Ultrasound in vasculitis

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ABSTRACT

Colour Doppler ultrasound displays a pathognomonic circumferential wall thickening in large-vessel vasculitis. Even rather small arteries like the temporal arteries can be easily examined with modern ultrasound equipment. In addition, ultrasound can detect stenoses and acute arterial occlusions. In large-vessel giant cell arteritis, the axillary arteries are most commonly involved. Takayasu arteritis affects particularly the left subclavian and the left common carotid arteries.

As ultrasound diagnosis at the temporal arteries becomes more difficult already after a few days of glucocorticoid treatment in some patients, institutions are implementing fast-track clinics for which patients receive an appointment within 24 hours. An experienced rheumatologist is able to establish a definite diagnosis in most cases with standardised history, clinical examination and ultrasound of temporal and axillary arteries. Furthermore, early diagnosis and treatment may prevent blindness.

Introduction

Ultrasound has become an important diagnostic tool for the rheumatologist within the last decade. Due to improved image quality and resolution even small arteries like the temporal arteries can be examined with ultrasound. Many studies have been published on ultrasound in vasculitis. The topic has been already covered by review articles in Clinical and Experimental Rheumatology in 2000 and in 2008 (1, 2). This article provides an update and focusses on practical issues of colour Doppler ultrasound particularly in large-vessel vasculitis.

In small-vessel vasculitides, ultrasound is used for determining disease extension and disease activity. Ultrasound can for instance evaluate renal, cardiac and pleural involvement (3). The diagnosis of small-vessel vasculitis needs to be confirmed histologically. In rare cases, small-vessel vasculitis can also affect larger arteries like the digital arteries (4, 5).

In the medium-vessel vasculitides, Kawasaki disease and polyarteritis nodosa, aneurysms frequently occur. These may be detected by ultrasound (6). Coronary aneurysms may complicate the course of the disease. Forty-four percent of patients had a coronary artery lesion (31% with ectasia, 13% with aneurysm) on the initial echocardiogram in a study of 100 patients with Kawasaki disease (7). Aneurysms may lead to coronary artery occlusion with cardiac infarction and impaired left ventricular function. Echocardiography is the imaging examination of first choice in suspected Kawasaki disease.

Ultrasound is particularly useful in the diagnosis of large-vessel vasculitis because characteristic wall thickening of affected arteries allows confirming a suspected diagnosis.

Temporal arteritis

Since the mid-1990s ultrasound has been used in diagnosis of temporal arteritis. Technology has significantly improved since then. In fact, a modern high-frequency probe provides both an axial and lateral resolution of 0.1 mm (100 µm). However, it is still advisable to use high-end technology. The linear probe should provide a frequency of at least 10 MHz for grey-scale ultrasound, preferably 15 MHz or more, and at least 7 MHz for colour Doppler ultrasound. The sonographer should have examined temporal arteries of about 30 to 50 healthy subjects and should have seen at least 3-5 patients with definite temporal arteritis before using this method for routine practice.

The patient lies supine looking at the ultrasound monitor. When the sonographer begins with a longitudinal scan anterior to the left ear (Fig. 1) examining the common superficial temporal artery (a), the patient can see the monitor. Then the sonographer continues

	Table L	 Settings 	for	ultrasound	of the	temporal	arteries
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Item	Setting	Comment	
B-mode frequency	10-20 (-50) MHz	As high as possible	
Colour Doppler frequency	7-12 MHz	50-70% of B-mode frequency	
Pulse repetition frequency	2-3 KHz		
Image depth	1-2 cm		
Focus position	4 mm	below skin surface	
Number of foci	1		
B gain	Bright enough	For distinguishing lumen and halo	
Colour gain	Not too high	Colour would cover halo	
Colour gain	Not too low	Pseudo halo at periphery of lumen	
Colour Doppler box	Maximum steering		

distally to the parietal branch (b) and returns scanning the parietal branch and the common superficial artery in transverse planes. From the bifurcation the sonographer follows the frontal branch in a longitudinal plane with regard to the course of the artery and returns using a transverse plane (c). The examination is than repeated on the right side. The temporal arteries should be examined as completely as possible. The pressure from the probe should be low, Otherwise the temporal arteries may be compressed and thus become invisible. In areas where the temporal arteries localise under hair, more ultrasound gel is needed, and pressure may be slightly increased in order to receive an adequate image of the artery (8).

