis and IBD do not overtly differ from those of patients with "primary" vasculitis and most of the treatments used for vasculitis are also effective against IBD. Future research may help to clarify the complex relationships and pathogenic mechanisms shared by these 2 diseases.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Financial support: Alice Sy was funded by the Abbott Summer studentship granted by the Canadian Rheumatology Association. The Vasculitis Clinical Research Consortium has received support from the National Institute of Arthritis and Musculoskeletal and Skin Diseases, USA (U54AR057319 and U01AR5187404), the National Center for Research Resources, USA (U54RR019497), the Office of Rare Diseases Research, and the National Center for Advancing Translational Science, USA.

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Appendix A. Supplementary information

Supplementary material cited in this article is available online at <http://dx.doi.org/10.1016/j.semarthrit.2015.07.006>.

Fig.
Algorithm of the literature search (ANCA, anti-neutrophil cytoplasmic antibody; *n*, number of cases; *x*, number of articles).

Table 1

Main demographic data and clinical characteristics of 32 patients with both IBD and vasculitis enrolled in the Vasculitis Clinical Research Consortium (VCRC) longitudinal studies, followed in Canadian Vasculitis research network (CanVasc) centers and/or in the University of Toronto's IBD clinic

Patient ID	Sex	Inflammatory bowel disease			Vasculitis			Disease status and treatment at last follow-up		
		Type	Age at dx (years)	Treatment	Type	Age at dx (years)	Clinical characteristics			
Large-vessel vasculitis										
1	F	CD	24	5-ASA	TAK	27	CONST, VASC, MSK, ART (+)	PDN, AZA	28	Recent flare; on PDN, MTX
2	F	CD	52	AZA, hemicolectomy	TAK	58	CONST, VASC, MSK, ART (+)	PDN, AZA	7.5	In remission; on AZA
3	F	CD	25	PDN, AZA, IFX, ADA	TAK	25	CONST, ARTH, ART (+)	PDN, AZA, IFX	5.5	In remission; on PDN, AZA, IFX
4	M	CD	13	IFX	TAK	17	CONST, HTN, VASC, MSK, ART (+)	PDN, MTX, IFX	1	In remission; on PDN
5	F	CD	15	5-ASA, PDN, IFX	TAK	17	CONST, VASC, ART (+)	MTX	NA	In remission; on PDN
6	F	CD	8	BUD, IFX, ileostomy, subtotal colectomy	TAK	17	CONST, HTN, VASC, PNS, SEM, CoA, ART (+)	PDN, AZA, MTX, RTX IFX, LEF, ADA, ABT, aortic stent	4.5	Recurrent flares; on PDN, MTX, IFX
7	F	CD	9	AZA, IFX, ADA subtotal colectomy	TAK	20	CONST, VASC, MSK, ART (+)	PDN, MTX	(new dx)	on PDN, MTX
8	F	CD	27	5-ASA, PDN, AZA, IFX	TAK	27	CONST, HTN, VASC, renal, ART (+)	PDN, AZA, MTX, IFX	8	NA
9	F	UC	16	5-ASA, PDN, 6-MP	TAK	29	CONST, VASC, ART (+)	PDN, ADA	1	Active disease; on PDN, ADA
10	F	UC	20	5-ASA	TAK	42	CONST, VASC, CNS, ART (+)	PDN, MTX	4	In remission; on PDN, MTX
11	F	UC	18	5-ASA, PDN, 6-MP	TAK	38	CONST, ART (+)	–	(new dx)	–
12	F	UC	34	PDN	TAK	49	CONST, VASC, PNS, ocular, ART (+)	PDN	(new dx)	on PDN
13	M	UC	30	PDN	GCA	57	CONST, PNS, PMR, ocular, ENT, biopsy (+)	PDN	1.5	In remission; on PDN
ANCA-associated vasculitis										
14	F	CD	8	5-ASA, 6-MP, MTX, IFX, ADA	GPA	20	CONST, MSK, CUT, ocular, ENT, PUL, atypical-ANCA (+), PR3 (+), biopsy (+)	PDN, MTX, Plasma exchange	(new dx)	PDN, MTX, Plasma exchange
15	F	UC	33	5-ASA	GPA	39	CONST, MSK, CUT, renal, ENT, c-ANCA (+), PR3 (+)	PDN, MTX, AZA, CYC	9	Low disease activity; on PDN

