Henoch-Schönlein purpura nephritis and IgA nephropathy: a comparative clinical study

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in revised form on March 15, 2013; accepted Clin Exp Rheumatol 2013; 31 (Suppl. 75): S45-S51.

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Key words: Henoch-Schönlein purpura, IgA nephropathy, nephritis.

Competing interests: none declared.

ABSTRACT

Objective. Henoch-Schönlein purpura nephritis (HSPN) and IgA nephropathy (IgAN) are related syndromes. In the present study we aimed to compare the clinical characteristics and outcome of a large and unselected series of patients diagnosed as having HSPN and IgAN. **Methods.** Comparative study of a wide and unselected population of HSPN (142 patient) and IgAN (61 patients)

(142 patient) and IgAN (61 patients) from a teaching hospital of Northern Spain.

Results. All of the following comparisons were expressed between HSPN vs. IgAN, respectively. HSPN patients were younger (30.6±26.4 vs. 37.1±16.5 years, p<0.001). Precipitating events, usually an upper respiratory tract infection and/or drug intake, were more frequently observed in HSPN (38% vs. 23%, p=0.03). Extra-renal manifestations were also more common in HSPN than in IgAN; skin lesions (100% vs. 1.8%; p<0.001), gastrointestinal (62%) vs. 7.4%; p<0.001), and joint involvement (61.3% vs. 3.6%; p<0.001). However, nephritis was less severe in HSPN, renal insufficiency (25% in HSPN vs. 63.4% in IgAN; p<0.001), nephrotic *syndrome* (12.5%, *vs*.43.7%; *p*<0.001), and nephritic syndrome (6.8% vs. 10.7%; NS). Leukocytosis was more frequent in HSPN (22.5% vs. 8.2%; p= 0.015) and anaemia in IgAN (12.7% in HSPN vs. 36% in IgAN, p<0.001). The frequency of corticosteroid (79.6% vs. 69%; NS) and cytotoxic drug (19% vs. 16.5%, NS) use was similar. The frequency of relapses was similar (38.6% in HSPN vs. 36.3% in IgAN).

After a median follow-up of 120.8 (IQR; 110-132) months in HSPN and 138.6 (IQR; 117-156) in IgAN, requirement for dialysis (2.9% vs. 43.5%; p<0.001), renal transplant (0% vs. 36%, p<0.001) and residual chronic renal insufficiency (4.9% vs. 63.8%; p<0.001) was more frequently observed in patients with in IgAN.

Conclusion. HSPN and IgAN represent different syndromes. IgAN has more severe renal involvement while HSPN is associated with more extra-renal manifestations.

Introduction

Henoch-Schönlein purpura (HSP) is an inflammatory vascular disease characterised by the involvement of the skin, joints, gastrointestinal tract and kidneys (1-5). HSP is generally considered as a benign and self-limited disorder. The prognosis of HSP is mainly due to renal involvement. Its frequency varies between 20 and 100%, depending on the definition of nephropathy and of patient selection as some series only included individuals assessed in nephrology referral services (6-8). HSP nephritis (HSPN) in adulthood is not only more common but also more severe than in childhood (3, 9-12).

IgA nephropathy (IgAN) is the most common cause of primary glomerulonephritis in developed countries (13-16, 20). IgAN may present at any age, but there is a peak of incidence in the second and third decades of the life (14, 17-21).

HSPN and IgAN are classically considered related syndromes. In both conditions the characteristic finding is the presence of prominent IgA deposits in the mesangium observed by immunofluorescence microscopy (19-23). This immunofluorescence pattern is usually indistinguishable in both syndromes (17, 20, 24-26). Also, in both entities the renal involvement may range from mild to severe including end-stage renal disease.

Although many studies have demonstrated a great deal of similarities, other

Funding: this study was supported by grants from "Fondo de Investigaciones Sanitarias" PI12/00193 (Spain), and also partially supported by RETICS Programme, RD08/0075 (RIER) from "Instituto de Salud Carlos III" (ISCIII), (Spain).

reports highlighted many differences between these two syndromes (17, 27). In addition, many of data previously reported in the literature were based on small or selected series of patients (4, 17).

Taking together all these considerations, in the present study we aimed to compare the clinical characteristics and outcome of a large and unselected series of patients diagnosed as having HSPN and IgAN.

