Henoch-Schönlein Purpura in Adults: Outcome and Prognostic Factors

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Abstract. Henoch-Schönlein Purpura nephritis (HSPN) has been extensively studied in children but, its natural history in adults is much less known. A cohort of 250 adults suffering HSP was retrospectively analyzed for a median follow-up period of 14.8 yr. All patients had biopsies consistent with HSP (predominant IgA mesangial deposits) associated with purpura, bowel angina, and/or abdominal pain. At presentation, palpable purpura was present in 96% of patients, and arthritis was reported in 61%, and gastrointestinal involvement in 48%. Thirty-two percent of the patients showed renal insufficiency (Creatinine clearance [CrCl] <50 ml/min), usually associated with proteinuria (99%) and/or hematuria (93%). Endocapillary glomerulonephritis was the most frequent lesion on renal biopsy (61%). At the end of follow-up, patient survival was only 74%. The first cause of death was carcinoma (most of them of respiratory or digestive tract). Regarding renal function, 11% of patients reached end-stage renal failure, 13% exhibited severe renal failure (CrCl <30 ml/min), and 14% moderate renal insufficiency (CrCl <50 ml/min). Clinical remission defined as the absence of proteinuria, hematuria, and a normal renal function was achieved in only 20%. This is a retrospective study; therefore, it is not possible to demonstrate any steroid and/or cyclophosphamide efficacy in diminishing the incidence of renal insufficiency. Multivariate analysis demonstrated that renal function impairment and proteinuria level at presentation and, on renal biopsy, the degree of interstitial fibrosis, percentage of sclerotic glomeruli, and presence of glomeruli with fibrinoid necrosis were associated with a poor renal prognosis. The data indicate that clinical presentation of HSPN in adults is severe and its outcome relatively poor, worse than in children. Identification of clinical and histologic prognostic factors may permit the design of appropriate therapeutic prospective studies.

Henoch-Schönlein purpura (HSP) is a leukocytoclastic vasculitis involving small vessels with the deposition of immune complexes containing IgA. It is characterized by the association of skin, joint, and gastrointestinal manifestations that may occur in successive episodes (1). In addition to these manifestations, renal involvement is common, and the long-term prognosis depends on its severity.

HSP primarily affects children, and its incidence is approximately 15 cases/100,000 children per yr (2); it is less common in adults. Although HSP has been extensively studied in children, much less is known about its natural history in adults.

Received October 23, 2001. Accepted January 28, 2002.
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1046-6673/1306-1271
Journal of the American Society of Nephrology
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DOI: 10.1097/01.ASN.0000138833.99976.22

Materials and Methods
Inclusion and Exclusion Criteria

This was a retrospective study of 250 patients aged 15 yr or more suffering from HSP nephritis. All patients underwent a renal biopsy...
between 1983 and 2000, in eleven different medical centers. HSP nephritis was suspected when hematuria, proteinuria, and/or renal failure were associated with a characteristic purpuric eruption and/or abdominal or joint pains (at least two of these three clinical signs). Predominant mesangial IgA immune deposits on renal biopsy were required for inclusion in the study. We excluded patients suffering from IgA nephropathy without systemic signs (Berger’s disease), those with other diseases associating nephropathy and purpuric rash, i.e., systemic lupus erythematosus and cryoglobulinemia, and those with thrombocytopenia (<100,000/mm³).

**Evaluation**

**Clinical and Biologic Data.** The characteristics of skin manifestations, gastrointestinal and joint symptoms, and renal involvement were recorded. Hypertension was defined according to World Health Organization criteria.

We recorded the levels of aspartate and alanine amino transferases (ASAT, ALAT), bilirubin, alkaline phosphatase, and γ-glutamyl phosphatase for hepatic disorders. Serum IgA levels were recorded when available.

Renal insufficiency was defined as creatinine clearance (CrCl) <50 ml/min (calculated by Cockroft formula [22]): moderate renal functional impairment as CrCl between 30 and 50 ml/min, and severe renal failure as CrCl ≤30 ml/min. Proteinuria was defined as proteinuria >0.1 g/d, and nephrotic syndrome as plasma albumin <30 g/L and proteinuria >3 g/d. Hematuria was defined as >10 red cells/mm³ in the urine, and was macroscopic if >1500 red cells/mm³.