Patient ID	Sex	Inflammatory bowel disease		Vasculitis		Age at dx (years)	Clinical characteristics	Treatment	Length of follow-up (years)	Disease status and treatment at last follow-up
		Type	Age at dx (years)	Type						
16	M	UC	58	5-ASA	GPA	71	CONST, CUT, PUL, c-ANCA (+), PR3 (+)	PDN, MTX	1	In remission; on PDN
17	F	UC	5	NA	GPA	55	CONST, MSK, ocular, ENT, c-ANCA (+), PR3 (+)	PDN, MTX	2	Recent flare; on PDN, RTX
18	F	UC	40	5-ASA, PDN, colectomy	GPA	50	CONST, ENT, PNS, PUL, C-ANCA (+), PR3 (+), biopsy (+)	PDN, CYC	14	In remission; on PDN
19	F	UC	52	5-ASA	GPA	54	CONST, MSK, renal, ocular, ENT, C-ANCA (+), PR3 (+), biopsy (+)	PDN, AZA, CYC	1	In remission; on PDN, AZA
20	F	CD	29	5-ASA	EGPA	65	CONST, MSK, CUT, PNS, asthma, PUL, c-ANCA (+)	PDN, AZA, CYC	6	In remission; on PDN, MMF
21	F	UC	14	5-ASA	EGPA	17	CONST, ocular, ENT, asthma, PUL, cardiac, p-ANCA (+)	PDN, AZA, MTX	10	In remission; off treatment
<i>Cutaneous vasculitis</i>										
22	M	CD	26	PDN, AZA, IFX	LCV	41	CUT, biopsy (+)	PDN, IFX	0.5	Active disease; on AZA, IFX, starting COL
23	F	CD	43	MTX	LCV	51	CONST, CUT, biopsy (+)	PDN, MTX	1	Active disease; on PDN, MTX, will begin IFX
24	M	CD	38	PDN, IFX	LCV	49	CONST, MSK, CUT, biopsy (+)	PDN	0.5	Active disease; on PDN, will begin IFX
25	M	CD	59	5-ASA	LCV	59	CONST, CUT, biopsy (+)	PDN, MTX	4	In remission; on MTX
26	F	UC	30	5-ASA	Cutaneous PAN	21	CUT	PDN, MTX, AZA, MMF	11	In remission; on MTX
<i>Other vasculitis</i>										
27	M	CD	13	5-ASA, PDN, MTX, IFX	Kawasaki	10	NA	NA	6	In remission; on IFX and MTX for CD
28	M	CD	13	PDN	IgA vasculitis	34	Renal, biopsy (+)	COL	6	Recurrent uveitis; considering MTX
29	M	CD	47	MTX, IFX	PAN	42	CONST, MSK, PNS	PDN, MTX	6	In remission; on MTX, IFX
30	F	UC	48	5-ASA, PDN, MMF	PAN	47	CONST, VASC, CNS, PNS, cardiac	PDN, MTX, CYC, HCQ, COL	1	Recurrent strokes; on PDN, MMF
31	F	CD	18	PDN	CNS vasculitis	49	VASC, CNS, ocular	PDN, MTX	6	Stable disease; on MTX, PDN

Patient ID	Sex	Inflammatory bowel disease		Vasculitis		Clinical characteristics	Treatment	Length of follow-up (years)	Disease status and treatment at last follow-up
		Type	Age at dx (years)	Type	Age at dx (years)				
32	F	UC	25	5-ASA, PDN, AZA, IFX	CNS vasculitis	30	MSK, CUT, VASC, CNS	4	Multiple strokes; on clopidogrel

5-ASA, 5-aminosalicylic acid; 6-MP, mercaptopurine; ABT, abatacept; ADA, adalimumab; ANCA, anti-neutrophil cytoplasmic antibody; ART, arteriography (+, positive with arterial abnormalities); AZA, azathioprine; BUD, budesonide; CD, Crohn's disease; CoA, coarctation of aorta; COL, colchicine; CNS, central nervous system; CONST, constitutional symptoms; CUT, cutaneous; CYC, cyclophosphamide; dx, diagnosis; EGPA, eosinophilic granulomatosis with polyangiitis; ENT, ear nose throat; GPA, giant cell arteritis; GPA, granulomatosis with polyangiitis; HCQ, hydroxychloroquine; IFX, infliximab; IgA, immunoglobulin A; LCV, leukocytoclastic vasculitis; LEF, leflunomide; MMF, mycophenolate mofetil; MSK, musculoskeletal symptoms; MTX, methotrexate; NA, not available; PAN, polyarteritis nodosa; PDN, prednisone; PMR, polymyalgia rheumatica; PNS, peripheral nervous system; PUL, pulmonary; RTX, rituximab; SEM, systolic ejection murmur; TAK, Takayasu arteritis; UC, ulcerative colitis; VASC, vascular.

