VASCULAR ARTERITIS

The vast majority of arterial vascular disease encountered in the world is the result of atherosclerosis. The remaining causes of arterial vascular disease, comprising about 20%, is made up of a combination of atypical diseases including inflammatory, congenital and acquired. Presenting symptoms of patients with these non-atherosclerotic diseases can be very similar to symptoms of patients with atherosclerosis which leads to confusion for the clinician. The term, vascular arteritis, is applied to several inflammatory diseases of the blood vessels. Symptoms are dependent on the specific vessels involved. Claudication and rest pain can be present when peripheral arteries are affected as well as those symptoms observed with cerebral ischemia such as vertigo and diplopia. The majority of arteritis patients vary from the average atherosclerotic patient by age and risk factors thus an accurate patient history is crucial to aid the diagnosis.

The etiology of arteritis in unknown in many cases but is thought to be immunologic in nature. Vessels with high concentrations of elastic tissue seem to be affected. Arteritis is an inflammatory process in which the media of the cell wall is infiltrated by various inflammatory white blood cells. The elastic and smooth muscular components erode and fibrosis develops. The result of this process is weakening of the blood vessels in addition to necrosis of the vessel walls.

Confirmation of the presence of arteritis utilizes various diagnostic techniques depending on the specific area affected. Blood tests
for various inflammatory markers, noninvasive vascular testing modalities, angiography and tissue biopsy all can be employed. Treatment and outcome are contingent upon the specific type of arteritis and the stage it is in when diagnosed.

Classification of arteritis is made by vessel size, microscopic features of the tissue reaction, or clinical features. A classification scheme for vascular arteritis based on vessel size is illustrated in Table 1.

Table 1.

Classification of Vascular Arteritis

Large Arteries:

Giant Cell Arteritis

Takayasu’s arteritis

Medium-sized Arteries:

Buerger’s Disease (Thromboangiitis obliterans)

Polyarteritis nodosa

Kawasaki’s disease

Behcet’s disease

Small-sized Arteries:

Wegener’s granulomatosis

Microscopic polyangiitis

Churg-Strauss Syndrome

Henoch-Schonlein purpura
Cryoglobulinemic vasculitis
The three most common types of arteritis that may be encountered during a vascular evaluation are: Takayasu's arteritis, Buerger's Disease (Thromboangiitis obliterans) and Giant Cell Arteritis (temporal arteritis). The following sections will describe each of these in more detail.

TAKAYASU'S ARTERITIS

Mikoto Takayasu, an ophthalmologist, reported in 1908 on some unusual ocular changes in a 21 year old female Japanese patient. He described a wreath-like appearance of blood vessels within the eye. These blood vessels were actually new vessel growth in response to arterial ischemia. Subsequently, other physicians provided accounts of similar manifestations with the addition of absent pulses in the upper extremities.
Takayasu's arteritis mainly affects the aortic arch and its large branches. The subclavian, renal and carotid arteries can also be involved. The involvement of the subclavian arteries occurs in 91-100% of cases examined while the common carotid arteries are involved in 58-60% of patients. Although bilateral common carotid artery involvement is generally observed, the left common carotid is typically more severely affected than the right. Its etiology is thought to include infection and autoimmune phenomena. It is known that an inflammatory process involving all three layers of the vessel occurs. This inflammatory process can either partially obstruct or completely occlude the vessels involved. The vessel walls may become weakened. This weakening can lead to fusiform or saccular aneurysm formations.
The incidence of Takayasu's arteritis is most common is Southeast Asia but also appears to be more frequently found in Mexico and India. It has been reported in all parts of the world and in all racial groups. The worldwide incidence of the disease is 2.6 cases per million individuals. It is eight times more prevalent in women then men. The vast majority of patients are under 40 years of age and less than 15% of the cases present in patients older than 40 years.
Takayasu's arteritis is usually divided into two stages: an early stage (prepulseless) and a late stage (pulseless). The early stage is characterized as a period systemic inflammation where patients may present with fatigue, malaise, weight loss and fever. Time of progression to the development of arterial lesions varies from the onset of these vague symptoms. The late stage is defined as the pulseless stage or vascular inflammatory stage where arterial stenoses and aneurysms can be observed. The majority of patients present for a vascular evaluation during the pulseless stage when one or more peripheral pulses may be absent. Symptoms during this late phase are reflective of the extremity or organ involved. Lightheadedness or vertigo is common in patients when the carotid or vertebral circulations are involved. Other symptoms for these patients may include amaurosis fugax, transient ischemic attacks, hemiparesis and diplopia. When the subclavian arteries are involved the presence of upper extremity claudication can occur in approximately 60% of the cases. The main finding in this group of patients is an absent upper extremity pulse or a brachial blood pressure difference greater than 30 mmHg.
Others have chosen to further distribute Takayasu's into four different categories based on location and vessels involved. These are noted in Table 2.