**Renal Pathology.** All renal biopsies were independently examined by two pathologists blind to clinical features. On immunofluorescence, the predominance of mesangial IgA among glomerular Ig deposits was required. To be adequate, at least ten glomeruli had to be present. We evaluated semiquantitatively: (1) endocapillary lesions and their focal or diffuse distribution; (2) extracapillary proliferation, graded according to the number of glomeruli involved; (3) interstitial fibrosis (% of the parenchyma involved); (4) interstitial cell infiltration, tubular necrosis, and red cell casts, graded from 0 to 3+ depending on the extent of the parenchyma involved; and (5) arteriolar hyalinosis and arteriosclerosis (from 0 to 3+). The proportions of glomeruli involved by crescents, fibrinoid necrosis, and global sclerosis were recorded. All biopsies were then classified according to the following classification:

1. Mesangiocapillary glomerulonephritis. Histologically normal glomeruli by light microscopy or minimal mesangial prominence.
2. Focal and segmental glomerulonephritis. Segmental endo- and extracapillary proliferation involving less than 50% of the glomeruli. The remaining involved and uninvolved glomeruli were either normal or exhibited minimal mesangial prominence.
3. Endocapillary proliferative glomerulonephritis, divided into two subclasses: 3(a), moderate pure endocapillary proliferative lesions; 3(b), severe endocapillary proliferation, possibly with extracapillary proliferation involving less than 50% of the glomeruli.
4. Endocapillary and extracapillary glomerulonephritis. Lesions were as above, with crescents involving more than 50% of the glomeruli.
5. Fibrotic kidney with global glomerular sclerosis involving more than 50% of glomeruli.

**Outcome.** We evaluated the outcome of each patient, as of the reference date of July 1, 2000. For patients who died, the cause of death and renal status at death were determined. When patients were lost to follow-up, their renal status at the last visit was recorded. Renal outcome was classified as remission (no renal failure, proteinuria, or hematuria); persistent proteinuria and/or hematuria without renal insufficiency; moderate or severe renal insufficiency as defined above; and end-stage renal failure (ESRF).

**Statistical Analyses**

Results were expressed as numbers (percentages) for categorical variables and as median (1st to 3rd quartiles; Q1 to Q3) or mean (± SD), as indicated, for continuous variables. Comparisons were based on the χ² test for categorical variables and Wilcoxon or Kruskall-Wallis tests for continuous variables. Survival curves from the day of renal biopsy were computed using Kaplan-Meier estimate. A Cox model was fit to evaluate the influence of the following variables on severe renal failure occurrence: age, CrCl, proteinuria level, hematuria, the pathologic classification, the percentages of crescents, necrotic glomeruli, sclerotic glomeruli, interstitial fibrosis, and the use of specific treatments. For model selection, we used stepwise forward selection. All tests were two-tailed, and P < 0.05 was considered significant. Statistical analyses were performed with SAS 6.12 software (SAS Institute, Cary, NC).

**Results**

**Extrarenal Presentation**

The median age at HSP onset was 50 (range, 15 to 86 yr). At the reference date, the median duration of follow-up was 14.8 (13.1 to 20.8) yr. Male/female ratio was 1.7. In 80 (32%) of our 250 cases, there was a recent history of intercurrent infection, mostly of the upper respiratory tract.

Most patients (96%) had purpura, always localized to the lower limbs. Other parts of the body were sometimes involved, but rarely the face or mucosa (5%). Blisters and hemorrhagic necrotic skin lesions occurred in 35% of the patients. Relapses of purpura were observed in 48%. Most of them only relapsed once, but in rare cases, up to ten times. Arthritis occurred in 61% of the cases, was symmetrical, and the joints most often involved were the knees or the ankles. Gastrointestinal involvement was observed in 120 cases (48%). The main symptom was colicky abdominal pain. Bleeding occurred in 61 cases of gastrointestinal involvement (51%) and was serious, requiring transfusion or surgery or leading to death, in 13 cases (11%). Purpura was the first clinical manifestation in 83% of the cases, arthritis in 9%, and gastrointestinal involvement in 8%. Renal manifestations preceded clinical symptoms in only two patients (4 and 5 mo before, respectively).

