Chapter

An Integrated Approach to the Role of Neurosonology in the Diagnosis of Giant Cell Arteritis

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Abstract

Giant cell arteritis (GCA) is a primary vasculitis that affects especially extra-cranial medium-sized arteries, such as superficial temporal arteries (TAs). Three findings are important for the ultrasound (US) diagnosis of TA: „dark halo" sign, which represents vessel wall edema, stenosis, and acute occlusions. US has a high sensitivity to detect vessel wall thickening in the case of large vessels GCA. The eye involvement in GCA is frequent and consists in arteritic anterior ischemic optic neuropathies or central retinal arterial occlusion, with abrupt, painless, and severe loss of vision of the involved eye. Because findings of TAs US do not correlate with eye complications in GCA, color Doppler imaging of the orbital vessels is of critical importance (it reveals low end diastolic velocities, and high resistance index), in order to quickly differentiate the mechanism of eye involvement (arteritic, versus non-arteritic). The former should be treated promptly with systemic corticosteroids to prevent further visual loss of the fellow eye.

Keywords: giant cell arteritis (GCA), temporal arteries (TAs), temporal artery biopsy (TAB), "dark halo" sign, ultrasonography (US), arteritic anterior ischemic optic neuropathies (A-AION), central retinal artery occlusion (CRAO), color Doppler imaging (CDI) of the orbital vessels, end diastolic velocities (EDV), resistance index (RI)

1. Introduction

Giant cell arteritis (GCA) is a primary (non-necrotizing granulomatous) vasculitis of autoimmune etiology, which especially affects extra cranial medium-sized arteries (branches of the external carotid arteries-ECAs-particularly the superficial temporal arteries-TAs) and sometimes large-sized arteries (aorta and its major branches). It is also recognized as Horton, temporal, or granulomatous arteritis. It causes narrowing of the artery, leading (by wall thickening) to partial (stenosis) or complete obstruction (occlusion) of local arterial blood flow, its clinical manifestations being expressed by signs of local ischemia [1–6].

GCA is the most common form of vasculitis that occurs in adults and in the elderly, being diagnosed over the age of 50's. Women are two to three times more

affected than men. It is well known that the disease can occur in every racial group but is most common in Caucasians, especially people of northern European descent, and others in northern latitudes. [1–6].

According to Hunder [7], and Jennette [8] a complete diagnosis of GCA requires the presence of American College of Rheumatology (ACR) classification modified criteria:

a. age over 50 years at the onset of the disease;

b. moderate, bitemporal, recently installed headache;

c. scalp tenderness, abnormal temporal arteries on inspection and palpation (**Figure 1**), reduced pulse, jaw claudication (pain in the jaw while/after chewing);

d. blurred vision or permanent visual loss in one or both eyes (since permanent visual loss due to ischemia is frequent, GCA should be considered an ophthalmic emergency requiring immediate management);

e. systemic symptoms (fatigue, weight loss, fever, pain in the shoulders and hips: polymyalgia rheumatica);

f. increased inflammatory markers (erythrocyte sedimentation rate greater than 50 mm/h, C reactive protein greater than 1,5 mg/dl);

g. representative histologic findings in temporal artery biopsy (TAB): mononuclear cell infiltration or granulomatous inflammation of the vessel wall, usually accompanied with multinucleated giant cells (**Figure 2**).

Several imaging techniques may be suitable in the diagnosis of GCA. [9] Compared to other imaging techniques, US is considered to be the most suitable in the evaluation of GCA patients, therefor it can easily be performed by the clinician (immediately after the general examination of patient), and it is significantly shortening the waiting period until another investigation is performed. [9–16].

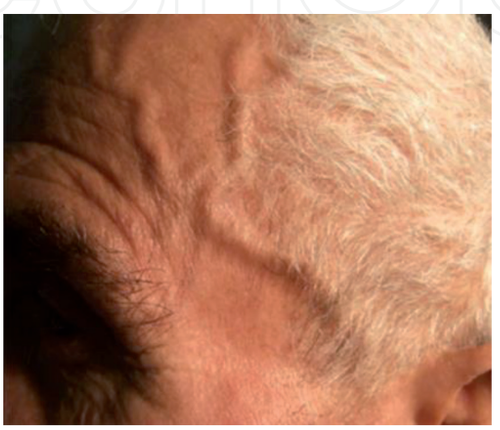

Figure 1.
Giant cell arteritis (GCA) of the left superficial temporal artery (TA) shows a prominent, tender and nodular artery, that is also hypo pulsating on palpation [9].

