INTRODUCTION

Systemic vasculitides have been classified according to several systems, all of which derive from the system originally proposed by Zeek in 1953. In 1990 the American College of Rheumatology published consensus definitions for the various forms of systemic vasculitis known at that time. Over the next few years it became clear that serologic tests for various anticytoplasmic neutrophil antibodies (ANCAs) would be very helpful in the clear separation of these disorders, and so in 1994 the American College of Rheumatology issued revised consensus criteria taking the new data into account. In this system, which is most widely used currently, the disorders are classified according to the size and type of vessel affected, the pattern of organ dysfunction, and various serologic markers. The histologic features are also regarded as an important element, but the authors stress that a correct diagnosis cannot be assured by biopsy findings alone.

<table>
<thead>
<tr>
<th>Table 1: SYSTEMIC VASCULITIDES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Large vessel</strong></td>
</tr>
<tr>
<td>Giant cell arteritis</td>
</tr>
<tr>
<td>Takayasu arteritis</td>
</tr>
<tr>
<td>Polyarteritis rheumatica</td>
</tr>
<tr>
<td><strong>Medium vessel</strong></td>
</tr>
<tr>
<td>Polyarteritis nodosa</td>
</tr>
<tr>
<td>Kawasaki disease</td>
</tr>
<tr>
<td><strong>Small vessel – ANCA associated</strong></td>
</tr>
<tr>
<td>Wegener’s granulomatosis</td>
</tr>
<tr>
<td>Churg Strauss syndrome</td>
</tr>
<tr>
<td>Microscopic polyangiitis</td>
</tr>
<tr>
<td><strong>Small vessel</strong></td>
</tr>
<tr>
<td>Henoch-Schönlein purpura</td>
</tr>
<tr>
<td>Behçet’s syndrome</td>
</tr>
<tr>
<td>Thromboangiitis obliterans</td>
</tr>
<tr>
<td>Leukocytoclastic vasculitis</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
</tr>
</tbody>
</table>
**Gastrointestinal Involvement by Systemic Vasculitides**

Most of the primary and secondary systemic vasculitides can affect the gastrointestinal tract, although involvement by thromboangiitis obliterans, Kawasaki disease, and the large vessel diseases (Takayasu arteritis, giant cell arteritis and polymyalgia rheumatica) are exceedingly rare. (These forms of vasculitis will not be discussed further in this handout).

G.I. biopsies from patients with systemic vasculitides, even those involving small and/or medium-sized vessels, typically reveal only generic ischemic changes, since the diagnostic vascular changes are usually limited to the submucosal, subserosal or mesenteric vessels. Surgical pathologists should be aware that all vessels located within the bowel wall in any part of the G.I. tract are regarded as “small-sized” in the context of the classification of systemic vasculitides. Only the largest named branches of the mesenteric blood supply to the GI tract qualify as “medium-sized”, and polyarteritis nodosa is the likely diagnosis when vessels of this caliber are involved.

When involvement of small intramural vessels in the G.I. tract is identified histologically the primary differential (based on the likelihood of G.I. involvement – see Table 2) is between microscopic polyangiitis and Churg-Strauss syndrome, with SLE, rheumatoid arthritis and Wegener’s granulomatosis as less likely alternatives. The histologic appearance of the vasculitis in all of these conditions is very similar. The vessels (arterioles, venules and small arteries) exhibit intense inflammatory cell infiltration, often with fibrinoid necrosis of the vessel wall. Fibrin thrombi sometimes produce luminal occlusion. The presence of eosinophils as part of the vasculitic infiltrate or as an extravascular infiltrate in the surrounding tissues strongly favors a diagnosis of Churg-Strauss syndrome. In addition, extravascular granulomas occur only in Churg-Strauss syndrome and Wegener’s granulomatosis. In the absence of these features a specific diagnosis cannot be suggested, and clinical correlation is required. Henoch-Schönlein purpura, in contrast, involves only vessels of the smallest caliber (capillaries, arterioles and venules), and has a distinctive leukocytoclastic appearance. Thus, it is unlikely to be confused histologically with the other systemic vasculitides. Small vessel vasculitis involving veins and venules can also be seen in Behçet’s syndrome, but histologic features of ischemia are usually not prominent. With the exception of the demonstration of IgA in vessel walls by immuno-fluorescence techniques in Henoch-Schönlein purpura, special studies are not useful in the diagnosis of systemic vasculitides involving the G.I. tract.
Table 2