We frequently observed mild, usually brief, liver disorders, with evidence of liver cell damage (15%) or cholestasis (87%). Elevated levels of IgA were found in 118 of the 196 patients tested (60%). Positive anti-neutrophil cytoplasmic antibody was found in 4 of the 105 patients tested (3.8%).

Clinical and biologic presentations differed among patients according to age, as shown in Table 1. More patients aged <30 yr had a recent history of intercurrent infection and arthritis than older patients. By contrast, in those aged >60 yr, purpura was much more frequently necrotic, IgA levels were higher, and CrCl was much lower (this last out of proportion to the differences expected on the basis of age).

**Renal Features**

Evidence of renal involvement was detected within a median period of 2 mo (range, 1 to 4 mo) after onset of the first clinical
symptoms. All patients exhibited some evidence of renal abnormality at the time of biopsy. Nineteen patients (36%) had high BP, but most of them had a past medical history of hypertension. Of the 250, 169 patients (68%) had normal and 81 (32%) impaired renal function. Renal function impairment was moderate in 46 cases (18%) and severe in 35 cases (14%).

Proteinuria was generally mild (66% had proteinuria ≤1 g/24 h, 8% had proteinuria 1 to 3 g/24 h, and 25% had proteinuria >3 g/24 h). Hematuria was generally mild (66% had no hematuria, 18% had microscopic hematuria, and 14% had macroscopic hematuria).

**Table 1. Clinical and biologic presentation of Henoch-Schönlein purpura (HSP) according to age**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Age &lt;30 yr (n = 54)</th>
<th>Age 30 to 60 yr (n = 111)</th>
<th>Age &gt;60 yr (n = 85)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recent history of infection, n = 80</td>
<td>54.7%</td>
<td>28.4%</td>
<td>23.5%</td>
<td>0.0004</td>
</tr>
<tr>
<td>Presence of arthritis, n = 153</td>
<td>71.7%</td>
<td>67.9%</td>
<td>48.2%</td>
<td>0.005</td>
</tr>
<tr>
<td>Necrotic purpura, n = 87</td>
<td>16.7%</td>
<td>36.4%</td>
<td>44.7%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Serum IgA level (g/L)</td>
<td>3 ± 0.2</td>
<td>4 ± 0.2</td>
<td>5 ± 0.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CrCl (ml/min)</td>
<td>99 ± 5</td>
<td>90 ± 3</td>
<td>46 ± 3</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*CrCl, creatinine clearance.

**Pathology**

The most frequent lesion in renal biopsies was proliferative endocapillary glomerulonephritis (class 3) (61%). Proliferative endo- and extracapillary glomerulonephritis (class 4) was only present in 21 cases (8%). In these cases, the mean percentage of glomeruli containing extracapillary proliferation was 62 ± 4%. Circumferential crescents involving all glomeruli were only seen in four biopsies. Fibrinoid necrosis of the glomerular tuft was present in 48% of biopsies. The mean percent of glomeruli per biopsy affected by fibrinoid necrosis was below 5% in classes 1, 2, and 3a, 14 ± 2% in class 3b, and 19 ± 5% in class 4. Inflammatory infiltrates and interstitial fibrosis were common, present in 50 and 54% of the biopsies, respectively. The quantity of red cell casts (117 biopsies) was correlated with the intensity of tubular necrosis (102 biopsies) (P < 0.0001). Only two patients exhibited necrotizing and granulomatous angiitis of the interlobular arteries. Arteriolar hyalinosis (13%) was most frequent among patients with diabetes, and arteriosclerosis (45%) among those with hypertension. They only coexisted in 8% of cases.

Almost all of the renal lesions were significantly worse in those aged >60 yr than in those aged <30 yr. This was true not only for vascular lesions and interstitial fibrosis, as might be anticipated, but also for tubular necrosis (0.69 ± 0.80 versus 0.37 ± 0.60; P = 0.015) and particularly for the presence of glomerular fibrinoid necrosis (1.9 ± 3.0 versus 0.7 ± 1.2; P = 0.008).

