Prognostic factors in small vessel vasculitis with renal impairment: monocentric study.

El youbi Randa*, Mohamed Arrayhani¹, and Tarik Sqalli¹

¹Department of Nephrology, Hassan II University Hospital, Fez, Morocco.

The kidney is one of preferred target for many forms of small vessels vasculitis. The objective of our work is to highlight risk factors of death and renal survival in small vessel vasculitis with renal impairment. A retrospective study conducted in the Department of Nephrology at the University Hospital Hassan II of Fez between April 2010 and April 2013. Of the 30 cases included, twenty-one patients had vasculitis associated to Anti-cytoplasmic antibodies neutrophil. The average age was 46.5 ± 16.17 (23-76 years old), with female predominance (sex ratio 0.6). The main reasons for hospitalization were severe kidney failure in 20% of cases, and hemoptysis in 53.3%. All patients have received corticosteroids and cyclophosphamide. After one year, the evolution was marked by complete remission in 26.6%, relapse in 13.3%, and chronic renal failure in 30%. Seven cases of deaths were noted. In univariate analysis, hypertension and the presence of sclerotic glomeruli were predictive factors associated with death. Renal prognosis was significantly correlated to early dialysis. We have identified a number of risk factor associated to unfavorable evolution which are: hypertension, presence of sclerotic glomeruli, and early dialysis.

Keywords: Dialysis, hypertension, sclerotic glomeral, kidney, prognosis, vasculitis.

INTRODUCTION

Systemic small vessel vasculitis is a group of disorders characterized by inflammatory disease of small arterial, venous and capillary blood vessels. Their clinical features are various. The kidney is a prime target for many forms of small-vessel vasculitis, necrotizing glomerulonephritis (GN) is the classical renal manifestation of the small-vessel vasculitis. The incidence and the prevalence of renal vasculitis in Europe is 10 20/million/an and 150-200/million respectively (Pagnoux, 2010; Kirsten, 2011). Vasculitis can be life-threatening, the morbi-mortality is the result of multi-visceral manifestations, especially renal. The aim of our study is to describe various aspects of kidney damage in small vessel vasculitis and highlight risk factors of unfavorable evolution.

METHODS

This is a retrospective study conducted in the nephrology department of Hassan II university hospital of Fez between April 2010 and April 2013.

Criteria of inclusion and exclusion

We included in this study all patients with kidney impairment caused by small vessel vasculitis. We have classified all vasculitis based on ACR 1990 criteria and Chapel Hill classification. We excluded from this study vasculitis of large and medium vessels.

Data collection

For all these patients, we analyzed the following parameters:
- Population: age, sex, history, extra-renal symptoms,
- Hypertension,
- Presence of sclerotic glomeruli.

*Corresponding author: El youbi Randa, Department of Nephrology, Hassan II University Hospital, Route sidi harazem, 30000 Fez, Morocco, E-mail: randa.ub@gmail.com
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Table 1. Different types of small vessels vasculitis with kidney impairment.

<table>
<thead>
<tr>
<th>Type of Vasculitis</th>
<th>Number</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasculitis associated to ANCA:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Granulomatosis with Polyangiitis (GPA)</td>
<td>21</td>
<td>70</td>
</tr>
<tr>
<td>Microscopic Polyangiitis (MPA)</td>
<td>12</td>
<td>40</td>
</tr>
<tr>
<td>Eosinophilic Granulomatosis with Polyangiitis</td>
<td>7</td>
<td>23.3</td>
</tr>
<tr>
<td>Non ANCA associated Vasculitides:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-GBM Disease</td>
<td>9</td>
<td>30</td>
</tr>
<tr>
<td>IgA Vasculitis (Henoch-Schönlein)</td>
<td>4</td>
<td>13.3</td>
</tr>
<tr>
<td>Cryoglobulinemic Vasculitis (CV)</td>
<td>3</td>
<td>10</td>
</tr>
</tbody>
</table>

- AKI: clinical, biological, etiology, proteinuria, urinary sediment, creatinine, as well as hematological, histological and immunological abnormalities.