Table 2

Summary of the cases of vasculitis associated with IBD in this series and reported in the literature

	Large-vessel vasculitides			Cutaneous vasculitides			ANCA-associated vasculitides			Other vasculitides		
	This series	Literature search		This series	Literature search		This series	Literature search		This series	Literature search	
No. of cases	13	144		5	66		8	19		6	78	
No. of Crohn's disease (%)	8 (62%)	70 (49%)		4 (80%)	43 (65%)		2 (25%)	12 (63%)		4 (67%)	45 (58%)	
No. of ulcerative colitis (%)	5 (38%)	74 (51%)		1 (20%)	23 (35%)		6 (75%)	7 (37%)		2 (33%)	33 (42%)	
Sex, female/male (%)	85%/15%	82%/18%		40%/60%	52%/48%		88%/12%	58%/42%		50%/50%	44%/56%	
Median age at diagnosis of IBD, years (range)	20 (8–52)	21 (10–56)		38 (26–59)	25 (2–80)		31 (5–58)	29 (10–53)		21.5 (13–48)	22 (10–59)	
Median age at diagnosis of vasculitis, years (range)	27 (17–58)	23 (12–52)		49 (21–59)	26 (2–80)		52 (17–71)	35 (16–78)		31 (10–49)	31 (10–59)	
Temporal relationship												
IBD first ^a	12 (92%)	87/127 (69%)		3 (60%)	32/55 (58%) ^b		8 (100%)	17 (89%)		3 (50%)	45/59 (76%)	
Vasculitis first	0	22/127 (17%)		2/5 (40%)	14/55 (25%)		0	2 (11%)		3 (50%)	10/59 (17%)	
Concurrent	1/13 (8%)	18/127 (14%)		0	9/55 (16%)		0	0		0	4/59 (7%)	

ANCA, anti-neutrophil cytoplasmic antibody; IBD, inflammatory bowel disease.

^aThe temporal relationship between the diagnoses of IBD versus vasculitis was reported or available for 126 cases of large-vessel vasculitides, 55 cases of cutaneous vasculitides, and 59 cases of other vasculitides.

^bIncludes cases of possible drug-induced vasculitis.

Table 3

Characteristics of patients with Takayasu arteritis (TAK) and an associated IBD from this series and the literature, and with TAK but no IBD from the Vasculitis Clinical Research Consortium (VCRC) longitudinal study

Characteristic	Patients from this series with TAK and IBD ^a , N = 12	Patients from the literature with TAK and IBD, N = 133	Patients from this series with TAK and no IBD (VCRC), N = 152
Female/male, no.	11/1	100/23 ^b	143/9
Age at diagnosis of TAK, years, median (range)	19 (8–52)	23 (10–69)	31 (4–63) ^c
Age ≥ 50 years old, no. (%)	11 (92)	104/105 (99) ^b	139 (91) ^c
Ethnicity, no. (%)		n = 62 ^b	
Caucasian	8 (67)	11 (18)	127 (84) ^c
Asian	3 (25)	45 (73)	14 (9) ^c
African American	1 (8)	3 (5)	7 (5%)
Middle Eastern	0	3 (5)	0 ^c
Native Indian	0	0	4 (3)
Clinical manifestations at time of TAK diagnosis, no. (%)		n = 67 ^b	
Claudication of extremities	8 (67)	19 (28)	96 (63) ^c
Decreased brachial pulse	9 (75)	36 (54)	92 (61)
Blood pressure difference between arms	7 (58)	35 (52)	70 (46)
Bruit over subclavian artery or aorta	5 (42)	35 (52)	77 (51)
Renal hypertension	4 (33)	9 (13)	20 (13)
Fever/weight loss/fatigue	7 (58)	31 (46)	42 (28) ^c
Abdominal pain, diarrhea	4/5 (80)	25 (37)	6 (4) ^c
Angina/dyspnea	2 (17)	14 (21)	14 (9) ^c
Carotidynia	1 (8)	14 (21)	31 (20)
Headache/dizziness	4 (33)	11 (16)	12 (8) ^c
Arthralgia	2 (17)	9 (13)	37 (24)
Duration of follow-up, years, median (range)	4.7 (0.75–28)	0.4 (0.1–28)	6.25 (0.25–31) ^c
Outcomes, no. with available data, no. (%)	n = 8	n = 68 ^b	n = 122
Remission of vasculitis at last follow-up	5 (63)	55 (81)	108 (89)
Stroke	0	4 (6)	9 (7)
Myocardial infarction	0	1 (1)	4 (3)
Deaths	0	6 (9)	0 ^c

ACR, American College of Rheumatology; BP, blood pressure; IBD, inflammatory bowel disease; TAK, Takayasu arteritis; VCRC, Vasculitis Clinical Research Consortium.

^aPatients from this series encompass patients from 3 different sources: the VCRC Longitudinal Studies cohorts, the Canadian Vasculitis research network centers and the Mount Sinai Hospital–University of Toronto referral center for IBD.

^bComplete clinical and demographics information was not reported for all cases from the literature.

^c $p < 0.05$ comparing patients with TAK and IBD from this series and the literature versus those with TAK but no IBD from the VCRC.

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