**Outcome**

The patient survival curve is shown in Figure 1A. Sixty-four patients (26%) died. Median survival time was 15 yr (range, 13 to 21). The mean age at death was 67.3 ± 1.5 yr. The most frequent cause of death was neoplasia in 17 patients (27% of deaths), involving lung in nine patients and upper respiratory and digestive tracts in five. Eleven of the seventeen patients dying of cancer never received any immunosuppressive treatment, four had been treated by corticosteroids alone, and two by corticosteroids associated with cyclophosphamide (P > 0.05). They thus did not differ significantly from the remaining patients as regards treatment. The mean delay between renal biopsy and death was 42 ± 7 mo (range, 5 to 118 mo).

The second cause of death was infection (16%). Eight of the twelve lethal infections were attributable to immunosuppressive treatment. The mean delay between renal biopsy and death there was 11 ± 3 mo (range, 2 to 41 mo). Death was secondary to HSP evolution in seven patients (11%), due particularly to severe digestive involvement. Cardiovascular diseases were responsible for the death of six patients (9%). The ratio of cardiac to cancer deaths in our patients was thus reversed compared with that in the general population.

The renal survival curve is shown in Figure 1B. Twenty-seven patients (11%) developed ESRF. Those who went into ESRF tended to do so rather rapidly, 13 (48%) of 27 by 3 yr, and all but 2 of 27 patients by 10 yr. Twenty-five patients were dialyzed, and 12 were renal transplant recipients. None of these recipients lost their graft because of a relapse of HSP. Thirty-

**Table 2. Renal data at the time of renal biopsy for patients with HSP**

<table>
<thead>
<tr>
<th>Renal function</th>
<th>% of patients (n = 250)</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal</td>
<td>67.6</td>
</tr>
<tr>
<td>moderately impaired</td>
<td>18.4</td>
</tr>
<tr>
<td>severely impaired</td>
<td>14.0</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Proteinuria</th>
<th>% of patients (n = 250)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.1 g/24 h</td>
<td>4</td>
</tr>
<tr>
<td>0.1 to 1 g/24 h</td>
<td>25.6</td>
</tr>
<tr>
<td>1 to 3 g/24 h</td>
<td>38.8</td>
</tr>
<tr>
<td>&gt;3 g/24 h</td>
<td>31.6</td>
</tr>
<tr>
<td>nephrotic</td>
<td>27.9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hematuria</th>
<th>% of patients (n = 250)</th>
</tr>
</thead>
<tbody>
<tr>
<td>no hematuria</td>
<td>5.6</td>
</tr>
<tr>
<td>microscopic</td>
<td>84.6</td>
</tr>
<tr>
<td>macroscopic</td>
<td>9.8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>% of patients (n = 250)</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal</td>
<td>55.7</td>
</tr>
<tr>
<td>moderately impaired</td>
<td>20.5</td>
</tr>
<tr>
<td>severely impaired</td>
<td>23.8</td>
</tr>
</tbody>
</table>
two patients (13%) had severe renal failure, and 35 (14%) had moderate renal insufficiency. In all, 94 (38%) of the 250 patients exhibited significant renal insufficiency.

At the end of the follow-up, only 20% of the patients were in clinical remission. Among the other patients, 50% had microscopic hematuria (isolated in 30 cases), 47% had minimal or moderate proteinuria, and 8% had nephrotic-range proteinuria. Thirty-eight patients (15%) were lost to follow-up after a median of 1.8 yr (range, 0.9 to 4.1). Seven of them were in clinical remission at the time of their last examination.

Therapy

Therapy was administered to 140 patients (56%). Steroids alone were given to 93 (37%), associated with cyclophosphamide to 47 (19%), and cyclophosphamide alone to only one patient. Levels of proteinuria (1.7 ± 0.2 g/24 h versus 3.7 ± 0.3; \( P < 0.0001 \)) and creatinine (125.4 ± 9.3 μmol/L versus 154.7 ± 12.6; \( P = 0.05 \)) were significantly higher in the treated group of patients. Treatments differed according to the glomerular classification. The worse the lesion, the greater the probability that the patient would be treated and that the treatment would be steroids combined with cyclophosphamide (Figure 2; \( P < 0.0002 \)). Seventy-five patients received converting enzyme inhibitors and/or angiotensin II receptor blockers. There were no differences between patients and regarding outcome between the patients receiving these agents and other patients.