<table>
<thead>
<tr>
<th>TYPE OF VASCULITIS</th>
<th>Frequency of G.I. Involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyarteritis nodosa</td>
<td>30 – 50 %</td>
</tr>
<tr>
<td>Wegener’s granulomatosis</td>
<td>5 – 10%</td>
</tr>
<tr>
<td>Microscopic polyangiitis</td>
<td>30 – 56 %</td>
</tr>
<tr>
<td>Churg-Strauss syndrome</td>
<td>37-62 %</td>
</tr>
<tr>
<td>Behçet’s syndrome</td>
<td>Up to 30 %</td>
</tr>
<tr>
<td>Takayasu’s arteritis</td>
<td>Up to 15 %</td>
</tr>
<tr>
<td>Giant cell arteritis</td>
<td>&lt; 1 %</td>
</tr>
<tr>
<td>Henoch-Schönlein purpura</td>
<td>50 – 75 %</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>&lt; 15 %</td>
</tr>
<tr>
<td>Rheumatoid arthritis vasculitis</td>
<td>Up to 10 %</td>
</tr>
<tr>
<td>(Enterocolic lymphocytic phlebitis)</td>
<td>( &gt; 90 %)</td>
</tr>
</tbody>
</table>

Special note must be made of vasculitis isolated to the G.I. tract. In the most common form small arteries are involved, and often exhibit fibrinoid necrosis similar to that seen in polyarteritis nodosa. Evolution to systemic involvement is uncommon. In the largest series of such patients with G.I. involvement the colon, appendix, or gallbladder was most often involved. The cases were thought to represent an isolated form of polyarteritis nodosa, but data regarding ANCA status were not available at the time the paper was published. It is possible that such cases actually represent a limited form of microscopic polyangiitis, based on the size of the vessels involved. A high titer of pANCA would be confirmatory. Phlebitis limited to a G.I. organ has also been described and has been designated as “enterocolic lymphocytic phlebitis”. This entity is discussed in detail at a later point in the handout.

Antineutrophil Cytoplasmic Antibodies (ANCA)

A relationship between ANCA and systemic vasculitis was first demonstrated for Wegener’s granulomatosis. Subsequently high serum ANCA titers were also found to be common in Churg-Strauss syndrome (CSS) and microscopic polyangiitis (MPA), but not any of the other systemic vasculitides. The vasculitis in all three of these disorders is histologically identical and affects small arteries.

ANCAs (either cytoplasmic or perinuclear) are identified by mixing the patient’s serum with normal peripheral blood neutrophils and using indirect immunofluorescence to detect antibody binding. Recent studies have demonstrated that in patients with systemic vasculitides the autoantigens responsible for ANCA positivity are proteinase 3 (PR3) and myeloperoxidase (MPO), and ELISA tests have been developed to identify them specifically. A high titer of cANCA (anti-PR3+) is highly sensitive (95%) and specific (90%) for active systemic Wegener’s
granulomatosis (WG). On the other hand, a high titer of pANCA (MPO+) does not distinguish between CSS, MPA or WG, and can also be seen in rheumatoid arthritis, Goodpasture syndrome, SLE and other connective tissue diseases. Also, a negative ANCA titer does not exclude WG, MPA or CSS, and is common during remission and after immunosuppressive therapy. It appears that ANCAs are directly involved in the vasculitic process, but the pathogenic mechanisms responsible for their formation and destructive effects are not well understood at present.

**Churg-Strauss Syndrome**

In 1951 Churg and Strauss described a type of systemic vasculitis distinct from PAN in 14 patients who presented with asthma, peripheral blood eosinophilia, and fever, and coined the term allergic granulomatosis and angiitis. Histological examination of affected tissues in these patients revealed small vessel vasculitis, extravascular eosinophil infiltration, and extravascular granulomas. The Chapel Hill consensus conference defined Churg-Strauss syndrome (CSS) as an eosinophil-rich and granulomatous inflammation involving the upper respiratory tract and necrotizing vasculitis affecting small to medium-sized vessels (capillaries, venules, arterioles and arteries), associated with asthma and eosinophilia. Recommended diagnostic criteria developed by the American College of Rheumatology in 1990 (before widespread use of serologic tests for ANCA) are listed below in Table 3:

<table>
<thead>
<tr>
<th>Table 3: DIAGNOSTIC CRITERIA: CHURG-STRAUSS SYNDROME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchial Asthma</td>
</tr>
<tr>
<td>Peripheral blood eosinophil count &gt; 10%</td>
</tr>
<tr>
<td>Mono- or polyneuropathy</td>
</tr>
<tr>
<td>Non-fixed pulmonary infiltrates on chest X-ray</td>
</tr>
<tr>
<td>Chronic paranasal sinusitis</td>
</tr>
<tr>
<td>Biopsy showing small vessel vasculitis &amp; extravascular eosinophils</td>
</tr>
</tbody>
</table>

[four of six required for diagnosis]

Patients with CSS typically first manifest a prodromal phase characterized by allergic rhinitis and nasal polyposis and asthma. This phase may last for up to 30 years. Next the patients experience systemic symptoms related to eosinophilic infiltration of tissue, most often the lung, but sometimes the G.I. tract. Pulmonary involvement can raise the possibility of chronic eosinophilic pneumonia or the hypereosinophilic syndrome. Finally systemic vasculitis develops, and the diagnosis is made. Of course, these three phases do not develop sequentially in every patient (16). Nonetheless, large case series emphasize that the correct diagnosis is often not made until years after the first symptoms develop. For instance, in one report
asthma (which is present in > 95% of CSS patients) was diagnosed at a mean of 9 years prior to the diagnosis of CSS (range 0 to 61 years). Asthma developing relatively late in life (> 35 years) should raise the possibility of CSS. Peripheral neuropathy (mononeuritis multiplex) is another common manifestation of CSS, due to both eosinophilic infiltration of nerves and vasculitis involving epineural arteries. Purpura due to dermal vasculitis is also typical, occurring in about 50% of cases. Cardiac involvement, producing rapid-onset heart failure, is more common in CSS than any of the other ANCA-associated systemic vasculitides.

Laboratory evaluation is helpful in confirming the diagnosis of CSS. Peripheral blood eosinophilia (> 1,500/ml) is almost invariably present, except in patients receiving high dose steroids for their asthma. In addition, a high titer pANCA (anti-MPO) is present in about 50-75% of cases. In <10% of cases cANCA is present. Recently elevated serum levels of exotaxin-3 were reported to be a useful diagnostic test for CSS. Radiographic examinations, including angiograms, are almost always normal.

Microscopic Polyangiitis

This entity, first designated “microscopic polyarteritis”, was developed to distinguish a subgroup of patients with apparent polyarteritis nodosa (PAN) in which renal involvement was characterized by segmental necrotizing glomerulitis due to small vessel vasculitis (rather than the multifocal renal infarct that occur in classic PAN patients due to vasculitis involving larger arteries). It later became clear that it was a distinct entity unrelated to PAN, and that the involvement of small vessels (capillaries, venules and arterioles) was indeed the defining feature that separated it from PAN. In addition, a high titer pANCA, MPO+ (or cANCA) is common in microscopic polyangiitis (MPA) and is not present in PAN.

Nephrologists report most cases of MPA, and thus renal involvement (rapidly progressive glomerulonephritis) is present in virtually every patient. Necrotizing glomerulonephritis with crescent formation occurs due to involvement of glomerular capillaries. Necrotizing arteritis involving the small renal arterioles may also be present. Musculoskeletal and cutaneous involvement are also common manifestations at presentation. Peripheral neuropathy and pulmonary involvement may also occur. (A form of MPA restricted to renal involvement has also been described).

Laboratory evaluation reveals evidence of impairment or renal function. As mentioned above, high titer pANCA (65%) or cANCA (35%) is present in about 75% of patients with MPA. The pANCA is usually of anti-MPO type. Recently it was reported that the anti-MPO antibodies in patients with microscopic polyangiitis are directed specifically against heat shock proteins.
Wegener’s Granulomatosis (granulomatosis with polyangiitis)

Wegener’s granulomatosis is a well-defined primary systemic vasculitis characterized by neutrophilic rich inflammation of the upper and lower respiratory tract and necrotizing vasculitis involving small to medium-sized vessels, ultimately leading to the development of granulomas surrounding central necrotic zones (Table 4). Renal involvement in the form of necrotizing glomerulonephritis is uncommon at presentation, but eventually occurs in 75-85% of patients, and is often progressive and severe. Skin, ocular, and musculoskeletal involvement frequently develops at some point in the natural history of the disease.

