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Original Investigation

Addition of Plasma Exchange to Glucocorticosteroids for the Treatment of Severe Henoch-Schönlein Purpura in Adults: A Case Series

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Background: Adult Henoch-Schönlein purpura (HSP) has been associated with poor outcome and end-stage renal disease in >20% of cases. Although the benefit of adding another immunosuppressant to steroids in severe adult HSP has not been shown, the benefit of plasma exchange (PE) therapy has been poorly evaluated.

Study Design: Case series.

Setting & Participants: 11 consecutive patients with severe and newly diagnosed HSP since 1988 who were treated with steroids and PE.

Outcome & Measurement: Patients' characteristics and outcome were analyzed. Birmingham Vasculitis Activity Score (BVAS), estimated glomerular filtration rate (eGFR), and proteinuria were measured at baseline, at the end of PE treatment, at months 6 and 12, and at the last visit. Side effects of corticoid treatment and PE were recorded.

Results: 11 patients were identified in 1988-2010. Patients received intravenous corticoid pulses in 64% of cases, followed by oral prednisone for a median of 6.6 months. They received a median of 12 PE sessions. BVAS, eGFR, and proteinuria improved significantly between baseline and the last PE at a median of 2 months. PE sessions were well tolerated, except in one patient who developed central catheter–associated septicemia. One patient required dialysis therapy 15 days after HSP diagnosis and did not recover kidney function. At the last medical evaluation at a mean follow-up of 6 years, median eGFR and proteinuria were 83 ± 22 mL/min/1.73 m^2 and protein excretion of 140 ± 10 mg/d, respectively. 3 women had pregnancy without complications.

Limitations: This case series did not have a control group.

Conclusions: The combination of PE and corticoid therapy in severe forms of HSP was associated with fast improvement and good long-term outcome.

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INDEX WORDS: Adult; Henoch-Schönlein purpura; nephritis; plasma exchange; steroids.

Henoch-Schönlein purpura (HSP) is a small-vessel vasculitis affecting the skin, joints, gut, and kidneys.[1] In adults, HSP occurs at a lower frequency than in children, but generally has more severity. In long-term follow-up, HSP nephritis with severe endo- and/or extracapillary proliferation can lead to end-stage renal disease in up to 20% of patients.[2,3]

Management of HSP in adults continues to be an area of controversy. Clinical prospective trials to guide the treatment of HSP are lacking. In the early phase of HSP, many patients experience transient nephritis. However, this not infrequently spontaneously resolves and thus no treatment is required. There is a paucity of specific information for the treatment of severe nephritis or severe digestive involvement in adults or children, but regimens based on those for other forms of systemic vasculitis are widely used. These have included steroids and cyclophosphamide, with the addition of methylprednisolone pulse in some cases.

The addition of plasma exchange (PE) in the initial treatment of severe adult HSP has been reported rarely in the literature and has never been evaluated.[4] The aim of this study was to analyze the outcome of patients with severe adult HSP treated with a combination of PE and steroids, which was the standard protocol used in our institution.

METHODS

We conducted a retrospective analysis of the medical records of all patients from our institution with newly diagnosed HSP from January 1988 to January 2011. Patients included in this study met the following criteria: (1) HSP diagnosis based on the Chapel Hill nomenclature conference criteria, (2) age older than 18 years, (3) severe organ involvement (biopsy-proven nephritis showing dif-

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fuse endocapillary proliferation [class 3] alone or with extracapillary proliferation [class 4], severe gastrointestinal involvement [hemorrhage, ischemia, perforation, or abdominal pain for >1 day unresponsive to standard analgesic]), (4) concomitant corticosteroid, (5) PE treatment, and (6) absence of other immunosuppressive treatment.[5] All patients with HSP with severe organ involvement were treated with PE and steroids from January 1988 to August 2002 and from October 2006 to January 2011 as a standard protocol in our department. Between September 2002 and September 2006, patients with HSP in our institution were included in a multicentric study evaluating cyclophosphamide addition to steroids in severe HSP.[6] A total of 3 patients were included in this study. These patients were excluded from the present study. Corticosteroid therapy was started at 1 mg/kg/d of oral prednisone, eventually preceded by intravenous methylprednisolone for 3 days (usually 10-15 mg/kg/d). Prednisone dosage gradually was tapered to 0.5 mg/kg/d at the end of the second month. Afterward, prednisone tapering was managed by the patient's physician and usually was stopped after 4-12 months of treatment. PE therapy was started as soon as possible and performed with a COBE Spectra Version 7.0 LRS Turbo (CarideanBCT, www.caridianbct.com). The following protocol was applied: usually 10-15 PEs were done over 2 months (usually 3 PEs in week 1, 2 PEs/wk in weeks 2 and 3, and 1-2 PEs/wk in weeks 4-8). PE consisted of a 1.25-1.5 plasma volume exchange with 4% human albumin. Plasma volume was calculated using the following formula: plasma volume (cc) = (body weight/13) × (1 − patient hematocrit), where body weight is in kilograms. Acid citrate dextrose was used as anticoagulation in a 1:22 ratio to whole blood flow.

