57 Systemic and Central Nervous System Vasculitides

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The vasculitides are a collection of diseases sharing the central feature of tissue injury caused by inflammation of blood vessels.[1] Although some vasculitides occur frequently, many are encountered rarely. Nonetheless, because compromise of the peripheral or central nervous system (CNS), or both, is a prominent part of these disorders, neurologists should know or be able to refer to studies on the classification, pathophysiology, treatments, and long-term complications of vasculitis.

Classification

The classification of the vasculitides is evolving.[2] There is no simple way to group the vasculitides that have neurological manifestations; however, a useful classification for discussing the diseases in relation to therapeutic approaches is given in Table 57.1. "Idiopathic systemic vasculitides" are noted for the constitutional features of systemic inflammation, a target group of affected organs, and requirement of biopsy for diagnosis. "Secondary vasculitides" are undoubtedly the largest group and most frequently encountered vasculitides. This group illustrates the wide variety and frequency of identifiable causes of vasculitis as well as the spectrum of clinical manifestations. "Focal vasculitides" are several types of vasculitis sufficiently restricted in their vascular territories or clinical presentations that they form a distinctive group. Examples are isolated angiitis of the CNS (a rare disorder characterized by recurrent inflammation of blood vessels within the dural reflections), Behçet disease (a small-vessel vasculitis encountered most frequently in the Middle East and South America), and Takayasu arteritis (a large-vessel vasculitis in which most of the neurological clinical manifestations present during the stage of scarring rather than during a stage of active inflammation). The major clinical problem in the management of isolated angiitis of the CNS is accurate diagnosis, particularly distinguishing it from the numerous infectious and neoplastic causes with similar clinical features.[15,19–21] This disorder is likely over-diagnosed and over-treated today.

Another group of disorders, "immune-mediated vasculopathies," is not truly inflammatory; thus, the term "vasculitis" would be a misnomer, but there is an immune component to the vessel damage. This is important because early recognition and therapy directed at the immune cascade likely minimize accrued damage. Increasingly, therapies to minimize disease progression in disorders, including transplant vasculopathy, systemic lupus erythematosus, cerebrovascular disease, and possibly atherosclerosis, use early anti-inflammatory or immunosuppressive agents.[22]

Pathophysiology

Inflammatory cells that bind to and pass through the blood vessel wall are a vital physiological process central to infection control and tumor surveillance functions of the immune system. The underlying sequential expression of cell surface molecules in response to proinflammatory stimuli is normally a well-regulated, self-limited process. Under various circumstances, persistent or recurrent inflammation in the blood vessel damages the structure or the function of the vessel, and tissue ischemia occurs. Multiple factors determine the susceptibility to and develop-

Table 57.1 Classification of vasculitides

Idiopathic systemic vasculitides
Wegener granulomatosis[3,4]
Churg-Strauss angiitis[5–7]
Polyarteritis nodosa[8]
Microscopic polyarteritis[9]
Temporal arteritis[10–13]
Secondary vasculitides
Hypersensitivity vasculitis
Infection-associated vasculitis
Hepatitis C
Hepatitis B
Human immunodeficiency virus
Bacterial
Aspergillus
Mucormycosis
Treponema
Drug-associated vasculitis
Neoplasia-associated vasculitis
Hodgkin disease
Connective tissue disease–associated vasculitis
Rheumatoid arthritis
Kawasaki disease[14]
Focal or restricted vasculitides
Isolated angiitis of CNS[15]
Takayasu arteritis[16,17]
Behçet disease[18]
Immune-mediated vasculopathies
Transplant vasculopathy
SLE vasculopathy

CNS, central nervous system; SLE, systemic lupus erythematosus.

ment of vasculitis. Inherited determinants increase the risk but are not themselves sufficient to induce disease. Infections are documented causes of many types of vasculitis and likely are important modulators and triggers of other cases. Defined mechanisms of vasculitis are associated with a specific agent: infection of the endothelial cells, overexpression of proinflammatory cytokines and adhesion molecules within the vessel wall, activation of monocytes, and circulating immune complexes. In other disorders, a spectrum of infections suggests a role for superantigen activation of autoreactive T and B lymphocytes.[23] Both the acute responses and the longer-term tissue responses to individual infectious agents vary considerably among patients, likely because of genetically controlled immune response factors. Tissue injury in the vasculitides ultimately results from diminished blood flow beyond the ability of other blood vessels or the tissue to adapt. Reduced blood flow accompanies inflammation and develops from 1) obstruction of the lumen by indurating inflammatory cells, 2) increased local thrombosis, and 3) vasospasm. Subsequent scarring and fibrosis of blood vessels may also cause ischemia in the chronic phase after inflammation has resolved.