Table 4: DIAGNOSTIC CRITERIA: WEGENER’S GRANULOMATOSIS

- Recurrent oro-nasal inflammation
- Fixed pulmonary infiltrates, nodules or cavities by chest X-ray
- Renal involvement (glomerulonephritis) - microhematuria
- Biopsy showing necrotizing vasculitis and (peri)vascular granulomas

[two of four required for diagnosis]

Polyarteritis Nodosa

Unlike the small vessel vasculitides (WG, CSS, MPA) constitutional symptoms (weight loss, fever, malaise) are more common and more prominent in polyarteritis nodosa (PAN). In addition, renal involvement in PAN (60-80% of cases) involves cortical ischemia due to medium-sized vessel vasculitis rather than necrotizing glomerulonephritis as occurs in the small vessel vasculitides. Visceral angiography is very useful in confirming a diagnosis of PAN. Microaneurysms and vascular stenoses in medium-sized vessels of the mesentery or renal arteries are diagnostic features for PAN and are not seen in any other of the vasculitides. Importantly, 7-22% of cases of PAN arise due to serum HBsAg antigenemia. Other viral infections (HIV, CMV, parvovirus B19, and HCV) have been reported rarely. Laboratory evaluation is not otherwise helpful in the diagnosis, except that ANCA titers are consistently negative.

In addition to the renal manifestations described above, cutaneous, musculoskeletal, peripheral nerve, and cardiac involvement are common. Involvement of the G.I. tract may be severe and dominate the clinical picture. Orchitis is a diagnostic feature of PAN, and may be a presenting symptom (Table 5).
Table 5: DIAGNOSTIC CRITERIA: POLYARTERITIS NODOSA

Weight loss > 4 kg (not related to dieting)
Livedo reticularis
Testicular pain or tenderness (orchitis)
Myalgias or weakness
Mono- or polyneuropathy
Hypertension (diastolic BP > 90 mmHg)
Elevated BUN or creatinine
Serum HBsAg antigenemia
Abnormal angiogram showing microaneurysms or occlusions
Biopsy showing active vasculitis involving medium-sized vessels

[Three of ten required for diagnosis]

Systemic Lupus Erythematosus

Systemic lupus erythematosus (SLE) is a systemic autoimmune inflammatory disease in which vasculitis sometimes occurs. The autoimmune nature of SLE is reflected by the presence of ANA and anti-dsDNA and anti-phospholipid antibodies. Gastrointestinal disease is common in SLE, but ischemia due to small vessel vasculitis (either arteritis or venulitis) is very rare. Immune complex deposition in vessel walls may be detected by immunofluorescence. Angiography is not helpful in demonstrating vasculitis in SLE. Mesenteric thrombosis due to the antiphospholipid syndrome is a more common cause of intestinal ischemia, but is also a rare manifestation.

Rheumatoid Arthritis

A small vessel vasculitis complicates the course of rheumatoid arthritis in about 20% of patients. Involvement of the gastrointestinal tract can be difficult to distinguish from drug induced injury (eg., NSAIDs). The vasculitis generally is not as intensely inflammatory as in the other systemic vasculitides.

Henoch-Schönlein Purpura

Henoch-Schönlein purpura is the most common systemic vasculitis of children. The hallmark of the disease is a non-thrombocytopenic purpura. Streptococcal
pharyngitis precedes the diagnosis in 30% of patients. Renal involvement in the form of acute glomerulonephritis is also common. Gastrointestinal involvement is also a diagnostic feature (Table 6). The vasculitis exclusively involves small vessels and is related to the deposition of immune complexes containing IgA in vessel walls. Neutrophils are evident in the vessel walls, sometimes with deposition of fibrin.

