Systemic Vasculitides: Treatment Myths and Pearls

BY SHARON WORCESTER
Southeast Bureau

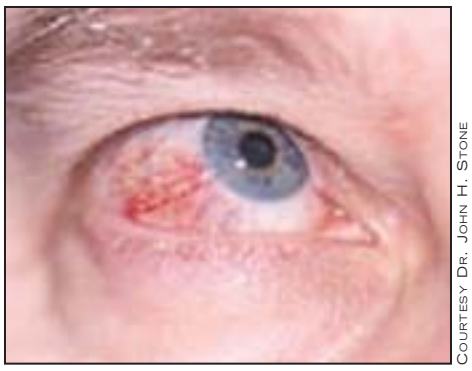
DESTIN, FLA. — Classic polyarteritis nodosa, or PAN, is curable in the majority of cases, Dr. John H. Stone said at the annual Rheumatology on the Beach.

The belief that this form of vasculitis is incurable is one of many myths about systemic vasculitides, he said, noting "classic PAN" means disease that does not include palpable purpura, glomerulonephritis, lung disease, or antineutrophil cytoplasmic antibody-positive disease.

In a study reported last year at the annual meeting of the American College of Rheumatology, two-thirds of PAN patients were cured, though that figure is likely high because patients other than those with classic PAN were included, noted Dr. Stone, a Boston-based rheumatologist and editor of Rheumatology UpToDate.

In his experience with classic PAN in the past 5 years, 17 of 21 patients were cured. Some were treated with steroids, and some were treated with steroids and cyclophosphamide; all were tapered completely off their drugs. The remaining four patients remained on low-dose steroids to control persistent skin disease, he said.

"As we understand PAN better, we are going to recognize that we can subclassify it phenotypically a bit more precisely," he said. Forms of the disease are tied to hepatitis B, there is the classic curable type, and there may be other subtypes.



COURTESY DR. JOHN H. STONE

Episcleritis often is an overlooked clue that a patient's vasculitis has flared.

To debunk another myth about systemic vasculitis, Dr. Stone described a patient with Wegener's granulomatosis who was diagnosed with rheumatoid arthritis based on the presence of arthritis and nodules on his elbows. Arthritis plus nodules does not necessarily equal RA, he said. The Churg-Strauss-type granulomas seen in this patient can be associated with Churg-Strauss syndrome, but another myth is that Churg-Strauss syndrome is the most common cause of the nodules. In fact, Wegener's granulomatosis is the most common cause, Dr. Stone explained.

Myths also exist about treatment for vasculitis. Chemotherapy with cyclophosphamide is indicated in patients with mononeuritis multiplex, central nervous system disease, rapidly progressing glomerulonephritis, mesenteric vasculitis, cardiac involvement, or alveolar hemorrhage. Nonhealing cutaneous ulcers or excessive steroid toxicity are also indications.

Data from one study, presented only in abstract form, show that intravenous cyclophosphamide treatment once every 2 weeks is as effective as oral daily cyclophosphamide but safer. However, daily oral treatment is currently the preferred approach for induction of remission. Some studies suggest oral therapy improves the chance of sustained remission. Oral cyclophosphamide can be titrated based on white cell count, another safety feature.

Patients who fail to respond to conventional daily cyclophosphamide should be considered to have an infection. Systemic vasculitis is almost always reliably controlled with conventional therapy, thus it is important to consider aspergillosis and other agents in refractory cases. Induction of neutropenia is not essential for achieving remission. The goal is to maintain white cell count above 3,500 or 4,000/mm^3. The current recommendation is that cyclophosphamide treatment be continued for 3-6 months after remission, followed by azathioprine. Errors with cyclophosphamide include failing to use it when needed, using it unnecessarily, and overdosing. The dose should be based on renal function and be lowered if function worsens. Elderly patients require half the dose, should have a biweekly complete blood count, receive steroids only in moderation, and receive pneumocystis pneumonia prophylaxis, Dr. Stone said. ■

Episcleritis Is Sign Of Vasculitis Flare

A frequent signal of disease flare in patients with systemic vasculitis is episcleritis, Dr. Stone said.

The Wegener's granulomatosis patient who was misdiagnosed with RA presented with this ocular condition—the most common ocular manifestation of systemic vasculitis—signaling renewed disease activity. The patient was having a flare but didn't realize it.

The onset of episcleritis is often overlooked. Recognizing it provides a very important clinical clue to renewed disease activity in many medium-to small-vessel vasculitides, including PAN, Wegener's granulomatosis, Churg-Strauss syndrome, microscopic polyangiitis, and rheumatoid vasculitis. The condition can also occur in the large-vessel vasculitis, Cogan's syndrome, which is characterized by a number of ocular manifestations, he noted.

Episcleritis may be striking, with bilateral redness of the eyes as was the case in this patient, or it can be more subtle and fleeting. But nonetheless, it is a harbinger of disease flare, Dr. Stone said.

