
Magnetic resonance imaging and magnetic resonance angiography in large-vessel vasculitides

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ABSTRACT

The role of imaging in diagnosis and monitoring of vasculitides has steadily become more important during the last years. As a result of the technological progress, its low invasiveness and its relatively good diagnostic reliability, magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) are increasingly used in the assessment of vasculitic changes of extra- and intra-cranial arteries. The aim of this review is to outline the significance of different imaging modalities, particularly the significance of MRI/MRA, in the context of large-vessel vasculitides, especially in regard to the first EULAR (The European League Against Rheumatism)-recommendations on the role of imaging in the process of diagnosis and monitoring of patients with suspected large-vessel vasculitides. Furthermore, some typical imaging findings as well as the basics of MRI technique are to be presented.

Introduction

The aim of this review is to outline the significance at this time of magnetic resonance imaging/angiography (MRI/MRA) in diagnosis and therapy monitoring of large-vessel vasculitides (LVV). The term large-vessel vasculitides refers to a group of primary vasculitides, multisystem disorders, characterised by autoimmunologically mediated granulomatous inflammatory processes of large and medium-sized blood vessels, predominantly affecting the aorta and its major branches with consecutive tissue necrosis (1). The two main forms of large-vessel vasculitides are giant cell (temporal) arteritis (GCA) and Takayasu's arteritis (TAK) (2).

The two entities differ in terms of clinical symptoms, the involvement pattern (or anatomic localisation) of the affected vessels, as well as in epidemiological conditions. Giant cell arteritis is

a disease of the elderly people, often associated with polymyalgia rheumatica, with a disease onset rarely before the age of 50 years. Takayasu's arteritis mostly affects younger people, rarely occurring after the age of 50 years (1, 3).

Both GCA and TAK involve the aorta and its major branches. In GCA, a predominance is seen of the supra-aortic vessels such as the subclavian, carotid, axillary, and superficial cranial arteries, in particular temporal and occipital artery. TAK affects predominantly the aortic arch and its major branches from the carotid to the external iliac artery (1, 4).

Vessel wall inflammation in large-vessel vasculitides may result in a number of severe complications, particularly due to the involved vessels' vicinity and relevance in terms of blood supply to the brain and its associated structures. While cerebrovascular involvement is well-known in TAK, it is controversially discussed in GCA (5-7). The most feared complications include irreversible vision loss as a result of anterior ischaemic optic neuropathy (AION) in case of giant cell arteritis, stenosis and occlusion of large arteries with the consequence of ischaemic (brain) injuries, and aortic aneurysms and dissections in case of TAK (8-10). These complications may be associated with considerable morbidity and mortality. Early diagnosis and adequate therapy is of essential value to prevent these severe complications.

Diagnosis of large-vessel vasculitides

Classification criteria for GCA and TAK of the American College of Rheumatology (ACR) which have been incorporated in most medical guidelines, include various clinical aspects and histopathological findings of the temporal artery in case of giant cell arteritis, but no imaging features to date (11, 12). It may be challenging to identify

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patients with large-vessel vasculitides, as they often present with a non-specific systemic inflammatory constellation in terms of clinical symptoms and laboratory values. Temporal artery biopsy is considered the “gold standard” in diagnosing the cranial form of giant cell arteritis (13-15).

Due to rapid technological progress in recent years, imaging plays an increasingly important role in diagnosis and monitoring of large-vessel vasculitides, more and more as the preferred complement to clinical examination and as a substitute to temporal artery biopsy. At this time, most common imaging modalities are colour-coded duplex sonography (CCDS), CT angiography (CTA), magnetic-resonance imaging/angiography (MRI/MRA), ¹⁸F-fluorodeoxyglucose positron emission tomography (FDG-PET), as well as catheter-based angiography (16, 17). EULAR (The European League Against Rheumatism) has recently released its first recommendations on the role of imaging in the process of diagnosis and monitoring of patients with suspected large-vessel vasculitides. These recommendations are mainly based on a systematic literature review (18), intended to guide primary, secondary and tertiary care physicians, such as neurologists, ophthalmologists or rheumatologists through diagnosis and monitoring in regard of application of imaging modalities (19). The most important statements among the 12 recommendations concerning imaging in large-vessel vasculitides (19) are summarised below:

