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POSTER PRESENTATION

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Elevated soluble Flt1 mediates an anti-angiogenic state in patients with ANCA-associated vasculitis

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Introduction

Anti-neutrophil cytoplasm antibody-associated vasculitides (AAV) represent a group of necrotizing small vessel vasculitides that include Wegener's granulomatosis, microscopic polyangiitis and Churg-Strauss-Syndrome. To date, little is known regarding endothelial cell survival and vessel regeneration in patients with AAV, despite the increasingly recognised role of vascular endothelial growth factor (VEGF) in mediating vessel repair.

Aim

Assess the role of sFlt1 in patients with AAV.

Material and methods

Were included 40 patients with PR3-AAV during active disease (n=20) or remission (n=20) and 23 patients with MPO-AAV during active disease (n=10) or remission (n=13). Eighteen additional PR3-AAV patients had paired serum samples drawn at the onset of the disease and at three months of follow-up.

Results

Serum levels of soluble Flt1 (sFlt1), a potent inhibitor of VEGF, are significantly increased during the acute phase of PR3-AAV (2592 ± 11347 pg/ml) and MPO-AAV (476 ± 4258 pg/ml) compared to controls (118 ± 269 pg/ml). sFlt1 levels decreased during disease remission but remained increased compared to controls in patients with PR3-AAV. sFlt1 serum levels correlated with serum levels of C5a, an anaphylatoxin released following complement activation. Serum from patients with acute

PR3-AAV induced the release of sFlt1 by human monocytes *in vitro*, but failed to induce a similar effect on endothelial cells. Pre-treatment of monocytes with an anti-C5a receptor blocking antibody attenuated sFlt1 release. Serum from patients with acute AAV induced a disruption of blood flow in the chicken chorioallantoic membrane assay and this effect was prevented by incubating patients' serum with an excess of human VEGF.

Conclusion

Our data indicate that a complement mediated-increase in sFlt1 occurs during acute AAV which leads to an "anti-angiogenic" state that hinders endothelial repair. "Pro-angiogenic" therapies, which would include complement activation inhibitors, may enhance endothelial repair during AAV and thus reduce renal vascular scarring.

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