Inflammatory Eye Diseases Call for Careful, Individualized Treatment to Maintain Vision

BY SARAH PRESSMAN LOVINGER
Contributing Writer

CHICAGO — Clinicians must become more aware of the prevalence and severity of inflammatory eye diseases, according to Dr. James Rosenbaum, of the Oregon Health and Science University in Portland.

"Uveitis is equal to diabetes as a cause of visual loss," said Dr. Rosenbaum at an American College of Rheumatology meeting.

Physicians may encounter several types of autoimmune uveitis in their practices. Blau syndrome, the rarest form, is an autosomal dominant disorder that causes a granulomatous uveitis and synovitis. Sometimes mistaken for sarcoidosis, it can lead to chorioretinal scarring.

Another form, tubulointerstitial nephritis and uveitis (TINU), can present with systemic symptoms of fever, myalgias, and fatigue. The sedimentation rate usually is quite high. "TINU tends to be a disease of children," said Dr. Rosenbaum. Patients respond to oral steroids. "TINU is a far more common disease than we think," he said.

In addition to uveitis, patients with systemic autoimmune disorders can present with scleritis. Dr. Rosenbaum said 40% of patients with scleritis have a systemic disease, most commonly rheumatoid arthritis (RA). Those with RA generally present with the typical features of joint pain and stiffness, and later develop scleritis. It is important to check antineutrophil cytoplasmic antibody (ANCA) levels in patients with scleritis, because the ANCA-positive form of this disease is very different from the ANCA-negative form. Some medications, including bisphosphonates, can induce a local form of scleritis, but this is rare, says Dr. Rosenbaum. Withdrawing medication generally will help to clear up this form of scleritis.

The overall treatment of scleritis depends on the severity of the disease. In the absence of infection, Dr. Rosenbaum recommends an oral nonsteroidal drug but that often is not adequate to provide symptom relief. Oral steroids then can be attempted, but some patients will require methotrexate.

As in scleritis, the treatment of uveitis is individualized. Options include topical corticosteroids, dilating drops, oral and intramuscular steroids, immunosuppressive medications, and implants. "It is such a varied disease," he said. "For some patients, drops are all that are needed."

Indications for using immunosuppressive treatment in patients with uveitis include visual limitations that interfere with daily activities, failure of oral and/or periocular steroids, and active inflammation. Immunosuppressive treatment options include antimetabolites, cyclosporine, combination medications, alkylating agents, and in some cases, biologic therapy.

Dr. Rosenbaum urges consideration before using TNF inhibitors to treat uveitis. In 31 patients treated with infliximab at the Oregon Health and Science University, the rate of severe toxicity was high. Three patients developed drug-induced lupus, two developed malignancies, two had pulmonary emboli, and one had a myocardial infarction. Fluocinolone implants represent one of the few medications approved by the FDA for the local treatment of uveitis. The implants deliver steroids continually for 30 months following implantation. Patients who get this treatment face hurdles—100% of patients develop a cataract in the treated eye, and most (70%) develop glaucoma. Of these, a high percentage will need surgery to repair the glaucoma. ■

Vessel Size Matters in Diagnosis of Vasculitis

SNOWMASS, COLO. — The most common pitfall in diagnosing vasculitides is failure to ask about the size of the involved blood vessels, Dr. John H. Stone said at a symposium sponsored by the American College of Rheumatology.

"That's really the key to sorting out these diseases clinically," said Dr. Stone, a rheumatologist at Massachusetts General Hospital in Boston.

Large-vessel diseases can be excluded because vessels larger than 150 mcm are not present in the skin and very rarely lead to cutaneous findings. Medium-size vessels (50-150 mcm) have muscular walls, and some can be visualized. Small vessels (under 50 mcm) can't be visualized.

Vasculitides can be classified by the size of involved vessels: pure small vessel, pure medium vessel, and small/medium vessel overlap, he said.

Pure small-vessel vasculitides include Henoch-Schönlein purpura, hypersensitivity vasculitis, and hypocomplementemic urticarial vasculitis. Signs include palpable and nonpalpable purpura, pustules, urticarial lesions, and blisters.

Pure medium-vessel vasculitides include polyarteritis nodosa and Buerger's disease. Medium-vessel lesions include nodules, ulcers, livedo reticularis, and digital ischemia. "Medium-size vessels, down deep in the dermis and in the fat, cause skin lesions that typically heal with scarring," said Dr. Stone.

There are two categories of small/medium vessel vasculitides: antineutrophil cytoplasmic antibody (ANCA)–associated vasculitides and cryoglobulinemia. ANCA-associated vasculitides include Wegener's granulomatosis, microscopic polyangiitis, Churg-Strauss syndrome, and drug-induced ANCA-associated vasculitis.

—Kerri Wachter