CLASSIFICATION OF TAKAYASU'S ARTERITIS

Type 1
Involving only the ascending aorta and its branches
Type 2
Involving the descending and abdominal aorta and its branches. (also called coarctation of aorta)

Type 3
Manifesting types one and two
Type 4
Involving all vessels in types one and two and pulmonary artery disease
The diagnosis of Takayasu's Arteritis will typically include evaluation for abnormal erythrocyte sedimentation rate and C-reactive protein concentration which are seen in the presence of an inflammatory process. A biopsy can unequivocally confirm the presence of Takayasu's arteritis. In most patients without a plan for surgical repair, biopsies are rarely done. Angiography can be used to examine the anatomy of the great vessels and the area reduction of the vessel lumen. Ultrasound is often used to provide hemodynamic information as to the significance of a stenosis as well as the location and extent of disease. A limitation of ultrasound in the diagnosis of
Takayasu's Arteritis is its inability to adequately visualize the aortic arch and the origin of many of its branches.
Figure 1 is an ultrasound image of a common carotid artery in a patient with Takayasu's arteritis. The color lumen is noticeably reduced in the proximal portion of the artery. The grey-scale ultrasound finding characteristically displays a homogeneous wall thickening (indicated at white arrows) which is concentric around the vessel walls. This is very different from the asymmetrical plaque patterns observed with atherosclerotic disease.

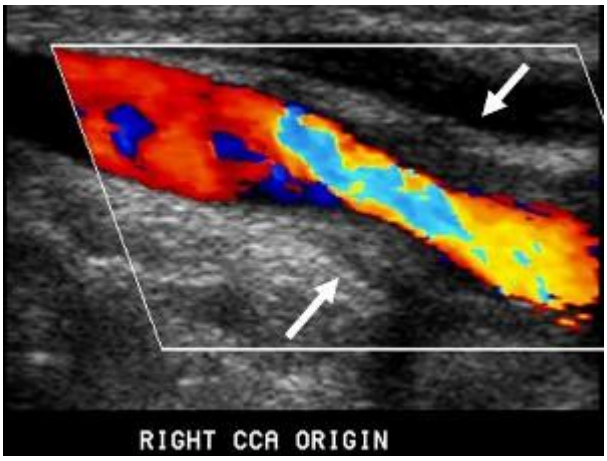

Figure 1. An ultrasound image of a common carotid
artery in a patient with Takayasu's Arteritis.
Color flow imaging demonstrates aliasing in area of lumen
reduction. White arrows point to homogeneous wall thickening.

In this patient the peak systolic velocity (PSV) at the level of narrowing is increased to 302 cm/s (Figure 2).

