Commentary on the recent international multicentre study (EUVAS) on antineutrophil cytoplasmic antibodies

Antineutrophil cytoplasmic antibodies (ANCAs)-associated vasculitis (AAV) is a group of potentially life-threatening conditions that require early and accurate diagnosis, most often based on a combination of clinical and serological features.[1] Most of the therapeutic modalities have immune-suppressing activity and can result in serious consequences, especially if applied to patients without AAV, such as those with infectious diseases, which may have clinical features that mimic AAV. Because an early and accurate diagnosis of AAV is a clinical imperative, both the differential diagnosis and the working diagnosis leading to urgent initial treatment are critical steps in the clinical care pathway. Even then, refinement of the diagnosis might be required during the clinical course after the initial choice of therapeutic strategies.

In this context and with interest we read the recent article by Damoiseaux *et al*[2] summarising the results from a large international multicentre study on ANCA. The findings seemed to indicate that (1) most anti-proteinase 3 (PR3) and anti-myeloperoxidase (MPO) solid phase immunoassays outperform the ANCA indirect immunofluorescence (IIF) test and (2) there is significant variability and lack of interlaboratory commutability between two IIF methods for the detection of ANCA. These findings led to the conclusion that only solid phase assays are needed for the screening of ANCA, especially because IIF ANCA results were not commutable between laboratories. Based on this observation, it is very encouraging that novel solid phase immunoassays for the detection of anti-PR3 and anti-MPO antibodies have evolved over the past years and reached a very high degree of performance. However, we suggest that before wide adoption of a new testing algorithm, it would be of high relevance to perform studies with more than two IIF ANCA tests and especially include assays that are most commonly used in diagnostic laboratories. This information can be easily obtained from proficiency testing reports such as through College of American Pathologists (CAP), United Kingdom National External Quality Assessment Service (UK NEQAS) or similar organisations in other jurisdictions. This is of special importance since one of the assays used was a 'home-made' assay. The data generated during the European Vasculitis Study (EUVAS) are of high value and we encourage the authors to further expand the study by analysing the data from different perspectives to provide more insights. Such additional analyses might include the assessment of likelihood ratios as a function of autoantibody levels and the potential value of combining results from different tests,[3] especially high-performing IIF ANCA assays with high-performing solid phase tests. Such combined results might offer increased likelihood and ORs for AAV as demonstrated recently for antinuclear antibody (ANA)-associated rheumatic diseases[3] and for ANCA testing.[4] In addition, multivariate analyses are needed to assess different combinations of test results which might prove extremely useful in patients with low pretest probability of disease. The authors also discuss the potential need for gating strategies for ANCA testing,[5] mostly to reduce testing requests in the setting of low pretest probability. Although we agree with this challenge, we want to point out that this can be a double-edged sword since in an emergency or intensive care setting, the immediate detection and diagnosis of AAV is an imperative and can be life-saving. In those cases, IIF and solid phase assays might provide an increased likelihood ratio for AAV. On the same note, patients who are double negative for ANCA by IIF and solid phase assay would represent a very low likelihood of suffering from AAV.

Finally, as pointed out by Damoiseaux *et al*, ANCA are not only used for the diagnosis of AAV but also used for other conditions, such as inflammatory bowel disease,[6–8] autoimmune hepatitis,[9] and primary sclerosing cholangitis.[7] Accordingly, it is important that laboratories clearly differentiate between test requisitions for AAV versus these other conditions.

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