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Long-term prognosis of Henoch–Schönlein nephritis in adults and children*

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Abstract

Background. The aim of this multicentre collaborative study was to compare the progression of renal disease in children and adults with Henoch–Schönlein purpura (HPS) nephritis selected on the basis of IgA-dominant renal deposits and biopsy material available for review.

Methods. The analysis was performed in 152 patients (95 adults and 57 children <16 years old at diagnosis) with a follow-up ($\geqslant 1$ year up to 20 years (4.9 ± 3.4 years in adults and 4.8 ± 3.9 years in children).

Results. Renal histology and clinical presentation were similar in both age groups: crescents were found in 36% of adults and 34.6% of children (in only 2.7% of adults and 1.9% of children involving $>50\%$ of glomeruli), nephrotic-range proteinuria in 29.5% of adults and 28.1% of children and functional impairment in 24.1% of adults and 36.9% of children. The outcome was similar for both age groups (remission, 32.5% of adults and 31.6% of children; renal function impairment, 31.6% of adults and 24.5% of children). End-stage renal disease was observed in 15.8% of adults and in 7% of children. Renal function survival at 5 years was not significantly different in the two groups (85% in adults and 95% in children) and at 10 years it was approximately 75% in both groups. None of the children died and adult survival was 97% at 5 years. In adults at presentation, renal function impairment ($P<0.02$) as well as proteinuria higher than 1.5 g/day ($P<0.02$) and hypertension ($P<0.001$) were negative prognostic factors. Multivariate analysis stressed the main statistical relevance of proteinuria (relative risk 2.37, $P<0.02$). Conversely, in children no definite level of proteinuria, hypertension or other data were found to be associated with poor prognosis.

Conclusions. Among patients with a clinical presentation which warrants renal biopsy, HSP nephritis has a similar prognosis in children and adults. The evolution is more predictable in adults than in children.

Key words: Henoch–Schönlein purpura nephritis; IgA nephropathy; prognostic indicators in nephritis; proteinuria; hypertension; paediatric nephrology

Introduction

Henoch–Schönlein purpura (HSP) is a vasculitis that often involves the kidneys and which can affect patients of any age [1–3]. An uneven distribution of prevalence and severity of renal disease is commonly observed, as the minimal renal involvement with transient haematuria without renal function impairment is far more frequent in children than in adults . However, recent long-term studies of selected pediatric cases reported progressive courses of disease, modifying the prognostic profile of a subset of these children [4]. Previously published reports have involved small series

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of patients [5–11] or, when more extensive [12–15], cohorts with limited age range. This study is unique because large groups of adults and children with HSP were selected based on homogeneous criteria, including the availability of renal biopsy samples and investigated in a parallel analysis.

The aim of this multicentre collaborative study of the Italian Group of Renal Immunopathology was to evaluate the progression of renal disease in children and adults with HSP nephritis severe enough to indicate renal biopsy, focusing the analysis on patients with follow-up longer than 1 year.

Subjects and methods

Selection of patients

The course of renal disease in HSP nephritis was evaluated in 152 patients (95 adults $\geqslant$16 years old at diagnosis, and 57 children $<$16 years at diagnosis) with a follow-up $\geqslant$1 year. This group also included patients who reached the end-point of death or irreversible renal failure within the first year of follow-up. The selection was made among 219 patients enrolled from 43 Italian centres of nephrology (14 of them paediatric) who satisfied the selection criteria of urinary abnormalities, IgA-dominant glomerular immune deposits, biopsy material available for review, palpable purpura (slightly raised haemorrhagic skin lesions, without thrombocytopenia) and/or bowel angina (abdominal pain worsening after meals or bowel ischaemia with bloody diarrhoea) [16].

