The Value of Vascular Ultrasonography in Defining Inflammatory Activity in Takayasu Arteritis: Case Reports

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Introduction

Takayasu arteritis (TA) is a rare large-vessel arteritis that primarily affects the aorta and its major branches.[1] The greatest challenge is to identify disease activity, since therapeutic measures modify the clinical course of the disease.

Vascular ultrasonography (VUS) is a promising tool for characterizing vessel wall inflammation and monitoring hemodynamic changes in response to therapy.[2]

We present 2 case reports that demonstrate the importance of VUS in identifying inflammatory activity in TA. The cases reflect the differences in thickened intima-media complex (IMC) between patients in active and non-active phases of the disease.

Case reports

First case: A 6-year-old boy who was suffering headaches but had no previous comorbidities was brought to a pediatrician. Clinical examination detected arterial hypertension (140 x 90 mmHg), and laboratory tests and VUS were scheduled to assess the renal arteries.

VUS revealed: 1) stenosis > 80% in the proximal segment of the left renal artery, and 2) thickened IMC of the abdominal aorta, with a lumen reduction of approximately 40% in the segment adjacent to the origin of the mesenteric vessels (Figure 1 B.C). Magnetic resonance angiography of the abdominal aorta and its branches was then performed (Figure 1D), with the findings confirming the VUS results.

Keywords

Vascular ultrasound; Takayasu's arteritis; vasculitis; intima-media thickness

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Examination of the carotid arteries was indicated, and significant thickening of the IMC was detected in both common carotid arteries, although the internal carotid artery was preserved, which is suggestive of TA (Figures 2 A-C).

VUS can be used to characterize vascular tissue as hypo- or hyperechogenic, and is validated by the adventitial layer or adjacent muscle. In this case, the IMC was characterized as hyperechogenic, suggesting fibrosis with no apparent disease activity.[3] The laboratory results showed no changes, with a C-reactive protein level of 0.1 mg/L and an erythrocyte sedimentation rate of 7 mm/h.

Clinical course: The patient was treated with antihypertensive drugs; the renal artery lesion was not treated with angioplasty due to his age. Ultrasound follow-up of the carotid arteries, aorta, and renal arteries 1 year after the initial examination showed no significant changes.

Second case: A 22-year-old woman presented with neck and axillary pain for the last 2 months, which worsened with movement and palpation. This was initially attributed to her physical activity. However, her neck and axillary pain worsened, and she progressed to fever and fatigue during light activity. She was evaluated by a rheumatologist, who requested laboratory tests and VUS of the carotid arteries, axillary vessels, and subclavian artery, in addition to magnetic resonance angiography of the cervical vessels.

VUS of the brachiocephalic trunk, the right common carotid artery, and the right supraclavicular region of the subclavian artery revealed increased diameters at the expense of significant intima-media thickening, causing subocclusion of these vessels (Figure 3A-C). The movement of the vessels was blocked, representing a drop in pulsatility, and the presence of hypoechoic areas probably represented vascularization of the wall of the right common carotid artery, which was detected by B-mode, color flow mapping, and amplitude Doppler imaging (Figure 4A-C). Retrograde flow in the external carotid artery flow was filling the internal carotid artery, which kept the flow at low speed, but in a cephalad direction. The caliber of both carotid branches was reduced, with no IMC involvement. The right vertebral artery was occluded (Figure 4D). The caliber of the infraclavicular region of the subclavian artery

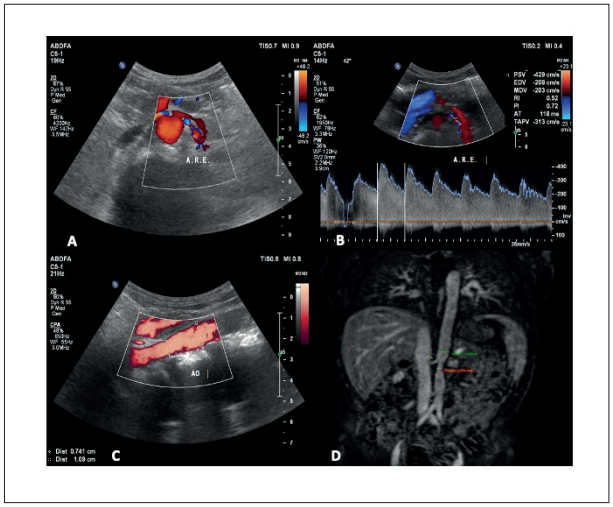

Figure 1 – *A) Color flow mapping shows lumen narrowing in the proximal course of the renal artery with flow turbulence; B) spectral Doppler analysis with PSV = 429cm/s and EDV = 208cm/s; C) measurement of the caliber of the abdominal aorta in the path with narrowing = 7.4mm, compared to the most distal path = 10.9mm; D) magnetic angioresonance of the abdominal aorta showing narrowing of the aorta in the path close to the origin of the mesenteric vessels.*

and the axillary artery was reduced due to IMC thickening, with low-amplitude single-phase flow.

