Gastrointestinal Involvement in Systemic Vasculitis

Gastrointestinal involvement is known to be associated with primary vasculitis. But in some cases, it may be IBD with secondary vasculitis, this review shows.

The gastrointestinal system has long been shown to be involved in both primary and secondary vasculitis, but so has inflammatory bowel diseases (IBD), which leads experts to question whether patients with primary vasculitis with inflammation in the gastrointestinal system have been accurately diagnosed. Could they, instead, have IBD with secondary vasculitis?

Writing in the journal Current Opinion in Rheumatology, Turkish researchers review the current literature on gastrointestinal involvement in different types of vasculitis. They address the variability of gastrointestinal involvement and clinical findings, as well as treatment.

An inflammatory bowel disease diagnosis usually precedes a diagnosis of vasculitis. A systematic review of the literature points to large vessel (mostly Takayasu arteritis), cutaneous vasculitis and ANCA-Associated Vasculitis (AAV) (mostly granulomatosis with polyangiitis, or GPA) as the three most common types of vasculitis associated with IBD.

Primary vasculitides most commonly associated with a higher frequency of gastrointestinal involvement include immunoglobulin A (IgA) and anti-neutrophilic cytoplasmic antibodies (ANCA)-associated vasculitis (AAV), polyarteritis nodosa (PAN) and Behcet’s syndrome.

Takayasu arteritis is associated with gastrointestinal symptoms that resemble inflammatory bowel diseases (IBD) in some patients. And, rheumatoid arthritis and systemic lupus erythematosus (SLE) can be associated with secondary vasculitis and gastrointestinal involvement.

Patients with vasculitis symptoms typically experience abdominal pain, fever, diarrhea, nausea, vomiting and sometimes bleeding. They can also experience aneurysms or occlusions in mesenteric, hepatic or splenic vessels.

An accurate diagnosis is difficult and usually includes imaging which may reveal an inflamed gastrointestinal tract with erosions, or ulcers that can lead to perforation, bleeding and bowel obstruction. Currently, angiography is the gold standard for diagnosis of mesenteric vascular lesions especially if endovascular therapeutic interventions are needed.

Vasculitis of solid organs in the pancreas, liver and gallbladder can occur in patients as well. Treatment depends on the type of vasculitis and is usually with high-dose corticosteroids and immunosuppressives. This article sums up the review as follows:

**Takayasu Arteritis**

Takayasu arteritis has long been associated with gastrointestinal symptoms and ulcerative colitis or Crohn’s disease, but the research has not yet definitively determined whether there is a true association between this large vessel vasculitis and IBD.

More than 100 case reports of Takayasu patients with ulcerative colitis or Crohn’s disease have been published. And, a multicenter retrospective survey concluded that ulcerative colitis is a major complication of Takayasu arteritis.

**Polyarteritis Nodosa**

Polyarteritis nodosa (PAN) causes inflammation of the medium-sized vessels and is characterized by microaneurysms found in hepatic, mesenteric, renal and splenic arteries. PAN one of the vasculitides is commonly associated with gastrointestinal involvement.

A similar inflammatory condition associated with a mutation in the CECR1 gene causing a deficiency of adenosine deaminase 2 (DADA2) and affecting middle and small sized arteries, demonstrates central nervous system as well as gastrointestinal involvement. When gastrointestinal symptoms are present in a child with a family history of vasculitis, DADA2 should be suspected.

**Antineutrophilic Cytoplasmic Antibodies-Associated Vasculitis**

Although an uncommon complication of antineutrophilic cytoplasmic antibodies-associated vasculitis (AAV), GI involvement can herald severe complications including bowel perforations, bleeding and death. When present, GI disease coupled with AAV can affect the entire alimentary tract from esophagus to intestines.

Several studies have cited linking antineutrophilic cytoplasmic antibody types (ANCA) to presentation and severity of GI involvement; T helper 17 cells with eosinophilic granulomatosis with polyangiitis (EGPA) and Crohn’s disease. Although rare, pancreatitis may complicate AAV and should be recognized early due to potentially fatal outcomes.

Nearly half of patients with AAV were shown to have abnormal liver function tests even more so if they also had granulomatosis with polyangiitis (GPA).

**IgA Vasculitis**

Gastrointestinal symptoms seen with immunoglobulin A (IgA) vasculitis include pain, bleeding and rarely intussusception in children. These problems are episodic and typically self-limited.

A systematic review showed that a way to distinguish IgA vasculitis from Crohn’s disease was the presence of leukocytoclastic vasculitis with IgA deposition on bowel biopsy. In this review, it was also discovered that IgA involvement produced no morbidity and could be treated successfully with immunosuppressive therapy such as corticosteroids. Azathioprine may have a steroid sparing effect.

Calprotectin has emerged as a useful predictive marker for inflammatory bowel disease and studies point to fecal calprotectin levels being higher in children that have both IgA vasculitis and gastrointestinal symptoms. Fecal calprotectin as a marker for IgA vasculitis had a sensitivity of 87% and specificity of 64% and may eventually be a good screening test.

**Behcet’s Syndrome**

Innate immunity appears to have a strong role in the development of gastrointestinal disease in Behcet’s syndrome, much like in Crohn’s disease in as much as they share IL23R and IL10 susceptibility and TLR5 as a mediator of this inflammatory response.

Gastrointestinal symptoms in Behcet’s differ from Crohn’s and appear as single large deep ulcers with a propensity to bleed and perforate. Treatment consists of 5-aminosalicylic acid (5-ASA) for mild cases, azathioprine (AZA) and mycophenolate mofetil possibly with steroids for moderate and severe disease.

A contemporary multicenter study out of Japan showed that using the anti-TNF drug adalimumab helped those with refractory GI disease 40 to 60% of the time at intervals 24 and 52 weeks out.
As with IgA vasculitis, fecal calprotectin levels also correlate with GI symptoms in Behcet’s Syndrome. Behcet’s also appears to have an association with myelodysplastic syndrome with gastrointestinal disease being the link.

**Systemic Lupus Erythematosus**

Mesenteric vasculitis is a rare but known complication of systemic lupus erythematosus. A large study showed that the common presentation with regards to gastrointestinal involvement includes from most common to least: mesenteric vasculitis, pancreatitis, appendicitis, acute gastroenteritis, peritonitis, intestinal pseudo-obstruction and renal vein thrombosis.

Mesenteric vasculitis is serious and can lead to death. Cyclophosphamide improved outcomes with rituximab being a possible alternative.

### Key Points

- Gastrointestinal involvement often accompanies the common vasculitides: IgA vasculitis, antineutrophilic cytoplasmic antibodies-associated vasculitis, polyarteritis nodosa, and Behcet’s syndrome.

- Vasculitis may impact any part of the GI tract, GI vessels and GI associated solid organs.

- Presentations may include enteral inflammation, erosions and ulcers with bleeding, obstructions and or perforations.

- Symptoms are non-specific and include common GI complaints such as diarrhea, nausea and vomiting, abdominal pain, bleeding and fever.

- Diagnosis is typically made with imaging techniques since biopsies can be difficult to obtain and are often too superficial.

- Treatment varies and includes corticosteroids and immunosuppressive agents.

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