data obtained for patients presenting with AAV over the same time period.

Results.—Eleven patients were identified, nine female, with an average age of 57 years and average follow-up of 80 months. Seven patients had antibodies to MPO and GBM and three to PR3 and GBM. One patient had antibodies to GBM, PR3 and MPO. All patients had renal involvement with a mean serum creatinine of 473 µmol. Five out of eleven patients required dialysis at presentation and one of these patients recovered renal function by 6 months. Two patients presented with pulmonary haemorrhage and 45% had radiological evidence of interstitial lung disease. Fifty-five percent of patients relapsed, all of whom had antibodies to PR3 and all relapses were associated with rising PR3 titres in the absence of anti-GBM antibodies. Five and 10 year renal survival was 100% in patients presenting dialysis independent and 20% of patients presenting dialysis dependent had independent renal function at 5 years. Overall renal survival, compared with AAV, is shown on Figure 1.

![Figure 1](image)

Renal survival.

Discussion.—This cohort of patients with "double positivity" experienced better overall patient and renal outcomes at one year than previously reported cohorts. They were generally treated as per local protocols for anti-GBM disease with 82% undergoing plasma-exchange. There was significantly reduced renal survival compared with AAV patients.

Conclusion.—GBM antibodies should be sought in any patients with AAV since double positive patients may require plasmapheresis despite the absence of organ threatening disease.

References


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A41

ANCA-associated vasculitis in Hispanics: An unrecognized severity

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Introduction.—ANCA-associated vasculitis (AAV) is now increasingly recognized in diverse ethnic populations. However, little is known about AAV and its severity among minorities in particular the Hispanic population in the United States. This study aims to describe the clinical severity and disease outcome in a group of Hispanic patients with AAV compared to a cohort of Caucasians living in the same geographical area.
Patients. – We identified 21 Hispanics and 25 Caucasians treated for AAV at Rush University in Chicago, IL from January 2006 to December 2011. Ethnicity was determined by self-report. Patient demographics, Laboratory data, Birmingham Vasculitis Activity Score (BVAS), and Vasculitis Damage Index (VDI) were analyzed. Student’s t-test and chi-square tests were employed, $P < 0.05$ was considered significant.

Results. – Of the 46 patients, 27 had GPA, 12 had MPA, seven had CSS. There was no difference in the median age at diagnosis, time to diagnosis, or in the gender distribution between Caucasians and Hispanics. Hispanics had a higher mean BVAS at presentation (16.75 ± 7.7 versus 12.4 ± 6.7, $P = 0.03$), a higher mean VDI at presentation (2.9 ± 1.5 versus 1.9 ± 1.2, $P = 0.03$) and a cumulative mean VDI (3.9 ± 1.7 versus 2.5 ± 1.9, $P = 0.01$) compared to Caucasians. The majority of Hispanics presented with renal involvement (89% of Hispanic versus 56% of Caucasians, $P = 0.06$) however the difference did not reach statistical significance. Seventy percent of Hispanics had acute renal failure (Mean highest creatinine = 4.01 ± 2.9 mg/dL) of whom half required dialysis, versus 29% of Caucasians (Mean highest creatinine = 1.98 ± 1.67 mg/dL, $P = 0.05$) and only two patient’s requiring dialysis. Two Hispanic patients (11%) died shortly after presentation. There were no deaths among Caucasians.

Conclusion. – Hispanics with AAV presented with more systemic and severe disease with higher damage index as compared to Caucasians. Whether these differences are due to genetic, socio-economic or healthcare access disparities is yet to be studied.

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A43

ANCA disease patients with increased expression of autoantigen genes produce an alternative PR3 transcript and synthesize autoantigen proteins

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Introduction. – Generally, mature neutrophils minimally synthesize RNA and protein. However, peripheral neutrophils from ANCA patients are transcribing genes, including the autoantigen PR3. Since mature neutrophils already contain stores of PR3 protein we asked two questions regarding increased PR3 expression in ANCA patients: Are there alternative PR3 transcripts produced in ANCA patients? Is PR3 message translated in mature neutrophils?

There are two annotated transcripts from the PR3 gene. One transcript contains all five exons of the PR3 gene; the other encodes a form originally described as myeloblastin (MBN). We explored the frequency of both PR3 and MBN transcripts in our patient population.

Methods. – Total leukocyte mRNA was isolated from patients with ANCA disease (BVAS range 0–26) and control subjects and screened for PR3 and MBN using transcript specific primers. Total PR3 transcript levels were monitored by qPCR. Potential translation of these transcripts was studied in cell lines and patient neutrophils.

Results. – Twenty-eight percent of MPO-ANCA samples ($n = 36$) and $20\%$ of the PR3-ANCA patient samples ($n = 55$) were positive for the MBN specific transcript, while all healthy subjects ($n = 18$) were negative. Sixty-one percent of ANCA patients with a qPCR value for total PR3 expression above 120 were positive for MBN compared to $0\%$ of patients with a qPCR value below 120. Expression of MBN is not due to an influx of progenitors into the periphery. Samples from patients with “left-shift” were negative for the MBN transcript.

The exclusive transcription of MBN in MCE-7 cell lines indicates that this gene can be translated. Neutrophils isolated from patients with ANCA vasculitis synthesize both PR3 and MPO in vitro.

Discussion. – ANCA patients actively synthesize an uncommon PR3 transcript. Also, mature neutrophils synthesize their autoantigen.

Conclusion. – The presence of MBN transcript and evidence of new ANCA antigen protein synthesis further support perturbed neutrophil physiology that may contribute to increased neutrophil activation and antigen exposure.

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