Ultrasound imaging of the left carotid, subclavian, and axillary arteries showed no abnormalities.

In maximum intensity projection reconstruction, magnetic resonance angiography of the intracranial vessels showed no opacification of the right internal carotid artery, suggesting chronic occlusion or subocclusion, and the right middle cerebral and right anterior cerebral arteries were visualized through the right anterior and posterior communicating arteries (Figure 5A). However, contrasted axial sections showed diffuse parietal thickening and thread-like flow in the right internal carotid artery (Figure 5B).

The patient's laboratory results showed increased inflammatory response, with a C-reactive protein level of 97 mg/L and an erythrocyte sedimentation rate of 114 mm/h.

Clinical course: Treatment consisted of prednisone 1 mg/kg and methylprednisolone pulse therapy 1000 mg for 3 consecutive days, associated with 6 monthly pulses of cyclophosphamide. Approximately 1 month after treatment began, the clinical picture improved and new VUS of the cervical arteries showed reduced arterial caliber and no signs of artery wall vascularization, but arterial obstruction had not reduced.

Discussion

TA is a chronic granulomatous panarteritis of unclear etiology that involves the large vessels, primarily the aorta and its major branches. The vast majority of cases (75% to 97%) occur women < 40 years of age.[1] There is no gold standard imaging or laboratory test with adequate sensitivity or specificity to diagnose TA. The diagnostic criteria for TA are a combination of physical examination, laboratory findings, and imaging studies.

Several authors have demonstrated the importance of VUS in diagnosis and follow-up of giant cell arteritis, suggesting that it should be included as a complementary exam in both TA and temporal arteritis.[3-5]

The recommended technique for evaluating IMC in patients with suspected arteritis is longitudinal ultrasound section imaging in B-mode with a high-frequency linear transducer. Measurement is made from the inner edge of the IMC to the outer edge of the adventitial layer of the vessel. Diffuse, homogeneous, and concentric increase in IMC, associated or not with loss of pulsatility, are considered positive criteria. The degree of echogenicity depends on disease stage. Vascularization in the arterial wall indicates

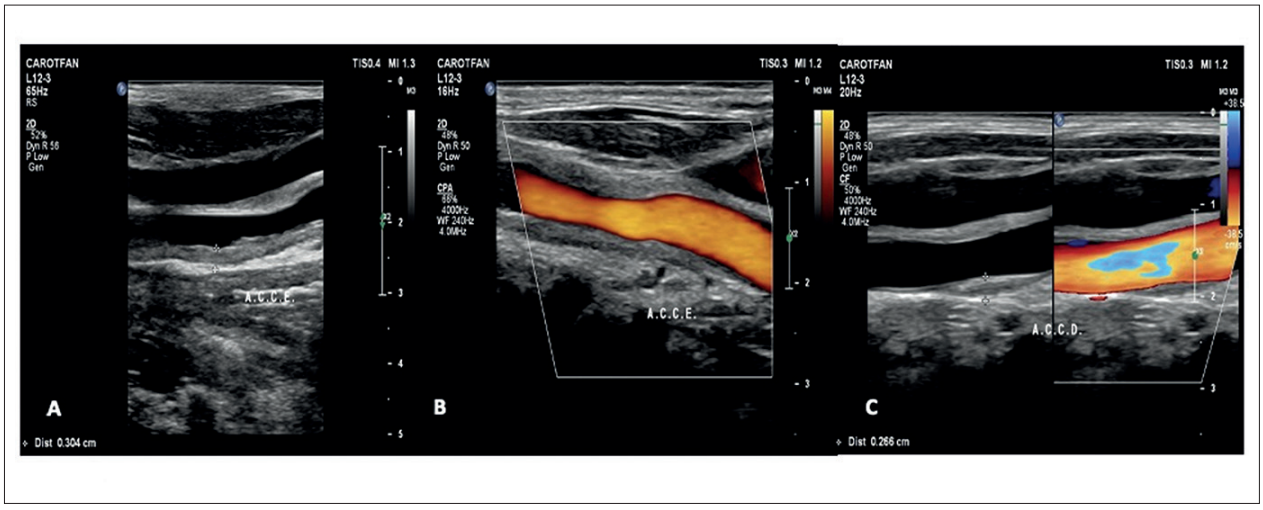

Figure 2 – *A) Diffuse and hyperechogenic thickening of the intima-media complex of the left common carotid artery; B) a reduction of the vascular lumen is observed as a result of the intima-media thickening; C) diffuse and hyperechoic thickening of the intima-media complex of the right common carotid artery.*