Prediction of Renal Outcome

Univariate Analyses. Table 3 shows the clinical and histologic data for patients at the time of renal biopsy categorized according to their renal outcome. Prognostic factors for severe renal impairment are shown in Table 4. Age over 50 yr at onset was a strong predictor of severe renal failure (relative risk [RR] = 2.53; \( P = 0.0012 \)); 66% of the patients with severe renal failure at their last visit were older than 50 yr at initial biopsy, and similarly, the mean age of patients with severe renal failure at the end of follow-up was significantly higher than that of patients with normal renal function (65 versus 43.5 yr). Clinical presentation, including purpura, arthritis, and abdominal involvement, was not associated with a significant difference in renal function at the end of the follow-up. The presence of renal failure at onset was the strongest predictive factor of renal failure at the end of follow-up (RR = 5.86; \( P < 0.0001 \)); thus 69% of the patients with severe renal failure at presentation had severe renal failure at the end of follow-up. Proteinuria >1 g/L (RR = 2.13; \( P = 0.0012 \)) and the presence of macroscopic hematuria (RR = 2.13; \( P = 0.038 \)) at biopsy correlated the CrCl at the end of follow-up, but the presence of nephrotic-level proteinuria was not predictive of a poor outcome.

As shown in Table 3, the pathologic process was more predictive of the renal prognosis than the clinical presentation. The glomerular classification was predictive of the renal outcome (\( P = 0.0002 \)). Of the 74 patients with class 1 and class 2 glomerulonephritis, 61 (82%) exhibited normal renal function at the final consultation, and only 11 (15%) exhibited severe renal failure. In contrast, of the 90 patients with severe endocapillary proliferative glomerulonephritis (biopsy classes 3b and 4), 47 (52%) exhibited normal renal function at the final consultation.

Figure 1. (A) Estimated Kaplan-Meier survival time after diagnosis of Henoch-Schönlein purpura (HSP) and its 95% confidence interval (CI): median, 178 mo (95% CI, 157 mo to not determined). (B) Estimated Kaplan-Meier time to occurrence of end-stage renal failure (ESRF) after diagnosis of HSP and its 95% (CI): median, 246 mo (95% CI, 189 mo to not determined). Analysis is somewhat hampered by the limited numbers of patients after 180 mo.

Figure 2. Number of patients with severe renal failure at the end of follow-up, according to their glomerular classification (classes 1, 2, 3a, 3b, 4, and 5) and the treatment received. \( n = 250 \) patients with Schönlein-Henoch nephritis. ■, no treatment; ■, corticosteroids alone; □, corticosteroids + cyclophosphamide.
Consultation, and 29 (32%) exhibited severe renal failure. The proportion of glomeruli affected by fibrinoid necrosis (RR = 1.95; P = 0.013) influenced the outcome, but the proportion of crescents in endocapillary and extracapillary glomerulonephritis did not. The number of global sclerotic glomeruli (RR = 2.94) and the degree of interstitial fibrosis (RR = 5) correlated strongly with poor outcome (P < 0.0001). The median proportion of interstitial fibrosis, glomerular fibrinoid necrosis, and glomerular sclerosis were found to be independent risk factors for severe renal failure.

**Multivariate Analyses.** As shown in Table 5, creatinine and proteinuria levels at the time of renal biopsy and the proportions of interstitial fibrosis, glomerular fibrinoid necrosis, and glomerular sclerosis were found to be independent risk factors for severe renal failure.

**Discussion**

The goal of this study was to define the long-term prognosis and risk factors for severe renal failure in adults with HSP nephritis. In contrast to previous outcome studies of comparable adult populations, multivariate analyses could be performed here because of the larger number of patients and the length of follow-up. We demonstrated that the clinical presentation of HSP is more severe in older adults and that the renal prognosis for HSP nephritis is poor compared with what is observed in series in children. It should be stressed that we studied a group of selected patients whose HSP-exhibited renal involvement severe enough to warrant renal biopsy.