Treatment

Therapy of vasculitis varies with the underlying cause and pathogenic mechanism. As therapy of individual diseases improves, two central issues that confront us are improving the accuracy of the diagnosis, including identifying any underlying infectious cause, and limiting the long-term damage both from disease and its treatment.[24] The underlying principal objectives are to remove the underlying cause of inflammation, to reduce inflammatory cells and pathogenic mediators by the method with least short- and long-term toxicity, and to restore the balance of healing within the vessel. Analysis of the efficacy and side effects of treatment regimens is difficult because 1) the natural history varies among populations of patients, 2) the rarity of many disorders complicates recruitment into randomized, controlled studies, 3) the nature of immunosuppressive therapy, both the obvious side effects and the need for dosage adjustments to achieve desired effects, confounds blinded studies, and 4) features of treatment failure resemble both the complications of therapy and the long-term manifestations of disease. Nonetheless, recent controlled studies have provided valuable information. The agents used most frequently to treat various vasculitides are listed in Table 57.2 and the treatment regimens for specific vasculitides are given in Table 57.3.

Many of the pharmacological agents used to treat immune-mediated diseases and chronic inflammation have been used to treat various diseases over the past 3 to 5 decades. Their efficacy in many diseases provides incentive to learn new ways to use these medications with greater efficacy and fewer side effects. In many studies, older agents are used in ways that restrict their action (more selective), restrict site (smaller distribution), or modify the dosage or route.

Complications of therapy for vasculitis can be divided into those that appear acutely and those that are longer term. Infection continues to be a major source of morbidity and mortality in patients with vasculitis. Recognition and treatment of infections in these patients is particularly difficult because the spectrum of potential pathogens is extensive and the clinical manifestations of infection simulate those of the underlying disease.[25–28] Osteoporosis and osteonecrosis are major problems with corticosteroid therapy; recent studies have suggested that the initial dosage rather than the duration or cumulative dosage is most culpable. The frequently encountered problems with hypertension and glucose intolerance (including frank diabetes mellitus and insulin resistance) are frequently recognized medical problems,

Table 57.2 Currently recommended medications for treatment of vasculitis

Disease/natural history	Recommended treatment	Small series
Wegener granulomatosis	Cyclophosphamide and prednisone Trimethoprime-sulfamethoxazole	Etanercept
Polyarteritis nodosa	Cyclophosphamide and prednisone	
Churg-Strauss angiitis	Cyclophosphamide and prednisone	Interferon-α
Temporal arteritis	Prednisone	Prednisone and methotrexate
Isolated angiitis of the CNS	Cyclophosphamide and prednisone	
Takayasu arteritis	Antiplatelet (?) Corticosteroid and cyclophosphamide	Mycophenolate mofetil Surgery
Behçet disease	Azathioprine Chlorambucil	Interferon-α Thalidomide Methotrexate
Secondary vasculitides		
Viral	Interferon-α, vidarabine, plasmapheresis	
Other infectious	Appropriate agent to treat underlying infection	
Kawasaki disease	Intravenous immunoglobulin, aspirin	
Toxic cause	Remove cause	

CNS, central nervous system.