Patients and methods

Patient population

An unselected series of patients diagnosed as having HSPN (142 cases) and IgAN (84 patients) at a teaching hospital since January 1977 to May 2012. HSP was diagnosed according to the criteria proposed by Michel et al, based on the American College of Rheumatology (ACR) database and methodology (Table I) (31, 32). HSP vasculitis was pathologically confirmed in 61 cases by a skin biopsy showing the characteristic histological findings consistent with leukocytoclastic vasculitis such as neutrophilic infiltration, leukocytoclasia, fibrinoid necrosis and red cell extravasation into the vessel wall of arterioles, capillaries, and post-capillar venules (28, 34). The remaining 81 patients without skin biopsy had typical nonthrombocytopenic symmetric palpable purpura, were usually children and all of them fulfilled previously proposed classification criteria (31).

To avoid selection bias, 21 of the 84 patients diagnosed as having IgAN were excluded since they had been sent to hospital from centers of other regions due to severe nephritis. IgAN was diagnosed by renal biopsy, according to the Oxford classification (29).

Clinical definitions

1) Classification by age groups: as proposed in previous reports (3, 31, 32, 35) those patients older than 20 years were considered as adults and those aged ≤ 20 as children. 2) Precipitating events: a drug or a mild infectious process (mostly an upper respiratory tract infection) were considered as the probable precipitating event if they occurred closely (within the preced-

 Table I. Criteria to differentiate Henoch-Schönlein purpura from hypersensitivity vasculitis (Traditional Format)*.

Criterion	Definition
1. Palpable purpura	Slightly elevated purpuric rash over one or more areas of the skin not related to thrombocytopenia.
2. Bowel angina	Diffuse abdominal pain worse after meals or bowel ischaemia usually including bloody diarrhoea.
3. Gastrointestinal bleeding	Gastrointestinal bleeding, including melena, haematochezia or positive test for occult blood in the stool.
4. Haematuria	Gross haematuria or microhaematuria.
5. Age at onset ≤ 20 years	Development of first symptoms at age 20 or less.
6. No medications	Absence of any medications at onset of disease which may have been a precipitating factor
The presence of any three of 87.1% .	or more of the 6 criteria yields a correct classification of HSP cases of

*Data reported by Michel et al. (31). J Rheumatol 1992; 19:721-8.

ing week) to the onset of the clinical syndrome. When a patient developed the clinical syndrome after drug intake for a mild infection, both the infection and the drug were considered as possible precipitating events. 3) Fever was defined as an axillary temperature >37.7°C. 4) Cutaneous involvement was defined as the presence of typical non-thrombocytopenic palpable purpura or other cutaneous lesions with leukocytoclastic vasculitis in the biopsy. 5) Joint symptoms included arthralgia and/or joint effusion. 6) Gastrointestinal manifestations encompassed the presence of bowel angina (diffuse abdominal pain worsening after meals), gastrointestinal bleeding (melena, haematozechia, or positive stool Guaic test), nausea and/or vomiting. 7) Nephropathy was categorised as mild or severe (35). Mild nephropathy included those patients with microhaematuria $(\geq 5 \text{ red cell/hpf})$ and/or proteinuria that did not reach the nephrotic syndrome range. A patient was defined as having severe nephropathy if he/she had: a) nephrotic syndrome (i.e. plasma albumin levels ≤25 gm/litre and either 1 gm of proteinuria/day/m² of body surface area in children, or >3.5 gm of proteinuria daily in adults), with or without oedema; or b) acute nephritic syndrome (i.e. haematuria with at least 2 of the following abnormalities: hypertension, increased plasma urea or creatinine levels, and oliguria). Renal insufficiency was considered if the plasma creatinine was >125% of the upper limit of normal. 8) Relapse was considered to be present when a patient previously diagnosed with HSPN or IgAN that was asymptomatic for at least one month, presented again a new flare of cutaneous lesions or other systemic complications, mainly renal disease, related to HSPN or IgAN (3).