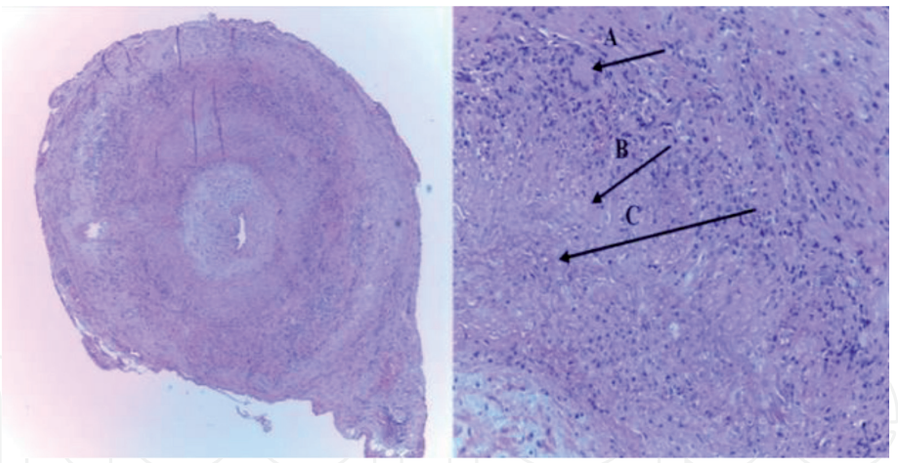

Figure 2.
The histopathological examination of the left superficial temporal artery biopsy (TAB) noted [10]. (A) Thickened vascular wall with inflammatory infiltration of multinucleated giant cells, (B) epithelioid cells and (C) dissolution of the internal elastic lamina (H&E stain).

2. Extracranial duplex sonography in giant cell arteritis (GCA)

Ultrasonography (US) is a safe, noninvasive, without radiations, widespread accessible, fast, and low-cost bedside screening technique which has the unique capacity of studying real-time hemodynamics. It presents the ability to evaluate the anatomy of vessel's wall, identifying equally parietal abnormalities (wall thickening, hypoechoic plaques, clotting, parietal hematoma, dissections) and the external diameter of the artery; it can rule out both stenosis and occlusion. Therefore, the use of US is widespread in neurological clinical practice, mainly in the evaluation of arterial atherosclerotic process but also for monitoring other diseases such as medium/large-vessel vasculitis. [17–19].

Olah noted that for US imaging of extracranial vessels different modes are being used:

a. *B-mode (brightness mode)*

- The strength of the echo is recorded as a bright dot, while the location of different gray dots corresponds to the depth of the target. [17]

b. *The duplex image*

- It associates a B-mode gray-scale image with pulse-wave (PW) Doppler flow velocities measurements.
- The B-mode image represents the anatomical localization of the vessels, indicating the zone of interest where a Doppler sample volume should be placed and where the velocities are measured.
- The Doppler angle can be measured correctly when the blood is parallel to the direction of the vessel. [17]

c. *Color Doppler flow imaging*

- Measure mean frequency shift in each sample volume.

- It represents color–coded velocity information, which is superimposed as a color flow map on a B-mode image.

- In each sample volume, the color reflects the blood flow velocity in a semi quantitative manner, as well as the flow direction relative to the transducer. Blood flowing toward or away from the transducer is shown by different colors (red and blue). Moreover, fast flow is indicated by a lighter hue and slow flow by a deeper one.

- The color flow map indicates the position and orientation of the vessels, as well as the site of turbulent flow or stenosis. Since color flow mapping is based on flow velocity measured by PW technology, aliasing occurs if the frequency shift is higher than half of the pulse repetition frequency (PRF). [17]

d.*Power Doppler mode*

- Uses the signal intensity of the returning Doppler signal instead of frequency shift.

- Power (intensity) of the signal is displayed as a color map superimposed on a B-mode image. Since the Doppler power is determined mainly by the volume rather than the velocity of moving blood, power Doppler imaging is free from aliasing artifacts and much more sensitive to detect flow, especially in the low-flow regions. However, it does not contain information about the flow direction or flow velocity. [17]

The advantages of US over other imaging techniques in GCA are represented by its safety, accessibility, tolerability, fast (may take about 15-20 minutes, if it's conducted by an experienced sonographer) and the more important, its high resolution (a high –frequency probe offers both an axial and a lateral resolution of 0.1 mm) [19–27]. The smaller the vessel diameter, the more difficult is to appreciate the vessel wall damages, so that, in this case, the most informative US data are based on Doppler spectral evaluation. This is also valid for the assessment of medium to small vessel inflammation such as intracranial vasculitis. Small vessel vasculitis (the ANCA-associated or the immune complex vasculitis) are not a domain of ultrasound. [19].

Furthermore, US has a higher sensitivity than TAB, the last one evaluating only a restricted anatomical region in a systemic disease. Using US, we can reveal pathological characteristics in GCA: non-compressible arteries (compression sign), the wall thickening ("halo" sign), stenosis and vessel occlusion. A normal intima-media complex (IMC) of an artery is represented by US as a homogeneous, hypoechoic or anechoic echo structure delineated by two parallel hyperechoic margins. [19–27].

There is imperative to underline the importance of establishing the arteries that should be routinely examined in a patient suspected for GCA and these are: the TAs, and axillary arteries. If US of these arteries does not reveal suggestive lesions, in the presence of a clear patient history and of an obvious clinical examination, other arteries should be examined: other branches of the ECAs (the internal maxillary, the facial, the lingual, the occipital arteries), the vertebral, the subclavian, the common carotid arteries-CCAs, and the internal carotid arteries-ICAs. [9, 19, 21].