The temporal arteries are localised superficially, about 4 mm below skin surface. Although they are rather small with a diameter of lumen and wall of about 0.7 mm, respectively, they are easily accessible with ultrasound. Ul-



Fig. 1. Anatomic scheme of the temporal arteries: **a**. common superficial temporal artery, **b**. parietal branch, **c**. frontal branch.

trasound allows assessing the whole length of the superficial temporal arteries (9). The grey-scale ultrasound image of a normal temporal artery displays the anechoic lumen. Examination is easier when using the colour Doppler mode. In this case the perfused lumen is color coded. The lumen is surrounded by a hyperechoic structure that represents the artery wall and the temporal fascia (Fig. 2-3). The temporal fascia encloses the distal common superficial temporal artery and its branches.

In case of acute temporal arteritis ultrasound shows a circumferential hypoechoic wall swelling due to oedema (Fig. 4-5). This phenomenon has also been called "halo sign" (9). It is hypoechoic (dark), not anechoic (black), and it represents inflammatory tissue. This tissue is not compressible (10). This wall swelling disappears after two to three weeks with glucocorticoid treatment in most patients with a wide range from 2 days to 6 months in some cases (11-15).

Often stenoses of short segments occur. Then colour Doppler shows a blurring mixture of colours (aliasing) together with persistent blood flow in the diastole. Pulsed wave-Doppler then displays an at least two-fold increase of the maximum systolic blood flow velocity in the stenosis compared to an area before or behind the stenosis. In addition, occlusions may occur, showing an artery that is not filled with colour Doppler signals.

For an examination of the temporal arteries the grey-scale frequency should be as high as possible. The colour frequency should be about 1/2 to 2/3 of the grey- scale frequency. The focus should be positioned at about 4 mm below skin surface. The sonographer should use colour Doppler mode not power Doppler mode. The average maximum blood flow velocities in the temporal arteries are rather high (around 50 cm/s), so that power Doppler mode is not necessary. The borderlines of the colour are often not as clear as with colour Doppler sonography. Stenoses may be missed by power Doppler sonography because it is insensitive to the aliasing phenomenon described above. The colour box needs to be steered in order to have the blood flow not completely parallel to the probe.

The pulse repetition frequency (PRF) should be adjusted around 2.5 to 3 KHz. The colour gain (colour sensitivity) should not be too low or too high. If it is too low, only the centre of the lumen would show colour signals leaving an anechoic (black) rim between lumen and wall. This phenomenon must not be confused with a wall thickening which is hypoechoic showing tissue. If the colour gain is too high, the inflamed area may be covered and disease may be missed (8).

Many studies have been conducted comparing temporal artery ultrasound with histology and with the clinical diagnosis of temporal arteritis. Three meta-analyses have been published (16-18). The sensitivity of temporal artery duplex ultrasound was 87% with regard to the clinical diagnosis, and the specificity was 96% in one of the meta-analvses (16). The presence of a bilateral halo seems to increase the specificity (17). Minor histological findings with small-vessel vasculitis of the vasa vasorum in the adventitia may be missed by ultrasound (19). Ultrasound probes with higher frequencies (50 MHz) might increase the sensitivity (20). With increasing experience and quality of the ultrasound equipment more centres achieve reliable results for the ultrasound examination and replace temporal artery biopsy in cases with definitive clinical and ultrasound findings (21-23). After training for temporal artery ultrasound inter- and intra-reader agreements have been shown to be excellent with kappa values over 0.8(24).