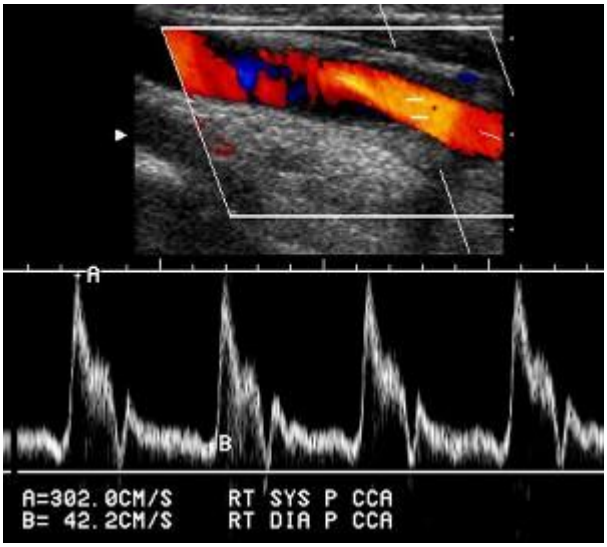

Figure 2. An increased PSV of 302 cm/s at area of narrowing produced by arteritis.

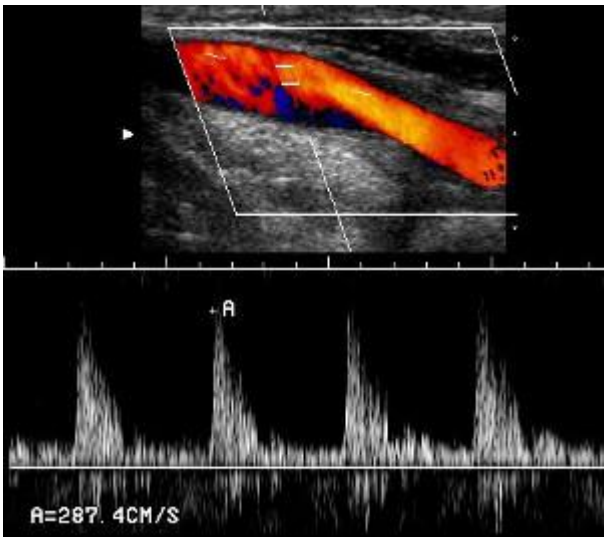

Figure 3. The distal common carotid area demonstrating post-stenotic turbulence with a PSV of 207 cm/s

Just distal to the stenosis, post-stenotic turbulence is clearly evident in the Doppler spectrum with a PSV of 207 cm/s (Figure 3). As with this case, distal to the area of concentric narrowing the adjacent segment of the vessel often appears disease free with a normal lumen.

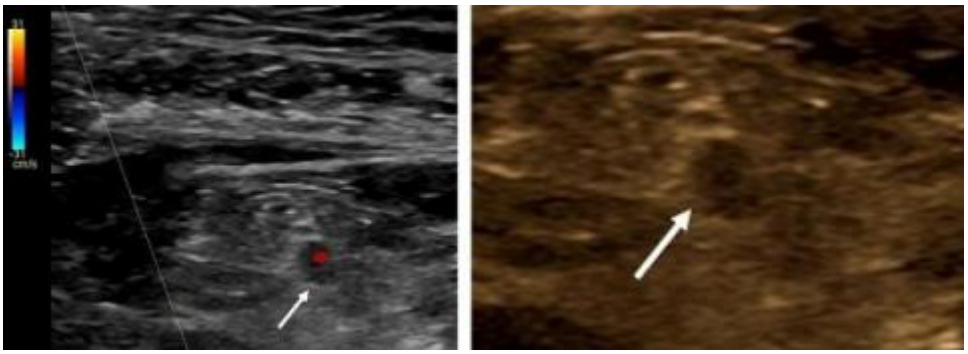
Figure 4. A patient with Takayasu’s arteritis affecting the axillary artery. The transverse views of the artery demonstrate the circumferential thickening characterized as the “macaroni sign”.