For each patient, the following data were extracted from patient records at baseline, at the last PE session, at months 6 and 12, and at the last visit: demographic characteristics, clinical data (blood pressure and body weight), biological data (serum creatinine concentration, glomerular filtration rate [GFR] estimated with the 4-variable MDRD [Modification of Diet in Renal Disease] Study equation, serum albumin concentration, hematuria, 24-hour proteinuria), and Birmingham Vasculitis Activity Score (BVAS).[7,8] The BVAS refers to new or worsening symptoms due to vasculitis activity. Dose and duration of steroid treatment and number, volume, and duration of PE sessions also were analyzed. Side effects that occurred during PE sessions were gathered from session files and the French Apheresis Registry, in which side effects are declared. All adverse events from the diagnosis of HSP to the end of follow-up (death or last visit) were recorded.

Kidney biopsy specimens were reviewed by 2 pathologists and classified as follows: class 1, mesangiopathic glomerulonephritis (GN); class 2, focal and segmental GN; class 3, endocapillary proliferative GN; and class 4, endo- and extracapillary GN.[2] The proportion of glomeruli involved by global sclerosis was recorded. Interstitial fibrosis was scored as follows: none or mild (0%-25%), moderate (25%-50%), and severe (>50%).

RESULTS

Clinical Features

Eleven patients were treated with PE in association with corticosteroids in our institution between January 1988 and January 2011. Demographic, clinical, and biological characteristics at baseline are listed in Table 1. Four men and 7 women with a mean age of 51.9 years at onset were included in this study. Comorbid conditions included chronic hypertension in 3 patients and diabetes in one patient. The most frequent clinical manifestation was purpura, which was necrotic or bullous in 2 of 11 patients (18.2%). Skin biopsy was performed in 6 patients, showing characteristic leukocytoclastic vasculitis. Joint manifestations were present in 4 of 11 patients (36.4%). Gastro-

Table 1. Demographic, Clinical, and Biological Characteristics at Baseline

Parameter	Value
No. of patients	11
Men	4 (36.4)
Age (y)[a]	51.9 ± 25.4 [18-85]
Comorbid conditions	
Hypertension	3 (27.3)
Diabetes	1 (9.1)
Physical examination	
Mean blood pressure (mm Hg)	143/76
Mean weight (kg)	65.7
Skin lesions	11 (100)
Type: purpura	11 (100)
Necrosis: bullous	2 (18.2)
Gastrointestinal involvement	7 (63.6)
Moderate	4 (36.4)
Severe	3 (27.3)
Joint manifestation	4 (36.4)
Biological tests	
CRP (mg/L)	45 [3-125]
Albumin (g/dL)	3.07 [2.3-4.4]
Serum creatinine (mg/dL)	1.06 [0.71-3.9]
eGFR (mL/min/1.73 m^2)	67 [11-108]
eGFR <60 mL/min/1.73 m^2	4 (36.4)
Proteinuria (g/24 h)	4.3 [2.1-7.2]
Proteinuria ≥1 g/d	10 (90.9)
Nephrotic syndrome	5 (45)
Hematuria ≥10 RBC/μL	11 (100)
Kidney biopsies	
No.	10
Glomerular score	
Focal and segmental GN (class 2)	1 (10)
Endocapillary proliferative GN (class 3)	6 (60)
Endo-/extracapillary proliferative GN (class 4)	3 (30)
Interstitial fibrosis	
None-mild (<25%)	9 (90)
Moderate (25%-50%)	0 (0)
Severe (>50%)	1 (10)
Skin biopsies	6
Leukocytoclastic vasculitis	6 (100)

Note: Unless otherwise indicated, categorical variables given as number (percentage); continuous variables given as mean ± standard deviation or median [range]. Conversion factors for units: serum albumin in g/dL to g/L, ×10; serum creatinine in mg/dL to mol/L, ×88.4; eGFR in mL/min/1.73 m^2 to mL/s/1.73 m^2, ×0.01667.

Abbreviations: CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; GN, glomerulonephritis; RBC, red blood cells.

[a]Range given in brackets.