**Table 6**

<table>
<thead>
<tr>
<th>Table 6: DIAGNOSTIC CRITERIA: HENOCH-SCHÖNLEIN PURPURA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palpable purpura (not related to thrombocytopenia)</td>
</tr>
<tr>
<td>Age &lt; 20 years at presentation</td>
</tr>
<tr>
<td>Bowel ischemia (clinical, radiographic, or pathologic evidence)</td>
</tr>
<tr>
<td>Leukocytoclastic vasculitis</td>
</tr>
<tr>
<td>[Two of four required for diagnosis]</td>
</tr>
</tbody>
</table>

**Enterocolic Lymphocytic Phlebitis**

This is the only type of vasculitis limited strictly to venous channels, and in almost all reported patients has affected only a single organ, usually within the G.I. tract. Only about 100 cases have been described in the literature. Most cases involve the colon or small bowel, but localization within the stomach and duodenum, gallbladder, liver, and mesentery, have also been documented. The pathogenesis of this disorder is unknown, although several authors have raised the possibility of a drug hypersensitivity reaction. This entity has not been discussed in the rheumatologic literature and no information is available regarding ANCA status in these patients.

Histologic examination reveals intense, predominantly mononuclear cell infiltrates within the walls of small and medium-sized venous channels, with complete sparing of all arterial vessels. A perivenular infiltrate is usually also present, and granulomas are present in a minority of cases. The affected organ usually exhibits ischemic changes secondary to the venous damage.

**Behçet’s Disease**

This primary systemic vasculitis predominantly involves small veins in any organ, but oral, genital, skin, and ocular involvement are most characteristic. Presentation generally occurs in the second to fourth decade of life, but children and older adults can also be affected. The etiology of Behçet’s disease is unknown, but a genetic
component is highlighted by the narrowly restricted geographic distribution of cases (along the silk route between the Mediterranean and East Asia) and the association with the HLA-B51 locus. In other parts of the world the incidence is significantly lower (Behçet’s disease is particularly uncommon in the United States). Immunologic studies suggest an altered host immune response with aberrant T-cell responses and formation of immune complexes, but a self-antigen has not been identified to date. An ongoing search to identify an infectious agent that might be a trigger for the development of Behçet’s disease has been fruitless thus far.

Since there is no single pathognomonic clinical feature, histologic finding or laboratory test to diagnose Behçet’s disease a variety of diagnostic algorithms have been proposed. A consensus classification proposed by an International Study Group has been validated and has gained wide utilization for research studies, and also as a diagnostic tool. In this system recurrent oral ulceration (at least three episodes in a year) must be present, along with at least two of the following: recurrent genital ulcers, ocular involvement, skin lesions and a positive pathergy test. Recurrent oral aphthous ulceration, the sine qua non of Behçet’s disease, may precede other systemic manifestations by decades. Cigarette smoking may suppress mouth ulcers, and relapse after cessation of smoking has been documented (similar to ulcerative colitis). Chronic relapsing ocular involvement, which occurs in 30-70% of patients, may manifest as uveitis, retinitis, scleritis, keratitis, or posterior uveitis. Pathergy, defined as hypersensitivity of the skin following minor trauma, is common in Middle Eastern patients but rare in other patient groups. It can be demonstrating by pricking the skin with a sterile needle, and is considered present if a sterile erythematous papule develops within 48 hours.

Gastrointestinal involvement has been reported in 3 to 26% of patients with Behçet’s disease, depending on the geographic location of the population studied. In patients from Turkey and the Mediterranean G.I manifestations are rarely reported while in the Far East patients may initially present with G.I symptoms. The common clinical manifestations of gastrointestinal involvement include G.I. bleeding, abdominal pain, anorexia, weight loss, and diarrhea. In about 75% of patients G.I involvement is localized to the ileocecal region. Endoscopic examination usually reveals rounded, punched out ulcers without evidence of surrounding colitis. Ulcers are commonly deep and perforation may be the presenting symptom. Surgical resection of an ulcerated or perforated segment of bowel is often followed by recurrent ulceration near the anastomosis.