Clinical presentation

Patients were stratified according to clinical presentation at diagnosis, including proteinuria (minimal, $\leqslant$1 g/day in adults and $\leqslant$10 mg/kg/day in children; moderate, $>1<3.5$ g/day in adults or $>10<50$ mg/kg/day in children; nephrotic, $\geqslant$3.5 g/day in adults and $\geqslant$50 mg/kg/day in children), gross haematuria and renal function (normal renal function (RF), serum creatinine (Cr) $\leqslant$1.5 mg/dl in adults or Cr clearance (CrCl) $\geqslant$90 ml/min/1.73 m^2 in children—calculated by Schwartz's formula: mildly impaired RF, Cr $>1.5\leqslant3$ mg/dl in adults and CrCl $<90\geqslant60$ ml/min/1.73 m^2 in children; severely impaired RF, Cr >3 mg/dl in adults and CrCl <60 ml/min/1.73 m^2 in children). Patients were considered hypertensive according to the WHO criteria.

Renal biopsy

The seven pathology committee members met regularly to decide on criteria for the examination and classification of renal biopsies. From then on, all renal biopsies, blinded as to clinical features, were independently examined and classified according to Emancipator [17] with minor modifications. Minimal glomerular lesions without crescents were termed Class I. The other three classes (class II with no crescents; class III with crescents in $<$50% of glomeruli; class IV with crescents in 50–75% of glomeruli and class V with crescents in $>$75% of glomeruli) were divided into subclasses (a) pure mesangial proliferation (MP), (b) focal–segmental endocapillary proliferation (EP), (c) diffuse EP. Class VI was pseudomembranoproliferative glomerulonephritis (GN) [17]. All equivocal cases were reconsidered by all members of the committee until a general consensus was obtained.

Outcome

The clinical outcome was classified as remission when normal RF as defined above was present without significant proteinuria ($<$200 mg/day in adults and $<$4 mg/kg/day in children); minimal or moderate proteinuria ($<$3.5 g/day in adults and $<$50 mg/kg/day in children); and normal RF, nephrotic proteinuria, and normal RF; moderately or severely impaired RF as defined above and end-stage renal failure (ESRF): patients on dialysis. Patients in remission or with minimal or moderate proteinuria and normal RF were considered to have a good outcome.

Statistical analysis.

Clinical and histological records were gathered using dBase IV software. Data were compared or analysed by means of the Chi-square test, Student's *t* test for unpaired data, and simple regression analysis when appropriate. Survival analysis was performed on patients with a known final event (death, ESRF, last record later than 1990) according to Kaplan and Meier, and the curves were compared by the Mantel–Cox test. Multivariate analysis was performed by the Peduzzi, Hardy, Hollford stepwise procedure as implemented on BMPD-UCLA.

Results

Clinical presentation and renal features

The 152 patients, 95 adults and 57 children with a follow-up evaluation $\geqslant$1 year, were aged 27.5 $\pm$ 18.3 (range 3–72) years, with most patients in their second decade of life. The mean follow-up was 4.9 $\pm$3.4 years in adults and 4.8 $\pm$3.9 years in children (up to 15 years in adults and up to 20 years in children). Male/female ratio was 1.5 in adults and 1.7 in children.

In both adults and children the single most prevalent histological pattern was a pure mesangial proliferative glomerulonephritis without extracapillary involvement (Table 1). Extracapillary proliferations were encountered with equal frequency in adults (36%) and children (34.6%). Most biopsies with crescents had associated endocapillary proliferation (74% of adults and 66.5% of children). A small number of adults and children had crescents within 50–75% of the glomerular samples, but no patient (adult or child) had $>$75% of glomeruli with crescents. The renal interstitium displayed limited areas of inflammatory infiltration in 9% of both groups.

IgA deposits associated with C3 were detected by immunofluorescence in 71.6 and 82.4% of adults and children respectively and fibrinogen was present in 68.4 and 75%. Less frequently IgM (37.4 and 47.4%), IgG (26 and 28%) and C1q (9.5 and 14%) deposits were found.

At diagnosis, most patients had normal renal function and minimal proteinuria (Table 2), together with microscopic haematuria which was evident in all cases.

