Seminars in Arthritis and Rheumatism 45 (2016) 475–482

Contents lists available at ScienceDirect

Seminars in Arthritis and Rheumatism

journal homepage: www.elsevier.com/locate/semarthrit

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

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ARTICLE INFO

Keywords:
Vasculitis
Takayasu arteritis
Inflammatory bowel disease
Crohn's disease
Ulcerative colitis

ABSTRACT

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

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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http://dx.doi.org/10.1016/j.semarthrit.2015.07.006

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).

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