L30. Assessment of vasculitis extent and severity

Introduction

Various criteria have been proposed to date to classify vasculitis. The diameter of the vessels involved is the main parameter upon which classification criteria are based, while additional parameters are the presence of granulomata and of antineutrophil cytoplasmic antibodies (ANCA). For the purpose of classification, small vessels are considered those whose caliber is inferior to 50 μm, medium vessels those with a caliber of 50 to 150 μm, and large vessels those with a caliber superior to 150 μm. Large-vessel vasculitides typically include giant cell arteritis (GCA) and Takayasu arteritis (TAK). Medium-vessel vasculitis is classically represented by polyarteritis nodosa (PAN), while ANCA-associated vasculitides (AAV) affect medium to small vessels. Herein, we reviewed the evidence on the classification, small vessels are considered those whose caliber is inferior to 50 μm, medium vessels those with a caliber of 50 to 150 μm, and large vessels those with a caliber superior to 150 μm. Large-vessel vasculitides typically include giant cell arteritis (GCA) and Takayasu arteritis (TAK). Medium-vessel vasculitis is classically represented by polyarteritis nodosa (PAN), while ANCA-associated vasculitides (AAV) affect medium to small vessels. Herein, we reviewed the evidence on assessment of disease extent and severity in the main types of vasculitides affecting large, medium and small vessels, respectively.

Large-vessel vasculitides

Clinical criteria to assess TAK were developed back in 1994 at the National Institute of Health (NIH) by Kerr et al. and still go by the name of Kerr or NIH criteria. These criteria encompass the following four parameters:

- systemic features (fever, musculoskeletal manifestations...);
- a raised erythrocyte sedimentation rate (ESR);
- manifestations of vascular ischemia (decreased/absent pulses, claudication, carotodynia, asymmetric blood pressure readings in the limbs);
- typical angiographic features (long, smooth stenoses). These criteria were developed from a population of 60 Takayasu patients followed up prospectively, of whom those with active disease received aortograms every 4 to 6 months. According to these criteria, active disease is defined by the presence of at least two of the above items. An analysis by the authors, however, revealed that their main drawback was a quite poor sensitivity, with 61% of patients judged as having “inactive” disease incurring progression of angiographic lesions.

More recent tools to assess disease activity of TAK are the Disease Extent Index.Takayasu (DEI.TAK) and the Indian Takayasu Activity Score (ITAS), which are both derived from the Birmingham vasculitis activity score (BVAS), the ITAS being a simplified version of the DEI.TAK. Both tools consider the presence of clinical features in organ-based domains, inflammatory markers (ESR and C-reactive protein) and physician global assessment (active/persistent/inactive). Clinical features must be specific for vasculitis and are scored as absent or present; for clinical features to be considered present, they must be new or have recently worsened. Disease is considered active if at least one organ system scores positive, while inflammatory markers and physician global assessment do not count per se toward assessment of disease activity. As these tools are remarkably similar, they show a high degree of correlation. A comparative analysis also demonstrated a high concordance between ITAS and Kerr indices in a population of patients with TAK. However, 31% of clinically active patients were in remission according to the DEI.TAK; conversely, the DEI.TAK was positive in 18% of patients felt to be clinically inactive. No specific tool has been yet designed to assess disease activity of GCA, although the Kerr and ITAS have empirically been used to do so in patients with large-vessel GCA. OMERACT 2011 has acknowledged the limitations inherent in the Kerr and ITAS indices and recognized the need to develop finer-tuned assessment tools.

In clinical practice and trials alike imaging procedures are the mainstay to assess large-vessel vasculitis. Color-Doppler sonography (CDS), magnetic resonance (MR) angiography (MRA) and contrast-enhanced computerized tomography (CT) combined with CT angiography (CTA) can visualize both the vessel wall and the lumen of large vessels. All these techniques are able to demonstrate early inflammatory signs (vessel wall thickening and mural inflammation) as well as late complications (stenoses and aneurysms). 18F-Fluorodeoxyglucose (FDG) positron emission tomography (PET) is able to detect increased FDG uptake by metabolically active cells, including inflammatory cells infiltrating the vessel wall in vasculitis, while digital subtraction angiography (DSA) is useful to demonstrate luminal changes.
Disease extent is better evaluated in early large-vessel vasculitis by techniques able to reveal early vascular changes, i.e., vessel wall thickening and mural inflammation (CDS, MR and CT). CDS lends itself particularly well to examining superficial vessels (epiaortic vessels, renal arteries and limb arteries), while CT and MR can also depict deep vessels such as the aorta. Alternatively, PET can be used. PET can reveal active inflammation in most vessels potentially affected by GCA and TAK except the temporal and renal arteries and is probably more sensitive than MR. Monitoring of luminal changes over time requires morphological imaging including CDS, MRA, CTA or DSA.