Clinical study

Besides a clinical history and physical examination, the following tests were performed routinely in most patients: Complete blood cell count (CBC), Westergren erythrocyte sedimentation rate (ESR)/1st hour, and routine urinalysis. In addition, most adults had an immunological profile taken including rheumatoid factor (RF), (performed initially by quantitative Latex agglutination test, and later on by nephelometry), antinuclear antibodies (ANAs), (by indirect immunofluorescence initially using rodent tissues as substrate or more recently Hep-2 cells), serum levels of C3 and C4, (firstly by radial immunodiffusion and more recently by nephelometry). Anti-neutrophil cytoplasmic antibodies (ANCAs) were performed in patients who had been diagnosed since 1992. They were initially carried out by indirect immunofluorescence on alcohol fixed neutrophils and later on by ELISA with purified proteinase-3 and mieloperoxidase. Other determinations were cryoglobulins (the composition of the cryoprecipitate was determined by double immunodiffusion with specific antibodies) and immunoglobulins that

were determined by nephelometry. Additional tests such as anti nDNA antibodies (by immunofluorescence with *Chrithidia Luciliae* as substrate), blood cultures, Guaic test for occult blood, serology for hepatitis B, or C or HIV infection, were performed only when it was considered to be indicated according to the clinical practice.

Anaemia was defined as a haemoglobin level ≤ 110 g/L. Leukocytosis as a white cell count $\geq 11 \times 10^{9}$ /L. The erythrocyte sedimentation rate (ESR) was considered to be increased when it was higher than 20 or 25 mm/1st hour for men or women, respectively (3, 36). Increased IgA levels were defined as total IgA level >400 mg/dl.

As mentioned before, a skin biopsy was performed in most adults with skin lesions but it was only generally performed in children. Renal biopsy was usually performed if there were laboratory data indicating severe renal disease such as protein excretion above 1 g/day, an elevated plasma creatinine concentration, or arterial hypertension (33). The pathognomonic and indistinguishable finding in both syndromes was the presence of prominent granular IgA deposits in the mesangium by immunofluorescence microscopy (Fig. 1).

Therapy, follow-up, relapses, need for dialysis or kidney transplantation and final outcome was assessed in all the patients.

Data collection

and statistical analysis

Information was retrieved and then analysed to compare the following: etiologic, clinical and laboratory data, treatment and prognosis. These data were extracted from the clinical records according to a specifically designed protocol, reviewed for confirmation of the diagnosis, and stored in a computerised file. To minimise entry error all the data were double checked.

The statistical analysis was performed using the STATISTICA software package (Statsoft Inc. Tulsa, OK, USA). Results were expressed as mean \pm standard deviation (SD) for variables with a normal distribution, or as median and range or interquartile range (IQR) (25th, 75th) for those not normally distributed.



Fig. 1. Glomerulus from a patient with Henoch-Schönlein purpura nephritis (HSPN) with granular mesangial deposits of IgA. (IgA immunofluorescence x 400)

Continuous variables (normally and not normally distributed) were compared with the 2-tailed Student's *t* -test or the Mann-Whitney U-test, respectively. The *chi*-square test or the Fisher exact test was used for the dichotomous variables. Statistical significance was considered as *p*-value <0.05.

Results

Based on the inclusion criteria 142 patients (88 men/ 54 women) were classified as HSPN and 61 (45 men/ 16 women) as IgAN. The main demographic and etiologic factors are summarised in Table II.

Demographic data

and etiological factors

HSPN patients were younger than IgAN patients. In this regard, the mean age at onset was 30.6 ± 26.4 years (range, 2.9–82.7) for HSPN and 37.1 ± 16.5 years (range, 14.7–78.5) for IgAN (p<0.001). Seventy-four (52%) of the 142 HSPN patients were children. In contrast, only 14 (22.9%) patients with IgAN were children. In both IgAN and HSPN the disease was more common

in men. HSPN onset was significantly more frequent in fall. At disease onset, 19% of HSPN and 11.5% of IgAN (p=not significant [NS]) were taking drugs, most of them for an upper respiratory tract infection. β -Lactam antibiotics were the most common drugs prescribed. Hepatitis virus infection was only found in 2 of HSPN and in 1 of IgAN patients (type B in all 3 cases). All patients were negative to HIV test.

Clinical features

The main clinical features are summarised in Figure 2. At disease onset renal disease was more frequently observed in IgAN patients (100%) than in those with HSPN (27.4%; p<0.001). In contrast, extrarrenal manifestations including skin, gastrointestinal and joint symptoms were more commonly observed in HSPN patients (Fig. 2A). During the clinical course, extrarrenal involvement remained to be statistically more frequent in HSPN (Fig. 2B). With respect to this, skin lesions, usually palpable purpura, were present in 100% of cases of HSPN but in only one case (1.8%) of the patients with IgAN

Table II. Main demographic and etiologic features of patients with Henoch-Schönlein purpura nephritis (HSPN) and IgA nephropathy (IgAN).