Regarding the adequate US equipment for the diagnosis of GCA, modern high-resolution linear probes providing Doppler mode should be used, especially for examination of TAs. We should take into consideration that tissue penetration increases with lower frequencies and the resolution of US increases with higher

frequencies. Probes that provide frequencies >20 MHz allow the clearly visualization of the normal IMC of TAs probes with frequencies ≥15 MHz are usually used for detection of minor wall thickening. [19, 21].

2.1 Ultrasonography (US) of the large cervical and cervico-brachial vessels

In 2012, during the Chapel Hill Consensus Conference [19, 28], large vascular vasculitis (LVV) was well-defined as a vasculitis involving the aorta and its major branches, although any size of artery may be affected. This definition does not state that LVV mainly affects large vessels because in many patients, the number of medium and small arteries affected is greater than the number of large arteries involvement. For example, in GCA, only few branches of the ECAs may be affected when there is involvement of numerous small branches extending into the eye and orbit (e.g., central retinal artery, posterior ciliary arteries). [29, 30] Less frequently, the CCA and the ICA are also affected (**Figures 3** and **4**). [9].

As Sturzenegger pointed up, angiography is not able to illustrate the vessel wall, so as to diagnose the inflammation of the large cervical and cervico-brachial vessels (aorta and its supra-aortic branches), the US can be very useful, since it can define alterations of the vessel wall with the use of B-mode imaging, while Doppler spectral flow velocity evaluation can help identify the stenosis or occlusion of the vessel. [19].

Color Doppler Duplex sonography (CDDS) is an excellent device used in screening the large vessels involvement. Agreeing with different authors, including Sturzenegger, there are two ultra-sonographic hallmarks of large vessels GCA:

1. Vessel wall thickening, that typically is homogeneous, circumferential and over long segments (**Figures 4** and **5**);

2. Stenosis, typically revealing slickly tapered luminal tightening (hour glass like) [19–27]

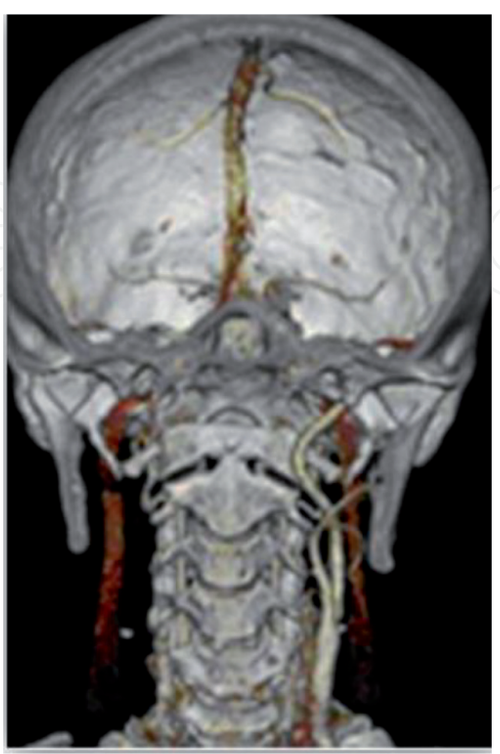

Figure 3.
Large vessels GCA; CT-angiography- occlusion of the left CCA, ECA, and ICA [9].

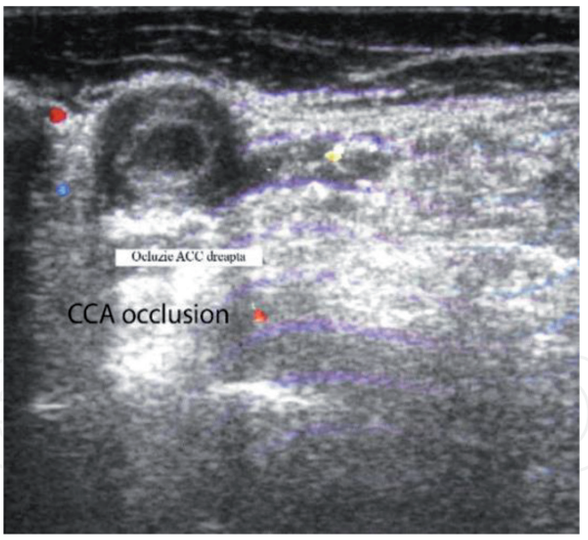

Figure 4.
Large vessels GCA, color Doppler ultrasound in transverse view of the right CCA. Hypoechoic wall swelling with right CCA occlusion [9].

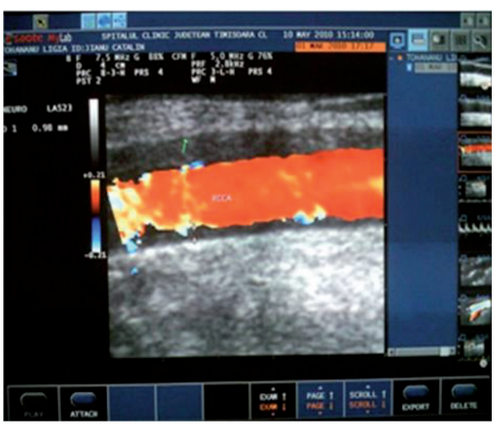

Figure 5.
Large vessel GCA, color Doppler ultrasound in longitudinal view of the right CCA with hypoechoic wall swelling [4].