Table 57.3 Current treatment regimens for specific vasculitides

Vasculitis	Regimen
Isolated angiitis of the CNS	Prednisone—40–60 mg/day orally at initiation; taper to 40 mg/day by end of first 4 weeks; taper in 5-mg increments every week to 15 mg; maintain 15 mg/day of prednisone for 6–9 months; reevaluate clinical features and taper 2.5 mg/day every 2 weeks until therapy is withdrawn Cyclophosphamide—500 mg intravenously every 3–4 weeks with 2 L of fluid for 9 months; after clinical reevaluation, cyclophosphamide dosage may be discontinued or reduced by half the dosage times for two additional treatments Alternative—prednisone as above with oral cyclophosphamide, 1–2 mg/kg daily If documented relapses occur with prednisone or cyclophosphamide regimen, therapy should be repeated with oral cyclophosphamide and prednisone for 1 year
Wegener granulomatosis	Prednisolone—on days 1–3, 0.5 g intravenously; on days 4–14, 1 mg/kg daily orally. By day 15, taper steroids with a reduction of 10 mg/week to a dosage of 30 mg/day. Then change tapering to 5 mg/week until a dosage of 15 mg/day. From there, tapering is 2.5 mg/week. Tapering is varied according to clinical features, but after 6 months the dosage of prednisolone should be 12.5 mg/day Cyclophosphamide—0.75 g/m^2 intravenously every 4 weeks *or* 2 mg/kg daily for 1 year
Hepatitis B-related polyarteritis nodosa	Plasmapheresis—3 exchanges a week for 3 weeks; then 2 exchanges a week for 2 weeks; then 1–2 times a week according to clinical situation Prednisone—1 mg/kg daily for 1 week; then taper over 1 week and stop Vidabarine—intravenously 15 mg/kg daily for 1 week; then 7.5 mg/kg daily for 2 weeks *or* Interferon-alfa-2b—3 million units a week for a maximum of 1 year Alternative Interferon-alfa-2b, 3 million units a week for a maximum of 1 year Lamivudine Prednisone, 1 mg/kg daily for 1 week
Temporal arteritis	Prednisone—60 mg/day in three divided daily doses for first week; then in single daily dose for second week; then taper by 10 mg/week until 40 mg/day. Thereafter, taper by 5 mg every 2 weeks until a dosage of 20 mg/day. The next step is taper prednisone by 2.5 mg every 2 weeks as tolerated by clinical symptoms. A lower dosage prednisone (10–15 mg/day) for 1–2 years is recommended by many but not all clinicians to minimize likelihood of relapse. Treat relapses by increasing prednisone dosage to minimal amount that controls symptoms Alternative—methotrexate, 10 mg (four 2.5-mg tablets) orally weekly for 1–2 years reduces the total cumulative amount of prednisone required for an equally effective treatment with fewer side effects

CNS, central nervous system.

occurring in 60% of patients in some series. Less acutely but equally troublesome is the burden of chronic disease, the high incidence of relapse, and the longer-term toxic effects of therapy. Glucocorticoid therapy effective in treating acute vascular inflammation may contribute to some of the long-term damage in the vessel.[29]

Pharmacological treatment

The role of antiplatelet agents (aspirin) in acute disease is not clear. With the prominent scarring and early atherosclerosis reported in long-term survivors of systemic vasculitis, maintenance with antiplatelet agents would appear useful, although long-term studies have not been done.[30] I recommend daily aspirin to patients after therapy for isolated angiitis and for various disorders involving vasculitis of the peripheral nervous system.

Nonsteroidal anti-inflammatory drugs (NSAIDs) have both anti-inflammatory and analgesic actions. They act by inhibiting the cyclooxygenase (COX) activities of prostaglandin endoperoxidase H (PGH) synthases that block the biosynthesis of prostanoids, including prostaglandins and thromboxanes.[31,32] The clinical efficacy and side effects of these medications depend on the relative potency of two isoenzymes, PGH synthase 1 (PGH_1) and 2 (PGH_2), also called COX 1 and COX 2, which are encoded by separate genes. Briefly, PGH_1 (COX 1) is constitutively expressed in all tissues; gastrointestinal tract cells particularly use PGH_1 to produce prostaglandins needed for housekeeping functions. PGH_2 (COX 2) is

produced largely in endothelial cells, fibroblasts, and macrophages in response to cytokines, growth factors, and tumor promoters. Most NSAIDs, including aspirin, indomethacin, ibuprofen, and naproxen, are more effective at inhibiting COX 1 than COX 2; this is apparent in the prominent gastrointestinal side effects. Although NSAIDs are potentially useful, their synergistic effect with corticosteroids on gastrointestinal tract disorders requires clinical judgment on their benefits early in the treatment of disease.

Selective COX-2 inhibitors are newer medications that reduce the inducible form of cyclooxygenase (COX 2), which is the major source of prostaglandin in the inflammatory response. Two agents, rofecoxib (Vioxx) and cerebrex, are selective COX-2 inhibitors and permit higher dosage of medication target at inducible enzymes with fewer side effects. Of note, COX-2 inhibitors do not affect platelet function. This is an advantage if bleeding is a potential complication. However, many physicians accustomed to using a nonsteroidal agent for its anti-inflammatory and anti-platelet actions need to remember to add a specific antiplatelet agent if needed.