In GCA, disease severity is mainly related to morbidity, while mortality is very rarely increased (in patients with thoracic aorta involvement that incur dissection). Risk factors for GCA-related ischemic events including visual loss comprise previous ischemic events, marked intimal hyperplasia on temporal artery biopsy, moderately (but not very high) serum inflammatory markers, older age at diagnosis, hypertension, previous ischemic heart disease and absence of systemic manifestations.

**Medium-vessel vasculitis**

PAN is the paradigm medium-vessel vasculitis. Disease extent is typically determined by clinical manifestations, if required supported by DSA especially to detect visceral vessel (micro-)aneurysms. The BVAS can also be used to systematically define the organs involved. Age over 65 years, hypertension, and severe gastrointestinal manifestations are independent predictors of death, whereas patients with cutaneous manifestations or PAN unrelated to chronic hepatitis B virus have a higher risk of relapses. An important prognostic tool for PAN is the five-factors score (FFS), which has been validated in a cohort of patients with PAN (which also included patients with microscopic polyangiitis [MPA]) and Churg-Strauss syndrome (CSS). The FFS includes five items:

- proteinuria greater than 1 g/24 h;
- serum creatinine greater than 140 μmol/l (1.58 mg/dl);
- specific cardiomyopathy;
- specific digestive system involvement;
- specific central nervous system involvement.

Five-year mortality rate is 12% when the FFS = 0, 25% when the FFS = 1, and 50% when the FFS ≥ 2. However, the FFS does not predict the risk of relapses. A revised version of the FFS (FFS2) has been validated for use in PAN, MPA, CSS and granulomatosis with polyangiitis (GPA). The revised FFS2 comprises five items, four with a positive score (+1) and one with a negative score (−1). The four items scoring positive are age over 65 years, cardiac involvement, gastrointestinal involvement and renal failure (creatinine > 1.7 mg/dl), while the item conferring a negative score is ENT involvement. Five-year mortality rate is 7.5% when the FFS2 = 0, 20% when the FFS2 = 1, and 47% when the FFS2 superior or equal to 2.

**Small-vessel vasculitis**

AAV affect small and small-medium vessels and comprise GPA, MPA and CSS. According to OMERACT 2011, the BVAS should be used to measure disease extent and activity in patients with AAV. The BVAS has also a prognostic value, with very high scores predicting fatal outcomes. A BVAS specifically generated for patients with GPA (BVAS/WG) is available. According to BVAS/WG, severe (life or organ threatening manifestations) include skin gangrene, scleritis, retinal involvement, sensineural hearing loss, mesenteric ischemia, alveolar hemorrhage, respiratory failure, an active urinary sediment with red cell casts, progressive renal failure and neurological involvement. Furthermore, as mentioned above, the FFS (2) can also be used to predict outcomes and thus tailor treatment accordingly. Finally, to assess the extent of both disease- and drug-induced damage OMERACT recommends that the Vasculitis damage index (VDI) be used.

**Disclosure of interest:** the authors have not supplied their declaration of conflict of interest.

**L31. A GWAS in ANCA-associated vasculitis: Will genetics help re-define clinical classification?**

Autoimmune diseases are a significant public health problem and are increasing in prevalence worldwide. They are a major cause of chronic morbidity as well as premature mortality. Anti-neutrophil cytoplasm antibody (ANCA)-associated vasculitis (AAV) is a severe, systemic autoimmune disease characterised by vascular inflammation and the presence of circulating auto-antibodies against neutrophil granule components, primarily proteinase 3 (PR3) and myeloperoxidase (MPO). AAV, which has a prevalence of 145/million in the UK [1], is comprised of...