Remarkably in some cases [9], the common carotid and the internal carotid arteries are also involved (large-vessel GCA) (**Figures 3**, **4**, and **5**).

2.2 Ultrasonography (US) of the temporal arteries (TAs)

Extracranial Duplex sonography investigates almost completely the whole length of the common superficial TAs, including the frontal and parietal branches, and founds that inflammation is segmental (intermittent arterial involvement) [19–27]. The common superficial TA derives from the ECA. It divides into the frontal and parietal ramus in front of the ear. The distal common superficial TA and the rami are localized between the two layers of the temporal fascia, which is like a bright band at ultrasound examination. [19–27].

2.2.1 Technical requirements

High-resolution color Doppler US can illustrate the vessel wall and the lumen of the TAs. One should use linear probes with a minimum gray scale frequency of 8 Mhz. Color frequency should be about 10 Mhz. [19–27].

2.2.2 Machine adjustments

The pulse repetition frequency (PRF) should be about 2.5 kHz as maximum systolic velocities are rather high (20-100 cm/s). Steering of the color box and the Doppler beam should be maximal as the rami are parallel to the probe. It is important that the color covers the artery lumen exactly. [19–27].

2.2.3 Sonographer training

The sonographer should perform at least 50 Duplex ultrasound of the TAs of subjects without GCA to be sure about the appearance of normal TAs before starting to evaluate patients with GCA. [19–27].

2.2.4 Sequence of the ultrasound examination

The investigation should begin with the TA, using the longitudinal scan. The probe should then be moved along the course of the TA to the parietal ramus. On the way back one should delineate the TA in transverse scans. Using the transverse scan, one can find the frontal ramus, which should then be delineated in both scans (longitudinal and transverse). If the color signal indicates localized aliasing and diastolic flow, one should use the pw-Doppler mode to confirm the presence of stenosis. [19–27].

In 1997 Schmidt et al. proved that the most specific (almost 100% specificity) and sensitive (73% sensitivity) sign for GCA was a concentric hypo-echogenic mural thickening, dubbed "halo", which the authors interpreted as "vessel wall edema". [24].

Other positive findings for GCA are the presence of occlusion and stenosis. [19–27].

In conclusion, there are three important items in the ultrasound diagnosis of temporal arteritis:

a. "dark halo" sign – a typically homogeneous, hypoechoic, circumferential wall thickening around the lumen of an inflamed TA - which represents vessel wall edema and a characteristic finding in temporal arteritis/GCA. It is well delineated toward the lumen (**Figure 6**).

b. stenosis are documented by blood-flow velocities, which are more than twice the rate recorded in the area of stenosis compared with the area before the stenosis, with wave forms demonstrating turbulence and reduced velocities behind the area of stenosis (**Figure 7**).

c. acute occlusions, in which the US image is comparable to that of acute embolism in other vessels, showing hypoechoic material in the former artery lumen with absence of color signals. [19–27]

Related ultrasound patterns can be found in other arteries: the facial, the internal maxillary, the lingual, the occipital, the distal subclavian and the axillary arteries.

The best time to perform ultrasound investigation is before initiating the corticosteroid treatment, or in the first 7 days of treatment, since with corticosteroid therapy the" halo" revealed by TAs ultrasound disappears within 2-3 weeks. The wall inflammation, stenosis, or occlusions of the larger arteries (CCA, ICA) remain for months, despite corticosteroid treatment. However, the diagnosis process should not postpone the initiation of therapy. Ultrasound may also detect inflamed

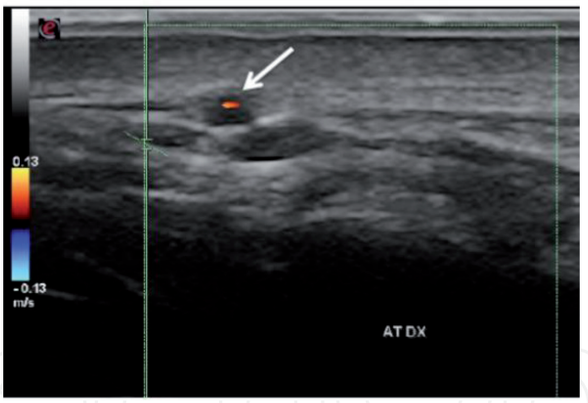

Figure 6.
Color Doppler ultrasonography (CDUS) of the right TA shows a hypoechoic halo around the lumen in transverse view (arrow). The "halo sign" corresponds to edema of the artery wall. [11].