The histologic features of gastrointestinal Behçet’s disease in biopsy specimens are entirely non-specific. Ulceration in a background of normal mucosa is the most common appearance. Interestingly, histologic features of mucosal ischemia are usually not mentioned in pathologic descriptions of Behçet’s syndrome. In resection specimens the characteristic vasculitis can be appreciated. It usually involves small vessels, particularly venules, and is characterized by intramural mononuclear cell and neutrophilic infiltrates, which can result in fibrosis and luminal occlusion. In early lesions the mural infiltrate appears to be primarily neutrophilic. The vessels
involved are scattered through the submucosa and subserosal fat. The vasculitis is histologically similar to that evident in cutaneous lesions. Although a few case reports mention the presence of granulomas, this is distinctly uncommon and is not reported in other involved organs. It is possible that some case reports of Behçet’s disease with granulomas actually represent examples of Crohn’s disease from areas where Crohn’s disease is uncommonly diagnosed.
REFERENCES


Systemic Vasculitis Involving the GI Tract

John Hart, M.D.
University of Chicago Medical Center
Histologic Features of Ischemia
Acute Phase

- Detachment and necrosis of surface epithelium
- “withered” appearance of superficial mucosa
- Lamina propria hemorrhage and hyalinization
- Very little inflammation except in ulcers
- Scanty pseudomembrane formation
- Normal crypt architecture
Histologic Features of Ischemia Chronic Phase

- Fibrosis of lamina propria
- Crypt architectural distortion
- Mucosal withering
- Hemosiderin laden macrophages (+ / -)
hemosiderin laden macrophages
Endoscopic Appearance

- **Acute phase:**
  - Segments of mucosal erythema and friability, with erosions or ulcers
  - Scanty pseudomembrane formation
  - Splenic flexure is a common colonic site, but any portion of the colon can be affected
  - Can be confused with IBD or infectious process

- **Chronic phase:**
  - Indurated nodular lesions
  - Stricture formation
  - Can be confused with malignancy
Severe acute ischemic colitis
Chronic ischemic colitis with stricture
Chronic ischemic colitis with nodularity
97-10372
Causes of G.I. Ischemia

- Non-occlusive mesenteric ischemia
- Vascular occlusive disease:
  - Systemic vasculitis
  - Thrombosis
  - Embolus
  - Amyloid deposition
- Mechanical causes:
  - Median arcuate ligament syndrome
  - Volvulus and intussusception
  - Mucosal prolapse
- Mimics:
  - E coli O:157h
  - Drugs
Why some areas of the colon are prone to ischemia

The colon is protected from ischemia by a collateral blood supply via the marginal artery of Drummond, a system of arcades connecting the major arteries. The anatomy is highly variable, however, and certain areas are more vulnerable in some people.

**The splenic flexure** (Griffith’s point) is vulnerable to ischemia because the marginal artery of Drummond is occasionally tenuous here and is absent in up to 5% of patients; a 1.2–2.8 cm² area may be devoid of vasa recta.

**The right colon** may be vulnerable in systemic low-flow states, as the marginal artery of Drummond is poorly developed here in 50% of the population.

**The rectosigmoid junction** (Sudek’s point) is also vulnerable because it is distal to the last collateral connection with proximal arteries.
Ischemic colitis: affected region

G.I. Involvement by Systemic Vasculitides

• Medium vessel:
  – Polyarteritis nodosa
  – Kawasaki disease

• Small vessel – cACNA positive:
  – Wegener’s granulomatosis
  – Churg-Strauss Syndrome
  – Microscopic polyangiitis

• Small vessel – cANCA negative:
  – Henoch-Schönlein purpura
  – Systemic lupus erythematosus
  – Rheumatoid arthritis

• Venous vasculitis:
  – Behçet’s syndrome
  – Enterocolic lymphocytic phlebitis
c-ANCA

p-ANCA

Small Vessel Vasculitis

Crohn’s Disease
Aorta

Large Artery

Medium Artery

Small Artery

Arteriole

Capillary

Venule

Small Vein

Polyarteritis Nodosa, Kawasaki’s

Takayasu’s, Giant Cell Arteritis

Wegener’s, Churg-Strauss, Microscopic Polyangiitis

Henoch Schönlein Purpura, SLE

ELP, Behçet’s
vascular supply to the GI tract

Small mesenteric artery
(piercing)

Muscularis

Submucosa

Mucosa/villus

Polyarteritis Nodosa

- Constitutional symptoms
- Renal involvement (60-80%) – infarcts
- Visceral angiography
- Serum HBsAg (7-22%)
- Other viral infections (HCV, HIV, CMV)
- Serum cANCA negative
- Systemic involvement:
  - Cutaneous, musculoskeletal, cardiac, G.I.
  - Orchitis
Polyarteritis Nodosa
Ha HK et al. Radiographics 2000; 20:29-42.
ANCA - associated Systemic Vasculitides