Corticosteroids are small lipophilic molecules that circulate in the blood bound mainly to corticosteroid-binding globulin and albumin.[33] Free corticosteroid molecules traverse cell membranes and interact with highly conserved corticosteroid receptors that reside in the cytosol of all nucleated cells. The mobility of the molecule and the breadth of its receptor are responsible for its pleomorphic effects. Occupancy of glucocorticoid and mineralocorticoid receptors throughout the body (including the hippocampus and hypothalamus) determines the net activity of many pathways. Both inadequate and excessive (endogenous or pharmacological) levels of cortisol damage the host.

The immunomodifying and anti-inflammatory actions of corticosteroids result from several processes, including a change in traffic patterns of leukocytes that impedes leukocyte accumulation and reduces expression of proinflammatory cytokines (interleukin [IL]-1, IL-2, IL-6, interferon-γ, and tumor necrosis factor [TNF]), thus inhibiting T-cell proliferation and T-cell dependent immunity. The anti-inflammatory effects of corticosteroids are probably greatest, or at least most discernible, on macrophages, where they inhibit cytokine gene transcription, PGH_2 (COX 2)-mediated production of prostanoids, and nitric oxide synthetase, thus reducing vasodilation. Immunological effects are considered high with doses more than the equivalent of 30 mg prednisone daily; medium, with 10 to 30 mg daily, and low, with less than 10 mg daily. The rationale for very high dosages does not appear to be based on definable immunological or inflammatory effects.

Glucocorticoid preparations are numerous. Prednisone is the least expensive corticosteroid and is available in many dose sizes. It is easily absorbed and converted to prednisolone. Methylprednisolone (4 mg is equivalent to 5 mg of prednisone) has a somewhat longer half-life and is more expensive. Dexamethasone, even more expensive, has a longer half-life but does not bind to corticosteroid-binding globulin and variably crosses the blood-brain barrier. Medication is often given intravenously, although the rationale is not clear unless a patient cannot tolerate any oral intake. Corticosteroid preparations are completely and rapidly absorbed orally.

The side effects are considerable and do not necessarily correlate with the length of treatment, although there is an association with cumulative dosage. Infections are an important complication of corticosteroid therapy. Other side effects include diabetes mellitus, hypertension, cataracts, osteoporosis, and aseptic necrosis. Furthermore, corticosteroids may contribute to chronic vasculopathy through hypertension, diabetes, effects on the shuttle of fatty acids in the vessel wall, and increased distribution of β-adrenergic receptors. In disorders such as polyarteritis nodosa and systemic lupus erythematosus, prednisone therapy is strongly suspected to contribute to the development of chronic vasculopathy. Strategies to minimize the side effects of corticosteroid therapy are outlined in Table 57.4.

Cyclophosphamide is a cytotoxic alkylating agent that was introduced nearly 40 years ago for the treatment of malignancies. An antimetabolite, it causes interstrand and intrastrand DNA crosslinks that result in dysfunction of the DNA template. These intracellular biochemical reactions lead to cell death, largely through apoptotic mechanisms. Cyclophosphamide exerts its effect throughout the cell cycle, but its greatest action is during cell division. The effect of cyclophosphamide on clonal expansion of lymphocytes is the basis of its use in immune-mediated disorders. Although the rapidity of its effect in some vasculitides suggests that it has an additional effect, possibly on endothelial cells, this has not been investigated.

Cyclophosphamide therapy improves morbidity and mortality in several of the vasculitides. It usually is administered in association with corticosteroids and is effective in the vasculitis of rheumatoid arthritis, Wegener granulomatosis, polyarteritis nodosa, isolated angiitis of the CNS, and in autoimmune processes without a central vasculitis, such as neuropsychiatric systemic lupus erythematosus. According to a recent report, cyclophosphamide alone was successful in the treatment of isolated angiitis of the CNS and amyloidosis.[37]

Patients usually tolerate cyclophosphamide well, but it must be administered with scrupulous attention to hydration (> 2 L daily) to avoid hemorrhagic cystitis and potential bladder malignancies. In some patients, prominent nausea develops and requires antiemetic therapy. Infrequently, allergic reactions, teratogenicity, and carcinogenicity (0.1% to 1% with long-term use) occur. Rarely, are cardiac, pulmonary, or liver disorders or the syndrome of inappropriate antidiuretic hormone encountered. For the dosages used to treat vasculitis (smaller than those used to treat cancer), the major side effects include infection, nausea, gonadal failure, and hemorrhagic cystitis.[38]