EULAR recommendations concerning the use of imaging in diagnosis and monitoring of patients with large vessel vasculitides (19) – the value of MRI in today’s guidelines

The preferred complement to clinical criteria in patients with suspected large-vessel vasculitides is an early imaging examination, presuming expertise, adequate equipment, operational procedures and settings. Preferably, imaging should take place before or as early as possible after initiation of therapy, as sensitivity is rapidly reduced under treatment with glucocorticoids (20-23). However, if adequate imag-

ing is not available in the foreseeable future, other diagnostic tests should be conducted in order to confirm or exclude the diagnosis. Considering the possible complications of large-vessel vasculitides, predominantly occurring before initiation of therapy, treatment of large-vessel vasculitides should never be delayed because of scheduled diagnostic (imaging) tests or biopsies.

i. Giant cell arteritis

In case of suspected predominantly cranial giant cell arteritis, colour-coded duplex sonography (CCDS) of temporal or/and axillary arteries is recommended as the preferred imaging modality, especially for its widespread and fast availability, good reliability, absence of procedural risks such as radiation and cost-efficiency. A hypoechoic, non-compressible halo sign is the typical finding in giant cell arteritis (24). If CCDS is inconclusive or not available, an alternative is high resolution MRI. Sensitivity and specificity of CCDS and high-resolution MRI in detecting mural inflammation signs in giant cell arteritis are comparable (18, 25).

In case of a positive imaging test in combination with a high clinical probability, giant cell arteritis may be diagnosed without any further test. In case of a negative imaging test combined with a low clinical suspicion, giant cell arteritis may be considered unlikely (19). If, after clinical examination and imaging test, there is still uncertainty, further steps need to be taken in order to confirm or exclude diagnosis of giant cell arteritis. Positron emission computed tomography (PET-CT) is not suitable to assess inflammation of intracranial arteries. However, CCDS, PET, MRI or CT may be used to assess inflammatory wall and/or luminal changes in extracranial arteries in the framework of giant cell arteritis.

Temporal artery biopsy is not supposed to be discarded as diagnostic procedure in GCA in favor of imaging by the new EULAR recommendations. Instead, imaging should be preferred over biopsy as a diagnostic procedure for its low invasiveness, rapid availability of imaging results and its superior evalua-

tion of disease extent and identification of other involved arteries in further localisations. This is of importance, since GCA is a systemic disease and most often affects more than one single vessel territory. However, under circumstances in which adequate imaging and expertise are not available, temporal artery biopsy is indicated to confirm clinically suspected GCA. Imaging is redundant, provided that temporal artery biopsy has already been conducted and is positive (19). A negative biopsy result does not rule out giant cell arteritis as there might be still unaffected segments of the temporal artery in an active vasculitis. In case of a negative or questionable biopsy, imaging might provide additional information.

ii. Takayasu’s arteritis

In the context of suspected TAK, MRI is recommended as the preferred diagnostic test to investigate luminal changes or mural inflammation, presuming expertise and availability. Alternatively, PET, CT and/or CCDS may be used for the assessment of inflammation processes or luminal changes in patients with TAK. However, value of CCDS in assessing the aorta and some of its branches is limited due to their anatomic localisation (19).

For long-term monitoring of large-vessel vasculitides as well as assessment of complications and structural damage, MRI/MRA, CTA and/or CCDS may be used. Modality and frequency of repeat scanning should be adjusted to the individual circumstances. However, routine imaging is not provided for patients in clinical and biochemical remission. Conventional angiography is not recommended anymore in diagnosis and monitoring of large-vessel vasculitides (26).

