ARTERITIS

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Introduction and Definition of Arteritis

Arteritis is formally defined as the inflammation of the walls of one or more arteries. This condition represents a significant subset of the broader category known as vasculitis, which encompasses inflammatory processes affecting any type of blood vessel, including veins (phlebitis) and capillaries. Arteritis is fundamentally a systemic disorder, meaning the inflammatory response, though localized to the vessel wall, can affect nutrient and oxygen supply to any organ system in the body, leading to potentially severe ischemic complications. The precise manifestation of arteritis is determined by the size and location of the affected arteries, which can range from large conduits like the aorta to medium-sized distributing arteries and the smallest arterioles. Understanding arteritis requires recognizing its potential to cause vascular wall damage, often resulting in luminal narrowing (stenosis), occlusion, or, conversely, aneurysm formation due to weakening of the vessel structure.

The inflammatory cascade inherent in arteritis typically involves infiltration of the arterial wall by immune cells, including lymphocytes, macrophages, and sometimes neutrophils, leading to the destruction of normal vascular architecture. This disruption is particularly critical in the tunica media, the smooth muscle layer responsible for maintaining vascular tone and integrity. The resulting proliferation of the intima layer, often in response to chronic injury, narrows the vessel lumen, thereby restricting blood flow. Because the tissues supplied by these inflamed arteries are starved of blood, the clinical consequence of arteritis is frequently ischemia, infarction, or necrosis in distal organs. Early and accurate diagnosis of arteritis is paramount, as delayed treatment can lead to irreversible damage, particularly concerning conditions affecting the cerebral or ocular circulation.

Arteritis can be classified as either primary, where the inflammation is the main disease process (e.g., Giant Cell Arteritis), or secondary, where arterial inflammation occurs as a manifestation of another underlying systemic disease, such as certain connective tissue disorders like systemic lupus erythematosus or rheumatoid arthritis. The nomenclature often reflects the primary anatomical site or the characteristic pathological features observed upon biopsy. For instance, the involvement of major arteries suggests large-vessel arteritis, while involvement of smaller, muscular vessels defines medium-vessel arteritis. The classification system is complex but crucial for determining appropriate therapeutic intervention, which often hinges upon the aggressive use of immunosuppressive agents to halt the ongoing destructive inflammation.

Classification and Primary Forms of Arteritis

The classification of arteritis is primarily based on the predominant size of the blood vessels affected, a system standardized by organizations such as the Chapel Hill Consensus Conference. Large-vessel arteritis (LVA) primarily affects the aorta and its major branches, exemplified by **Giant**

Cell Arteritis (GCA) and Takayasu Arteritis (TA). GCA, the focus of much arteritis research due to its commonality in the elderly, preferentially targets the arteries originating from the aortic arch, particularly those supplying the head and neck, such as the temporal and ophthalmic arteries. TA, conversely, typically affects younger individuals, particularly women of Asian descent, often resulting in pulseless disease due to severe stenosis in the subclavian and aortic arch vessels.

Medium-vessel arteritis (MVA) involves the main visceral arteries and their branches, which penetrate the organs. A classic example is **Polyarteritis Nodosa (PAN)**, a necrotizing vasculitis that historically targeted arteries of the kidney, gastrointestinal tract, and nervous system, often sparing the pulmonary circulation. The term "panarteritis," referenced in early descriptions, refers to the inflammation extending through all layers (pan-) of the arterial wall, which is characteristic of PAN. Unlike GCA, PAN typically does not involve granulomatous inflammation and is not strongly associated with anti-neutrophil cytoplasmic antibodies (ANCA). Another prominent MVA is Kawasaki disease, primarily affecting pediatric populations, where coronary artery involvement is a significant risk factor for long-term morbidity.

Small-vessel arteritis (SVA) involves arterioles, capillaries, and venules, often presenting with cutaneous manifestations like palpable purpura. This category largely overlaps with ANCA-associated vasculitis (AAV), including Granulomatosis with Polyangiitis (GPA, formerly Wegener's) and Microscopic Polyangiitis (MPA). While these conditions are often referred to as vasculitis, they involve inflammatory damage to the smallest arteries and are distinct in their pathogenesis, frequently characterized by the presence of autoantibodies targeting neutrophil components. The distinction across these classifications is essential because the clinical spectrum, prognosis, and initial therapeutic approaches differ markedly depending on the vessel size involved.

Focus on Temporal (Giant Cell) Arteritis (GCA)

Temporal Arteritis, also known as Giant Cell Arteritis (GCA) or Horton's disease, stands out as the most common form of primary systemic vasculitis affecting adults globally. It is classified as a chronic, granulomatous inflammation predominantly affecting medium and large arteries. The disease has a striking epidemiological profile, almost exclusively affecting individuals over the age of 50, with peak incidence occurring in the seventh and eighth decades of life. Furthermore, individuals of Northern European descent, particularly Scandinavian populations, exhibit the highest rates. GCA rarely occurs in younger patients, and its prevalence increases sharply with age, suggesting a complex interplay between immunosenescence and genetic predisposition.