All patients were treated according to EULAR protocol, they received a corticosteroid bolus of methylprednisolone (15 mg / kg / day) for three days relayed by oral corticosteroids (1 mg / kg / day) for one month, then we have reduce prednisone dose slowly, down to 10 mg / day at the six month. They have also received bolus of cyclophosphamide (0.75 g/m2). The cyclophosphamide was administered as a bolus IV, the dose was adjusted depending on the age and renal function. It was administered according to the following protocol:

- A bolus every 2 weeks for the first 3 bolus;
- Then a bolus every 3 weeks for 3-6 following bolus for six to nine months

Definitions

Renal impairment was selected to the presence of one or more of the following criteria:
- Renal failure: creatinine greater than 15 mg / l
- Proteinuria greater than 0.3 g/24 h.
- Presence of macroscopic or microscopic hematuria.
- Complete remission is defined by an improvement in renal function (creatinine less than 15mg/l), disappearance of hematuria and vasculitis symptoms.
- Relapse is defined by increased creatinine, onset of hematuria, recurrence of manifestation or appearance of new vasculitis symptoms.
- FFS score: prognostic score, based on the following five clinical items, with the presence of each being accorded one point for a maximum score of 5:
  - Renal failure( creatinine ≥ 140μmol/l)
  - Proteinuria≥ 1g/day
  - Central nervous system involvement
  - Cardiomyopathy
  - Severe gastrointestinal involvement.

Statistics

Descriptive analyzes have been conducted in collaboration with the epidemiology laboratory from Medicine and Pharmacy faculty of Fez, using the SPSS 17.0. Qualitative variables were expressed as percentages and quantitative variables as median or mean. The Student t test was used to compare continuous variables. The comparison of qualitative variables was performed by chi² test. The results are significant if p <0.05. The univariate analyzes was subsequently used to highlight factors associated with unfavorable evolution.

RESULTS

We have collected 30 patients with kidney impairment caused by systemic vasculitis of small vessels. Their average age was 46.5 ± 16.17 (23-76 years old), with a female predominance (sex ratio M/F:0.67).

Systemic vasculitis were revealed by renal symptoms in 53.3% of cases, clinical presentation was mainly dominated by rapidly progressive renal failure in 20% of cases, with a mean creatinine at 72.4 ± 49.16 mg / l. Nephrotic syndrome was noted in 13.3% of cases, and a complete anuria in two cases.

The main clinical signs of extra renal involvement were hemoptysis in 23% of cases, purpura in 43%, arthralgia in 60%, weakness in 76.6%, and hypertension in 63.3% of cases.

Anti-neutrophil cytoplasmic (ANCA) antibodies were positive in 19 patients (63.3%) with the presence of anti-myeloperoxidase (MPO) in seven patients (38.9%) and an anti-proteinase 3 (PR3) in twelve cases (63.1%). Anti-glomerular basement membrane antibodies were positive in 13% of cases.

Granulomatosis with polyangiitis was the most common cause of systemic vasculitis (43.3%), followed by microscopic polyangiitis (23.3%) (table 1).
Table 2. Risk factors associated to death in our series.

<table>
<thead>
<tr>
<th></th>
<th>Died(N=6)</th>
<th>Alive(N=24)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex-ratio (M/F)</td>
<td>0.6</td>
<td>0.7</td>
<td>0.86</td>
</tr>
<tr>
<td>Olig-anuria</td>
<td>37.5%</td>
<td>36.3%</td>
<td>0.95</td>
</tr>
<tr>
<td>Creatinine at admission (mg/l)</td>
<td>87.00±60.09</td>
<td>70.27±41.74</td>
<td>0.39</td>
</tr>
<tr>
<td>HTA(mmhg)</td>
<td>87%</td>
<td>45.5%</td>
<td>0.04</td>
</tr>
<tr>
<td>sclerotic glomeruli (%)</td>
<td>100%</td>
<td>54.54%</td>
<td>0.02</td>
</tr>
<tr>
<td>Complications (%)</td>
<td>62.5%</td>
<td>77.2%</td>
<td>0.41</td>
</tr>
<tr>
<td>Dialysis (%)</td>
<td>62.5%</td>
<td>50%</td>
<td>0.54</td>
</tr>
</tbody>
</table>

Table 3. Risk factors of unfavorable evolution of renal failure.