Table 1. Renal histological features of patients with HSP nephritis according to Emancipator (see text for detailed classification)

	Adults (%)	Children (%)
Class I	2.7	1.9
No crescents and minimal lesions		
Class II	56	55.8
No crescents		
(pure MP)	(33.3)	(38.5)
(focal-segmental EP)	(13.3)	(7.7)
(diffuse EP)	(9.3)	(9.6)
Class III	33.3	32.7
Crescents in $<50\%$ glomeruli		
(pure MP)	(9.3)	(9.6)
(focal EP)	(10.7)	(11.5)
(diffuse EP)	(13.3)	(11.5)
Class IV	2.7	1.9
Crescents in 50–75% glomeruli		
Class V		
Crescents in $>75\%$ glomeruli	0	0
Class VI	5.3	nf(7.7
Pseudomembranoproliferative		

MP mesangial proliferation; EP endocapillary proliferation.

Table 2. Clinical presentation at diagnosis of HSP nephritis

		Adults (%)	Children (%)
Proteinuria			
Minimal proteinuria	with normal RF	33.7	17.5
	with impaired RF	5.2	10.5
Moderate proteinuria	with normal RF	19	10.5
	with impaired RF	8.4	14.1
Nephrotic proteinuria	with normal RF	19	21.1
	with impaired RF	10.5	7
Gross haematuria	with normal RF	4.2	14
	with impaired RF	0.0	5.3
Renal function			
Normal RF		75.9	63.1
Moderately impaired RF		13.6	24.6
Severely impaired RF		10.5	12.3
Blood pressure			
Hypertension		21	21

Patients were stratified based on clinical presentation at diagnosis, according to proteinuria (minimal proteinuria: $\leqslant 1$ g/day in adults and $\leqslant 10$ mg/kg/day in children; moderate proteinuria: $>1<3.5$ g/day in adults or $>10<50$ mg/kg/day in children; nephrotic proteinuria: $\geqslant 3.5$ g/day in adults and $\geqslant 50$ mg/kg/day in children), gross haematuria and renal function (normal renal function (RF): serum creatinine (Cr) $\leqslant 1.5$ mg/dl in adults or Cr clearance (CrCl) $\geqslant 90$ ml/min/1.73 m^2 in children — calculated by Schwartz's formula: mildly impaired RF, Cr >1.5 $\geqslant 3$ mg/dl in adults and CrCl <90 $\geqslant 60$ ml/min/1.73 m^2 in children; severely impaired RF, Cr >3 mg/dl in adults and CrCl <60 ml/min/1.73 m^2 in children).

About 30% of the adults and children had nephrotic-range proteinuria at onset. Renal function was impaired in 24.1% of adults and 36.9% of children. Hypertension was found in 21% of both adults and children.

In 18% of adults and 30% of children no treatment for HSP nephritis was performed. In the others, treatment consisted of steroids (in 73.7% of adults and in 60% of children), often in association with immunosuppressive drugs (in 26.3% of adults and 17.5% of children) or antiplatelet agents (in 23% of adults and 19.3% of children). Plasma exchange was used in a minority of patients (4.2% of adults and 3.5% of children). Proteinuria higher than 2 g/day in adults was significantly associated with steroid treatment ($P<0.02$) even though nephrotic proteinuria was not a uniform guideline for treatment, particularly in younger patients (23.8% of nephrotic children vs 15.8% adults were not treated). Conversely, clinical onset of renal functional impairment was generally considered an indication for treatment in both adults (93.3%) and children (100%), as well as patients with extracapillary proliferation (88.1% of adults and 77.7% of children with crescents).

Outcome

At the end of the follow-up period, one-third of the patients were in clinical remission (Table 3) without microscopic haematuria or proteinuria. Another third had minimal or moderate proteinuria, while a few cases still had nephrotic range proteinuria. Renal function impairment, varying in severity, was observed in 31.6% of adults and 24.5% of children. Fifteen adults (15.8% of adults) and four children (7% of children) started renal replacement therapy. The interval between clinical onset and dialysis ranged from a few days to several years (3.2 ± 3 year up to 11.3 in adults; 10.2 ± 6.1 up to 20 years, in children). The actuarial renal survival at 5 years was 85% in adults and 95% in children. At 10 years, figures are superimposable in adults (74.1%) and children (73.1%) (Figure 1).

Seven adult patients died (7.3% of adults) from neoplasia or cerebrovascular accidents. Survival rates in adults were 97.8% at 5 years and 88.1% at 10 years.

