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ANCA vasculitis and atypical hemolytic uremic syndrome: An association with poor outcome

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Introduction.--Atypical hemolytic uremic syndrome (aHUS) secondary to vasculitis is a rare but serious complication.

Patients.--We described two patients and review previous 32 reported cases of patients with aHUS associated to small vessel renal vasculitis (SVV).

Results.--Case 1.--A 70-year-old male with a diagnosis of microscopic polyangiitis (MPA) presented because of worsening kidney function to end stage renal disease (ESRD) and appearance of aHUS with C3 serum reduction. Kidney biopsy showed SVV. Steroids, cyclophosphamide and PE were started. Hemolysis recovered. After 20 months follow up he started dialysis.

Case 2.--A 79 years old male with a recent diagnosis of MPA presented for aHUS. He had C3 serum severe reduction. Kidney biopsy showed SVV, acute thrombotic microangiopathy associated and C3 positive immunofluorescence. PE, steroids and cyclophosphamide were started. Hemolysis recovered but kidney function never improved and the patient died because of pneumonia.

All the patients were negative for genetic mutations in the complement pathway (CFH, CFB, MCP, CFI) and for anti-CFH antibodies. ADAMTS 13 activity was normal.

Discussion.--aHUS is associated to the most severe cases of renal vasculitis; despite the addiction of PE to burn out hemolysis the outcome was negative.

In the literature review we identified 32 cases (Supplementary data). Similarly to our cases, 81% of the patients were treated with PE; nevertheless 61% of the patients died or presented ESRD. Alternative complement pathway (AP) hyperactivation seems to play an important role in SVV; indeed disease progression could be prevented by C3 depletion in animal models and human neutrophils involved in ANCA vasculitis.

Conclusion.--All the patients with SVV with sudden deterioration of kidney function, anemia and thrombocytopenia should be suspected to have aHUS. Starting an early appropriate treatment with PE or complement blocking agents such as eccluzimab could improve patient’s morbidity and mortality.

Supplementary data associated with this article can be found on the website of La Presse Médicale (http://www.em-consulte.com/revue/lpm).

Table I Cases report of vasculitis syndrome aHUS associated

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Long-term outcome of severe alveolar hemorrhage in ANCA-associated vasculitis: A retrospective cohort study

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Introduction.--Alveolar hemorrhage (AH) is a major cause of early death in ANCA-associated vasculitis (AAV). There is a paucity of information regarding the outcomes of AAV patients presenting with severe AH.

Patients.--A retrospective cohort study. Patients with severe AH were identified from a case review of 824 AAV patients. Demography, presenting features, treatment and outcomes were described.

Results.--Fifty-three patients (M/F 33/20; median age 59) were identified, 37 (69.8%) with granulomatosis with polyangiitis (Wegener’s), 16 with microscopic polyangiitis; 36 PR3-ANCA and 17 MPO-ANCA. AH was the first disease manifestation in 46 (86.8%). Assisted ventilation was required in 36 (67.9%), renal involvement was present in 52 (98.1%) and 28 (52.8%) required dialysis. Forty (75.5%) received plasma exchange. At 3 months, 44/53 (83.0%) were alive. The mean follow-up was 49 months when 31 (58.5%) were alive and 24 (45.3%) dialysis independent. Mortality was higher in those requiring dialysis at entry (57.1% vs. 24%, P = 0.02), in patients >65 years (71.4% vs. 30.8%, P = 0.01), and tended to be higher in those requiring intubation (54.5% vs. 32.2%, P = 0.1).

Conclusion.--Severe AH was more commonly associated with PR3-ANCA (vs. MPO-ANCA) and strongly correlated with renal vasculitis. Current treatment of severe AH leads to remission but long-term mortality remains high. Concurrent renal failure and older age were associated with higher mortality.

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P166
Acute respiratory distress syndrome (ARDS) as primary manifestation in ANCA-associated vasculitis

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Introduction.--ANCA-associated vasculitis (AAV) often presents with pulmonary and renal involvement. Alveolar hemorrhage can progress into life-threatening respiratory dysfunction requiring admission to the intensive care unit (ICU) and ventilator support. Rarely lung involvement may even lead to acute respiratory distress syndrome (ARDS).

Patients.--A retrospective chart review identified 14 patients treated for AAV and ARDS during the last two decade at our institution. Data for analysis were available in 13 of these patients.

Results.--The study population consisted of 9 female and 4 male patients (mean age 40.4 ± 13.2 years). Diagnosis of AAV was established by screening all patients for ANCA serology, occasionally confirmed by skin or renal biopsy. PR3-ANCA was positive in 12 patients (92%), MPO-ANCA was positive in one patient (8%). Renal involvement was present in 11 patients (81%). All patients were severely ill (APACHE II score 17.3 ± 4.2) and presented with severe respiratory dysfunction requiring mechanical ventilation (PaO2/FIO2 109 ± 36.8 mmHg, PEEP 15.2 ± 4.6 mbar on day one). All patients fulfilled the criteria for ARDS, three patients required venovenous extracorporeal membrane oxyge-
nation (ECMO). Symptoms resolved during treatment with prednisolone and cyclophosphamide. Six-months-mortality was 15%, however deaths were not directly related to the lung involvement (one patient due to bowel ischemia, one patient due to multi-organ failure).

Discussion.-- Among patients with ARDS routine screening for ANCA can rapidly establish the diagnosis of AAV, whereas biopsy is often difficult to obtain. ARDS was more commonly associated with PR3-ANCA positivity. Early mortality was not related to pulmonary involvement. Overall outcome of patients with AAV and ARDS was favourable, even in patients requiring ECMO therapy.