<table>
<thead>
<tr>
<th></th>
<th>Favorable evolution</th>
<th>Unfavorable evolution</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>45.86±17.9</td>
<td>46.78±16.03</td>
<td>0.89</td>
</tr>
<tr>
<td>Sex-ratio</td>
<td>0.4</td>
<td>0.76</td>
<td>0.48</td>
</tr>
<tr>
<td>Olig-anuria (%)</td>
<td>14.3%</td>
<td>43.5%</td>
<td>0.16</td>
</tr>
<tr>
<td>Creatinine at admission (mg/dl)</td>
<td>64.71±33.94</td>
<td>77.78±50.30</td>
<td>0.52</td>
</tr>
<tr>
<td>Nephrotic syndrome (g/dl)</td>
<td>28.6%</td>
<td>8.7%</td>
<td>0.16</td>
</tr>
<tr>
<td>Dialysis (%)</td>
<td>14.2%</td>
<td>65.2%</td>
<td>0.02</td>
</tr>
<tr>
<td>sclerotic glomeruli (%)</td>
<td>28.5%</td>
<td>69.5%</td>
<td>0.54</td>
</tr>
</tbody>
</table>

All patients were treated according to EULAR protocol. Sixteen patients have required hemodialysis for advanced renal failure. No patient has received plasma exchange because of lack of means. According to FFS score, twenty-two patients have score at 0, six patients at 1 and two patients have a score ≥ 2.

After one year, the evolution was marked by a complete remission in 23.3% of cases, relapse in 13.3% of cases, and chronic renal failure in 30% of cases. Four patients (13.3%) were lost to follow up, and six patients (20%) died by alveolar hemorrhage in 66.6% of cases, and septic shock in 33.3%.

In univariate analysis, dialysis at admission was a risk factor associated to an unfavorable evolution of kidney injury (p = 0.018). Hypertension and the presence of sclerotic glomeruli were predictive factors of death (p 0.04 and 0.02 respectively) (Table 2.3).

DISCUSSION

The kidney is a prime target for many forms of small-vessel vasculitis (Puéchal, 2007). The frequency of kidney impairment in small vessel vasculitis is highly variable (Droz, 2000;; Agard, 2003). It is estimated at 79% in granulomatosis with polyangitis, between 8% to 83% in microscopic polyangitis and 10-20% in the Churg and Strauss (Brillet, 2007;; Canveau, 2008). The most common vasculitis in our series was a GW (40%), followed by PAM (23.3%) and a Sd Churg and Strauss in 6.7%.

In our series, the average age of our patients was 46.5 ± 16.17 years (23-76 years old), similar results have been reported by other studies [Chedadia, 2009; Esqalli, 2012]. Systemic vasculitis were revealed by renal symptoms in 53.3% of cases, with the presence of rapidly progressive glomerulonephritis in two-thirds of cases, these results are comparable to literature data [9,10]. The etiologies of systemic vasculitis were different between our series and other studies like Bejia S (2009) and Stegeman CA (2002) studies (ennette,1997;, Slot, 2003), Stegeman, (2002).

In our series, the evolution was marked by a complete remission in 23.3% of cases, relapses in 13.3% , and a chronic renal failure in 30% of patients . The death rate was high (26.6%) compared to other series (Table 4).

In univariate analysis, hypertension and the presence of sclerotic glomeruli were predictive factors of death, and early dialysis was significantly associated to unfavorable evolution of renal failure. In literature, other parameters have been identified as factors associated to unfavorable evolution of renal failure, mainly: resistance to initial treatment, renal relapses, higher age, the presence of interstitial fibrosis and / or glomerulosclerosis (Hauer, 2002; Hauer, 2007). Booth AD and al (2003), have showed that mortality was associated to age (>60 years) (p <0.001), presence of chronic renal failure (p <0.001), and sepsis (p <0.048) (Booth, 2003).
Table 4. Evolution after one year of treatment.

<table>
<thead>
<tr>
<th></th>
<th>Remission(%)</th>
<th>Relapse(%)</th>
<th>CKF(%)</th>
<th>Death(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tunis(9)</td>
<td>40</td>
<td>-</td>
<td>50</td>
<td>10</td>
</tr>
<tr>
<td>Marrakech(10)</td>
<td>23,5</td>
<td>-</td>
<td>41,2</td>
<td>29,4</td>
</tr>
<tr>
<td>Our study</td>
<td>23,3</td>
<td>13,3</td>
<td>30</td>
<td>26,6</td>
</tr>
</tbody>
</table>

CKF: chronic kidney failure

CONCLUSION

Vasculitis of small vessels with renal impairment remains severe. Through this study, we have identified a number risk factors of death and renal prognosis: hypertension, the presence of sclerosic glomeruli and early dialysis. New treatment can improve patient survival and renal prognosis, although they are not without risk in the medium to long term.

Conflict of Interest: none

REFERENCES


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