The anatomical predilection of GCA is centered on the branches of the **carotid arterial system**, particularly the external carotid artery branches, including the superficial temporal, occipital, and facial arteries. Crucially, the ophthalmic artery, a branch of the internal carotid artery, is also frequently involved. Inflammation in the temporal artery is often palpable, presenting as

tenderness, nodularity, or decreased pulsation. The inflammation within the vessel wall is segmental, meaning areas of disease are interspersed with normal segments, a feature that significantly complicates diagnostic procedures such as biopsy. Because GCA is systemic, inflammation is not restricted to the head; large arteries like the aorta and its major branches can also be affected, leading to potential complications such as aortic aneurysm or dissection many years after the initial diagnosis.

GCA often coexists with or is preceded by **Polymyalgia Rheumatica (PMR)**, an inflammatory disorder characterized by aching and stiffness, particularly in the shoulders and hips. Approximately 15 to 20 percent of PMR patients eventually develop GCA, and conversely, 40 to 60 percent of GCA patients also experience symptoms of PMR. This strong association suggests a shared underlying immunopathogenesis. Recognizing PMR symptoms in an older patient is critical, as it raises the index of suspicion for impending or concurrent GCA, necessitating vigilant monitoring for classical signs of vascular inflammation, especially the onset of headaches or visual symptoms.

Pathophysiology and Histological Markers

The pathogenesis of GCA is complex, involving an autoimmune response directed against components of the arterial wall, though the specific initiating antigen remains elusive. Current understanding suggests a robust T-cell mediated inflammatory process. Dendritic cells within the arterial wall capture unknown antigens and present them to T-lymphocytes, leading to the activation and proliferation of CD4+ T helper cells. These activated T cells migrate into the layers of the arterial wall, primarily the adventitia and the media-intima border, releasing large quantities of pro-inflammatory cytokines, notably Interleukin-6 (IL-6) and Interferon-gamma (IFN-γ). These cytokines drive the systemic symptoms (fever, malaise) and recruit macrophages, which fuse together to form the pathognomonic cellular structures.

The defining histological characteristic of GCA is the presence of a granulomatous inflammatory infiltrate within the arterial wall. This infiltrate includes epithelioid cells and the characteristic large, **giant, multinucleate cells**, which are fused macrophages. These giant cells are typically found near the fragmented internal elastic lamina, suggesting that the elastic layer may be the target of the inflammatory attack. The inflammation leads to severe disruption and fragmentation of the internal elastic membrane, followed by intimal hyperplasia--the proliferation and thickening of the innermost layer of the artery. This proliferation acts to dramatically narrow the lumen of the artery, impeding blood flow.

The consequence of this intimal proliferation and subsequent luminal stenosis is a critical reduction in blood supply, leading to ischemia in the tissues supplied by the affected vessel. For example, inflammation of the temporal artery causes local symptoms like headaches and tenderness, but the

most devastating complication arises from the occlusion of the ophthalmic artery. When the ophthalmic artery becomes ischemic due to inflammation and narrowing, it causes ischemia of the optic nerve head, known as anterior ischemic optic neuropathy (AION). This process is rapid and often irreversible, underscoring why GCA represents a medical emergency requiring immediate high-dose immunosuppression to prevent permanent visual impairment.

Clinical Presentation and Symptomology

The clinical presentation of GCA is highly variable, but certain symptoms are classic and demand immediate attention. The most common presenting symptom is a severe, new-onset headache, usually localized to the temporal or occipital area, and often described as boring or throbbing. Unlike typical tension headaches or migraines, GCA headaches are often refractory to standard analgesics and may be unilateral or, frequently, **bilateral in the temporal area**. Palpation of the superficial temporal artery may reveal tenderness, thickening, or nodularity, and in advanced cases, the pulse may be diminished or absent due to severe luminal occlusion.

Beyond the headache, systemic features are prominent and reflect the high level of circulating inflammatory cytokines. Patients often present with constitutional symptoms such as unexplained fever, profound fatigue, night sweats, and unintentional weight loss, which can sometimes precede the vascular symptoms by several weeks or months. A specific symptom strongly suggestive of GCA is **jaw claudication**, characterized by pain, aching, or fatigue in the jaw muscles or tongue upon chewing or prolonged talking, which is relieved by rest. This symptom arises from ischemia of the muscles of mastication supplied by branches of the external carotid artery.

The most urgent and feared complication of GCA involves the ocular system. Visual disturbances are a critical sign of impending or established ischemia of the optic nerve. Patients may report transient monocular vision loss (amaurosis fugax), often described as a curtain coming down over the eye. If treatment is not initiated immediately, the inflammation can lead to irreversible ischemic damage, resulting in permanent vision loss, most commonly **loss of sight in one eye**. This vision loss is typically sudden, painless, and represents an ocular emergency. Less common, but still serious, symptoms include involvement of the large arteries leading to upper limb claudication, or neurological symptoms such as stroke or transient ischemic attacks, although these are less frequent than ocular complications.