It is also possible to examine the occipital arteries which may be exclusively



Fig. 2. Colour Doppler ultrasound image of a normal temporal artery using a 10-22 MHz probe in a longitudinal view.



Fig. 3. Colour Doppler ultrasound image of a normal frontal branch (**a**) and parietal branch (**b**) using a 6-18 MHz probe in a transverse view.

involved in some patients, particularly if they are presenting with retroauricular pain (25). The facial arteries are particularly involved in patients with jaw claudication (26).

As the wall swelling of the temporal arteries disappears quickly and reoccurs only in severe flares, follow-up ultrasound examinations do not need to be routinely done. Patients' history and the monitoring of CRP and ESR usually provide enough information if the disease is active or not.

Large-vessel giant cell arteritis

Increased use and quality of imaging shows that extracranial arterial involvement in GCA is much more common than previously assumed. About 50% of the newly diagnosed GCA patients

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have axillary artery involvement (27, 28). Adding axillary ultrasound to temporal artery ultrasound in a protocol increases the diagnostic yield for GCA in routine practice, particularly as only 60% of patients with large-vessel GCA have temporal artery involvement. An experienced sonographer examining both the temporal and axillary arteries should find more GCA patients than biopsy with histology of a 1–2 cm long segment of one of the branches of the common superficial temporal arteries (29).

When comparing patients with classic cranial temporal arteritis to patients with proximal arm artery involvement (large-vessel GCA), patients with large-vessel GCA tend to be younger (66 years vs. 72 years); and more of them are female (83% vs. 66%). Time between onset of symptoms and diagnosis is longer (7 months vs. 2 months) (27, 30). Duration of treatment and prednisolone doses are similar. Patients with large-vessel GCA are developing less commonly anterior ischaemic optic neuropathy (31, 32). Critical limb ischemia usually does not occur in the course of the disease (31, 33). The axillary arteries are more commonly involved than the subclavian and brachial arteries (27, 28). Bilateral vessel involvement is present in most patients (27, 28, 34). Patients with large-vessel GCA may either present with classic cranial temporal arteritis, with pure PMR, arm claudicatio or pyrexia of unknown origin.

The axillary arteries can be easily and quickly examined with ultrasound. The probe is placed longitudinally in the axilla along the humeral head and neck (8). This scan is identical with the axillary shoulder scan for detecting glenohumeral joint effusions. The axillary artery localises either at the level of the humerus or 1 to 2 cm medially to it. It runs proximally to the circumflexa humeri artery. The area distal to the circumflexa humeri artery is the proximal brachial artery which may also show vasculitis. In order to receive a good colour Doppler image the colour box needs to be steered as described for the temporal arteries above, in order to avoid a blood flow perpendicular to



Fig. 4. Colour Doppler ultrasound showing acute temporal arteritis using a 10-22 MHz probe. The hypoechoic wall swelling is seen even outside the colour box in the grey-scale (B-mode) image (**a**). At this segment the diameter of the swollen wall is 0.6 mm (**b**). The brighter colour with a mixture of colours (**c**) indicates aliasing as a sign of a stenosis.



Fig. 5. Transverse view of the same artery in temporal arteritis. The arrows indicate the "halo".

the sound waves. To evaluate the artery wall with grey-scale, the probe and vessel should be as parallel as possible. A normal vessel shows an intima-media complex of less than one millimeter (Fig. 6). A bright line represents the interface between artery lumen and vessel wall followed by a dark line representing wall tissue and another bright line representing the interface between media and adventitia.

In case of large-vessel vasculitis the artery wall is thickened, usually more than 1 mm (Fig. 7). For the author, a homogeneous wall swelling, preferably circumferential, of 1.5 mm or more is pathognomonic for the diagnosis of

axillary vasculitis (27). Vasculitis may lead to stenosis showing aliasing as explained above in the temporal arteries and characteristic pulsed wave (pw)-Doppler curves with increased systolic and diastolic flow velocities. Sometimes axillary or proximal brachial arteries are occluded due to vasculitis.

