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Multimodal Imaging in the Diagnosis of Large Vessel Vasculitis: A Pictorial Review

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Vasculitis is a pathologic process characterized by vessel inflammation with leukocyte infiltration into the vessel wall. The large vessel vasculitides (LVV), such as giant cell arteritis (GCA) and Takayasu arteritis (TA) involve similar histologic abnormalities but differ in the age of onset and vessels that are preferentially targeted [1]. Both present with systemic symptoms, such as fever and raised inflammatory markers. GCA occurs in patients exclusively older than 50 years and classically involves the extracranial aortic branches of internal and external carotid arteries, in particular, the temporal arteries, although any organ system can be involved. Involvement of the subclavian, axillary, and proximal brachial arteries leads to the aortic arch syndrome of claudication of the arms and absent or asymmetric pulses [2]. TA is mostly seen in women under the age of 40 years and has the greatest prevalence in Asians [3]. It primarily involves the aorta and its branches, in particular, the subclavian arteries [4]. The abdominal aorta and pulmonary vessels are involved in up to half of the cases. An angiographic classification (types I-V) exists based on the site of involvement of the aorta [4]. A recent patient series that involved 25 patients with TA found type V to be the most common type, which involves the entire aorta, including the renal arteries [5]. The mainstay of treatment is immunosuppression with agents such as corticosteroids.

Imaging studies are vital for early diagnosis because LVV can present with a variety of symptoms. We obtained images by using various modalities, including duplex ultrasonography (US), catheter-directed angiography (CDA), computed tomography (CT) and magnetic resonance angiography (MRA), and positron emissions tomography (PET) and CT. A literature review was carried out to determine their effectiveness in diagnosis and follow-up.

Duplex US

US (Figures 1 and 2) can assess both vessel anatomy and luminal status, and may demonstrate early wall changes before detectable lumen changes are seen on angiography [6]. Sensitivities ranged from 91%-100% compared with histology and from 78%-100% compared with clinical diagnosis in a review of 13 studies, with findings that included wall oedema, stenoses, and occlusion [7].

Characteristic findings include increased diffuse, circumferential intima-media complex thickness in transverse sections ("macaroni sign") thought to reflect oedema, increased vascularity, or both [8]. A similar finding, the so-called halo sign, is a long, smooth, homogenous circumferential thickening of the arterial wall [9].

A recent meta-analysis reviewed the diagnostic value of colour Doppler in GCA by using either histology or American College of Rheumatology (ACR) criteria as reference...
Figure 1. (A) Duplex ultrasound (US) of the left axillary artery of a 71-year-old woman (patient 1) with giant cell arteritis. Vessel-wall inflammation is demonstrated by the long hypoechoic signal (white arrows) surrounding the colour flow. (B) US of the same patient's right axillary artery 5 weeks later, demonstrating similar findings. This figure is available in colour online at http://carjonline.org/.

Figure 2. Ultrasound of the right common carotid artery (white arrow) in the same patient as in Figure 1, demonstrating a diffusely thickened hypoechoic arterial wall. The right internal jugular vein (asterisk) is lateral to it. This figure is available in colour online at http://carjonline.org/.

Figure 3. Repeated ultrasound of the left (A) and the right (B) axillary artery in patient 1 after 6 weeks of treatment, showing near resolution of wall inflammation of the left axillary artery and improvement of the right axillary wall inflammation (white arrows). The left axillary artery is not entirely in plane here, which accounts for the apparent narrowing seen (it was normal on this study). This figure is available in colour online at http://carjonline.org/.

standards. The sensitivity and specificity of the halo sign were 69% and 82%, respectively, compared with biopsy and were 55% and 94%, respectively, compared with ACR criteria. Stenosis or occlusion was an almost equally sensitive marker compared with biopsy (sensitivity 68%) or ACR criteria (sensitivity 66%) [10].

US is comparable with other noninvasive modalities. The results of high-resolution magnetic resonance imaging (MRI) and colour US in detecting suspected GCA in 59 patients were compared with a final diagnosis as made by ACR criteria and a 6-month follow-up study; 61% were ultimately diagnosed with GCA. Sensitivity of high-resolution MRI and US was 69% and 67%, respectively, specificity was 91% and 92%, respectively, positive predictive value was 93% and 92%, respectively, and negative predictive value was 66% and 64%, respectively. Temporal artery biopsy was positive in 24 of 41 patients (59%). Sensitivity of high-resolution MRI and US compared with biopsy was 83% and 79%, specificity was 71% and 59%, sensitivity was 71% and 59%, positive predictive value was 80% and 73%, and negative predictive value was 75% and
Figure 4. (A) Computed tomography (CT) of the thorax with contrast in a 29-year-old woman with Takayasu arteritis, presenting with chest pain. The image shows aortic mural thickening of the ascending aorta (red arrows). (B) An arterial phase CT images of abdomen, showing marked wall thickening and enhancement of the upper abdominal aortic wall (red arrows). (C) Multiplanar reconstructions of CT of the thorax in the same patient, demonstrating ascending aorta and aortic root mural thickening (white arrows). This figure is available in colour online at http://carjonline.org/.