Conclusion.-- Outcome of patients with AAV and ARDS is favourable. Early mortality was not related to pulmonary involvement. Among patients with ARDS routine screening for ANCA can rapidly establish the diagnosis of AAV.

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P167 Focal necrotizing and crescentic glomerulonephritis in patients with normal serum creatinine


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Introduction.-- Focal necrotizing (FNGN) and crescentic glomerulonephritis (CGN) are common renal manifestations of systemic vasculitis. They usually present as rapidly progressive glomerulonephritis and have a poor prognosis if untreated. These pathological findings, however, are not always accompanied by abnormalities of renal function. We aimed to establish the frequency and outcomes of patients presenting with FNGN/CGN and normal serum creatinine at our centre.

Patients.-- We conducted a retrospective review (1995–2011) of all adult patients who presented with native renal biopsy proven FNGN/CGN and normal serum creatinine (<120 micromol/L)

Results.-- Thirty-eight patients were identified, median age 57 years (range 17–78), 29% male. Biopsies showed median 14 glomeruli (4–33), with 32% (4–100%) of glomeruli affected by necrosis/crescents. All patients received immunosuppression in accordance with local protocols. Median duration of follow-up was 45 months (2–184).

Clinical features and outcomes are summarised in table I -- as shown, the vast majority of patients had good outcomes at 1 year and at last follow-up. The majority of patients had extra-renal manifestations of vasculitis or autoimmune rheumatic disease. Two patients progressed to ESRF (both secondary to lupus nephritis, at 21 & 29 months) and four patients died during follow-up (at 2, 12, 96 & 122 months).

Discussion.-- FNGN/CGN may occasionally present in patients with normal serum creatinine. This occurs most commonly in patients with pauci-immune GN secondary to ANCA-associated vasculitis. Abnormal urinary findings in association with extra-renal manifestations of disease may alert clinicians to this diagnosis. Confirmation of organ-threatening involvement on renal biopsy may significantly influence treatment decisions.

Conclusion.-- Low threshold of clinical suspicion for FNGN/CGN, prompt biopsy and early initiation of treatment may prevent irreversible kidney damage and improve long-term outcomes in these patients.

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| Table I |

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of cases (%)</th>
<th>% affected glomeruli</th>
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<tbody>
<tr>
<td>Pauci-immune GN</td>
<td>23 (74%)</td>
<td>32% (4–100%)</td>
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<tr>
<td>Lupus Nephritis</td>
<td>7 (18%)</td>
<td>17% (4–50%)</td>
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<tr>
<td>Anti-GBM disease</td>
<td>2 (5%)</td>
<td>36% (26–47%)</td>
</tr>
<tr>
<td>IgA Nephropathy</td>
<td>1 (3%)</td>
<td>50%</td>
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Biochemistry                  | At biopsy            | At 1 year¹           | At last follow-up¹ |
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<tr>
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<tbody>
<tr>
<td>Creatinine (µmol/L)</td>
<td>84.00 (52–115)</td>
<td>82 (58–145)</td>
<td>77.0 (57–107)</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>29.0 (10–40)</td>
<td>38 (30–46)</td>
<td>37.0 (22–45)</td>
</tr>
<tr>
<td>uPCR (mg/mmol)</td>
<td>71.2 (0–681)</td>
<td>23 (0–272)</td>
<td>15.0 (0–238)</td>
</tr>
</tbody>
</table>

¹Results expressed as median (range). Censored for ESRF/death.

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P168 Clinical and pathological study on 34 patients with primary ANCA-associated systemic vasculitis with renal immune complex deposition

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Introduction.-- To analyze the clinical and pathological characteristics of Chinese patients with primary antineutrophil cytoplasmic autoantibody (ANCA)-associated systemic vasculitis (AASV) with renal immune complex deposition.

Patients.-- Thirty-four patients diagnosed with ANCA-associated systemic vasculitis in Shanghai Ruijin Hospital with renal immune complex deposition were enrolled in this study. Their clinical and pathological data were collected and studied, and compared with other 76 AASV patients having classic pauci-immune glomerulonephritis.

Results.-- Of the 34 patients, 27 patients were microscopic polyangiitis (MPA), six patients were Wegener’s granulomatosis (WG) and one patient was Churg-Strauss syndrome (CSS). The mean age was 56.4 ± 16.4 years with a male/female ratio of 1:1.27 (19/15). Kidney and lung were the most common organs involved, taking 100% (34) and 76.5% (26) respectively. 79.4% (27) of patients had impaired renal function, with an average serum creatine of 390.3 ± 284.9 (median 352, 46–1067) umol/L. C3 (82.4%) and IgM (50%) were the most common immune complex deposits observed in kidney, mostly located in mesangial areas and capillary loops. During the follow-up [median 39 (1–120) months, average 39.5 ± 31.7 months], all following a therapy of daily oral OCS combined with immunosuppressants, six (17.7%) patients died and 11 (32.4%) finally progressed to end-stage renal disease (ESRD). Compared with patients having classical pauci-immune glomerulonephritis, patients with renal immune complex deposition had more significant proteinuria, with a higher prevalence of nephrotic syndrome and hypocomplementaemia, and also a higher risk for progressing to ESRD.

Conclusion.-- Our study found that AASV patients with renal immune complex deposition had significantly more proteinuria, more hypocomplementaemia and a higher risk for progressing to ESRD than those having classic pauci-immune glomerulonephritis, and that might indicate a worse renal prognosis.

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