Arteriosclerosis is uncommon both in the temporal or axillary arteries. It is hyperechoic, inhomogeneous and often asymmetric. The carotid, femoral and popliteal arteries are much more often affected by arteriosclerosis. In some few cases it may be difficult to differentiate hypoechoic plaques from vasculitic lesions. However, most often it is easy to differentiate arteriosclerosis from vasculitis with ultrasound (29).

Other arteries like the subclavian, common carotid and vertebral arteries can also be easily examined by ultrasound. However, these arteries are rarely affected in GCA without involvement of either the temporal or axillary arteries. Therefore, routinely examining these arteries will not greatly increase the sensitivity of ultrasound. Carotid artery stenoses are rarely caused by GCA. Most stenoses in the age group around 70 to 75 years are due to arteriosclerosis. However, stenoses and occlusions may occur in the vertebral arteries causing cerebral ischaemia and stroke (35). The clinical examination of patients with GCA should include the palpation of the pedal pulses. If these pulses are not palpable and particularly if patients complain about lower limb claudication the arteries of the lower leg should be examined by ultrasound. Particularly the superficial femoral arteries and the popliteal arteries are commonly involved in GCA (36).

With medical treatment alone, the prognosis of GCA of the arm arteries is benign in nearly all cases (24, 26). Ultrasound may be performed every 6 months for follow-up in order to measure the maximum wall thickness. If the diameter decreases or remains the same, the disease activity presumably has been under control during this period (37).

Polymyalgia rheumatica

Shoulder and hip ultrasound increases the specificity for diagnosing PMR. Therefore musculoskeletal ultrasound has been incorporated into the new EULAR / ACR classification criteria (38). Patients in whom ultrasound revealed inflammation in the shoulder and hip region respond better to glucocorticoid treatment (39). A subgroup of PMR patients reveals largevessel vasculitis. In 7% of patients with "pure PMR", e.g. PMR without symptoms of temporal arteritis, temporal artery ultrasound was positive (40). Adding ultrasound of axillary arteries about 15% of patients with "pure PMR" will be diagnosed with large-vessel vasculitis (29).



Fig. 6. Longitudinal (a) and transverse (b) view of a normal axillary artery.



Fig. 7. Longitudinal (a) and transverse (b) views of an axillary artery in large-vessel GCA. The arrows indicate the vasculitic wall swelling.

Takayasu arteritis

GCA and Takayasu arteritis are similar regarding histology and initial response to treatment. However, Takayasu arteritis never affects the temporal arteries. Patients with Takayasu arteritis are significantly younger at disease onset; and they experience more severe flares with vascular complications than GCA patients. Duration of treatment is far longer. Takayasu arteritis usually occurs less symmetrically. It most commonly affects the left subclavian and common carotid arteries (34).

The ultrasound images are similar in GCA and Takayasu arteritis. In acute flares the wall is hypoechoic because of wall oedema (41). It becomes more hyperechoic with treatment (42). Contrast-enhanced ultrasound may show increased vascularity of the artery wall in active disease (43). In most cases the diagnosis of Takayasu arteritis is not established before stenoses occur.

However, early praestenotic disease can be detected by ultrasound because of its high resolution and excellent depiction of the artery walls (44). In suspected disease the carotid, subclavian and vertebral arteries should be examined together with the abdominal aorta. The renal arteries should be examined in case of arterial hypertension (29). Echocardiography may reveal the following abnormalities: 1. Leftventricular hypertrophy as arterial hypertension caused by renal artery stenosis may be missed because of subclavian artery stenoses or occlusions; 2. Vasculitic

wall swelling of the ascending aorta. The first 4 cm of the ascending aorta are well visible with transthoracic echocardiography. 3. Aortic valve insufficiency due to vasculitis of the ascending aorta. 4. Pericardial effusion. 5. Pulmonary hypertension due to vasculitic stenosis of the pulmonary arteries (45).