- Churg-Strauss Syndrome
- Microscopic polyangiitis
- Wegener’s granulomatosis

- Vasculitis:
  - Small vessels
  - Fibrinoid necrosis
Churg Strauss Syndrome

- Asthma and/or sinusitis
  - 95% of patients (suspect in patients > 35 y.o.)
  - Mean of 9 yrs. prior to Dx of CSS (0 to 61 yrs)
- Peripheral blood eosinophilia (>1,500/ml)
- Pulmonary involvement
- Mononeuritis multiplex
- Cardiac involvement – more common than other ANCA positive vasculitides
- Purpura in 50% of cases
- cANCA (anti-MPO) in 50-75%
Churg Straus Syndrome
Histologic Features

- Necrotizing small vessel vasculitis
  - Focal involvement
  - Eosinophils are prominent component

- Extravascular infiltrates of eosinophils

- Extravascular granulomas
Clinical History
Case courtesy of Dr. Hong Chen, St. Mary’s Hospital, Centralia, IL

- 43-year-old male presented with an acute abdomen
- Exploratory laparotomy revealed a colonic perforation
- Ileocecectomy was performed
Additional History

• The patient had a long history of asthma and sinusitis
• WBC count at the time of surgery revealed 21% eosinophils.

Final Dx: Churg Strauss Syndrome
• 76 year old female with asthma and peripheral neuropathy
• Presents with lower G.I. bleeding
• Colonoscopy - right colonic erythema & scanty pseudomembranes
• Peripheral blood eosinophil count is elevated.
Churg- Strauss vasculitis
Microscopic Polyangiitis

- Necrotizing small vessel vasculitis
  - Capillaries, arterioles, venules
  - Distinct from polyarteritis nodosa
- Renal involvement:
  - Rapidly progressive glomerulonephritis
  - Segmental necrotizing glomerulitis with crescents
  - Occurs in > 90%; can be limited to kidney
- Musculoskeletal and cutaneous involvement
- Peripheral neuropathy
- Pulmonary involvement
- pANCA (2/3) or cANCA (1/3) in 75% of cases
Microscopic polyangiitis
Ha HK et al. Radiographics 2000; 20:779-
Localized Vasculitis of the Gastrointestinal Tract

Allen P. Burke, M.D., LtCol, USAF, Leslie H. Sobin, M.D. and Renu Virmani, M.D.

<table>
<thead>
<tr>
<th>Type of vasculitis</th>
<th>No. of cases</th>
<th>Mean age (yr)</th>
<th>Sex ratio (M:F)</th>
<th>No. of patients with follow-up (mean duration)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyarteritis</td>
<td>33</td>
<td>52.8</td>
<td>18:15</td>
<td>23 (5.8 yr)</td>
</tr>
<tr>
<td>Phlebitis</td>
<td>12</td>
<td>57.0</td>
<td>7:5</td>
<td>7 (5.5 yr)</td>
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<tr>
<td>Churg-Strauss angiitis</td>
<td>8</td>
<td>49</td>
<td>5:3</td>
<td>5 (6.0 yr)</td>
</tr>
<tr>
<td>Small-vessel vasculitis</td>
<td>6</td>
<td>48.5</td>
<td>3:3</td>
<td>5 (6.1 yr)</td>
</tr>
<tr>
<td>Buerger’s disease</td>
<td>2</td>
<td>44</td>
<td>2:0</td>
<td>1 (4 yr)</td>
</tr>
<tr>
<td>Giant-cell arteritis</td>
<td>1</td>
<td>68</td>
<td>1:0</td>
<td>1 (1 mo)</td>
</tr>
</tbody>
</table>
Necrotizing Arteritis of the Vermiform Appendix

A Clinicopathologic Study of 12 Cases

Terence N. Moyana, MD

Arch Pathol Lab Med 1988; 112:738-41.