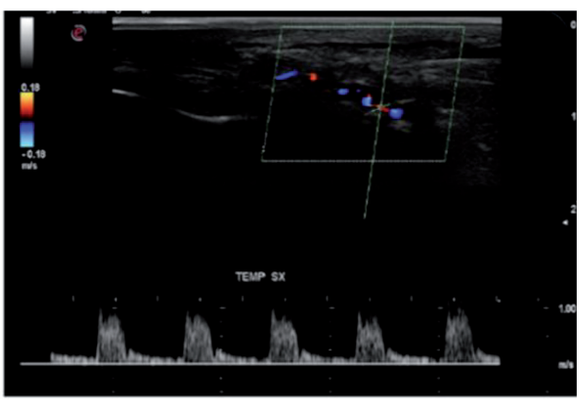

Figure 7.
Longitudinal view of the right TA by color Doppler ultrasonography (CDUS) shows a hypoechoic halo of the TA and the presence of turbulent and weak flow, suggesting the presence of stenosis. The PSV is 1 m/s, that is double compared to the segment without stenosis. [11].

TAs in patients with clinically normal TAs. Some patients with the clinical image of polymyalgia rheumatica, but with hidden TAs may be diagnosed using ultrasonography. [9–16, 19–27].

In 2010, Arida et al. [26] evaluated a number of studies that examined the sensitivity and specificity of the "halo" sign confirmed by TA ultrasound (US) for GCA diagnosis versus the American College of Rheumatology (ACR) 1990 criteria for the classification of this vasculitis (used as a reference standard). Only 8 studies involving 575 patients, 204 of whom received the final diagnosis of GCA, achieved the technical quality criteria for US. This meta-analysis disclosed a sensitivity of 68% and a specificity of 91% for the unilateral "halo" sign, as well as 43% and 100%, respectively, for the bilateral "halo" sign in TA US for GCA diagnosis when the 1990 ACR criteria are used as the reference standard. The authors established that the halo sign in US is of great utility in diagnosing GCA. [19–27].

In the case of consistent clinical and sonographic results, temporal arteries biopsy (TAB) does not appear to be useful and justified. [19, 27].

Sturzenegger affirmed that differential diagnosis with arteriosclerosis is important in patients over 50 years, taking into consideration that GCA with large vessels disease disturbs almost exclusively this category of patients. There are some characteristic features of the arteriosclerotic wall: the thickening usually appears less homogeneous; there are calcified arteriosclerotic plaques ulcers; stenosis extends over shorter segments, they are not concentric, not tapering, and location of lesions differs (e.g., mainly bifurcations). [19].

Besides, agreeing to Sturzenegger, differential diagnosis with the other LVV, especially Takayasu arteritis, has to be reflected:

- Takayasu arteritis usually affects women below the age of 40 years;
- symptoms like tender scalp or polymyalgia syndrome are exceptional;
- the involvement of CCA is more frequent in Takayasu arteritis, while the involvement of temporal artery in Takayasu arteritis is not known;
- US image of wall thickening ("halo") is brighter in TA than in GCA probably due to a larger mural edema in GCA which is a more acute disease than TA. Reflected. [19–27]

2.3 Color Doppler imaging (CDI) of orbital (retro-bulbar) vessels

Approximately 25% of patients with temporal artery biopsy (TAB) - proven GCA have ophthalmologic complications: usually unilateral visual loss (due to the vasculitic involvement of orbital vessels:

a. of posterior ciliary arteries (PCAs) - represented by arteritic anterior ischemic optic neuropathies (A-AION), or

b. of central retinal artery (CRA) - represented by central retinal artery occlusion (CRAO). [31–35]

Schmidt compared the results of TAs-US examinations with the occurrence of visual ischemic complications (A-AION, CRAO, branch retinal artery occlusion, diplopia, or amaurosis fugax) in 222 consecutive patients with newly diagnosed, active GCA. [21–24].

However, findings of TAs US did not correlate with eye complications. [21–24].

This is the reason why we always have to exam the orbital (retrobulbar) vessels in GCA patients or in patients with unilateral abrupt visual loss [9–16] (**Figure 8A,B**).

2.3.1 Orbital (retrobulbar) vessels

The ophthalmic artery (OA) branches in several arteries, including (**Table 1**):

a. the central retinal artery (CRA) (**Figure 8 A**), and

b. the posterior ciliary arteries (nasal and temporal branches-nPCAs, tPCAs) [28, 31, 32] (**Figure 8B**), (**Table 1**). [15, 28, 31, 32]

OA finishes in the a. supra-trohlearis and *A. dorsalis* nasi.

2.3.2 Probe selection

Standard neurovascular ultrasound machines equipped with linear-array transducers emitting 6-12 MHz (up to 15 MHz) are adequate for identifying (by Color Doppler sonography), and measuring (by spectral analysis pulsed Doppler sonography) the blood flow in the orbital vessels: the OA, the CRA and central retinal vein (CRV), PCAs, and the superior ophthalmic vein (SOV). [28, 31, 32].