Follow-up examinations are done as in

large-vessel GCA to evaluate increase or decrease of wall swelling and stenoses. The use of imaging for follow-up has yet to be proven in larger trials (46).

Aortitis

Isolated aortitis is rare. Aortitis is common in GCA and Takayasu arteritis. The abdominal aorta is fairly well visible with ultrasound if the patient is not obese. Most parts of the thoracic aorta are accessible only by transoesophageal ultrasound.

Two similar entities affect the wall and/ or the tissue around the abdominal aorta: aortitis / periaortitis and retroperitoneal fibrosis with or without IgG 4 relation (47). CRP and ESR are increased in both entities. However, the increase is most commonly greater in aortitis. Usually, only retroperitoneal fibrosis leads to hydronephrosis. Treatment of both diseases includes immunosuppressive therapy, notably glucocorticoids. Both MRI and CT are the imaging procedures of choice for the diagnosis for retroperitoneal fibrosis (48). Ultrasound is disappointing for detecting retroperitoneal fibrosis as it fails to clearly differentiate the affected tissue from the surrounding tissue. However, ultrasound clearly delineates an inflamed aortic wall in abdominal aortitis (29).

Ultrasound and other imaging techniques

Ultrasound has many advantages: It is widely available; and it can be performed by the rheumatologist himself. The suspected diagnosis can be confirmed or excluded immediately. Ultrasound is non-invasive and has no relevant side effects. During the examination findings can be already discussed with the patient. The sonographer needs to be well trained in vascular ultrasound in order to provide reliable results. A good reliability is possible as mentioned above. An experienced sonographer can do a standardised ultrasound examination of temporal and axillary arteries in 10 minutes. An extensive ultrasound examination of all arteries that may be potentially affected by vasculitis would be very time consuming.

High quality magnetic resonance imaging (MRI) with dedicated coils can be

used for examining the temporal arteries. The diagnostic power for diagnosing temporal arteries is similar for MRI and ultrasound (49). MRI can also depict the artery walls; and it is superior to ultrasound for examining the thoracic aorta. MR-angiography (MRA) provides a good overview of affected arteries. Computed tomography (CT) and CT-angiography (CTA) are alternatives to MRI and MRA (50). However, CT has not yet been used for examining the temporal arteries. Positron emission tomography (PET) and PET-CT provide also a good overview, but they are limited by high radiation exposition, high costs and the inability to examine the temporal arteries (51). Ultrasound and PET correlate well for diagnosing GCA (52). Conventional angiography is invasive and does not depict the artery wall. It has still its place for interventional treatment, particularly in Takayasu arteritis.

Practical application of ultrasound

Fast-track clinics for the diagnosis of giant cell arteritis help initiate treatment before complications such as blindness occur. In such clinics, patients receive appointments within 24 hours. Clinical examination and ultrasound of temporal and axillary arteries are performed by an experienced rheumatologist. Other arteries may be examined depending on clinical findings. In most cases this allows to clearly determine if GCA is present or not. Temporal artery biopsy is done in ambivalent cases. Other imaging techniques like MRI, MRA, CT, CTA or PET can be done particularly if aortitis is suspected and ultrasound findings are not clear. MRA may provide an overview of involved vessels particularly for patients with Takayasu arteritis in order to have information about the vascular pattern before treatment. Conventional angiography is only used for interventional treatment. Particularly ultrasound is a valuable tool for follow-up particularly for large-vessel GCA and Takayasu arteritis.

In conclusion, ultrasound has become a valuable diagnostic tool for largevessel vasculitis. It helps establish the diagnosis early and thus may prevent complications such as blindness.

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