Figure 5. Computed tomography (CT) coronary angiogram in the same patient as in Figure 4, demonstrating a significant 70% stenosis in the origin of the left main coronary artery (white arrows) and approximately 60% stenosis at the origin of the right coronary artery (white arrowheads). There also is mural thickening of the aortic root (small red arrows). This figure is available in colour online at http://carjonline.org/.

Figure 6. Arterial phase multislice computed tomography angiography in 42-year-old Caucasian woman with Takayasu arteritis, demonstrating thickening of the superior aspect of the aortic arch, and extending to the brachiocephalic branch (white arrows) and left common carotid artery (white arrowheads). The left subclavian artery is not demonstrated here due to occlusion.
Figure 7. A 3-dimensional reconstruction of the computed tomography angiography in the same patient as in Figure 6, demonstrating a long-segment left subclavian artery occlusion (white arrows, denoting normal projected course) due to stenosis from its origin at the aortic arch (asterisk). The artery has reconstituted distally (white arrowheads). This figure is available in colour online at http://carjonline.org/

Figure 8. Arterial phase (A), portal venous phase (B), and delayed phase (C) images in a 79-year-old man, demonstrating mural thickening (white arrowheads) and enhancement of the distal abdominal aorta. He presented with abdominal pain.

Figure 9. Sagittal arterial (A) and portal venous phase (B) images, in the same patient in Figure 8, demonstrating mural thickening and enhancement of the aorta (white arrowheads) as well as an aortic aneurysm (black arrowheads).

67%, respectively [11]. Portability, lack of ionizing radiation, and relative cost effectiveness make US an ideal modality for diagnosis and follow-up (Figure 3) of patients with LVV. Its limitations include dependence on operator skill and difficulty in imaging deep segments like the thoracic aorta [6].

CT Angiography

CT and CT angiography (CTA) are useful in demonstrating both vessel wall and luminal changes and can aid early diagnosis [12]. CTA findings include stenosis, dilatation, and aneurysms, as well as wall thickening and calcifications [13]. Characteristic findings (Figure 4) are demonstrated in precontrast, arterial phase, and delayed phase images. Precontrast scans can reveal high wall attenuation; arterial phase images (Figures 5–7) may show circumferential wall thickening and enhancement, whereas delayed phase images (Figures 8 and 9) demonstrate similar findings, including concentric low attenuation rings inside the arterial wall, which correlates with active disease [14].

CT also can be used to evaluate response to therapy and can assess for progression. In a small study of follow-up CTs of patients with both inactive and persistent TA (by erythrocyte
Figure 10. Computed tomography angiography with multiplanar reconstruction, of the patient whose ultrasound images are seen in Figures 1 and 2, demonstrating long stenosis in the right axillary artery (white arrowheads). There is evidence of collateral flow. This figure is available in colour online at http://carjonline.org/.

sedimentation rate levels), imaging findings correlated with activity. The thickness and CT attenuation values of the aortic wall on precontrast, arterial, and venous phases were measured on the initial and follow-up scans. Initial findings included wall thickening and enhancement in arterial and venous phases, whereas a low-attenuation ring was demonstrated in the venous phase in 15 patients (83%). Follow-up images showed a decrease in mean mural thickness and mean mural attenuation ratio. A low attenuation ring was identified in 7 patients (39%) with active persistent arteritis [15]. In another study, of 20 patients with TA that was conducted in Japan, CTA demonstrated findings, including stenosis (Figure 10) and occlusion, with about 95% accuracy. Overall sensitivity and specificity were 95% and 100%, respectively [13]. The limitations of CT in evaluation and follow-up lie in the relatively large amount of ionizing radiation and the necessity to use intravenous contrast [10]. This is an especially important consideration in female patients of childbearing age. It has an advantage over conventional angiography because it can provide additional mural information.

Figure 11. Maximum intensity projection magnetic resonance angiography images of thoracic vessels in a 60-year-old woman diagnosed with Takayasu arteritis who presented with left upper limb pains and elevated erythrocyte sedimentation rate. The image demonstrates high-grade stenosis (white arrows) of the right subclavian and the proximal left subclavian artery (white arrowheads). The patient was treated with corticosteroids and methotrexate.