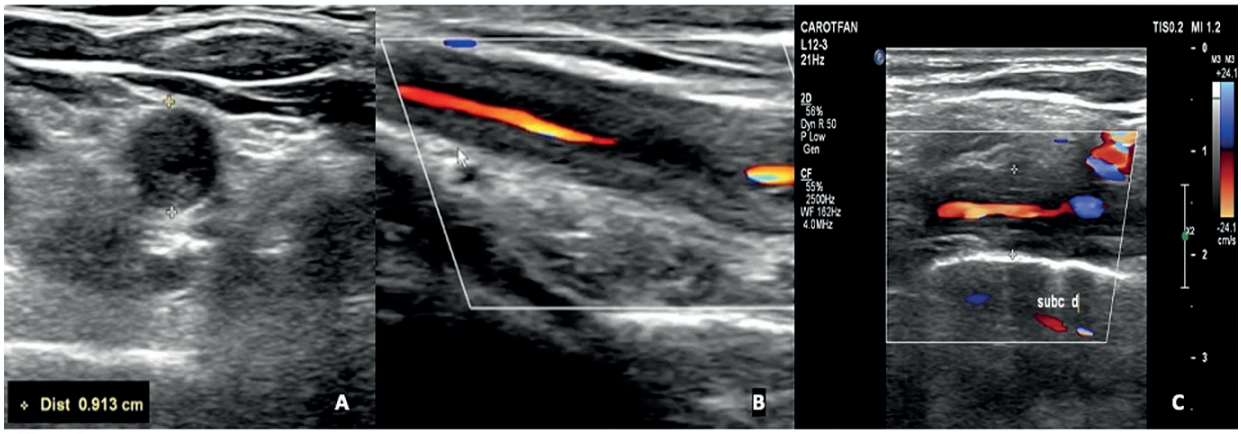

Figure 3 – *A) Transverse section of the right common carotid artery with increased anteroposterior diameter (9.13mm); B) Longitudinal section of the right common carotid artery, with marked thickening of the intima-media complex, with color flow mapping showing significant reduction of the vascular lumen; C) right subclavian artery, in its supraclavicular course, with increased diameters and accentuated intima-media thickening.*

disease activity, which can be further investigated through ultrasound with contrast-enhancing agents.[6]

After the creation of fast-track clinics, which provide clinical and laboratory tests and VUS within 24 hours, the importance of ultrasound assessment for patients with suspected arteritis has become clear. The decreased number of patients with permanent vision loss and the reduced number of biopsies in patients with suspected temporal arteritis, which have been demonstrated in 2 important studies, reinforce the value of VUS in the rapid diagnosis of this disease, as well as arteritis in general.[7,8]

Increased IMC thickness, which is identified through B-mode VUS, reflects inflammation in the vessel wall due to the mobilization and migration of myofibroblasts to the IMC.[9] This increase in mural thickness can cause stenosis, occlusion and, consequently, ischemia and damage to the target organ tissue.[10]

In ultrasound assessment, an arteritic IMC will be concentrically and homogeneously arranged, which must be differentiated from non-homogeneous, asymmetrical, and partially calcified alterations of the arterial wall, which are typically observed in atherosclerosis.[11]

IMC thickening, which is associated with vessel caliber > 10 mm and neovascularization, has been described as a sign of disease activity.[12] As has been described in the diagnosis of temporal arteritis, an inflammatory halo, representing low IMC echogenicity, may be a sign of disease activity in a thickened IMC in TA. The opposite is also true, ie, hyperechogenic areas in a thickened IMC indicate the presence of fibrotic material, characterizing a more chronic stage of the disease.[13]

Svensson et al.[14] compared IMC characteristics in patients with and without disease activity, characterizing the different stages into five grades. Grades I, II and V are considered disease activity:

Grade I: - Increased IMC, low-to-medium echogenicity and hypoechoic areas in the IMC

