Comparison of PR3-specific ANCA assays performance for diagnosis of granulomatosis with polyangiitis (GPA)

A. Radice¹, L. Bianchi², S. Gionna², B. Trezzi², U. Maggiore³, R.A. Sinico²
1. San Carlo Borromeo Hospital, Microbiology Institute, Milan, Italy
2. San Carlo Borromeo Hospital, Nephrology and Clinical Immunology, Milan, Italy
3. Maggiore Hospital, Nephrology and Transplantation, Parma, Italy

Introduction.– PR3-ANCAs are usually detected by immunometric assays, with purified PR3 directly coated onto the solid-phase. Novel methods for PR3-ANCA detection have been proposed with the goal of improving the traditional PR3-specific assays, although little is known about their diagnostic performance in real-life clinical settings.

The purpose of this monocentric retrospective study was to investigate and compare the diagnostic performance of nine different commercial PR3-specific assays, representative of the 1st, 2nd, and 3rd generation tests (direct, capture and anchor assays). The third generation assay, employing both human and recombinant PR3, was also evaluated.

Methods.– The study population consisted of 55 GPA, 175 disease controls, including 52 microscopic polyangiitis and 20 healthy subjects. GPA pts were selected on the basis of the clinical diagnosis, according to the international criteria & definitions available. Median age of GPA was 53.5 yrs (13–82), 31 were ♂. The primary evaluation of test sensitivity was carried out using cut-off points, which provided adequate and identical specificity for each test.

Results.– Although sensitivity & area under the ROC curves did not differ significantly between any of the PR3-specific assays, substantial differences in sensitivity at 98% specificity were found in some instances (Supplementary data, P < 0.001).

Discussion.– Our study shows that, compared to direct PR3-ELISAs, most of the capture/anchor tests improve the PPV for GPA diagnosis. Indeed, some of the 2nd & 3rd generation assays show a better performance than the traditional direct ones when the relevant cut-point is selected to guarantee the high specificity (98%) requested for such critical investigations. In addition, most of the 2nd and 3rd generation assays make easier the discrimination between +ve and –ve samples due to the reduction of borderline ANCA values.

Conclusion.– The usefulness of the new assays in monitoring the disease activity needs to be ascertained.

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PR3-ANCA: A promising biomarker for the differentiation of ulcerative colitis and Crohn’s disease

M. Mahler¹, C. Bentow¹, D. Blockmans², S. Vermeire³, P. Rutgeerts⁴, X. Bossuyt⁴
1. INOVA Diagnostics, San Diego, USA
2. University Hospitals, General Internal Medicine, Leuven, Belgium
3. University Hospitals Leuven, Gastroenterology, Leuven, Belgium
4. University Hospitals Leuven, Department of Microbiology and Immunology, Laboratory Medicine, Leuven, Belgium

Introduction.– Anti-PR3 antibodies represent an established and widely applied marker for the diagnosis of small vessel vasculitis, such as granulomatosis with polyangiitis (GPA). However, the prevalence of anti-PR3 antibodies in inflammatory bowel disease (IBD) patients is poorly defined. Although anti-PR3 antibodies have also been detected in IBD patients, their impact on diagnosis is unclear. Here we used three independent automated methods (QUANTA Flash, ELiAs, BioPlex 2200) to evaluate the prevalence of anti-PR3 antibodies in IBD.

Methods.– Sera from 76 ulcerative colitis (UC) and 55 Crohn’s disease (CrD) patients were collected (University Hospitals of Leuven, Belgium). The diagnoses were made based on current standard clinical, radiological, endoscopic and histological criteria. Additionally, samples from vasculitis patients (n = 55) were collected. As controls, patients with celiac disease (Cd) and patients with systemic rheumatic diseases were tested.

Results.– Anti-PR3 antibodies in IBD were detected by all three methods, albeit at a lower level than in GPA. The antibodies were mainly found in ulcerative colitis (UC) patients (prevalence varied between 15.8 and 71.1%, depending on the method) and rarely in patients with CrD (prevalence varied between 1.8 and 30.9%, depending on the method). Using receiver operating characteristics (ROC) analysis the cut-off selection was identified as the major cause of discrepancies. The likelihood ratios (LR+/LR−) for UC vs. CrD were 15.2/0.74 for QUANTA Flash and BioPlex 2200 and 8.7/0.86 for ELiAs. Overall, 15.8% of UC, but none of the CrD patients were positive by all three methods.

Discussion.– Anti-PR3 antibodies can be detected in UC patients using three independent methods. The putative clinical association between GPA and UC has to be investigated.

Conclusion.– Anti-PR3 antibodies are found in patients with UC and colitis has to be excluded in patients with a positive test result. Anti-PR3 antibodies represent a promising tool to help differentiating UC from Cd.

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