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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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