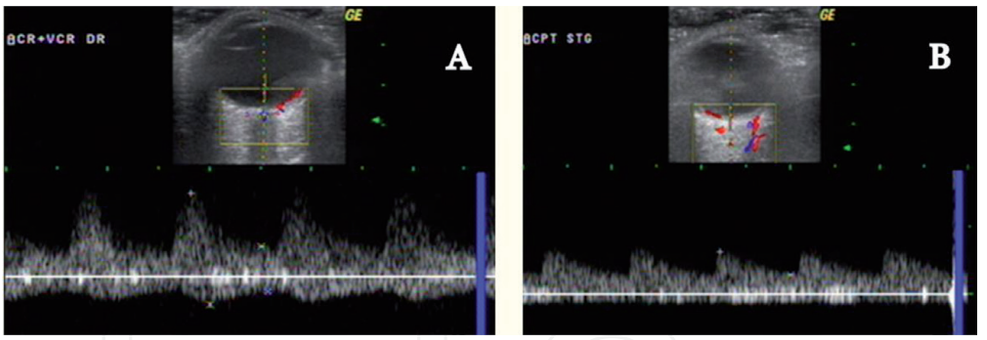

Figure 8.
Color Doppler imaging (CDI) of orbital (retro-bulbar) vessels: (A). central retinal artery (CRA); (B). posterior ciliary arteries (PCAs) [15].

Parameter	OA	CRA	PCA (temporal)	PCA (nasal)	SOV (superior ophthalmic vein)
PSV (cm/s)	45,3 ± 10,5	**17,3 ± 2,6**	**13,3 ± 3,5**	**12,4 ± 3,4**	10,2 ± 3,8
EDV (cm/s)	11,8 ± 4,3	**6,2 ± 2,7**	**6,4 ± 1,5**	**5,8 ± 2,5**	4,3 ± 2,4
RI	0,74 ± 0,07	**0,63 ± 0,09**	**0,52 ± 0,10**	**0,53 ± 0,08**	

Note: These are the normal flow velocities and resistances index in orbital vessels which are generally accepted by the specialists.

Table 1.
Normal flow velocities and Resistance Index in orbital vessels [15, 31, 32].

The CRA, a distal branch of the OA, enters the optic nerve (ON) approximately 1-1.5 cm distal from the bulbus coming from the dorsolateral direction. Parallel to this is the CRV.

The PCAs are located near the optic nerve (ON) (the nasal-nPCA and the temporal-tPCA branches). [28, 31, 32].

If the vessels are difficult to display, the power should be elevated for a short time if the clinical question is important. [28, 31, 32].

2.3.3 Arterial blood supply of the anterior part of the optic nerve

The optic nerve head (ONH) consists of (from anterior to posterior):

a. the surface nerve fiber layer - mostly supplied by the retinal arterioles. The cilioretinal artery, when present, usually supplies the corresponding sector of the surface layer. [36–40]

b. the prelaminar region - situated anterior of the lamina cribrosa. It is supplied by centripetal branches from the peripapillary choroid. [36–40]

c. the lamina cribrosa region - supplied by centripetal branches from the posterior ciliary arteries (PCAs), either directly or by the so-called arterial circle of Zinn and Haller (when is present). [36–40]

d. the retrolaminar region - is the part of the ONH that lies immediately behind the lamina cribrosa. It is supplied by two vascular systems: the peripheral centripetal and the axial centrifugal systems. The previous represents the main source of stream for this part. It is formed by recurrent pial branches arising from the peripapillary choroid and the circle of Zinn and Haller (when present,

or the PCAs instead). In addition, pial branches from the central retinal artery (CRA) also supply this part. The latter is not present in all eyes. When present, it is formed by inconstant branches arising from the intraneural part of the CRA.

From the description of the arterial supply of the ONH given above, it is obvious that the PCAs are the main source of blood supply to the ONH. [36–40].

2.3.4 Pathophysiology of factors controlling blood flow in the optic nerve head (ONH)

The blood flow in the ONH depends upon [36–40]:

a. resistance to blood flow - depends upon the condition and caliber of the vessels supplying the ONH, which in turn are influenced by: the efficiency of auto-regulation of the ONH blood flow, the vascular variations in the arteries feeding the ONH circulation, and the rheological properties of the blood.

b. arterial blood pressure (BP) - both arterial hypertension and hypotension can influence the ONH blood flow in several ways. In an ONH, a fall of blood pressure below a critical level of auto-regulation would decrease its blood flow. Decrease of BP in the ONH may be due to systemic (nocturnal arterial hypotension during sleep, intensive antihypertensive medication, etc.) or local hypotension.

c. intra-ocular pressure (IOP) - there is an opposite relationship between intra-ocular pressure and perfusion pressure in the ONH.

The blood flow in the ONH is calculated by using the following formula:

Perfusion pressure = Mean BP minus intraocular pressure (IOP).
Mean BP = Diastolic BP + 1/3 (systolic - diastolic BP) [6, 13].

3. Anterior ischemic optic neuropathies (AIONs)

AION is the consequence of an acute ischemic disorder (a segmental infarction) of the ONH supplied by the PCAs. Blood supply interruption can occur with or without arterial inflammation. Therefore, AION is of two types: non-arteritic AION (NA-AION) and arteritic AION (A-AION). The prior is far more common than the last, and they are distinct entities etiologically, pathogenically, clinically and from the management point of view. [36–40].

A history of amaurosis fugax before an abrupt, painless, and severe loss of vision of the involved eye, with concomitant diffuse pale optic disc edema is extremely suggestive of A-AION. None of these symptoms are found in NA-AION patients. [36–40].