Risk factors for progressive nephritis

Renal lesions

Both cohorts included almost exclusively cases with crescents in $<50\%$ of glomeruli. Moderate or severe chronic renal failure developed in 38.9% of adults and 18.5% of children with extracapillary proliferation (Figure 2). Renal failure progressed to require dialysis

Table 3. Outcome of HSP nephritis

Outcome	Adults (%)	Children (%)
Remission	32.5	31.6
Minimal or moderate proteinuria, normal RF	32.7	42.1
Nephrotic proteinuria, normal RF	3.2	1.7
Moderate functional impairment	13.7	12.2
Severe functional impairment	2.1	5.3
End-stage renal failure in dialysis	15.8	7

See Table 2 for detailed definitions.

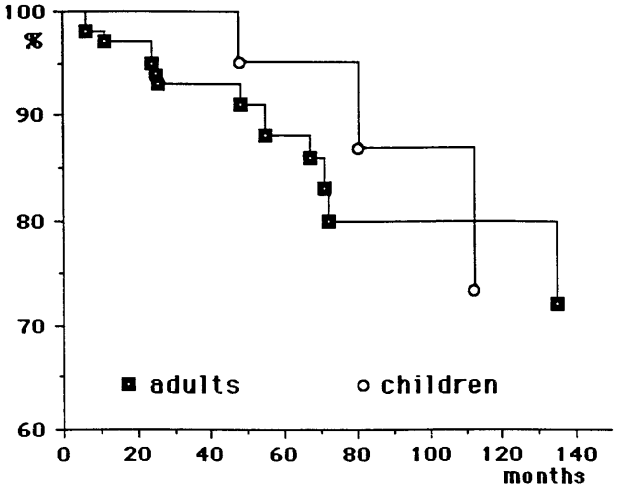

Fig. 1 Actuarial renal survival in adults and children with HSP nephritis.

in 17% of adults and 7.5% of children with crescents in their biopsies. Renal function also deteriorated in 19.5% of adults and 23.6% of children without crescents in the biopsy, with 4.5% of adults and in 2.4% of children in this group requiring dialysis. Survival analysis failed to show any significant difference between presence or absence of crescents on histopathology. In class VI patients, two of the five adult patients but none of the five children ultimately needed dialysis.

Renal functional impairment at onset

Renal functional impairment at presentation was a negative prognostic factor in adults. Indeed 45.5% of adults with severe renal failure and 18.7% of those with moderate functional impairment eventually required chronic dialysis vs only 2.7% of adults with normal renal function at onset ($P<0.02$). This association was not found in children; 12.5% of those with severe impairment and 6.2% of those with moderate functional impairment as well as 6.2% of those with normal renal function at onset deteriorated to the point of requiring dialysis.

Hypertension

A favourable outcome (remission or moderate proteinuria with normal renal function) was observed in 70.6% of the normotensive adults vs 45% of hypertensive ones ($P<0.01$). Accordingly, 35% of hypertensive adults needed chronic dialysis treatment vs only 10.6% of normotensive ones ($P<0.02$). Kidney function survival analysis of hypertensive vs normotensive adult patients showed a significant difference between the two groups (5-year survival to end-point dialysis, 87.4% in hypertensive vs 98.6% in normotensive patients; Mantel–Cox $P=0.0008$).This difference was not found in children; a positive outcome was found in 75% of hypertensive vs 73.1% of normotensive patients while 8.3% of hypertensive vs 6.6% of normotensive patients required dialysis ($P=$NS). However, with a more sensitive end-point of slightly reduced renal function ($CrCl<80$ ml/min/1.73 m^2), the difference between hypertensive and normotensive children became significant (4% vs 31% reached this end-point, $P=0.008$).

