Factors Determining the Clinical Utility of Serial Measurements of Antineutrophil Cytoplasmic Antibodies Targeting Proteinase 3.

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Abstract

OBJECTIVE:

Relapse following remission is common in antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), particularly with ANCs directed at proteinase 3 (PR3). This study was undertaken to evaluate the association of an increase in PR3-ANCA level with subsequent relapse.

METHODS:

Data from the Rituximab versus Cyclophosphamide for ANCA-Associated Vasculitis (RAVE) trial were used. Starting from the time of achieving complete remission, serial measurements by direct and capture enzyme-linked immunosorbent assays (ELISAs) were analyzed in 93 patients with PR3-ANCA, using Cox proportional hazards regression.

RESULTS:

An increase in PR3-ANCA level was identified in 58 of 93 subjects (62.4%) by direct ELISA and in 59 of 93 (63.4%) by capture ELISA. Relapses occurred in 55 of 93 subjects (59.1%), with 25 and 21 occurring within 1 year after an increase by direct ELISA and capture ELISA, respectively. An increase by direct ELISA was associated with subsequent severe relapses (hazard ratio [HR] 4.57; P < 0.001), particularly in patients presenting with renal involvement (HR 7.94; P < 0.001) and alveolar hemorrhage (HR 24.19; P < 0.001). Both assays identified increased risk for severe relapse in the rituximab group (HR 5.80; P = 0.002 for direct ELISA and HR 4.54; P = 0.007 for capture ELISA) but not the cyclophosphamide/azathioprine group (P = 0.103 and P = 0.197, respectively).

CONCLUSION:

The association of an increase in PR3-ANCA level with the risk of subsequent relapse is partially affected by the PR3-ANCA detection methodology, disease phenotype, and remission induction treatment. An increase in PR3-ANCA level during complete remission conveys an increased risk of relapse, particularly severe relapse, among patients with renal involvement or alveolar hemorrhage and those treated with rituximab. Serial measurements of PR3-ANCA may be informative in this subset of patients, but the risk of relapse must be weighed carefully against the risks associated with therapy.

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