complain of symptoms that in Nov 2010 were found consistent with
Horton arteritis. He resumed steroids and symptoms remitted. At
the time of admission, the steroid dosage was 7.5 mg/day. TAVI was
uneventful except for a valve in valve procedure due to a “low”
valve implantation with a final mild aortic regurgitation. Twelve
hours later, pt developed a rash that persisted for 4 days. From day
5, severe increase in CRP with normal procalcitonin values and
reduction in plt count (nadir on the day 680,000/μL) were demon-
strated. On day 6, pt started to complain of shortness of breath and
hemoptysis, and from day 8, of fever. Chest X-ray and CT-scan
showed diffuse interstitial-alveolar infiltrates. ANCA were confirmed
negative as were anti-GBM, anti-DsDNA, anti-phospholipids. Com-
plement fractions were normal. Sputum cultures were repeatedly
negative, as was an extensive work up for infectious conditions.
Normal valve position and ventricular function were demonstrated
by frequent echocardiographic controls. Pt was treated with steroids
and supportive care. Pt continued to cough blood until day 19 and
20, when he was treated with nebulized rFVIIa that stopped bleed-
ing. After a transient improvement of clinical and radiological
picture, respiratory conditions deteriorated and on day 32 pt died.
Autopsy revealed hyperemic lungs at gross examination, with firm
gray-brown or pale edematous areas. Histologically pneumonia
organizing aspect was prevalent, associated to rare suppurative foci.
Only minimal intra-alveolar blood was observed at the periphery of
organizing areas. Both septal and interstitial vessels were dilated and
congested. Only focal alveolar or interstitial hemosiderin-laden
macrophages were present at Pearsl stain.
Conclusion.—The clinical spectrum of diffuse alveolar haemorrhage is
wider than previously considered. Besides the well-known vasculitic
syndromes, immune or hypersensitivity reactions to medications and
foreign materials, direct toxic effects to alveolar capillaries, coagula-
tion defects, hemodynamic and vascular conditions, infectious
causes should be taken into account. Identification of different
causes and treatment based on the different etiologies are challeng-
ing tasks.

http://dx.doi.org/10.1016/j.lpm.2013.02.270

P200
Microscopic vasculitis associated to Sjögren’s syndrome. About 4 cases
I. Ben Ghorbel, N. Belfeki, T. Ben Salem, A. Hamzaoui, M. Khanfir,
M. Lamloum, M. Miled, H. Houman
La Rabta hospital, department of internal medicine, Tunis, Tunisia

Introduction.—Glomerular involvement during Sjögren’s syndrome is
extremely rare and necessitates an etiological investigation. Hereby,
we report 4 observations of patients with primary Sjögren’s syn-
drome associated to proliferative nephritis related to microscopic
polyangiitis.

Methods and results.—The report is about 4 patients whose mean age
was 68 years. The first presented with arthritis, the second with lower
limb edema, the third and the fourth with paresthesias. All patients
reported ocular and oral dryness. Biological investigations revealed in
cases an inflammatory syndrome, a hypoalbuminemia, and a 24-
hour-proteinuria over 0.5 g/24 hours. Renal biopsy was performed in 3
cases and revealed diffuse extracapillary proliferative glomerulone-
phritis with crescents in 1 case and focal segmental glomerulonephritis
with crescents in 2 cases. The electromyogram objectified an axonal
sensorimotor neuropathy in 3 cases and the nerve biopsy concluded to a
necrotizing vasculitis in one case. In all cases, Salivary gland biopsy
showed stage 4 chronic lymphocytic sialadenitis according to Chisholm
and Mason criteria. The immunological findings revealed positive anti-
nuclear antibodies at a rate higher than 1/400 in all cases, as well as
positive anti DNA, anti SSA, anti SSB in 3 cases. P-ANCA antimitochondri-
onxydase antibodies were detected in all cases. The diagnosis of micro-
scopic polyangiitis associated to Sjögren’s syndrome was retained in all
cases. All patients underwent a course of corticosteroids associated to
12 monthly pulses of cyclophosphamide relayed by azathioprine.
The evolution was favourable in all cases with the mean decline of 40
months.