When viewed transversely, the circumferentially thickened intima-media complex is clearly identified and often referred to as the “macaroni sign”. The ultrasound images in figure 4 are from a patient with Takayasu’s Arteritis affecting the axillary artery. The color-flow image on the left depicts the reduced lumen. On the right, the colorized grey-scale image displays the circumferential wall thickening or “macaroni sign”. The wall thickening will often extend over along segment of an artery for several centimeters.

The treatment of Takayasu’s Arteritis varies depending on disease severity. Most patients receive anti-inflammatory drugs such as corticosteroids. If the response is poor to the corticosteroids, immune-suppressive medications can be added. Further treatment can involve bypass surgery or endovascular repair. Bypass surgery can be performed on the various segments affected with low morbidity and mortality. The major surgical procedures include aortocervical bypass, cervicosubclavian bypass, various aortic bypass grafts and renovascular bypass. Continued advances in endovascular techniques make this a frequently used method of treatment for Takayasu’s Arteritis. Either percutaneous transluminal angioplasty alone or with stenting can be performed on the subclavian, renal and carotid arteries as well as the aorta. Medical, endovascular and surgical treatment have all improved the prognosis of patients with Takayasu’s Arteritis.

BUERGER’S DISEASE (THROMBOANGIITIS OBLITERANS)

Buerger’s disease or Thromboangiitis obliterans is an inflammatory vasculitis affecting small to medium size vessels in the upper and lower extremities. This disease can involve the digital, palmar, plantar, tibial, peroneal, radial and ulnar arteries. It was first described in 1879 by Felix von Winiwarter who called it endarteritis. A detailed description was published in 1908 by Leo Buerger who referred to the disease as thromboangiitis obliterans.

The exact cause of Buerger’s Disease is unknown but an essential component for its development and progression is the use of tobacco. It is believed an immunologic reaction occurs which leads to vasodysfunction and inflammatory thrombi. Patients with the disease exhibit a hypersensitivity to intradermally injected tobacco extracts. Elevated levels of various serum antibodies as well as impaired endothelial-derived vasorelaxation also are present. A genetic component to the disease may also play a part as there is an increased prevalence of several human leukocyte antigens.

Buerger’s disease has a male to female ratio of 3:1 and typically presents in patients under the age of 40 years. It affects all races but is more prevalent in the Middle and Far East than in in Europe and the United States. The incidence in the United States is reported at 12.6-20 per 100,000 individuals. One of the highest incidences of the disease is among Israeli Jews of Ashkenazi descent. It is rare among African-Americans.

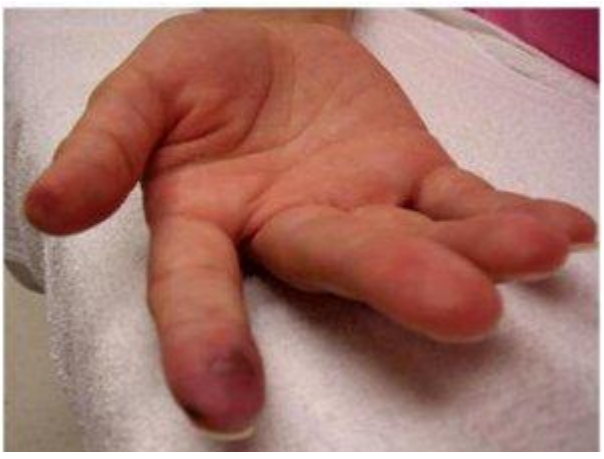

Figure 5. A patient with Buerger's disease with ischemic changes to the first and second digits.

The common clinical presentation of distal ischemic ulcerations or rest pain involving the toes, feet or fingers is observed in 70-80% of patients with Buerger's Disease (figure 5). Gangrene of the digits is also often present. The disease appears to begin in distal vessels and then progresses proximally. Symptoms can also include a sensation of cold, numbness and pain confined to a digit. Another clinical feature of the disease is impaired distal pulses in the presence of normal proximal pulses. Greater than 80% of patients have involvement of three of the four limbs. Almost half of the patients with Buerger's Disease may have episodes of recurrent superficial thrombophlebitis.