Figure 12. Gadolinium-enhanced 3-dimensional fast low-angle shot magnetic resonance angiography, showing similar findings 3 months later with high-grade stenosis of the right subclavian artery (white arrows), 2 cm beyond its origin and a stenosis of the left subclavian artery (white arrowheads).

Figure 13. Precontrast axial T1-weighted magnetic resonance image (A) and after gadolinium magnetic resonance (B), demonstrating mural thickening (white arrowheads) and enhancement (white arrows) of the infrarenal abdominal aorta in a 40-year-old Asian woman.
Figure 14. (A) Sagittal T1-weighted fast low-angle shot of the same patient as in Figure 11 demonstrating smooth tapering of the infrarenal abdominal aorta (white arrowheads). (B) Postcontrast maximum intensity projection image of the same patient in Figure 11, demonstrating the same finding (white arrows).

Figure 15. Transmural enhancement of the abdominal aorta (arrow) in a 62-year-old woman with giant cell arteritis, seen on double inversion recovery T1-weighted magnetic resonance imaging, after administration of gadolinium. Reprinted with permission from the American Journal of Roentgenology [9].

MRA

MRA and MRA (Figures 11 and 12) play an important role in early diagnoses of LVV [16]. Spin-echo sequences can depict early aortic-wall thickening, along with significant enhancement in and around the aorta and carotid arteries in the acute phase of the disease [17]. Bley et al performed contrast-enhanced high-resolution MRI in 64 patients with suspected GCA [18]. Mural thickness, lumen diameter, and a mural contrast enhancement score were assessed with T1-weighted spin-echo images. A final diagnosis according to ACR criteria was used as the criterion standard. Evaluation of the mural inflammatory MRI signs for diagnosing vasculitis resulted in a sensitivity of 80.6% and a specificity of 97.0% [18].

MRI findings (Figures 13–15) of vascular inflammation include wall thickness and oedema and increased mural enhancement on postcontrast T1-weighted images [19,20]. It can provide high-resolution anatomic information and physiological data, such as measurements of degree of wall enhancement and the presence of oedema, and this also can be used in follow-up evaluation. In a study of patients with proven GCA, a comparison of initial and follow-up MRIs after treatment demonstrated decreased intensity of inflammatory enhancement, which correlated with clinical and
serologic remission in 15 of 17 patients. One of the patients with active disease had persisting mural inflammation in keeping with relapsing disease [21].

PET

As a relatively new modality, $^{18}$F fluorodeoxyglucose (FDG) PET, also has a pertinent role in the diagnosis of LVV (Figures 16 and 17), particularly in the initial diagnosis of patients presenting with nonspecific symptoms [22]. The early stage of the disease is characterized by an inflammatory cell infiltrate into vessel walls. Webb et al [23] performed PETs in 18 patients suspected of having TA, all of whom had full clinical and laboratory assessment, cross-sectional imaging, and angiography. Sixteen of the 18 patients met the ACR criteria for diagnosis. PET correctly identified 11 of 12 patients with active disease, which achieves a sensitivity of 92%, a specificity of 100%, and negative and positive predictive values of 85% and 100%, respectively, in the initial assessment of active vasculitis. It also correctly identified all 6 patients with inactive disease.

$^{18}$F-FDG PET has a role in the follow-up of patients with LVV, although the amount of data is limited. In a study that compared PET with MRI in the diagnosis and follow up of patients with aortitis, follow-up PETs of 30 involved arterial regions in 6 patients showed normalization of uptake in 24 regions after treatment. This correlated with clinical and laboratory findings. PET also identified more vascular regions involved in the inflammatory process than MRI [24]. Limitations of $^{18}$F-FDG PET include a lack of information regarding vessel wall constitution or status of luminal flow. It is also limited by its restricted availability and high cost.

Angiography

Angiography, particularly digital subtraction angiography, has traditionally been the procedure of choice for the diagnostic evaluation of TA [12] and can demonstrate a number
of findings, including stenosis (Figure 18) and frank occlusions but cannot provide information about the vessel wall. It also can be used to guide interventional procedures such as angioplasty or stent placement in patients with stenoses [25]. Its limitations include its invasive nature, high-radiation dose, and the need for iodinated contrast with its associated complications.

Conclusion

Imaging plays a central role in the early diagnosis and follow-up in patients with LVV such as GCA and TA. Relatively newer and noninvasive imaging techniques, such as CTA, MRA, duplex US and PET-CT, are safer than traditional catheter-directed angiographic techniques. In addition, these techniques provide information about vessel-wall changes along with luminal changes and are thus a valuable tool to assess disease activity in patients without symptoms of vessel lumen compromise. Portability, availability, radiation dose, and vessel location are important considerations in choosing between modalities, especially because repeated imaging is often required for follow-up in women of childbearing age.

References