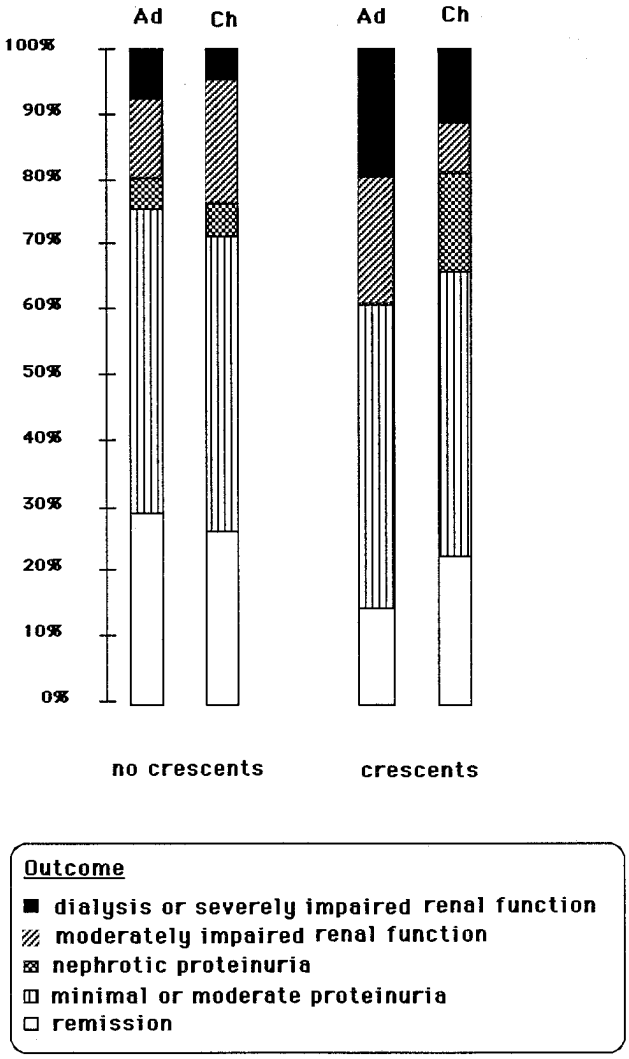

Fig. 2. Predictive value of renal lesions for final outcome in adults (Ad) and children (Ch) with Henoch–Schönlein purpura nephritis.
No crescents: histological class I (minimal changes) and class II (moderate changes).
Crescents: class III (crescents in $<50\%$ of glomeruli); class IV (crescents in 50–75% of glomeruli). No patient was in class V ($>75\%$ of glomeruli with crescents).
Outcome: remission with no significant proteinuria (<200 mg/day in adults, <4 mg/kg/day in children), with normal renal function (RF) defined by serum creatinine (Cr)$\leqslant 1.5$ mg/dl in adults or Cr clearance (CrCl) $\geqslant 90$ ml/min/1.73 m^2 in children); minimal or moderate proteinuria (<3.5 g/day in adults and <50 mg/kg/day in children) and normal RF; nephrotic proteinuria and normal RF; moderately impaired RF with Cr>1.5 mg/dl in adults and CrCl <90 ml/min/1.73 m^2 in children; severely impaired RF (Cr>3 mg/dl in adults and CrCl<60 ml/min/1.73 m^2 in children) or end-stage renal failure requiring dialysis.

Proteinuria

Outcome was favourable in adults with proteinuria <1 g/day, as 89% of them completely recovered or

had mild proteinuria and only 2.7% progressed to end-stage renal failure ($P<0.001$ vs nephrotic patients). Patients with higher levels of proteinuria had a less favourable outcome, although no clear-cut difference was observed between non-nephrotic (56% in remission or mild proteinuria and 15.4% requiring dialysis) and nephrotic patients (56% with a positive outcome and 28% in dialysis, $P=$NS *vs* non-nephrotic). Renal survival analysis comparing adults with nephrotic or non nephrotic proteinuria did not show significant differences (Mantel–Cox $P=0.06$). There was a significant difference between groups of patients with lower levels of proteinuria (<1.5 g/day vs $\geqslant 1.5$ g/day) with respect to dialysis as an end-point; Mantel–Cox $P=0.02$. Similar figures were found with Crs $\geqslant 4$ mg/dl as end-point (Mantel–Cox $P=0.009$).