Conclusion.—Extracapillary proliferative glomerulonephritis with posi-
tive p-ANCA in Sjögren’s syndrome is a rare condition and needs to
search for an associated systemic vasculitis. In these cases corticosteroids
associated to immunosuppressive agents are still the main treatment to ameliorate the renal prognosis.

http://dx.doi.org/10.1016/j.lpm.2013.02.271

Side effects

P201
Quantifying the effect of rituximab on changes in serum immunoglobulin G
D. Roberts, R. Smith, R. Jones, F. Alberici, H. Marco, D. Jayne
Renal Medicine, Addenbrooke’s Hospital, Cambridge, United Kingdom

Introduction.—Rituximab (RTX) decreases production of pathogenic
immunoglobulins in autoimmune disease. Hypogammaglobulinaemia
(hypoG; IgG < 7 g/L) is a potential complication and assessment of the
rate of change in IgG after RTX may assist in the determination of risk
factors.

Methods.—Patients receiving RTX for vasculitis or SLE with sequential
IgG levels and no subsequent immunosuppressive treatments known to
affect IgG were studied. The rate of change in IgG pre- and post-RTX was
determined using linear regression. The regression fit was assessed using
the Run’s test and visual inspection.

Results.—Sixty-four patients were identified: median age 47 years,
42 female, and 38 (59%) had previously received cyclophospha-
dime. The median number of data points and the duration of periods
of observation were 8 and 23 months pre- (n = 52) and 10 and 25
months post-RTX (n = 64). Compared to the nadir IgG pre-RTX, the
incidence of IgG < 7 g/L was increased post-RTX (P = 0.0395), but
not for IgG < 5 g/L (P = 0.1765) or IgG < 3 g/L (P = 0.5864). There
was an association between the nadir IgG post-RTX and IgG at the
time of RTX (P < 0.001). Marked intra-individual variability was
observed pre- and post-RTX so temporal IgG trends were not sig-
nificant in a number of patients. A decrease in IgG was seen in 23
(35%) (in 3/18 IgG was already decreasing pre-RTX), compared to
an increase in 9 (14%). In those with a declining IgG, the median rate
was 0.05 g/L/month, range 0.02 to 0.2 g/L/month. However, in 13
(25%) patients whose IgG was declining pre-RTX, IgG stopped
decreasing post-RTX in 10, including an upward trend in two. The
rate of change in IgG did not correlate with the total RTX dose (up to
20 g, median 6 g), cyclophosphamide (up to 163 g, median 5 g), age
or sex.

Discussion.—Linear regression provided an indication of the direction
and extent of changes in IgG. RTX was associated with a slow overall
decrease in IgG in one third of patients, while in some IgG increased. Factors influencing the rate of change were not confirmed.

http://dx.doi.org/10.1016/j.lpm.2013.02.272

P202
Risk of malignancy with long-term immunosuppression in ANCA-associated vasculitis
C. Rahmattulla1, A. Göçeroğlu1, M.E.J. Reinders2, E.C. Hagen3, J.A. Brujin1, I.M. Bajema1
1. Leiden University Medical Center, Department of Pathology, Leiden, Netherlands
2. Leiden University Medical Center, Dept of Nephrology, Leiden, Netherlands
3. Meander Medical Center Amersfoort, Dept of Nephrology, Amersfoort, Netherlands

Introduction. — Recent studies indicate that patients with ANCA-associate
ded vasculitis (AAV) have a significantly higher risk of developing
malignancies [1], that the mortality in AAV patients is 2.6 times higher
than that of the general population, and that malignancies are the
second cause of death after the first year of diagnosis [2]. Drawbacks
from these studies are a relatively short follow-up, and possibly, under-
reportage due to lack of access to registries.

Methods. — We investigated the occurrence of malignancies in 187
histologically confirmed AAV patients after diagnosis at our center
between 1982 and 2011 by performing a search in PALGA, a Dutch
national pathology database which covers all the histologically con-
firmed malignancies diagnosed in the Netherlands.

Results. — One hundred and thirty-six patients with AAV had a follow-up
of at least 1 year; 46 of those developed 93 malignancies during a mean
follow-up of 12.3 years. There were 63 non-melanoma skin cancers
(NMSC) of the skin. Thirteen malignancies occurred more than once:
four of the bladder, four of the prostate, three of colon/rectum and two
of the lung. There was a variety of one time occurring malignancies. The
mean age of AAV patients developing a malignancy was similar to
patients without a malignancy (58 years).