3.1 Spectral Doppler analysis of the orbital (retro-bulbar) vessels in A-AION

In acute stage, blood flow cannot be detected in the PCAs in the clinically affected eye of any of the GCA patients with A-AION. Low end diastolic velocities (EDV) and high resistance index (RI) are identified in all other orbital vessels (including the PCAs in the opposite eye) of all A-AION patients. [9–14, 41].

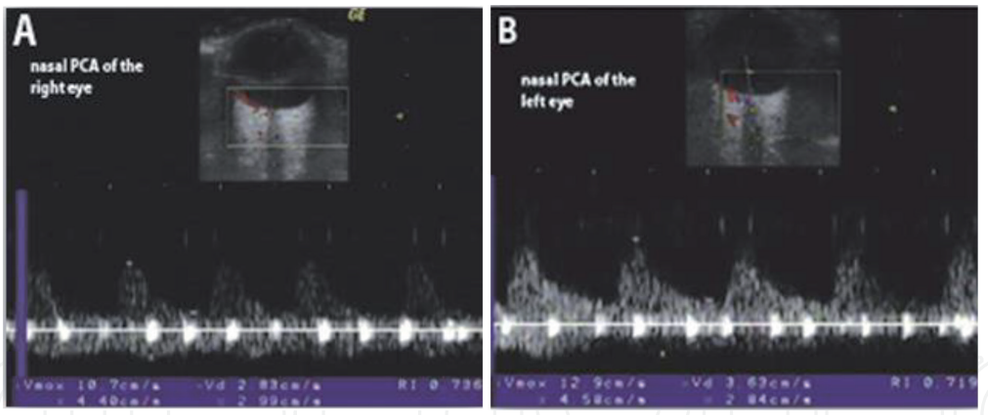

Figure 9.
CDI of the PCAs in A-AION: (A). Decreased EDV in the nasal PCAs of the clinically affected right eye, and (B) of the clinically unaffected left eye.

Over 7 days, Spectral Doppler analysis of the orbital vessels highlights blood flow alterations in all A-AION patients even with a high-dose corticosteroids therapy. Severely reduced blood flow velocities (especially EDV) in the PCAs of the affected eye (both nasal and temporal branches), compared to the unaffected eye, are observed. An increased RI in the PCAs is noted (the RI is higher on the clinically affected eye as compared to the unaffected eye). [9–14, 41] (**Figure 9A,B**).

Fewer abnormalities are detected in the CRAs: high RI are measured in both sides, with decreased peak systolic velocities (PSV) in the CRA of the clinically affected eye. [9–14, 41].

Similar abnormalities are noted in the OAs: high RI are measured in both sides. [9–14, 41].

At 1 month, after treatment with high-dose corticosteroids, CDI examinations of orbital blood vessels reveals that blood flow normalization is slow in all A-AION patients. [9–14, 41].

In conclusion, the Spectral Doppler Analysis of the orbital vessels in A-AION indicates (after several days of corticosteroid treatment) low blood velocities, especially EDV, and high RI in all orbital vessels, in both orbits. These signs represent characteristic signs of the CDI of the orbital vessels in A-AION. [9–14, 41].

3.2 Spectral Doppler analysis of the orbital (retro-bulbar) vessels in NA-AION

In contrast, the patients with NA-AION present the following characteristics in acute stage, and at 1 week of evolution:

- minor reduction of PSV in PCAs (nasal and temporal) in the affected eye, compared to the unaffected eye.

- slight decrease of PSV in CRA of the affected eye, due to papillary edema. [9–14, 41]:

- in OAs, PSV are variable: normal to decreased, according to ipsilateral ICAs status.

Severe ICA stenosis (≥70% of vessel diameter) combined with an insufficient Willis polygon led to diminish PSV in ipsilateral OA. [9–14, 41].

In 1 month, CDI examinations of orbital blood vessels reveal that blood flow normalization is reached. The exceptions are the cases with severe ipsilateral ICA stenosis/occlusion. [9–14, 41].

In conclusion, in NA-AION, blood velocities and RI in PCAs are preserved. Similar results were obtained in other studies. [9–14, 41].

Fluorescein angiogram and CDI of the orbital vessels data support the histopathological evidence of involvement of the entire trunk of the PCAs in the A-AION (impaired optic disc and choroidal perfusion in the patients with A-AION). On the other hand, in the NA-AION, the impaired flow to the optic nerve head (ONH) is distal to the PCAs themselves, possibly at the level of the para-optic branches (only 1/3 of the flow of the PCAs). [36–40].

These branches supply the ONH directly (impaired optic disc perfusion, with relatively conservation of the choroidal perfusion). [36–40].

Extremely delayed or absent filling of the choroid has been depicted as a fluorescein angiogram characteristic of arteritic AION and has been suggested as one useful factor by which A-AION can be differentiated from NA-AION. [36–40].

4. Central retinal artery occlusion (CRAO)

CRAO is the result of an abrupt diminuation of blood flow in CRA, severe enough to cause ischemia of the inner retina. Due to the fact that there are no functional anastomoses between choroidal (PCAs) and retinal circulation (CRA), CRAO determines severe and permanent loss of vision. Therefore, it is very important to identify the cause of CRAO, in order to protect the contralateral eye. Frequently, the site of the blockage is within the optic nerve substance and for this reason, it is generally not visible on the ophthalmoscopy. The majority of CRAO are caused by thrombus formation due to systemic diseases, including GCA. For this reason, all patients with CRAO should undergo a systemic evaluation. [42–44].