	HSPN	IgAN	<i>p</i> -value
Number of patients	142	61	
Mean age \pm SD (years)	30.6 ± 26.4	37.1 ± 16.5	<i>p</i> <0.001
Sex (men/women)	88/54	45/16	p=0.1
Seasonal pattern, no. (%)			
Spring	30.3%	31.1%	p=0.9
Winter	24.6%	32.8%	p=0.25
Fall	31%	14.7%	p=0.02
Summer	14%	21.3%	p=0.3
Etiological factors, no. (%)	54 (38%)	14 (23%)	<i>p</i> =0.03
Infections	50 (35.2%)	15 (24.6%)	p=0.13
URTI*	43 (30.5%)	13 (23.6%)	p=0.33
Hepatitis virus infection	2 (3.7%)	1 (2.4%)	p=0.72
Drugs at disease onset	27 (19%)	7 (11.5%)	p=0.18
b-lactam antibiotics	8 (30.7%)	3 (42.8%)	p=0.54
Analgesics/NSAIDs	1 (3.8%)	2 (28.6%)	p=0.04
others	18 (66.6%)	2 (28.6%)	p=0.8

*URTI: upper respiratory tract infection; NSAIDs: Non-steroidal anti-inflammatory drugs.

(p<0.001). Gastrointestinal involvement was more frequent in HSPN (62% vs. 7.4%, p<0.001). The main symptom was the typical colicky abdominal pain. Other gastrointestinal symptoms such as nausea and/or vomiting (17.8% vs. 1.7%; p=0.005) and melena/rector-rhagia (32.7% vs. 0%, p<0.001) were also more frequent in HSPN. Stool Guaic test was positive in 56.8% (25 of 44 tested) of HSPN and in 0% of IgAN (0 of 6 tested) (p=0.009).

Joint manifestations (arthralgia and/ or arthritis) occurred more frequently in HSPN (61.3% vs. 3.6%, p<0.001). However, joint swelling on physical examination was only observed in 38% of HSPN but in none of IgAN patients. The most frequent joint pattern observed was a non-erosive oligoarthritis affecting the ankles and/or knees.

Renal involvement was more severe in IgAN (Fig. 3): nephrotic syndrome (12.5% in HSPN vs. 43.7% in IgAN; p<0.001), nephritic syndrome (6.8% vs. 10.7%; p=0.5), and renal insufficiency (25% vs. 63.4%; p<0.001). The average amount of proteinuria (gr/24 h) was higher in patients with IgAN (median; IQR) (1; 0.5–2.2 in HSPN vs. 3.1; IQR 1.4–7.7 in IgAN) (p<0.001). Also, serum creatinine (mg/dl) was higher



Fig. 2. Main clinical features of 142 patients with Henoch-Schönlein purpura nephritis (HSPN) and 61 with IgA nephropathy (IgAN), at disease onset (**A**) and when the disease was fully established (**B**).

in patients with IgAN (1.2; 1–2.4 in HSPN vs. 1.8; 1.2–3 in patients with IgAN) (p=0.01).

Laboratory data

The main laboratory findings are summarised in Table III. Routine laboratory tests were done in all of the patients at the time of diagnosis. Anemia was present more frequently in IgAN (12.7% in HSPN vs. 36% in IgAN; p < 0.001) while leukocytosis was more common in HSPN (22.5% vs. 8.2%; p=0.015). The mean ESR was similarly increased in HSPN (47.1±30.2 mm/1st hour) than in IgAN (49.2±24.7 mm/1st hour). Serum IgA levels were increased in 60% (15 of 25 tested) of patients with HSPN and in 53.8% (21 of 39) of those with IgAN (p=0.62). The mean \pm SD value of IgA was similar in both conditions (HSPN: 442±240 mg/dl; IgAN: 447.2 ± 242.3) (p=0.97). Other immunological tests such as RF, and ANAs were generally negative in both groups and in the few cases in whom they were positive they were at low titer and other diseases such us rheumatoid arthritis, systemic lupus erythematosus or other connective tissue disease were excluded in all of them. In those patients with cryoglobulins the precipitate was scarce (+/+++, or trace amounts), and none of them could be classified as having cryoglobulinemic vasculitis. ANCAs were negative in all patients with HSPN and only positive in 2 patients with IgAN (p=0.17) (one cANCA and one pAN-CA; in both cases at low titer and without fulfilling definitions for primary systemic necrotising vasculitis).