Our study extends the findings of previous studies (4–14,15) conducted in smaller series. The patients in our population were roughly comparable to those previously described by...
much more common and became increasingly so with age. In our adult patients, by contrast, necrotic purpura was
neous necrosis is uncommon and affects fewer than 5% of
(Table 1). All the studies of children (24–26) show that cuta-
nous necrosis is uncommon and affects fewer than 5% of
cases. In our adult patients, by contrast, necrotic purpura was
much more common and became increasingly so with age.

Pathologically, we found that 8% of patients had endocap-
illary and extra-capillary proliferative glomerulonephritis (class
4), which is within the previously described range (3 to 23%)
(4). This great disparity in histologic severity is probably due
to different indications for renal biopsy in different countries.
Furthermore, numerous studies were performed before the
International Study of Kidney Disease in Children classification
was instituted, and precise data regarding the pathology
were not always available.

In our series, mortality was high and was in most cases
secondary to neoplasia. Cancer was the leading cause of mor-
tality, accounting for 27% of deaths, a frequency far higher
than that for cardiovascular disease (9%), the leading cause of
death in the general population. This was not correlated with
the use of immunosuppressive treatment; in fact, 8 of 17
patients either had their cancers or precursor conditions, such
as emphysema, at the time of diagnosis of HSP. Furthermore,
these cancers were more likely to be neoplasms of the lung
(14%) and of the upper respiratory and digestive tracts (8%),
than those occurring in general French population (4 and 2%
respectively) (27). To our best knowledge, this high proportion
of deaths related to cancer has never been described in prior
cohort studies of HSP nephritis. Most of the neoplasms in our
patients involved the upper respiratory and digestive tracts,
whose mucosa secrete IgA. It is of interest that the pathophys-
ology of HSP has been attributed to abnormal IgA clearance
(28,29). Here, however, we found no evidence for a possible
paraneoplastic origin of HSP. The proportion of alcohol and
tobacco abusers in our population was quite high (more than
10%); therefore, it might follow that HSP is most often found
in this setting, a possibility that would also favor the develop-
ment of neoplasms (30).

The renal prognosis for our series was poor, because nearly
25% of patients reached renal insufficiency. Other studies have
shown better renal outcome. However, our study and that of
Fogazzi et al. (14) are the only ones to have a long follow-up.
This may explain the even poorer renal prognosis reported by
the latter authors (renal insufficiency in almost 50% of cases).
In this respect, HSP nephropathy may resemble IgA nephe-
rophy. Many authors indeed had initially reported a favorable
outcome for IgA nephropathy until the point in time when
follow-up was long enough to enable them to conclude that
end-stage renal disease was a frequent complication (31–35).
We were able to identify several risk factors for severe renal
failure. As in other studies, extrarenal clinical manifestations
and gender did not affect the renal prognosis. Age, the presence
of macroscopic hematuria, initial renal insufficiency, and pro-
teinuria >1 g/24 h were found by univariate analysis to be
prognostic factors for a decline in renal function; by multivar-
iate analysis, however, only initial renal insufficiency and
proteinuria were associated with renal insufficiency. Regarding
macroscopic hematuria, HSP nephropathy therefore differs
from IgA nephropathy, as several authors have shown that
macroscopic hematuria is associated with better long-term
renal function (36,37). However, other authors (38,39) have
shown that episodes of macroscopic hematuria are frequently
associated with acute renal failure during IgA nephropathy. In
our patients, these episodes were frequently associated with