MRI in large-vessel vasculitides

Large-vessel vasculitides are systemic inflammatory diseases and have variable involvement patterns. The superficial temporal artery with its branches and the superficial occipital artery are common sites of vascular inflammation in giant cell arteritis, typically with a segmental involvement pattern (27-29). The aortic arch and its branches includ-

ing the pulmonary artery are classically affected in TAK. However, in both, GCA and TAK, involvement patterns are variable and may include coronary, carotid, external iliac, as well as intracranial arteries. Therefore, MR-imaging should preferably include as much of the potentially affected vasculature as possible to capture the entire disease extent.

Several studies have shown that MRI is suited to reveal vasculitic changes of superficial cranial arteries (30, 31). MR-imaging is suitable for the assessment of both extracranial “deep” arteries, including the large body vessels, and extracranial superficial arteries, particularly the superficial temporal and occipital arteries, as well as intracranial arteries simultaneously. Settings and technical parameters vary and depend on the anatomic localisation to be examined.

MRI findings

Characteristic MRI findings in the context of vasculitides can be divided into direct and indirect signs (32). Direct signs of vessel inflammation include particularly mural thickening and contrast enhancement of the affected vessel. A 4-point ranking scale, classifying the vessel affection according to wall thickness and mural contrast enhancement with the cut-off value of 600 μm for the diameter of the vessel wall can be used for the assessment, graduation and standardisation of vasculitic changes (31).

MRI-visible mural inflammatory changes of the vessel wall resolve under treatment with corticosteroids, resulting in a substantial decrease of sensitivity in detecting signs of vessel inflammation in MRI after 5 or more days of therapy (33). However, imaging should not be delayed if imaging is not available.

Indirect signs of vasculitides, indicating already incurred complications, include non-arteriosclerotic vascular stenosis and, in case of brain-supplying arteries, cerebral ischaemic infarction or perfusion deficit and intraparenchymatous or subarachnoid haemorrhage (32). Vascular stenosis caused by inflammation is characterised by a circular contrast enhancement and narrowing of the lu-

menal diameter, in contrast to eccentric plaque and stenosis in case of arteriosclerotic changes (32, 34).

MRI technique

i. Cranial MRI

For assessment of vasculitic changes of intracranial and extracranial superficial arteries, a 3.0 T MRI scanner and at least an 8-channel head-coil are used preferentially. Routinely, T1-weighted spin echo, gadolinium contrast-enhanced, fat-suppressed, high-resolution (for example inplane $195 \times 260 \mu\text{m}^2$, slice thickness 3 mm, repetition time (TR) / echo time (TE) 500/22 ms) sequences should be acquired. T2-weighted turbo spin echo, non-contrast-enhanced imaging (TR/TE 9000/143 ms) is significantly less sensitive (19). Transversal slices are angulated parallel to corpus callosum in standard assessments.

ii. Body MRI

For assessment of vasculitic changes of the large body vessels, a 3.0 T MRI scanner and minimum an 8-channel head and neck coil and a 16-channel body coil are used preferentially. In order to capture as many affected arteries as possible, MR angiography of the aorta and its major branches should include vessels from the carotid bifurcation to the iliac arteries in coronal acquisition to include the axillary and brachial arteries. Possible vasculitic changes include stenoses, occlusions and aneurysms; therefore, assessment of vessel lumina is important. In order to assess mural inflammation, T1-weighted, fat-suppressed, contrast-enhanced sequences as well as black blood imaging (*e.g.* 1 navigated three-dimensional TSE, spatial resolution $1.2 \times 1.3 \times 2 \text{ mm}^3$, TR/TE 1000/35 ms) are preferentially used. T2-weighted TSE sequences are more prone to artefacts and less sensitive to detect oedema in mural inflammation (19).

