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Editorial

Quantifying disease involvement in Takayasu's arteritis

Scoring with colour-Doppler ultrasound

Large vessel vasculitis has been the poor relative of primary systemic vasculitides, taking ideas on pathology and therapy like hand-me-down clothes from well-developed studies in small-vessel vasculitis (SVV), whether they fit or not. Takayasu's arteritis (TA), more frequent in Eastern countries with less well endowed medical science resources, particularly lacks an evidence base for therapy. This cannot be achieved without standardized assessments of disease activity and damage, which need to be TA specific, since the clinical expression is very different from SVV. Symptoms in TA relate to the characteristic vessel stenosis that often develops insidiously, promoting collateral flow with intermittent ischaemia rather than acute tissue infarction. Both inflammation and thrombosis may contribute to stenosis, often in the absence of raised acute phase response (APR). There is no biomarker for diagnosing TA, nor one for assessing activity, hence the reliance on angiography for diagnosis as well as to define the sites involved.

In practice, therapy decisions in TA are directed by clinical disease activity, the APR and imaging [1]. This physician's global assessment (PGA) is heavily dependent on the doctor's experience. A standardized approach to scoring clinical activity [Indian Takayasu Activity Score (ITAS)] was recently reported from India [2]. The score can also incorporate ESR or CRP (ITAS.A). Imaging has relied on angiography, but it reveals luminal blockage rather than vessel wall involvement. Magnetic resonance angiography (MRA) can show vessel wall thickening, but this tissue oedema correlates poorly with clinical score or ESR. PET scans may light up extensive linear areas in the vessel wall, particularly in early TA. This is often interpreted as inflammation, but the scans do not regularly correlate with symptoms nor do they clear coincidentally with clinical improvement. Similar aortic scans are seen in temporal arteritis not associated with clinical involvement and not progressing to the stenosis characteristic of TA [3]. Thus the nature of the lesions underlying hot PET scans needs further study [4].

Vascular involvement in other forms of GCA has been imaged extensively using US [5]. This has the advantages of avoiding the high radiation doses of angiography or PET and is cheaper and more widely available—particularly relevant in Asia, hence the importance of the study by Sinha *et al.* [6] in Kolkata, India applying colour Doppler US imaging (CDUS) to TA. US has been applied to image stenosis in TA before. The key advance of the Sinha *et al.* study is that it examines 19 vascular regions in a standardized fashion, scoring each for both stenosis and flow pattern. This produces a quantitative score, CDUS-Kolkata (CDUS-K) that reflects the vessels where pulse loss can be detected clinically in TA. However, it is not clear whether including all the main downstream vessels is useful. If there is a femoral artery lesion, does US of the popliteal and dorsalis pedis arteries provide extra information? Fewer vessels scanned could shorten the 50 minutes required, which may be important in routine follow-up.

The correlation with the angiography score is reassuring, but CDUS is the most user-dependent radiological method. Intrathoracic vessels such as the commonly involved subclavian are especially difficult to visualize and produced the lowest kappa values in this study. CDUS-K needs urgent study in other centres to confirm its practicality in practice. A second major drawback of the study is its cross-sectional nature, so the sensitivity to change is unknown. CDUS-K scores each vessel dichotomously (as 0 and 1), thus limiting the assessment of further changes in the vessel lumen [7]. How will increased stenosis, aneurysm development or increased vessel wall involvement be determined? This can be a serious issue when clinical signs or APR point to a new relapse, and the physician might have to turn to conventional imaging for sensitive assessment of the vessel changes. Serial assessments with angiography plus ITAS are essential to clarify these issues.

Another question is whether CDUS is simply a cheaper way to gain diagnostic information on vessel occlusions or whether it provides something extra. The ability to distinguish between stenosis resulting from current active inflammation and that due to the scars of previous disease would have a major influence on therapy decisions. Future studies of the nature of the lesions detected by CDUS and their relationship to vessel wall abnormalities detected by PET and by MRA, as well as to clinical features, may tell us more about the nature of pre-stenotic lesions in TA. The current study showed good correlations between CDUS-K and the clinical activity score, but we do not know how much that reflects a stenosis score *vs* a score of more diffuse alterations in flow patterns. The ESR data are provided but they have not been related to the CDUS-K score. A longitudinal study is again essential to establish if it changes in response to clinically successful therapy.

The exciting point for those interested in TA is that we possess a quantitative clinical disease activity score in ITAS2010, a way to integrate that with the acute phase response in ITAS.A [2] and now an apparently quantitative way to score vascular images acquired by a patient-friendly technique. These may not be ideal tests, but they do cover the three factors (clinical activity, acute phase and vessel imaging) defined as important to estimate PGA [7]. These assessments are not necessarily in their final state and wider experience will doubtless hone the details. The best way to assemble these scores into a compound index also requires work, but experience with the 28-joint DAS and all its variants in RA [8] suggests that committing to collect data using standardized scores may be more important than trying to establish precisely which compound score offers most. The PGA may suffice for experienced experts, but a standardized score will be more reproducible for the wider mass of practitioners seeing uncommon disease. The immediate hope is that the combination of validated clinical activity assessments plus quantitative imaging may now form the basis for much needed clinical trials. The evidence base for therapy in this serious progressive disease currently resembles the emperor's new clothes. The mainstay of steroids has never been tested and the EULAR guideline on adding immunosuppressive agents [9] is recommended in the absence of hard evidence. A concerted effort is needed to improve this dire situation and the means to start work on it now appears to be at hand.

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