Several tests may be performed to aid in the diagnosis of Buerger's Disease. Blood tests in these patients are normal and thus not helpful in the diagnosis. Biopsies of the affected areas can also be performed. However, biopsies are performed primarily to exclude other disorders such as lupus or scleroderma. Noninvasive physiologic testing is helpful in identifying digital ischemia. Plethysmographic waveforms can provide qualitative documentation digital blood flow. Digital pressure measurements can also be recorded and used to calculate a toe-brachial index (TBI) for the toes or digital-brachial index (DBI) for the fingers. In all forms of digital ischemia regardless of the underlying cause, these indices fall to less than 0.7. Patients with severe digital disease will demonstrate a marked reduction in pulsatility in their digital tracings while upper extremity plethysmographic waveforms are often relatively normal (Figures 6 & 7).

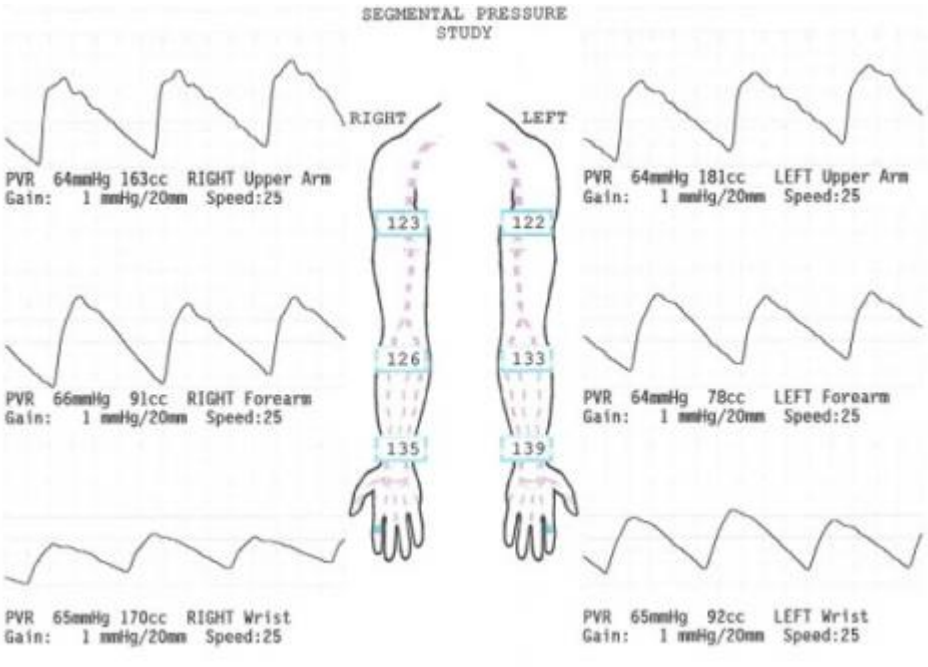

Figure 6. Upper extremity pulse volume recordings and segmental pressures in a patient with Buerger's Disease. These waveforms and pressures are within normal limits with only a slight delay in the upstroke of the waveforms.

