letters to the editor

Table 2. Laboratory data

<table>
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<tr>
<th>Weeks of gestation</th>
<th>4</th>
<th>8</th>
<th>12</th>
<th>16</th>
<th>20</th>
<th>24</th>
<th>28</th>
<th>32</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>9.2</td>
<td>9.7</td>
<td>9.8</td>
<td>9.4</td>
<td>8.4</td>
<td>9.8</td>
<td>10.3</td>
<td>9.4</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td>27</td>
<td>29.1</td>
<td>30.9</td>
<td>27.0</td>
<td>24.4</td>
<td>29.0</td>
<td>30.1</td>
<td>27.8</td>
</tr>
<tr>
<td>Calcium (mg/dl)</td>
<td>8.2</td>
<td>9.2</td>
<td>9.7</td>
<td>10.1</td>
<td>9.4</td>
<td>9.1</td>
<td>9.9</td>
<td>9.6</td>
</tr>
<tr>
<td>Bicarbonate (mmol/l)</td>
<td>21.8</td>
<td>24.2</td>
<td>25.4</td>
<td>25.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-dialysis urea (mg/dl)</td>
<td>104</td>
<td>109</td>
<td>92</td>
<td>68</td>
<td>63</td>
<td>101</td>
<td>64</td>
<td>96</td>
</tr>
</tbody>
</table>

Conflicts of interest

The authors affirm that they have no conflicts of interest related to the content of this article.


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C1q Nephropathy and Malignancy
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Dear Editor,

C1q nephropathy (C1qN) is an idiopathic glomerular disease characterized by extensive mesangial deposition of C1q with associated mesangial immune complexes, in the absence of evidence of systemic lupus erythematosus1.

The prevalence of C1qN has been estimated from 0.2% to 16%3-8. Light microscopy (LM) findings range from no glomerular abnormalities to mesangial proliferation1,4,9,11,12 or focal segmental glomerulosclerosis (FSG)2,4,6,8,13. Clinical presentations vary from asymptomatic urinary anomalies3,7,9,11,13, and macroscopic hematuria14, to nephritic syndrome5,15 and corticorresistant nephrotic syndrome (NS)2,4,6,14. Earlier reports found a poor response to steroids and a high risk of progression to end-stage renal disease (ESRD)2,5,6,12,13, particularly those with FSG. Patients presenting asymptomatic urinary anomalies have been found to have a good prognosis5,12,3. The variability in the prevalence, clinical presentation and prognosis of C1qN has been attributed to different ages and ethnicities of the patients included in the series, and to different thresholds to perform a renal biopsy.

The association between NS and malignancy has been reported in various glomerulopathies, but not with C1qN. Recognition of malignancy-associated glomerulopathies is important to prevent ineffective and potentially harmful treatment.

A 56-year-old male was admitted to our Department with NS. He reported persistent peripheral edema lasting for two months. He was a smoker of 80 packs/year. He had exuberant edema of lower extremities and abdominal wall. Laboratory findings revealed hypoalbuminemia (1.1g/dL), proteinuria (10g/day) and microscopic hematuria; serum creatinine was 1.1mg/dL and urea: 48mg/dL. Hyperlipidemia (total-cholesterol: 320mg/dL) was also noted. HBs-antigen, HCV-antibody and HIV-antibody were all negative. Serum protein electrophoresis was unremarkable; complement levels, ANCA, ANA, cryoglobulins and anti-phospholipid antibodies were normal. Ultrasonography of the kidneys was unremarkable. Abdominal ultrasonography showed small volume ascites, and chest X-ray revealed small pleural effusions, without any other abnormal findings.

A renal biopsy was performed, whose histological findings are shown in Figure 1. Fifteen glomeruli were observed, showing segmental thickening of glomerular basement membranes (GBM) and mesangium by an eosinophilic Congo-
red negative amorphous material. Spike formation or stippling of the GBM was absent in periodic-acid methenamine-silver staining. Immunofluorescence (IF) revealed predominant presence of comma-shaped C1q mesangial deposits.

We started prednisolone (1mg/Kg/day), cyclosporine (3mg/Kg/day) and acenocumarol. One month later, he had an acute pyelonephritis, with worsening renal function (creatinine: 1.6mg/dL). Prednisolone dose was reduced to 0.5mg/Kg/day.

Two months later, his clinical condition deteriorated, with asthenia, anorexia and anasarca. Laboratory findings revealed a serum creatinine of 3.9 mg/d, with proteinuria (39g/day) and hypoalbuminemia (1.1g/dL); trough levels of cyclosporine were 176ng/mL. In an attempt to reduce proteinuria, non-steroidal anti-inflammatory drugs were tried, without response. Cyclosporine was stopped and a right nephrectomy was performed. FSG was noted in all of the 15 glomeruli, with persistence of mesangial C1q deposits. It is plausible that the first biopsy was not representative, or maybe this findings represented the rapid course of the disease.

In the post-operative period, the patient developed signs of hyperhydration and started haemodialysis. Hypoalbuminemia and signs of hyperhydration gradually improved, but he maintained severe proteinuria. When clinical euvoeemia was achieved, a right pleural effusion persisted. A CT scan was performed, revealing a disseminated neoplasm (Figure 2). A pleural exudate without malignant cells was drained. Tumor markers Ca 19.9 (95.2U/L, normal <27U/L) and neuron specific enolase (NSE) (96.6U/L, normal <15.2U/L) were elevated.

The patient’s general condition rapidly deteriorated with marked cachexy and, later on, respiratory failure. Invasive investigation was not possible, as the patient was not fit. A week later, he died with a nosocomial respiratory infection. Histological characterization of the neoplasm was not possible, as the patient’s family refused an autopsy.

C1qN can present with NS, typically with histological phenotype of either MCD or FSG. In a report of 15 pediatric patients with C1qN, 9 children had corticosterine NS. FSG was diagnosed in four cases with poor outcome. Markowitz et al. reported 19 patients with C1qN, 79% of which with nephrotic proteinuria. Renal biopsy disclosed FSG in 17 patients and MCD in two. Four patients with FSG had progressive renal insufficiency and two developed ESRD within 27 months. In a report of 20

Figure 1. Kidney biopsy specimen. H&E (A), PAS (B) and Masson trichrome (C) magnification x 400, show segmental thickening of glomerular basement membranes and mesangium by an eosinophilic amorphous material, without mesangial hypercellularity. Immunofluorescence study (x 400) revealed predominant mesangial deposits of C1q (D).

Figure 2. CT scan. CT scan shows bilateral pleural effusion, with atelectasis of the lower right and lower left lung lobes, associated with lymphatic mediastinal metastases (A), and multiple diffuse hepatic nodules (B).
Failure to recognize paraneoplastic glomerulonephritis can subject patients to ineffective and potentially harmful therapy. It is important to highlight the possible association between C1qN and malignancy. Before refractory NS associated with C1qN, an underlying malignancy should be suspected.

Conflicts of Interest
The authors declare that there is no conflict of interest associated with this manuscript.


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