Table 57.4 Strategies to minimize side effects of corticosteroid and cyclophosphamide therapy

Agent	Side effect	Strategy
Corticosteroids	Infection	Vigilance for infections, including blood cultures for patients with fevers or "failure to thrive"
	Osteoporosis[34]	Calcium, 1500 mg/day Vitamin D, 400–800 IU/day Exercise Check for hypogonadism—if present, hormone replacement therapy, annual bone scans, add antiresorptive therapy if > 2% bone loss in a year
	Hypertension	Frequent office and home monitoring Treat elevations promptly
	Diabetes mellitus, glucose intolerance	Monitor fasting glucose level Appropriate high protein, low carbohydrate diet with onset of therapy
	Suppression of hypothalamic-pituitary-adrenal axis	After discontinuing medication, patients need to carry identification that they have been adrenally suppressed and need to receive a stress dose of medication in the event of emergency
Cyclophosphamide	Infection[35]	Vigilance for infections, maintain blood neutrophil count > 1.5×10^9/L
	Nausea	Antiemetic medication, alizapride or ondansetron
	Hemorrhagic cystitis	Fluid intake > 2 L/day, monitor urine for red blood cells and specific gravity
	Gonadal toxicity[36]	Amenorrhea may occur in 20%–30% of women Teratogenicity is difficult to quantitate but patients should be aware of risks

Strategies to minimize the side effects of cyclophosphamide therapy are outlined in Table 57.4.

Combination therapy with cyclophosphamide and prednisone

The systemic vasculitides, including Wegener granulomatosis, Churg-Strauss angiitis, microscopic polyarteritis, and polyarteritis nodosa, as well as systemic vasculitis complicating rheumatoid arthritis and isolated angiitis usually are treated successfully with a combination of cyclophosphamide and a glucocorticoid agent. With the reduction in disease mortality comes the newer questions: how can disease morbidity and morbidity from the medications be reduced and how can the relapse rate be decreased? Several prospective randomized trials have investigated the treatment of systemic vasculitis with several dosages and routes of cyclophosphamide. It is difficult to compare these studies because they did not measure the same outcomes or agree on the escalation therapy for treatment failures. In one review comparing induction of remission, frequency of remission, number of relapses, and complications of therapy (particularly infection, bladder-related side effects, and malignancies), the Vasculitis Group at Birmingham U.K. found that pulse cyclophosphamide-prednisolone was slightly less effective but less toxic than a continuous oral regimen of prednisolone and cyclophosphamide (with the latter replaced after 3 months with azathioprine). More recent studies have tried to distinguish between patients with a better prognosis who can receive shorter or intermittent therapy and patients at higher risk for early death who should receive more aggressive therapy.[39–46]

Methotrexate is a potent folate antagonist that has been used successfully to treat rheumatoid arthritis and psoriasis. It has been investigated recently for the treatment of Takayasu arteritis, Wegener granulomatosis, and neuropsychiatric Behçet disease.[47,48]

Chlorambucil is a cell-cycle nonspecific agent from the alkylating class of anticancer drugs. Among the vasculitides, it may be useful for Behçet disease. Short-term therapy with high-dose chlorambucil was given to five patients who had intractable sympathetic ophthalmia and to six patients who had severe Behçet disease. The total cumulative doses ranged from 306 mg to 4.2 g, with duration of therapy no longer than 36 weeks (most patients were treated for fewer than 24 weeks).[49] Adverse effects include myelosuppression that may result in leukopenia and thrombocytopenia. Hepatotoxicity, pulmonary fibrosis, bronchopulmonary dysplasia, sterility, peripheral neuropathy, seizures, and acute pneumonitis have also been described.