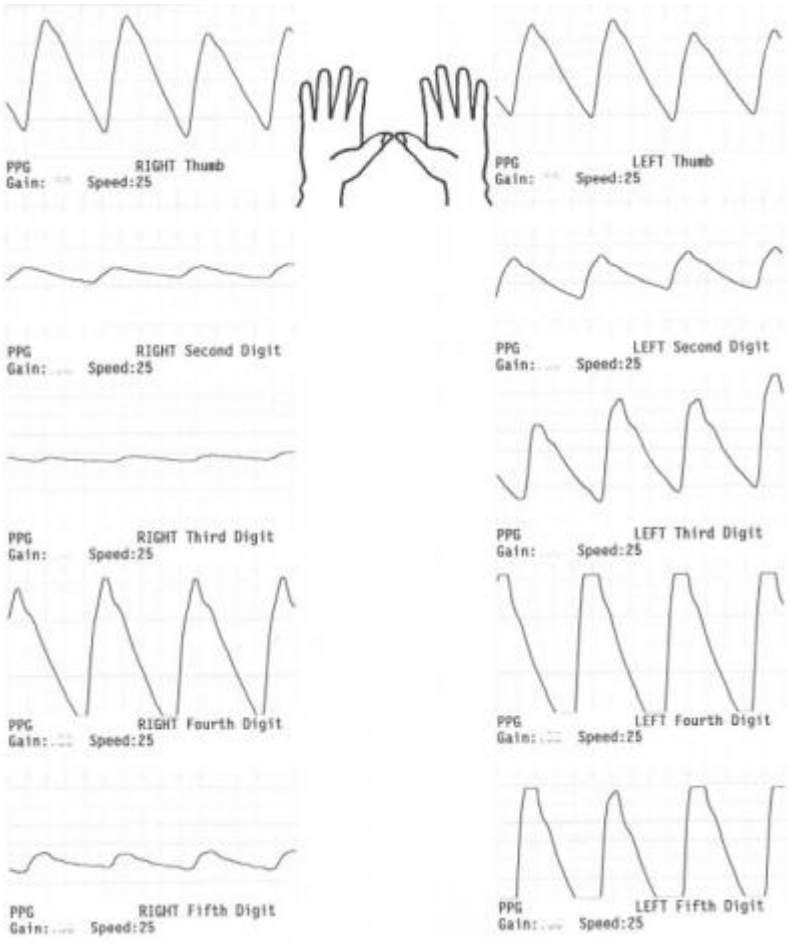

Figure 7. Digital photoplethysmographic (PPG) waveforms from the same patient in Figure 6. The PPG waveforms are severely diminished in second and third digits of the right hand, moderately diminished in the fifth digit of the right hand and mildly diminished in the second digit of the left hand.

Ultrasound can be used to check for the lack of atherosclerotic lesions and the identification of distal arterial occlusion. Angiography
is typically used in the diagnosis of Buerger's Disease. A smooth, non-atherosclerotic arterial wall proximal and distal to the sites of arterial occlusions is considered a key finding observed on angiography. The absence of atherosclerotic irregularities on angiography helps to aid in the differentiation of Buerger's Disease. A "corkscrew" like image is often demonstrated in angiographic findings due to excessive collaterals within the affected area.
Cessation of tobacco use is the primary treatment for patients with Buerger's Disease. It is essential that all tobacco use is discontinued including any nicotine replacement products. Anticoagulants and antiplatelet therapies can be prescribed. Vasodilators such as calcium channel antagonists or prostaglandin (PGE) infusions may also aid in treatment. Surgical revascularization is not typically an option due to the location and extent of this pathology. Amputation may be necessary if infection or gangrene is present.

GIANT CELL ARTERITIS (TEMPORAL ARTERITIS)

Giant Cell Arteritis is an arteritis which mainly affects medium sized arteries that supply the head, eyes and optic nerve. It commonly is seen in the branches of the external carotid artery, in particular the temporal artery. This is why it is often referred to as temporal arteritis. While there is earlier mention of

temporal artery inflammatory processes, it was not until the 1930's when cases were described suggesting an association of temporal arteritis and blindness. It is the most common form of vascular arteritis seen in adults.

Like other vascular inflammatory disease, the exact etiology is unknown but does appear to be immune-mediated. The name Giant Cell Arteritis describes the appearance of multinucleated giant cells in affected vessels. The internal elastic membrane of the vessel walls is attacked by these giant cells and ultimately becomes necrotic.

Giant Cell Arteritis has a female to male ratio of 3:1 and almost exclusively affects people over 50 years old with an average age of onset of 70 years. It also occurs more frequently in Caucasians of northern European descent and rarely in African-Americans and Asians.