A contrast-enhanced, fat-suppressed, high-resolution T1-weighted spin echo sequence is the most valuable sequence for detecting mural inflammatory changes in GCA. MR-angiography, especially TOF (Time-of-Flight)-angiography in case of assessment of the intracranial arteries and contrast-en-

hanced time-resolved TWIST (Time-resolved angiography With Interleaved Stochastic Trajectories)-angiography in case of assessment of the large body vessels, are helpful to evaluate the lumen diameter and detect eventual vessel stenosis or occlusion. Unenhanced T1-weighted, T2-weighted or diffusion weighted imaging, etc. might add important anatomic and functional information and may be helpful in detecting vasculitic complications, such as infarctions or hemorrhage. However, they are not mandatory for diagnosis, and may be omitted in order to reduce scanning time. Long T1-weighted sequences may be used without impairment of their diagnostic value, as contrast enhancement usually persists relatively long in the inflamed vessel walls after the contrast agents has left the vascular system.

Discussion

MR-imaging plays a significant role in diagnosis and monitoring of patients with large-vessel vasculitides, and will probably be of increased importance in the future. The diagnostic value of both MRI and CCDS in the assessment of inflammatory vessel changes in giant cell arteritis is comparable, with pooled sensitivity of MRI: 73%; specificity: 88% (18), and similar values in a retrospective direct comparison with a sensitivity of 69% in MRI and 67% in CCDS and a specificity of 91% in both modalities (25). MRI, however, is characterised by a higher standardisation in regard to data acquisition and reproduction. MRI is a non-invasive imaging modality, featuring anatomy and vasculature in three dimensions and with high spatial resolution without using radiation. Multiple extra- and intra-cranial arteries can be investigated simultaneously, thus enabling assessment of disease extent within one single imaging test. This feature is of importance since large-vessel vasculitides are systemic disorders and display a segmental or rather intermittent distribution pattern of inflamed vessel segments. MRI and CCDS enable reliable detection of affected vessel segments, with the inherent possibility of indicating the inflamed segment prone

to biopsy, potentially contributing to a reduction of the number of false-negative biopsies (33).

Another imaging modality, rather known for its significance in oncology is ¹⁸F-fluorodeoxyglucose positron emission tomography (FDG-PET), which reveals abnormal metabolic activity in the wall of inflamed vessels by means of functional imaging. Recent data suggest that FDG-PET is more suitable to assess disease activity while MRI is superior in evaluating disease extent and vascular damage in large-vessel vasculitides, so that both modalities provide complementary information (35). Also, MRI does not use ionising radiation and is suitable for repeat studies in young patients with TAK.

Limitations of imaging

Nonetheless, imaging has its constraints. Sensitivity of all imaging modalities decreases after treatment initiation with glucocorticoids. It is reported that sensitivity of MRI decreases significantly within five days after therapy initiation (33), and the halo-sign in CCDS disappears about 14–21 days after initiation of glucocorticoid treatment (36). However, within several days after treatment initiation, diagnosis through imaging may be difficult in some cases (37).

In contrast to these imaging tests, temporal artery biopsy seems to be valuable up to 4 weeks after treatment initiation (38).

Furthermore, general aspects of MRI represent limitations; availability of MRI is still restricted, its costs are relatively high, the imaging times are quite long and require, to a certain extent, the patients' compliance. In addition, administration of contrast agent may, although in rare cases, entail severe consequences.

Conclusions

On the basis of ongoing technological progress and despite of certain limitations, imaging has gained great importance in diagnosis and therapy monitoring of large-vessel vasculitides, increasingly replacing invasive tests such as temporal artery biopsy or conventional angiography. Today's

EULAR-guidelines concerning diagnosis of large-vessel vasculitides recommend an imaging test as first complement to clinical examination - CCDS as preferred imaging modality in suspected giant cell arteritis, with MRI as equivalent alternative in case of inconclusive results, and MRI as first choice in suspected TAK. MRI/MRA, CTA, FDG-PET and/or CCDS often provide complementary information and may be used depending on and coordinated with individual circumstances for long-term monitoring of large-vessel vasculitides. MRI has promising potential to gain priority in imaging of vasculitis, due to its variable potential applications in terms of intra- and extracranial vessel assessment and as a non-invasive, radiation-free technique.

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