4.1 Spectral Doppler analysis of the orbital (retro-bulbar) vessels in CRAO

The patients with an unilateral CRAO present at the Spectral Doppler analysis of the retrobulbar vessels the following aspects [9, 15, 16]:

a. an elevated RI in the CRAs (the RI is higher on the affected side, than it is on the unaffected side); with severe diminished blood flow velocities (especially EDV) in the CRA.

b. fewer abnormalities are observed in the PCAs, and in the OAs (**Figure 10**).

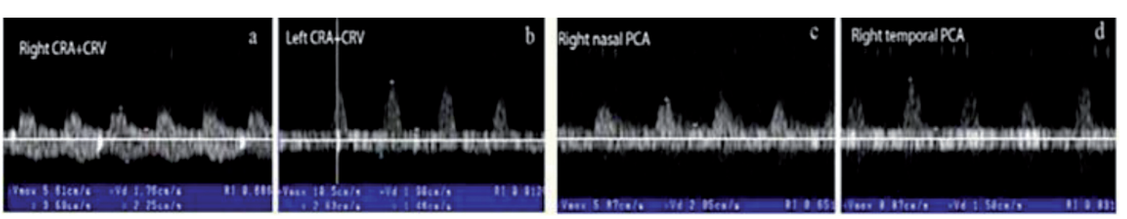

Figure 10.
CDI of orbital vessels revealed severely diminished EDV and high RI in both CRAs (a, b) despite the fact that the left eye had the normal aspect at ophthalmoscopy. Fewer abnormalities were observed in the PCAs (c, d). [15].

5. US and others imaging techniques

Other imaging techniques, such as high-resolution magnetic resonance imaging (MRI), magnetic resonance-angiography (MR-A), computer tomography angiography (CT-A), positron emission tomography (PET) provide valuable information regarding the structure of large vessels, highlighting with much greater precision the thoracic aorta, compared with US. [45–47].

There are few studies that compared US with other imaging techniques. Some of them indicated that there is a good correlation between US and PET, even though PET might have a little more sensitivity for vertebral arteries examination. [45–46] 18F-fluorodeoxyglucose-positron emission tomography/ computed tomography (FDG-PET/CT) has a higher sensitivity for detection of large arteries and aortic involvement - analysis of the arterial wall. [45, 46] The diagnostic power of high-resolution MRI and color-coded duplex US of extra-cranial arteries in detecting GCA are equivalent [47].

The disadvantages of this techniques are: they are more expensive, hardly accessible, some of them are limited by invasiveness, nephrotoxicity (angiography) and exposure to high radiations (CT,PET), this is why they might be unnecessary (excepting those patients with exclusively thoracic aorta involvement) and are not accepted as diagnostic methods in GCA. They should only be used when interventions are required [45–47].

All these imaging techniques should always be performed by well-trained specialists, using suitable equipment and operational protocols. [45–47].

Nevertheless, US is particularly useful in examining the orbital vessels. [9–16, 28, 31, 32, 41].

The diagnostic work-up of AION benefits from the combined used of fluorescein angiography and noninvasive multimodal imaging, including CDI of the orbital vessels and structural Optical Coherence Tomography (OCT) of the optic nerve head (ONH) and OCT angiography [10, 48]. They provide very detailed information regarding the structural (retinal nerve fiber layer-RNFL-thickness/optic disc edema) and vascular impairments (microvascular defects-vessel tortuosity, and vessel density reduction) of the ONH, respectively [10, 48].

6. Conclusions

US should be used as a first-line diagnostic investigation for patients presenting with clinical and biological features suggestive for GCA, taking into consideration that it has a high sensitivity to detect vessel wall thickening (dark hallo sign) in the case of large/medium vessels. In a few cases of our studies, the CCAs and the ICAs were also involved.

In consequence, in our department, CCDS has emerged as a safe and reliable alternative to TAB as a point of care diagnostic tool in the management of temporal arteritis.

The eye involvement in GCA is frequent and consists in A-AIONs or CRAO, with abrupt, painless, and severe loss of vision of the involved eye.

Because findings of TAs US do not correlate with eye complications in GCA, CDI of the orbital vessels is of critical importance, in order to quickly differentiate the mechanism of eye involvement (arteritic, versus non-arteritic). This US tehnique may be helpful to detect the blood flow in the orbital vessels, especially in cases of opacity of the medium, or when the clinical appearance of ophthalmologic complications in temporal arteritis is athypical.

The Spectral Doppler Analysis of the orbital vessels in GCA with eye involvement reveals low blood velocities, especially EDV, and high RI in all orbital vessels, in both orbits, for all patients (especially on the affected side).

A huge advantage of CDI of orbital vessels is that it provides immediate information that can be used to inform treatment decisions, including a potential reduction in loss of sight and avoidance of unnecessary long-term steroid treatment by early exclusion of mimics.

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