Diagnostic Procedures and Imaging

The diagnosis of GCA relies on a combination of clinical presentation, laboratory findings, and definitive tissue confirmation. Laboratory tests typically reveal markedly elevated levels of acute phase reactants. The **Erythrocyte Sedimentation Rate (ESR)** is often extremely high, frequently exceeding 50 mm/h and sometimes reaching over 100 mm/h. Similarly, C-Reactive Protein (CRP)

levels are usually significantly elevated. While these markers indicate systemic inflammation, they are non-specific; however, a normal ESR or CRP in a patient with suspected GCA should prompt careful re-evaluation, although it does not entirely rule out the disease. Mild to moderate normochromic anemia and thrombocytosis are also common findings.

The gold standard for confirming the diagnosis remains the **Temporal Artery Biopsy (TAB)**. Given the segmental nature of the inflammation (skip lesions), a sufficient length of the artery (ideally 1.5 to 2.5 cm) must be excised to maximize diagnostic yield. Histopathological examination confirms the presence of the characteristic transmural inflammation, often granulomatous, containing giant cells and fragmentation of the internal elastic lamina. Importantly, high-dose corticosteroid therapy must be initiated immediately upon strong clinical suspicion, especially if visual symptoms are present, without waiting for the biopsy procedure or results, as delay can cause irreversible blindness. The biopsy remains diagnostic even if performed within two weeks of starting steroid therapy, although the inflammatory findings may be attenuated.

In recent years, non-invasive imaging techniques have played an increasing role in diagnosis, particularly in cases where the biopsy is negative or impractical. High-resolution color Doppler ultrasonography of the temporal arteries is highly useful, often revealing the characteristic "halo sign," which represents the edema and thickening of the arterial wall. Magnetic Resonance Angiography (MRA) and Positron Emission Tomography (PET) scanning are employed to assess involvement of the large arteries, such as the aorta and subclavian vessels, which often occurs silently. PET scanning, in particular, can detect increased metabolic activity indicative of active inflammation in the walls of the great vessels, aiding in the diagnosis of large-vessel vasculitis components of GCA.

Management and Therapeutic Strategies

The management of GCA is centered on the rapid suppression of inflammation to prevent irreversible ischemic complications, particularly vision loss. Due to the urgent nature of the disease, treatment must be initiated immediately upon clinical suspicion. The cornerstone of therapy involves high-dose corticosteroids. If vision is threatened or symptoms are severe, intravenous methylprednisolone is often administered for three days before transitioning to high-dose oral prednisone (typically 40 to 60 mg/day). This aggressive initial dosing is maintained until symptoms resolve and acute phase reactants normalize.

Following initial disease control, the challenge shifts to long-term management and preventing relapse while minimizing the severe side effects associated with prolonged high-dose glucocorticoid use. The corticosteroid dose is gradually tapered over many months, often 1 to 2 years, based on clinical status and monitoring of ESR and CRP. Relapse is common during tapering and necessitates a return to a higher dose. Prophylactic measures against corticosteroid

side effects, such as calcium and Vitamin D supplementation, bisphosphonates for osteoporosis prevention, and gastric protection, are crucial components of the care plan.

In recent years, steroid-sparing agents and biologic therapies have emerged to manage refractory cases or to reduce cumulative steroid exposure. Methotrexate has been used, though its efficacy is modest. More significantly, Interleukin-6 (IL-6) inhibition has revolutionized treatment. Tocilizumab, a monoclonal antibody targeting the IL-6 receptor, has demonstrated efficacy in maintaining remission and allowing for more rapid and sustained steroid tapering, significantly improving long-term outcomes for many patients with GCA. Ongoing research continues to explore other targeted immunosuppressants to further refine the therapeutic strategies for this chronic inflammatory condition.

Related Conditions and Differential Diagnosis

Arteritis must be distinguished from various other conditions that present with similar systemic or localized inflammatory symptoms. The primary distinction is made against other forms of vasculitis. For instance, Takayasu Arteritis, while also a large-vessel vasculitis, typically affects individuals under 40 and often presents with symptoms related to limb ischemia rather than the severe headaches and ocular involvement characteristic of GCA. Furthermore, the inflammatory pattern differs histologically.

The differentiation from **Polyarteritis Nodosa (PAN)** is also essential, especially considering the historical overlap implied by the term "panarteritis." While PAN also involves medium-sized arteries, it typically presents with microaneurysms, livedo reticularis, mononeuritis multiplex, and renal involvement (sparing the glomeruli). Unlike GCA, PAN is a necrotizing vasculitis without granuloma formation and is not associated with the classic systemic findings of GCA in the elderly population. The presence or absence of the giant, multinucleate cells is a key differentiator between GCA and PAN.

Finally, GCA must be differentiated from non-inflammatory causes of headache and visual loss. Severe headaches, especially in the temporal area, can be symptoms of structural brain lesions, complicated migraines, or trigeminal neuralgia. Acute visual loss can result from central retinal artery occlusion (CRVO), glaucoma, or non-arteritic anterior ischemic optic neuropathy (NA-AION). The presence of systemic inflammatory markers (elevated ESR/CRP), jaw claudication, and temporal artery tenderness are the crucial clinical features that guide the physician toward an immediate diagnosis of GCA, necessitating rapid initiation of life-saving steroid therapy.