Discussion. — This study shows a higher incidence of malignancies than
was recently reported for a European study group. One explanation for
this discrepancy could be the accurate data reporting through the Dutch
PALGA system by which virtually no malignancy could have been
missed. There was no significant age difference between patients with
and without malignancies. Notably, there was a high number of NMSCs
which is most likely related to the immunosuppressive therapy these
patients receive. In the management and treatment of patients with
AAV, it is of major importance to monitor closely for developing
malignancies.

Conclusion. — This study on the development of malignancies after AAV
from a large single center experience shows a high incidence of
malignancies in AAV patients after diagnosis.

References
patients treated for antineutrophil cytoplasm antibody-associated vascu-
litis: follow-up data from European Vasculitis Study Group clinical trials.

http://dx.doi.org/10.1016/j.lpm.2013.02.273

P203
Infectious complications related to treatment in an inception cohort of antineutrophil cytoplasmic antibody associated vasculitis
J. Mcgregor1, R. Negrete-Lopez2, C. Poultón1, J. Kidd1, S. Weaver1,
L. Goetz1, Y. Hu1, P. Nachman1, R. Falk2, S. Hogan1
1. UNC School of Medicine, Chapel Hill, USA
2. Hospital Universitario-UNAM, Monterrey, Mexico

Introduction. — The objective of this study was to describe factors
associated with infections related to immunosuppression in an inception
cohort of patients with biopsy-proven AAV.

Methods. — Four hundred and ninety patients diagnosed with AAV
between 1/2000–12/2011, treated with immunosuppressive therapy
and not at end stage renal disease (ESRD) on presentation were
enrolled. Infectious events within 24 months were assessed.

Results. — Median age was 59 IQR (45,70), 47% female, 54% MPO
positive and 25% diagnosed with GPA. Mean follow up was 3.9 ± 3.7
years. Age was increased across infection frequency groups (56 years
[43,65] – 0 infections (inf); 60 years [47,71] – 1–2 inf; 64 years
[47,72] – ≥ 3 inf). More leukopenia events were associated with
increasing numbers of infections (1 ± 0.99 l events – 0 inf; 1.24 ± 0.96
events – 1-2 inf; 1.55 ± 1.12 events – ≥ 3 inf; P = 0.03). Relapse episodes were higher across increasing numbers of
infections (0.53 ± 0.66 relapses–0 inf; 0.85 ± 0.81 relapses–1-2 inf;
0.95 ± 0.62 relapses–≥ 3 inf; P = 0.001). Greater number of infections
within 24 months was associated with a higher likelihood of ever
having a severe infection (27 severe infections (22%) – 0 inf; 87 severe
infections (41%) – ≥ 2 inf; 66 severe infections (60%) – ≥ 3 inf;
P = c.0.001). Death from any cause was also associated with more
infections (3 deaths (2.5%) – 0 inf; 21 deaths (10%) – 1-2 inf; 9 deaths
(10%) – ≥ 3 inf; P = 0.025).

Conclusion. — Higher frequencies of infections within 24 months are
associated with death from any cause, development of severe infects,
more relapses, more episodes of leukopenia and advancing age.

http://dx.doi.org/10.1016/j.lpm.2013.02.274

P204
Cyclophosphamide effect on immunoglobulins levels in AAV patients treated with long-term pre-emptive rituximab maintenance
E. Besada1, W. Koldingsnes2, J. Nossen3
1. UNC School of Medicine, Chapel Hill, USA
2. University hospital North Norway, Troms, Norway
3. Royal Darwin Hospital, Darwin, Australia

Introduction. — Rituximab (RTX) is an anti-CD20 antibody used in
ANCA-associated vasculitis (AAV) for induction and maintenance of
remission. The objective of this study is to determine the effect of CYC on Ig levels
in patients treated with long-term pre-emptive RTX maintenance.

Methods. — Retrospective study of 38 patients (35 with GPA and with
3 with CSS) treated with RTX between April 2004 and September
2011 for active disease. 58% of the patients had renal involvement.
The cumulative cyclophosphamide (CYC) dose was 14 g (0–250).
Twelve patients (32%) were treated with combination CYC-RTX at
initiation. RTX was initiated as tw10 g infusion 2 weeks apart (RA
protocol) and thereafter 2 g RTX was administered annually

http://dx.doi.org/10.1016/j.lpm.2013.02.273