Established in 1871
Swiss Medical Weekly
Formerly: Schweizerische Medizinische Wochenschrift
An open access, online journal • www.smw.ch

Viewpoint | Published 1 March 2017 | doi:10.4414/smw.2017.14405
Cite this as: Swiss Med Wkly. 2017;147:w14405

Large vessel vasculitis: which imaging method?

Marco A Cimmino[a], Dario Camellino[b]

[a] Research Laboratory and Academic Division of Rheumatology, University of Genova, Genova, Italy
[b] Autoimmunology Laboratory, Department of Internal Medicine, University of Genova, Genova, Italy

Imaging has dramatically changed our understanding of large vessel vasculitides. They can be identified with ultrasound, ^{18}F-fluorodeoxyglucose positron emission tomography (PET), combined or not with computed tomography (CT), and magnetic resonance imaging (MRI) [1]. With these techniques, large vessel vasculitides have also been recognised in patients presenting with only nonspecific signs or symptoms, such as malaise and fever, or increased inflammatory indices.

Large vessel vasculitides are not a homogeneous group of conditions since they include several diseases in addition to giant-cell arteritis and Takayasu's arteritis [2]: IgG4-related disease, rheumatoid arthritis, systemic lupus erythematosus, Behçet's syndrome and Cogan's syndrome can also affect the aorta and its branches.

In their retrospective study published in *Swiss Medical Weekly* [3], Adler et al. showed a high positive predictive value (92%) of magnetic resonance angiography (MRA) of the aorta for diagnosing large vessel vasculitis. Their most striking finding was that glucocorticoid treatment for more than 5 days reduced the chance of classifying MRA as positive by 89.3%. In giant-cell arteritis, MRI is very effective for assessing inflammation of the temporal arteries, with a sensitivity of 93.6% (assuming temporal artery biopsy to be the reference standard) [4].

In this study, 51/75 patients who underwent MRA were judged as "imaging negative". Six of these patients, however, were considered to have large vessel vasculitis on the basis of their clinical picture, and five showed positive histology of the temporal artery, despite more than 5 days of glucocorticoid treatment. This finding suggests that temporal artery biopsy, in spite of being an invasive procedure and lacking sensitivity, maintains its pivotal role in the diagnosis of giant-cell arteritis. Conversely, three patients with negative temporal artery biopsy showed positive MRA, confirming that inflammation is flighty in choosing its targets and that a combined approach is therefore needed to identify both cranial and extra-cranial sites of arteritis.

PET/CT could appear a more appealing method in detecting large vessel vasculitis, because it allows a panoramic visualisation of the aorta and its branches. However, its role in patients receiving glucocorticoids has been not defined and the temporal artery cannot be visualised because of its small diameter and the presence of the very intense adjacent brain uptake. In addition, the interpretation of PET/CT in large vessel vasculitis is still controversial, as reflected by the many published scoring methods [5]. Anecdotal observations of temporal artery inflammation detected by PET have been made [6], however.

Early reports have suggested that MRI is better for identifying anatomical abnormalities such as stenosis and dilation, whereas PET seems better for active inflammation [7]. This issue will probably be overcome by the use of combined PET/MRI machines. An MRI protocol able to simultaneously evaluate cranial arteries and aorta in the same session has been proposed [8]. Although this approach needs to be validated, it could represent the ideal imaging tool in this condition. In fact, MRI and MRA are safe in the large majority of patients, whereas PET/CT exposes patients to ionising radiation, a crucial issue, especially in patients with Takayasu's arteritis, who are typically women of reproductive age. Definition of vasculitis and scoring methods for MRI are consistent between different studies, especially regarding giant-cell arteritis, focusing on thickening and enhancing of the arterial wall in T1 sequences. T2-weighted images can show high signal intensity related to mural oedema, although this latter finding, if isolated, is not considered pathognomonic of vasculitis.

Recently, simultaneous MRI evaluation of arterial wall thickness and enhancement, contour aspects, T2 signal, and presence of stenosis has been proposed [9]. In a small and heterogeneous cohort of patients, a poor correlation between this score and clinical and laboratory parameters was found.

The most important limitation of ultrasound, MRI and PET studies in large vessel vasculitis is the lack of histological confirmation of imaging findings: a definite diagnosis by an expert clinician is usually taken as reference standard [10], an approach representing "circular reasoning". The cases, usually identified on the basis of clinical suspicion, are investigated with an imaging tool and the confirmation of the diagnosis (and therefore of the truthfulness of imaging findings) is then based on clinical evaluation, which is influenced by the results of imaging. Except for anecdotal reports [11], histological confirmation of large vessel vasculitis is not feasible in the vast majority of patients and most of our knowledge still relies on old necropsy studies [12].

A possible limitation of the study by Adler et al. is that it merged all patients with large vessel vasculitis. Takayasu's arteritis and giant-cell arteritis are differentiated on the basis of age, but the debate as to whether their differences exceed their similarities is still open [13]. Moreover, isolated aortitis is an increasingly recognised entity, which should probably be separated from giant-cell and Takayasu's arteritis, because it is characterised by younger age compared with giant-cell arteritis and a higher risk of aortic damage requiring surgery. Isolated aortitis has been classified separately in the latest Chapel Hill Consensus Conference as "single organ" vasculitis [2], but many reports consider it together with other large vessel vasculitides. The scenario is further complicated by the observation of large vessel vasculitis at imaging in at least one third of patients with apparently clinical isolated polymyalgia rheumatica [14], raising the doubt whether it represents an incomplete form of giant-cell arteritis or a disease *per se*. Giant-cell arteritis, Takayasu's arteritis, vasculitis associated with polymyalgia rheumatica and isolated aortitis share pathological characteristics, but evidence for considering these forms of large vessel vasculitis a single entity is still lacking. As a consequence, each of these diseases should probably be studied separately.

In the end, which is the best imaging method for detecting large vessel vasculitis? The answer has yet to come. A PubMed search of the terms "large vessel vasculitis AND positron emission tomography" performed on 23 October 2016 yielded 95 results published in the last five years, in comparison with 83 for "large vessel vasculitis AND magnetic resonance imaging". This indicates that both tech-

niques continue to be under the spotlight, at least in the research field.

Disclosure statement
No financial support and no other potential conflict of interest relevant to this article was reported.

Correspondence
Marco Amedeo Cimmino, MD
Università di Genova
Viale Benedetto XV, 6
I-16132 Genova
cimmino[at]unige.it

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