Treatment and outcome

Corticosteroids and cytotoxic drugs were the usual therapy for both diseases. Corticosteroids were generally prescribed because of persistent skin lesions or visceral involvement such as severe abdominal pain, gastrointestinal bleeding or nephropathy. Cytotoxic drugs were usually prescribed either as corticosteroid-sparing agents or as additional therapy in patients with severe renal involvement.

The frequency of corticosteroids and immunosuppressive drug use was similar in both groups: corticosteroids



Fig. 3. Comparison of renal involvement between 142 patients with Henoch-Schönlein purpura nephritis (HSPN) and 61 with IgA nephropathy (IgAN):

Nephrotic syndrome (*i.e.* proteinuria of 1 gm/day/m² of body surface area or >3.5 gm/day with plasma albumin \leq 25 gm/litre). Nephritic syndrome (*i.e.* haematuria with at least 2 of the following: hypertension, increased plasma urea or creatinine, and oliguria). Renal insufficiency (Plasma creatinine >125% of the upper limit of normal).

Table III. Routine and immunological laboratory findings in patients with Henoch-Schönlein purpura nephritis (PSHN) and IgA nephropathy (IgAN).

	PSHN (n=142)	IgAN (n=61)	<i>p</i> -value
Leukocytosis	22.5% (142/142)	8.2% (61/61)	<i>p</i> =0.015
Anaemia	12.7% (142/142)	36% (61/61)	<i>p</i> <0.001
Increased ESR	88.9% (48/54)	83.3% (20/24)	p=0.5
Increased IgA levels	60% (15/25)	53.8% (21/39)	p=0.62
Positive rheumatoid factor	2.5% (2/79)	4.5% (1/22)	p=0.62
Positive antinuclear antibodies	13.8% (12/87)	18.2% (6/33)	p=0.54
Positive ANCAs	0% (0/27)	6.4% (2/31)	p=0.17
Cryoglobulins	16.7% (8/48	20% (3/15)	p=0.76
Low C3 and/or C4	12.8% (13/101)	12.7% (6/47)	p=0.98

Routine laboratory tests were performed to all of the patients at the time of diagnosis. Values are percentages (no. positive/total no. tested).

Leukocytosis was defined as a leukocyte count $\geq 11 \times 10^9$ /litre, anaemia as haemoglobin <110 gm/litrr, elevated erythrocyte sedimentation rate (ESR) as $\geq 20 \text{ mm/1}^{st}$ hour- (as higher than 20 or 25 mm/1st hour for men or women, respectively) and increased IgA levels as total IgA level >400 mg/dl.

(79.6% in HSPN vs. 69% in IgAN; p NS) and cytotoxic drugs (19% in HSPN vs. 16.5% in IgAN, p= NS). The following cytotoxic drugs were used in HSPN (azathioprine in 7, cyclophosphamide in 6 and mycophenolate mofetil in 2) and IgAN (cyclophosphamide in 8 and cyclosporine in 2). The duration of corticosteroid treatment was higher in patients with IgAN (median: 6 moths, IQR 1–48 months) than in patients with HSPN: median: 2 months, IQR 1–7) (p<0.001).

After a median follow-up of 120.8 (IQR; 110–132) months in HSPN and 138.6 (IQR; 117–156) months in IgAN, the outcome was better in HSPN than in IgAN. Complete recovery was observed

more frequently in HSPN (69.7% vs. 26.5%; p<0.001). Although a persistent, usually mild, haematuria was observed more frequently in HSPN (14.8% vs. 2%; p<0.03), chronic renal insufficiency was more frequent in IgAN (4.9% in HSPN vs. 63.8%; in IgAN p<0.001). During the acute phase of these conditions and throughout the complete follow-up dialysis was required in 43.5% (27/61) of patients with IgAN while only in 2.9% (4/142) of HSPN (p < 0.001). None of the patients with HSPN required kidney transplant while it was performed in 36% (22/61) of IgAN (p < 0,001). The disease relapsed in 38.6% of patients with HSPN and in 36.3% with IgAN (*p*=0.8).

Discussion

The classical clinical triad of HSP is characterised by the presence of skin lesions, abdominal symptoms and joint involvement. In addition, the occurrence of nephropathy is relatively common and it determines the prognosis. Previous studies on HSPN have vielded disparate results. Discrepancies could be related to several factors: 1) Selection bias because some studies are the result of nephrology series in which renal involvement may be overrepresented (36). 2) The use of variable criteria for the classification of HSP, often requiring biopsy for a diagnosis, although in typical cases of HSP in children with mild renal disease a kidney biopsy is not generally performed (36). 3) The absence of standardised therapeutic management of HSP, especially in cases of nephropathy.