Newer pharmacological agents for vasculitis

Mycophenolate mofetil is the morpholinoethyl ester prodrug of mycophenolic acid, an immunosuppressant drug that acts by impairing de novo purine synthesis. This drug is relatively selective for lymphocytes and inhibits antibody production by B cells more than other immunosuppressants do. Recently, the U.S. Food and Drug Administration approved the use of mycophenolate mofetil for the prevention of rejection in renal transplantation. Success has been reported with this medication in the maintenance phase of systemic vasculitis after traditional induction with cyclophosphamide and pred-

nisone and in Takayasu arteritis. If the low side effect profile continues, mycophenolate mofetil may decrease the long-term morbidity of traditional vasculitis therapies.[50,51]

Thalidomide appears to have a specific inhibitory activity on the production of TNF-α. Its usefulness is being reevaluated because recent studies have indicated it is effective in erythema nodosa leprosum, acquired immunodeficiency syndrome, graft-versus-host disease, and Behçet disease. Side effects include peripheral neuropathy, drowsiness and somnolence, orthostatic hypotension, and teratogenicity.[52,53]

Biological modifiers

Biological modifiers encompass monoclonal antibodies, cytokines, receptor antagonists, gene promotors, and other agents almost invariably cloned, sequenced, and synthesized that diminish or enhance biological pathways.[54] As a group, a major attraction is their use of natural pathways and their ability to target focused aspects of an immune response. Limitations to their use, at least for chronic diseases, is their short effect times and the frequent development of host antibodies, which limit their efficacy when used repeatedly.

As a class, interferons possess antitumor, antiviral, and immunomodulating activity. They are species-restricted and receptor-dependent, and they must bind to specific cell-surface receptors to be active. Interferon-α is a primary therapeutic agent in the treatment of viral vasculitis, specifically that associated with hepatitis B viremia.[55,56] Success has been reported with its use in Churg-Strauss angiitis and Behçet disease.[57,58] Of note, interferon-α has been suspected to either induce or exacerbate vasculitis.[59] Characteristic side effects of alpha interferons are flulike symptoms and gastrointestinal disturbances, but alopecia, neutropenia, thrombocytopenia, and increases in liver enzyme levels also occur. In addition, the neurological, psychiatric, and autoimmune side effects of interferon-α therapy may be considerable.[60,61]

Agents that interfere with activity of tumor necrosis factor-α

TNF promotes inflammation by binding to receptors on various cells and stimulating them to release a host of other inflammatory mediators. Soluble TNF receptors are cleaved from the membrane portion of the cell complex and appear to function as a natural counterbalance to TNF.

Etanercept is an expressed protein containing two chains of a soluble TNF receptor linked by the Fc portion of an immunoglobulin molecule (soluble TNF receptor [p75]:Fc fusion protein [TNFR:Fc]). The molecule functions by absorbing excess circulating TNF and keeping it from binding to its natural receptor. Several studies have indicated its efficacy and safety in patients with rheumatoid arthritis and Wegener granulomatosis.[62]

Infliximab is a chimeric (part-mouse, part-human) monoclonal antibody to TNF. It, too, reduces inflammation and is currently indicated for treatment of Crohn disease. An issue with monoclonal antibodies as therapy is the development of antibodies to the monoclonal antibody that may reduce the efficacy of the medication.

Gene therapy

Currently, several strategies of gene therapy are used to treat vascular disease. Most promising is the potential of diminishing chronic changes associated with proliferative responses in the vessel wall.[63,64]

Interventional procedures and maneuvers

Plasmapheresis may be effective therapy for vasculitis when circulating autoantibodies or immune complexes contribute to the pathogenesis of the vasculitis. It is most effective in essential mixed cryoglobulinemia but may be useful in Kawasaki disease. A controlled study that compared glucocorticoids alone with glucocorticoids and plasmapheresis did not demonstrate improved short-term or long-term outcome in patients with polyarteritis nodosa or Churg-Strauss angiitis. Except for patients with refractory systemic vasculitis, plasmapheresis is not recommended for routine or initial treatment. Both the complications of central venous access and the high cost limit its use. Its main side effects are hypotension and occasional clotting abnormalities.

Intravenous immunoglobulin is the treatment of choice for Kawasaki disease.[65] It is variably effective in treating systemic vasculitis, although no controlled studies have been performed. Its side effects include fever, chills, hypotension, nausea, abdominal pain, headache, dizziness, and rarely anaphylaxis.

Surgery

Currently, the only vasculitis for which surgical treatment is beneficial is Takayasu arteritis. Because the CNS manifestations result from obliterative and hypertensive vascular changes occurring during the fibrotic stage of the disease, bypass procedures have occasionally proved beneficial.[66,67]

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