The clinical outcome for children with absent or mild proteinuria was generally more favourable (82.1% were in remission or had mild proteinuria and 3.6% required dialysis) than those with higher levels of proteinuria, but statistical significance was not reached. No significant difference in outcome was found between children with non nephrotic proteinuria (63% in remission or with mild proteinuria and 4.5% requiring haemodialysis at the end of the follow-up period), and nephrotic proteinuria (remission or mild proteinuria in 75% and dialysis in 12.5%). No statistical difference in cumulative proportional survival was found in children, stratified according to different proteinuria levels.

Systemic extrarenal signs of vasculitis

No significant difference in renal function was found at the end of the follow-up period between patients who presented with the three major signs of organ involvement *versus* those with limited syndrome. The presence or absence of eliciting factors also had no prognostic value.

Treatment

Attention was focused on the group of patients with nephrotic syndrome and/or those with $\geqslant 50\%$ glomeruli with crescents. This cohort included 34 adults (6 of whom were not treated) and 27 children (6 untreated). At follow-up, 42.7% of treated and 50% of untreated adult patients were in remission or had moderate proteinuria and normal RF, while 25% of treated and 16.6% of untreated patients needed to start a chronic dialysis programme. In children, 38% of treated and 33.3% of untreated patients had a good outcome, while 14.1% of treated and 16.6% of untreated had moderately or severely impaired renal function at the end of the follow-up. Since treatment was not given randomly, no definite conclusion can be drawn from this study.

Renal function survival multivariate analysis

A multivariate analysis was performed in the adult population to test the value of several covariates (proteinuria at a threshold of 1.5 g/day, hypertension, age at onset of clinical disease, sex, polysymptomatic presentation) in predicting the risk of developing end-stage renal failure. Because renal function impairment was likely to behave as a confounding factor, it was not entered in the stepwise analysis. Proteinuria and hypertension were significant predictors only when separately added to the model (proteinuria: relative risk 2.37, $P=0.02$; hypertension: relative risk 1.93, $P=0.001$) However, these two elements were strictly related and when added together to the model, only proteinuria maintained its significance. The multivariate analysis in children was not reported because the low number of events in children (end-stage renal failure in 4 cases only) limiting the value of this analysis.

A simple regression analysis was calculated on the whole cohort of patients, looking for the influence of age at onset on the progression to dialysis, but no correlation was found even considering the entire range of ages.

Discussion

Although there is a general agreement that HSP nephritis is more benign in children than in adults, reports in the literature vary widely. Series of unselected children indicate that the vast majority of them (up to 90%) enjoy resolution of disease with a few mild or no sequelae and only 2–13% eventually develop renal failure [20–23]. Conversely, reference centres report remission rates below 50% and poor outcome in 10–25% of children [8,14] and the disease accounts for 3% of all children on dialysis in Europe [15]. In adults, chronic renal failure is reported in 8–68% of patients with HSP [8,9,24,25], indicating that most studies suggest a lower prevalence of disease resolution in adults than in children [6,8,21]. The collaborative work of the Italian Group of Renal Immunopathology allowed the analysis of a large cohort of patients affected by HSP nephritis and a direct comparison of long-term follow-up outcomes between groups of different ages meeting the enrolment criteria. Only patients with a clinical picture severe enough to warrant renal biopsy were admitted to the study. Therefore our results cannot be generalized to the entire spectrum of HSP nephritis since minor forms of nephritis, particularly common in childhood, which are likely to have a good prognosis [6–16], were not included. However this is the first report directly comparing the long-term evolution of HSP nephritis in adults and children of HSP nephritis with disease severe enough to warrant renal biopsy.

It should be noted that the simple criterion of the need of renal biopsy, adopted by 43 different nephrology centres, resulted in a remarkably homogeneous group of children and adults with respect to renal histological patterns and clinical features. Compared to other series from the literature [14,18], minimal glomerular lesions were similarly unusual, while crescent formations were less frequent than reported by

Emancipator's review [17] or in Habib's analysis of a single world-wide reference centre [14]. The prevalences of the different histological classes, as well as the frequency of impaired renal function at presentation were similar in adults and in children. The cohort of children investigated had more impairment of renal function and more severe nephrotic syndrome than those reported in the literature [10,14,18,20].