The American College of Rheumatology has published criteria to help differentiate Giant Cell Arteritis from other forms of vascular arteritis. Three of the following five criteria must be met for the diagnosis: age > 50 years, new onset of localized headache, temporal artery tenderness or decreased pulse, erythrocyte sedimentation rate > 50 mm/hr or abnormal histology.

Other symptoms include jaw claudication, various visual symptoms (amaurosis fugax, diplopia), low-grade fever and scalp tenderness, which occurs in more than 25% of patients. Since the ophthalmic arteries are also commonly involved, loss of vision can occur being either a partial or complete defect. Optic nerve ischemia can lead to a permanent deficit in one or both eyes.

The definitive method for diagnosis is a temporal artery biopsy. If a unilateral biopsy is negative, a contralateral biopsy will be performed. The biopsy will reveal mononuclear cells and giant cells around the elastic lamina within the media of the cell wall. Other tests may be done prior to temporal biopsy such as measurement of the erythrocyte sedimentation rate and C-reactive protein.

Ultrasound can be useful in detecting Giant Cell Arteritis and can identify specific areas of stenosis. Collateral pathways can be assessed in those patients with vessel occlusion. Typical ultrasonic findings of a stenosis will include a focal increase in velocity noted within inflamed segment and post-stenotic turbulence distal to this segment. Temporal artery velocities may increase to 130 cm/s or greater within a stenotic segment as compared to 40-60 cm/s in a normal segment. Ultrasound of the temporal artery often reveals a characteristic dark halo surrounding the vessel (Figures 8 & 9).

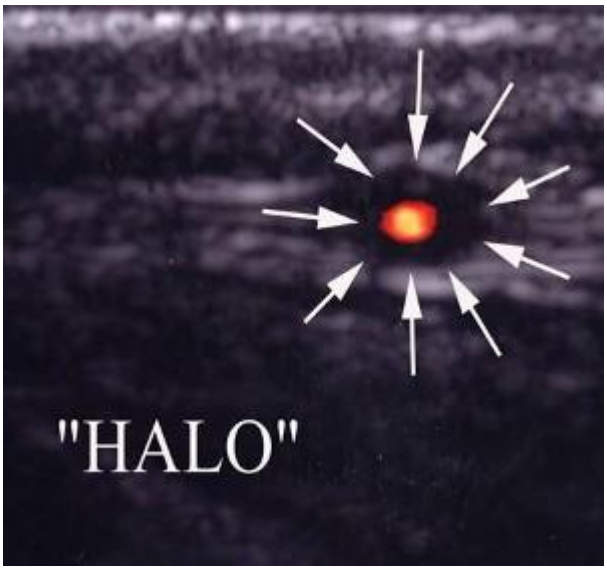

Figure 8. A transverse view of the temporal artery

illustrating the anechoic halo around the artery which
is characteristic of Giant Cell or Temporal Arteritis.