- 12 patients; 10 female; 11–57 years old
- Incidence of 0.30% (11/3686)
- Systemic vasculitis in 3 of 9 followed a mean of 6.8 years (colonic involvement)
- Acute or recurrent RLQ pain in 6
- Acute appendicitis in 2
Henoch Schönlein Purpura

- Most common systemic vasculitis in children
- Non-thrombocytopenic palpable purpura
- Streptococcal pharyngitis in 30%
- Acute glomerulonephritis (IgA)
- Arthropathy
- Bowel ischemia is a diagnostic criterion
- Abdominal pain in 50%; G.I. bleeding in 20%
- Perforation and intussusception
- Leukocytoclastic vasculitis
10 children presenting with abdominal pain, weight loss, diarrhea
Endoscopy revealed patchy mucosal ulceration & erythema
Diagnosis: IBD (n = 5), non-specific mucosal inflammation (n = 5)
Follow-up over 2 to 24 months:
- radiographic or pathologic evidence of systemic vasculitis
- polyarteritis nodosa (n = 9), microscopic polyangiitis (n = 1)
Visceral angiography:
- important to proper diagnosis
- classic diagnostic features masked by immunosuppressive Rx
Biopsy of other organs (skin, kidney, skeletal muscle)
Enterocolic Lymphocytic Phlebitis

- More than 40 cases reported
- Colon, small bowel, gallbladder, stomach & duodenum, liver
- Acute abdominal symptoms
- Cured by resection
- ? Drug hypersensitivity reaction
- Pathologic features:
  - Lymphocytic phlebitis involving venules and veins
  - Granulomatous component in some cases
  - Complete sparing of all arteries
  - Ischemic changes are uncommon
Behçet’s Disease

- Primary systemic vasculitis involving small veins and venules
- Presentation in the 2nd to 4th decades; M > F
- Multi-system involvement:
  - Oral ulcers
  - Genital ulcers
  - Ocular lesions
  - Skin involvement
  - Gastrointestinal involvement
- Relapsing course
– Similar cases noted by Hippocrates in his *Third book of Endemic Diseases* published in the 5th century B.C.
– Single case reported by Benedict Adamantiades in 1931 in *Ann Ocul* (Paris)
Abb. 3. Aphthöse Erscheinungen im Mund und an der Lippe

Abb. 5. Aphthöse Erscheinungen auf der Zunge. Rezidive zu verschiedenen Zeiten
Clinical Manifestations

- Vary by population studied
- Relapsing oral ulceration is the *sine qua non*
- Ocular involvement in 30-70%:
  - Uveitis, retinal vasculitis, iridocyclitis, scleritis etc.
  - Leads to blindness in up to 25% of patients
- Genital ulcers (75-90%)
- Skin disease:
  - Erythema nodosa, papulopustular lesions etc.
  - Pathergy (Middle East >> Far East >> Europe & USA)
- Gastrointestinal disease (30%)
- Association with HLA-B51
Behçet’s Disease
Gastrointestinal Involvement

- G.I. bleeding, abdominal pain, anorexia
- Ileocecal region involved in 75%
- Punched out ulcers with surrounding normal mucosa
- Can cause perforation
- Recurrence common after surgical resection
- Phlebitis evident microscopically
- Ischemic changes not prominent

Behçet's Disease vs. Crohn’s Disease

- **Similar to Crohn’s disease:**
  - Any portion of G.I. tract, ileocecal ds. most common
  - Systemic manifestations; relapsing course
  - Serum ASCA titers elevated in 50%
  - Responds to anti-TNF therapy

- **Unlike Crohn’s disease:**
  - Genital and oral lesions
  - Perianal disease and fistulas very rare
  - Intestinal perforation is common
  - Vasculitis (phlebitis)
  - Granulomas very rare
  - Pathergy test positive in some populations
  - NOD2/CARD15 mutations not reported
Diagnosis of Behçet’s Disease
International Study Group Criteria

- Oral Ulceration – 3 episodes in one year
  PLUS any two of the following:
  - Recurrent genital ulceration
  - Eye disease – uveitis, retinal vasculitis
  - Skin lesions - Erythema nodosum etc.
  - Positive pathergy test

Systemic Vasculitis Involving the GI tract

- The vessels of the GI tract present in resection specimens are “small vessels” in the systemic vasculitis classification schema.

- Knowledge of the clinical history, laboratory results and radiographic findings is necessary in most cases to arrive at an exact diagnosis.

- Mucosal ischemic changes may not be prominent in some cases of GI vasculitis.