Dear Sir,

High levels of neutrophil elastase have been described in the hemolytic-uremic syndrome (HUS) [1]. Elastase is stored within the primary granules of neutrophils which may circulate in a degranulated form in HUS [2]. Moreover, an increased adherence of neutrophils to the endothelium has been found [3]. All these experimental data would suggest that proteinases released by neutrophils would attack the endothelium and participate in the pathophysiology of HUS.

Based on these considerations, we evaluated antineutrophil cytoplasm antibodies (ANCA) in several sera of 4 patients affected with HUS.

ANCA were evaluated with immunofluorescence (cytoplasmic and perinuclear pattern) and ELISA, using the Biocarb Diagnostics ‘Anti-neutrophil cytoplasm antibodies quantitative kit’ (Biocarb Diagnostics, Lund, Sweden) which detects antibodies against proteinase 3 (PR3 Abs) [4]. Antimyeloperoxidase (MPO) Abs were also tested with ELISA (‘Anti-myeloperoxidase antibodies quantitative kit’, Biocarb Diagnostics). Moreover, antielastase (E) and antilactoferrin (L) Abs were tested. For this purpose, plastic micro-titer plates were coated with E (1 µg/ml in carbonate buffer; Sigma, Chemical Co, St. Louis, Mo., USA) and L (5 µg/ml in carbonate buffer, Sigma). After incubation with patient and control sera, the binding of specific Abs was recognized by alkaline phosphatase-conjugated goat antihuman IgG Ab (Sigma). Samples were regarded as positive when their absorbance reading was greater than the mean + 2 SD of healthy subjects.

Four of 5 patients were negative for all the tests.

0.02 NHS

Table 1.

One patient showed positive results for PR3, MPO and E Abs. L Abs were negative. Immunofluorescence showed a borderline cytoplasmic positivity (table 1).

Several points are interesting: (1) HUS is not an ANCA-associated disease, so that positive data are striking. However, there were no clinical or laboratory characteristics and no histologic lesions on renal biopsy which could suggest an underlying vasculitis. (2) The association of PR3- and MPO-Abs-positive values is unusual, but has previously been described [5]. (3) The
presence of E Abs in HUS has never been reported in the literature. Generally, E Abs behave as perinuclear ANCA [5]; our data would then have been concordant if a perinuclear immunofluorescence pattern had been found. Aspecificity of the Biocarb Diagnostics kit also seems unlikely, since the coated 29-kD antigen is obtained with a Triton X-100 extraction of the α-granules and successive purification, so that this kit detects Abs directed against PR3 [4]. Moreover, if the Abs recognized by the kit included E Abs, the titer of E Abs would have been much greater (table 1). It seems more logical to conclude that this patient presented different types of ANCA: PR3, MPO and E Abs.

An interesting speculation about the presence of E Abs in a case of HUS, which approaches the topic of Milford’s [1] letter, might follow the hypothesis proposed by Falk [6]. Primed neutrophils could express the antigen on their surface (in this case E). E Abs could then interact with the antigen, inducing neutrophil activation and degranulation, with release of elastase in the subendothelium and participation in the pathophysiology of HUS.

An alternative explanation might be that an excessive release of E by stimulated neutrophils could in some way induce an autoimmune reaction against this enzyme.

Our results widen the scope of the patho-genetic hypotheses concerning HUS and hence need to be further explored.

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References