In our study groups, similar long-term outcomes were observed in adults and children, with remission seen in about one-third, often without urinary abnormalities and hypertension and one-third ending in impaired renal function. As expected, adults needed dialysis more often than children; however, the analysis of cumulative proportional survival did not show any significant difference and at 10 years it was approximately 75% in both groups. Single and multiple regression analyses confirmed that the age at diagnosis was not significantly related to outcome. Though HSP nephritis is often considered separately from idiopathic IgA nephropathy, the two conditions are thought to represent phenotypic variations of the same disease [28]. The actuarial renal survival at 10 years in large populations of patients with idiopathic IgA nephropathy, according to the recent literature, is sligthtly better than in the HSP cohort examined, ranging from 78 to 87% [27].

Crescents involving $>50\%$ of glomeruli in other series were associated with poor prognosis [15,17]. In our cohort, the small number of such patients did not allow such a statistical comparison. In terms of clinical prognostic factors, hypertension was a risk factor for progression with greater impact in adults than in children. The low prevalence of renal failure in children may, however, bias the analysis. Indeed, hypertension emerged as a risk factor in children when less severe functional impairment was chosen as an end point. The predictive value of proteinuria appeared to be different in adults and children affected by HSP. In both groups the absence of proteinuria or, at the other extreme, the presence of nephrotic-range proteinuria, was associated with a high rate of remission or functional impairment respectively. However, the outcome associated with moderate proteinuria was less clear-cut. In adults, proteinuria above or below 1.5 g/day could discriminate between favourable and unfavourable long-term renal survival. In children it was impossible to find such a cut-off point, and heavily proteinuric children were found to have the same prognosis as mildly proteinuric ones. Renal functional impairment at onset was a reliable predictor of outcome, but attained statistical significance only in adults. Progressive renal functional impairment, hypertension, and proteinuria were somehow interrelated; proteinuria was the only parameter which was statistically significant as an independent variable in multivariate analyses.

In conclusion, the comparison of children and adults with HSP nephritis severe enough to indicate renal biopsy showed astonishing similarities in terms of renal lesions, clinical onset and long-term outcome. Risk factors for progression were more apparent in adults, as low levels of proteinuria, normal blood pressure, and preserved renal function were significantly associated with good prognosis. These features, including minimal or absent proteinuria, were associated with a good prognosis in children as well, even though the clinical course in children was more unpredictable. Among patients with a clinical presentation warranting renal biopsy, HSP nephritis cannot be considered to be more benign in children than in adults.