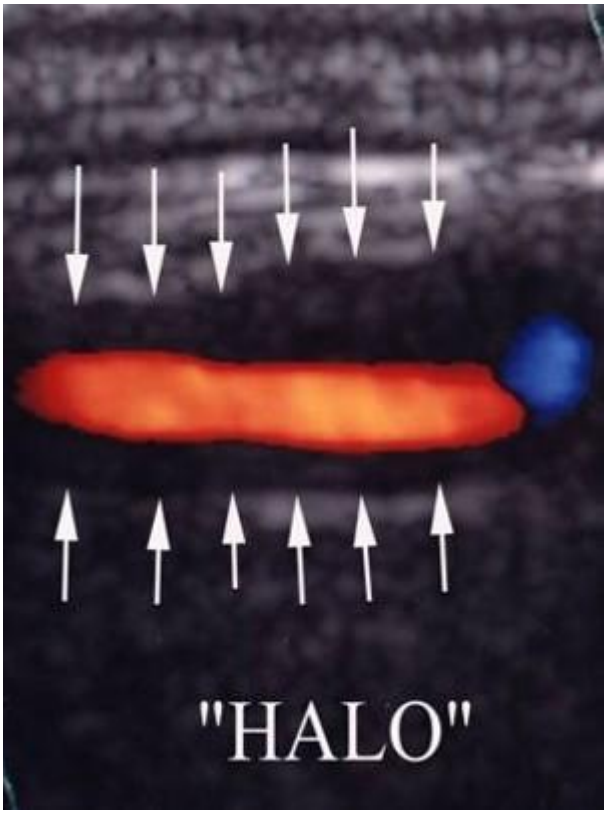

Figure 9. The sagittal view of the temporal
artery in the same patient as shown
in Figure 8.

This may be due to infiltration of white blood cells. Some reports describe a high sensitivity and specificity of this halo in predicting temporal arteritis. Others suggest a halo may be present in approximately 80% of patients examined by ultrasound. Most laboratories report specificity values in excess of 95% for the halo appearance. A generalized wall thickening is also observed on ultrasound and appears circumferential, characteristic of the inflammatory process. In those patients presenting with absent or
diminished upper extremity pulses, angiography is performed to evaluate the vessels for indications of arteritis.

Treatment should start immediately to prevent total blindness. Glucocorticoids such as prednisone are the drug of choice for treatment of temporal arteritis. In addition, immunosuppressants may also be prescribed.

CONCLUSION

Most patients seen in the vascular laboratory are evaluated for ischemic symptoms due to the result of atherosclerosis. There are a small portion of patients which may present with arterial ischemia and symptoms related to vascular arteritis. The patients with arteritis are distributed into specific demographic groups with unique clinical presentations. Physiologic and ultrasound testing results display distinctive findings identifiable to these inflammatory processes. Understanding the various types of vascular arteritis and their vascular laboratory findings will aid in the proper diagnosis and treatment of these patients.

REFERENCES

- Butteriss DJA, Clarke L, Dayan M, Birchall D. Use of colour duplex ultrasound to diagnose giant cell arteritis in a case of visual loss of uncertain aetiology. Br J Radiol 2004; 77:607-609.
- Chaubal N, Dighe M., Shah M. Sonographic and color Doppler fndings in aortoarteritis (Takayasu Arteritis). J Ultrasound Med 2004; 23:937-944
- Garcia LA. Epidemiology and pathophysiology of lower extremity peripheral arterial disease. J Endovasc Ther 2006; 13 (suppl II):II-3-II-9
- Klippel JH. The Pocket Primer on Rheumatic Diseases, 2nd ed. London: Springer-Verlag, 2010; 149-164.
- Maeda H, Handa N, Matsumoto M, et al. Carotid lesion detected by B-mode ultrasonography in Takayasu's arteritis: 'macaroni sign' as an indicator of the disease. Ultrasound Med Biol 1991; 17: 695-701.
- Meini S, DeFranco V, Auteri A, Pieragalli D. Takayasu's Arteritis: The "Macaroni Sign" Circulation 2006; 114:e544.
- Puechal X, Fiessinger JN. Thromboangiitis obliterans or Buerger's disease: challenges for the rheumatologist. Rheumatology 2007; 46:192-199.
- Olin JW. Thromboangiitis obliterans (Buerger's disease) N Engl J Med 2000; 343:864-869.
- Tato F, Hoffman U. Giant cell arteritis: a systemic vascular disease. Vascular Medicine 2008; 13:127-140.
- Tenny E. A rare diagnosis of common symptoms: Vascular sonography in Takayasu Arteritis. J Diagnostic Med Sonography 2012; 28:33-38.
- Washko PA, Smith SW. Special considerations in evaluating nonatherosclerotic arterial pathology. Kupinski AM, ed. Diagnostic Medical Sonography: The Vascular System Lippincott, Williams & Wilkins, Philadelphia, 2013:193-208.