IgAN is the most common cause of primary glomerulonephritis in developed countries (13-16, 20). IgAN is more common in men than in women (male: female ratio 2:1). The onset of IgAN may be associated with infections in the upper respiratory tract (20). Patients with IgAN usually present with one of the following features: episodes of macroscopic haematuria that may coincide with an infection of the upper respiratory tract or abnormal sediment in the urine and proteinuria in patients without symptoms. The clinical course of IgAN is highly variable and can range from complete recovery to end-stage renal disease. In this regard, according to the different series, up to 15-40% of patients with IgAN may develop an end-stage renal disease (13, 14, 19).

Different studies have demonstrated many similarities between HSPN and IgAN (13, 17, 27). In both syndromes the increased synthesis of IgA1 by B lymphocytes is the pathogenic characteristic feature. It leads to an increase in serum IgA1, circulating immune complexes containing IgA1 as well as increased tissue deposition of IgA (37). However, data on demographic features, clinical, laboratory, renal disease and its treatment and outcome in both syndromes are highly variable depending on the series under consideration. As stated before, it may be due to pa-

tient-selection. Thus, the main aim of our present study was to assess an unselected series of patients diagnosed as having HSPN and IgAN.

As expected, demographic features disclosed a predominance of males in both syndromes, being patients with HSPN younger than those with IgAN (3, 13, 36), since HSP is more frequent in the childhood. Also, precipitating events were similar in both groups, generally an upper respiratory tract infection and/or related to drug intake (3, 20). In keeping with previous studies, extra-renal manifestations, such as skin, gastrointestinal and joint manifestations occurred more commonly in patients with HSPN while they were only seen in a limited number of cases with IgAN (3, 13, 36). In contrast, renal involvement was more severe in patients with IgAN (20, 36). In this regard, in our series, nephrotic syndrome and renal insufficiency were statistically more common in patients with IgAN than in those with HSPN. With regard to laboratory findings, we observed differences in anaemia, which was more frequent in IgAN while the leukocytosis was more frequent in the HSPN. The percentage of patients with increased IgA serum levels was similar in both groups. With respect to this, no major differences were observed when our results were compared with those from other studies (36, 14, 19).

Although renal involvement was more severe in patients with IgAN, the number of patients who received treatment with corticosteroids and/or cytotoxic agents was similar in both groups, probably due to the frequent extra-renal manifestations that were present in patients with HSPN. Our study showed a better long-term prognosis in patients with HSPN with a greater number of patients recovering completely and a lower frequency of HSPN patients with chronic renal insufficiency, dialysis or kidney transplant compared to those patients with IgAN.

When compared with other series, our patients with HSPN developed less severe renal involvement. Therefore, we observed a smaller number of cases that had to be dialysed (36). In contrast, the percentage of IgAN who progressed to

end-stage renal disease was higher than in other studies (13, 19).

When we were about to submit our study, we disclosed a recent report that compared biopsy-proven HSPN with IgAN (38). The study included a large series of Chinese patients seen at a referral nephrology centre. The authors did not observe differences in the clinical outcome (frequency of endstage renal disease or death) between HSPN and IgAN patients. The different results observed in this study when compared with our data may be the result of a different genetic background and selection bias as this series only included biopsy- proven HSP patients, some of them with severe nephritis that required study at a nephrology unit. In contrast, our cohort included patients with HSPN regardless of the severity of the renal involvement associated to this vasculitis.

A potential limitation was that due to retrospective nature of our study, we could not calculate the BVAS. We realise that it could have been informative to calculate the BVAS at the diagnosis in both groups of patients also considering that the performance of BVAS has been recently evaluated also in pediatric vasculitis (39).

In conclusion, our results indicate that HSPN and IgAN may represent different clinical syndromes. IgAN has more severe renal disease with higher frequency of nephrotic and renal insufficiency, while HSPN has more frequent extra-renal manifestations. In unselected patients the outcome is better in HSPN than in IgAN.

Acknowledgements

We are greateful to the members of the Rheumatology, Dermatology, Paediatrics and Pathology Services of Hospital Universitario Marqués de Valdecilla, Santander, Spain.

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