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References

1. Mills JA, MichelI BA, Bloch DA *et al*. The American College of Rheumatology 1990 criteria for the classification of Henoch–Schoenlein purpura. *Arthritis Rheum* 1990; 33: 1114–1121
2. Jennette JC, Falk RJ, Andrassy K *et al*. Nomenclature of systemic vasculitides. Proposal of an International Consensus Conference. *Arthritis Rheum* 1994; 2: 187–192
3. Knight JF. The rheumatic poison: a survey of some published investigations of the immunopathogenesis of Henoch–Schönlein purpura. *Pediatric Nephrol* 1990; 4: 533–541
4. White RHR. Henoch–Schönlein nephritis: a disease with significant late sequelae. *Nephron* 1994; 68: 1–4
5. Lee HS, Koh HI, Kim MJ, Rha HY. Henoch–Schönlein nephritis in adults. A clinical and morphological study. *Clin Nephrol* 1986; 26: 125–130
6. Faull RJ, Aarons I, Woodroffe AJ, Clarkson AR. Adult Henoch–Schönlein nephritis. *Aust NZ J Med* 1987; 47: 396–401
7. Fogazzi GB, Pasquali S, Moriggi M *et al*. Long-term outcome of Schoenlein–Henoch nephritis in the adult. *Clin Nephrol* 1989; 31: 60–66
8. Sinniah R, Feng PH, Chen TM: Henoch–Schonlein syndrome: a clinical and morphological study of renal biopsies. *Clin Nephrol* 1978; 9: 219–228
9. Chen WP, Lin CY, Hsu HC, Cheng JH: Purpura nephritis in chinese children from Northern Taiwan. *Child Nephrol Urol* 1988; 9: 331–336
10. Kobayashi O, Wada H, Okawa K, Takeyama I. Schoenlein–Henoch's syndrome in children. *Contrib Nephrol* 1987; 4: 48–71
11. Farine M, Poucell S, Geary DL, Baumal R. Prognostic significance of urinary findings and renal biopsies in children with Henoch–Schönlein nephritis. *Clin Pediatr* 1986; 25: 257–259
12. Cream JJ, Gumpel JM, Peachey RDG. Schoenlein–Henoch purpura in the adult. A study of 77 adults with anaphylactoid or Schoenlein–Henoch purpura. *Q J Med* 1970; 39: 461–484
13. Levy M, Broyer M, Arsan A, Levy-Bentolila D, Habib R. Anaphylactoid purpura nephritis in childhood natural history and immunopathology. In: Hamburger J, Crosnier J, Maxwell MH, ed. *Advances in Nephrology*. Year Book Medical, Chicago, 1976; 183
14. Habib R, Niaudet P, Levy M. Schonlein–Henoch purpura nephritis and IgA nephropathy.In: Tisher C, Brenner BM, ed. *Renal Pathology: With Clinical and Functional Correlations*. 2nd edn. Lippincott, Philadelphia, 1994; 472
15. Goldstein AR, White RHR, Akuse R, Chantler C: Long-term follow-up of childhood Henoch-Schonlein nephritis. *Lancet* 1992; 339: 280–282
16. Gruppo di Immunopatologia Renale Società Italiana di Nefrologia: Aspetti sistemici e renali della sindrome di Schoenlein-Henoch. R.Coppo Editor, Wichtig, Milano, 1995
17. Emancipator SN. Primary and secondary forms of IgA nephritis, Schoenlein-Henoch syndrome. In: Heptinstall RH, ed. *Pathology of the Kidney,* 4th edn, Vol 1. Little Brown, Boston, 1992; 389–476
18. Meadow SR, Glasgow EF, White RHR, Moncrieff MW, Cameron JS, Ogg CS. Schonlein-Henoch nephritis. *Q J Med* 1972;163: 241–258
19. Ayoub EM, Hoyer J. Anaphylactoid purpura: streptococcal antibody titers and beta-1 globulin levels. *J Pediatr* 1969; 75: 193–201
20. Stewart M, Savage JM, Bell B, McCord B. Long term renal prognosis of Henoch-Schonlein purpura in an unselected childhood population. Eur J Pediatr 1988; 147: 113–115
21. Koskimies O, Sevgi MIR, Rapola J, Vilska J. Henoch-Schonlein nephritis: long-term prognosis of unselected patients. *Arch Dis Child* 1981; 56: 482–484
22. Counahan R, Winterborn MH, White RHR *et al.* Prognosis of Henoch-Schonlein nephritis in children. *Br Med J* 1977; 2: 11–14
23. Yoshikawa N, White RHR, Cameron AH. Prognostic significance of the glomerular changes in Henoch-Schonlein nephritis. *Clin Nephrol* 1981; 5: 223–229
24. De Groc F, Baurnelou A, Beaufils H, Bendia H. Glomerulonephrite du purpura rhumatoide de l'adulte. In: *Seminaire de néphrologie pediatrique, Hopital Necker Enfant Malades,* Flammarion, Paris, 1987; 31
25. Kuster S, Andrassy R, Waldherr R, Ritz E. Contrasting clinical course of Henoch-Schonlein purpura in younger and elderly patients. In: Sessa A, Meroni M, Battini G, ed. *Glomerulonephritis in the Elderly*. Basel, Karger,1993; 93
26. Knight JF, Cameron JS. Henoch-Schonlein nephritis in adults: a report from UK glomerulonephritis registry. (abstract). *Nephrol Dial Transplant* 1987; 2: 415
27. D'Amico G, Ragni A, Gandini E, Fellin G. Typical and atypical natual history of IgA nephropathy in adult patients. *Contrib Nephrol* 1993; 104: 6
28. Meadow SR, Scoot DG: Berger disease: Henoch-Schoenlein syndrome without the rash. *J Pediatr* 1985; 106: 27

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