<table>
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<tr>
<th>Variable at Biopsy</th>
<th>Relative Risk</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥50 yr</td>
<td>2.53</td>
<td>1.44 to 4.45</td>
<td>0.0012</td>
</tr>
<tr>
<td>Creatinine &gt;120 μmol/L</td>
<td>5.86</td>
<td>3.30 to 10.44</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Proteinuria &gt;1 g/24 h</td>
<td>2.13</td>
<td>1.6 to 6.64</td>
<td>0.0012</td>
</tr>
<tr>
<td>Macroscopic hematuria</td>
<td>2.13</td>
<td>1.04 to 4.35</td>
<td>0.038</td>
</tr>
<tr>
<td>Corticosteroids alone</td>
<td>1.98</td>
<td>1.14 to 3.44</td>
<td>0.015</td>
</tr>
<tr>
<td>CS + Cy</td>
<td>1.5</td>
<td>0.82 to 2.74</td>
<td>0.19</td>
</tr>
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<table>
<thead>
<tr>
<th>Biopsy classification</th>
<th>Relative Risk</th>
<th>95% CI</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>class 1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>class 2</td>
<td>9.02</td>
<td>1.14 to 71.29</td>
<td>0.037</td>
</tr>
<tr>
<td>class 3a</td>
<td>6.52</td>
<td>0.86 to 49.59</td>
<td>0.07</td>
</tr>
<tr>
<td>class 3b</td>
<td>11.7</td>
<td>1.57 to 87.33</td>
<td>0.016</td>
</tr>
<tr>
<td>class 4</td>
<td>11.99</td>
<td>1.44 to 99.75</td>
<td>0.022</td>
</tr>
<tr>
<td>class 5</td>
<td>64.48</td>
<td>6.61 to 629</td>
<td>0.0003</td>
</tr>
<tr>
<td>Presence of crescents</td>
<td>0.78</td>
<td>0.28 to 2.16</td>
<td>0.64</td>
</tr>
<tr>
<td>Glomerular necrosis &gt;10%</td>
<td>1.95</td>
<td>1.15 to 3.31</td>
<td>0.013</td>
</tr>
<tr>
<td>Glomerular sclerosis &gt;10%</td>
<td>2.94</td>
<td>1.71 to 5.05</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Interstitial fibrosis &gt;10%</td>
<td>5</td>
<td>2.58 to 9.68</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

* For biopsy classification, see Materials and Methods (Renal Pathology). CS, corticosteroids; CY, cyclophosphamide.

Table 5. Significant prognostic factors for severe renal failure by multivariate analysis

<table>
<thead>
<tr>
<th>Variable at Biopsy</th>
<th>Relative Risk</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine &gt;120 μmol/L</td>
<td>4.27</td>
<td>0.963 to 0.987</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Proteinuria &gt;1 g/24 h</td>
<td>2.98</td>
<td>1.72 to 7.98</td>
<td>0.0045</td>
</tr>
<tr>
<td>Glomerular necrosis &gt;10%</td>
<td>1.83</td>
<td>1.036 to 1.78</td>
<td>0.04</td>
</tr>
<tr>
<td>Glomerular sclerosis &gt;20%</td>
<td>2.12</td>
<td>1.053 to 4.54</td>
<td>0.02</td>
</tr>
<tr>
<td>Interstitial fibrosis &gt;10%</td>
<td>3.83</td>
<td>1.036 to 1.78</td>
<td>0.0008</td>
</tr>
</tbody>
</table>

others, but they were older on average, and more of them were
hypertensive. Note, however, that the World Health Organiza-
tion has recently lowered the measures that define hypertension
(23).

We show here that the presentation of HSP differs signifi-
cantly with age, as older patients exhibited much more severe
renal and extrarenal manifestations than younger patients.
Coppe et al. (3) has shown that children differ from adults by
more frequent joint manifestations, and that this difference
persists in adulthood, with decreasing joint manifestations as
patients age, a finding that our study confirms and extends
(Table 1). All the studies of children (24–26) show that cuta-
nous necrosis is uncommon and affects fewer than 5% of
cases. In our adult patients, by contrast, necrotic purpura was
much more common and became increasingly so with age.

Pathologically, we found that 8% of patients had endocap-
acute renal failure, possibly because of the tubular necrosis associated with macroscopic hematuria (P = 0.00012). This, in turn, may be responsible for the association of macroscopic hematuria with chronic renal failure seen on univariate analysis (Table 4). By contrast, contrary to the general impression, macroscopic hematuria was not correlated with the number of crescents.