- Increased IMC, low-to-medium echogenicity and neovascularization
- Increased IMC, low-to-medium echogenicity, and increased vessel diameter

Grade II: Increased IMC, medium echogenicity (no increase in diameter or hypoechoic areas)

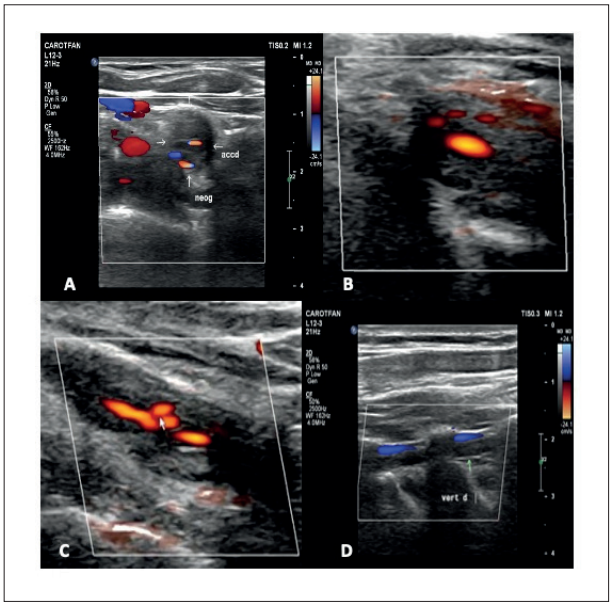

Figure 4 – *A) Transverse section of the right common carotid artery with color flow mapping showing areas of neovascularization intermingled in the thickened mediointimal complex; B) areas of vascularization in the arterial wall evidenced by amplitude Doppler in the transverse section; C) longitudinal section of the common carotid artery; D) absence of flow on color flow mapping in the right vertebral artery (occlusion).*

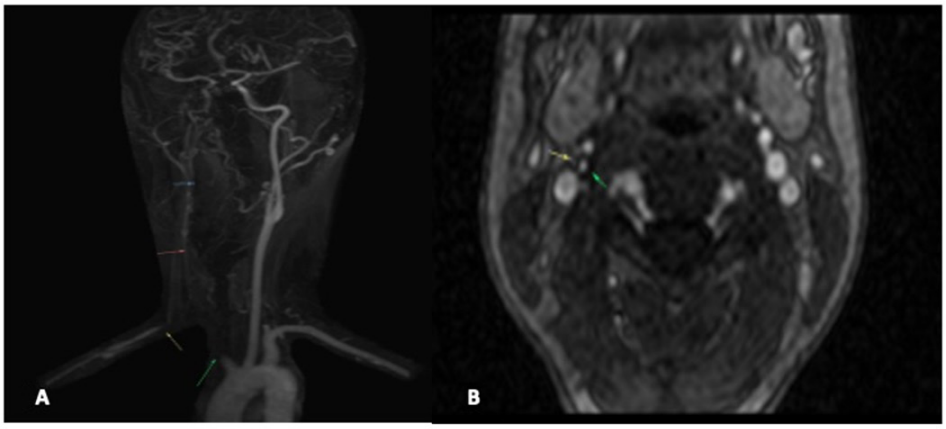

Figure 5 – *AngioRM of intracranial vessels. A) MIP reconstruction of cervical AngioMR: absence of flow in the right brachiocephalic trunk, right subclavian artery, ACCD and in most of the ACID; B) Axial section of MRA, with contrast: ACID with diffuse parietal thickening and marked luminal reduction, with threadlike flow inside it.*

Grade III: Increased IMC, medium echogenicity and fibrotic areas

Grade IV: Increased IMC, high echogenicity and fibrotic areas

Grade V: Grade III or IV with any signs of grade I

Conclusions

VUS is a non-invasive method that can aid in the diagnosis and monitoring of inflammatory changes in the vessel wall of patients with TA. Increased artery diameter at the expense of a thickened hypoechoic IMC or with signs of increased vascularization of the arterial wall are suggestive of disease activity. Thickening of the IMC, which is characterized by greater echogenicity and the appearance of fibrotic elements in the wall, suggests disease stability and a lack of inflammation.

Author Contributions

Conception and design of the research, acquisition of data and analysis and interpretation of the data: Barros FS; writing of the manuscript and critical revision of the manuscript for intellectual content: Barros FS, dos Santos SN, Storino J, Freire CMV, Barros FS.

Potential Conflict of Interest

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Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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