In agreement with previous studies (3), we show here that the degree of proteinuria is a significant prognostic factor. As far as we know, no other study has demonstrated the role of initial renal function. Some authors (20) have shown that the presence of a high percentage of crescents has an unfavorable effect, but this was not confirmed by others (3,12) or by our own study. Similarly, we found that no single class of glomerular lesions has a prognostic value by multivariate analysis. Among the acute lesions considered, the only histologic variable that was an independent prognostic factor was the presence of glomerular fibrinoid necrosis. By contrast, we demonstrate that chronicity factors, such as the percentage of interstitial fibrosis and of global sclerotic glomeruli, are unfavorable risk factors. These variables are usually described in other glomerulonephritis, particularly IgA nephropathy (32,35,40,41).

As to the efficacy of specific treatments by steroids alone or combined with cyclophosphamide, it is difficult to draw any conclusions; their efficacy in reducing the incidence of severe renal insufficiency could not be demonstrated. On univariate analysis, steroids even seem to worsen the course of renal evolution. As in most previous retrospective studies of HSP nephropathy, the limitation of the present investigation was that the distribution of established renal risk factors was different in treated versus untreated patients. No study has so far been able to demonstrate the efficacy of treatment of this nephropathy in adults. The importance of irreversible histologic lesions, such as interstitial fibrosis and glomerular sclerosis, as indices of poor prognosis makes the efficacy of treatment doubtful. Nevertheless, the prognostic value of glomerular fibrinoid necrosis provides some hope of improvement with steroids. The results of pediatric therapeutic studies (42-44), even though none was prospective and randomized against untreated patients. No study has so far been able to demonstrate the efficacy of treatment of this nephropathy in adults. The importance of irreversible histologic lesions, such as interstitial fibrosis and glomerular sclerosis, as indices of poor prognosis makes the efficacy of treatment doubtful. Nevertheless, the prognostic value of glomerular fibrinoid necrosis provides some hope of improvement with steroids. The results of pediatric therapeutic studies (42-44), even though none was prospective and randomized against placebo, were mostly positive.

In conclusion, although earlier small series have suggested a relatively poor prognosis in HSP in adults as compared with children, this is the first large study with long follow-up to confirm and refine this impression. It further identifies independent prognostic factors, such as initial renal failure, the level of proteinuria, and the histologic quantification of interstitial fibrosis and glomerular sclerosis. Because of the retrospective nature of this study and despite the absence of positive impact of corticosteroids and cyclophosphamide treatment, we cannot definitely reject such treatments until their failure to benefit is confirmed in a placebo-controlled clinical trial with randomized treatment allocation.

Acknowledgments

We are grateful to the following pathologists, who provided listings of the HSP nephropathy patients and slides of their renal biopsy:

Hélène Beaufils (Hopital Pitié Salpêtrière, Paris, France), Dominique Droz (Hopital St Louis, Paris, France), Béatrice Mougenot (Hopital Tenon, Paris, France), and Francine Walker (Hopital Bichat, Paris, France). We are also grateful to the following clinicians from Internal Medicine Services or from the Groupe d’Études Néphrologiques d’Île de France (GENIF) for their cooperation: Valérie Caudwell and Olivier Kourilsky (Hopital d’Evy, Evry, France), Dominique Chauveau, Philippe Lexavre and Jean Pierre Grünfeld (Hopital Necker, Paris, France), Michel Delahousse (Hopital Foch, Suresnes, France), Gilbert Deray (Hopital Pitié Salpêtrière, Paris, France), Christian Jacquot and Jean Bariéty (Hopital Européen Georges Pompidou, Paris, France), Henri Kreiss (Hopital Necker, Paris, France), Frank Martinez and Christophe Legendre (Hopital St Louis, Paris, France), Luc Moulounguet (Hopital A. Paré, Boulogne, France), Jean Charles Pette (Hopital Pitié Salpêtrière, Paris, France), Eric Rondewa and Jean Daniel Sraer (Hopital Tenon, Paris, France), Jérôme Rossert and Pierre Ronco (Hopital Tenon, Paris, France), and François Vrtovsnik and Françoise Mignon (Hopital Bichat, Paris, France).

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