EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 5
Issue: 4
01-05
Year: 2018

DEVELOPMENT OF HENOCH-SCHONLEIN PURPURA NEPHRITIS AND MIGRATORY POLYARTHRITIS IN A PATIENT WITH IG A NEPHROPATHY

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Article Received on 22/01/2018 **Article Revised on 11/02/2018** **Article Accepted on 03/03/2018**

ABSTRACT
Henoch-Schonlein purpura is a type of systemic vasculitis characterized by deposition of IgA on the vascular wall. Skin, joints, kidney, gastrointestinal tract and other organs may be affected. In this paper we present a patient diagnosed as IgA nephropathy with renal biopsy 12 years ago and nowadays presented with Henoch-Schonlein purpura with purpura, hematuria and migratory polyarthritis.

KEYWORDS: Henoch-Schonlein purpura, IgA nephropathy, migratory polyarthritis.

INTRODUCTION
Henoch-Schonlein purpura (HSP) is a leukocytoclastic vasculitis characterized by deposition of immune complex containing IgA in the small vessels. In HSP skin, gastrointestinal tract, joints, kidneys and less frequently other organs may be affected.[1,2] HSP primarily affects children and in adults is rare.[3] Renal involvement is common and long-term prognosis depends on the degree of renal involvement. The degree of renal involvement varies from 20% to 100% in different studies.[4]

IgA nephropathy (IgAN) is one of the most common forms of primary glomerulonephritis worldwide.[5] It is characterized by mesangial IgA deposition and mesangial proliferation without evidence of a systemic disease symptoms.[6] Relationship between HSP and IgAN is interesting and controversial. Because of the fact that both may be seen in the same patient consecutively[7] and have similar pathological and biological properties, HSP and IgAN are considered to be related diseases.[8,9] IgAN is suggested to be a variant of HSP because of described cases in different individuals of the same family[10] or in identical twins.[11] However, HSP is associated with more extra-renal involvement and IgAN presents with severe kidney involvement so they may thought to be different syndromes.[12]

In this paper we present a 24 year- old male patient diagnosed as IgA nephropathy with renal biopsy 12 years ago and nowadays presented with Henoch-Schonlein purpura with hematuria and migratory polyarthritis.

CASE REPORT
A 24-year-old man was admitted to our department of nephrology after two weeks of migratory polyarthritis on arms and legs and macroscopic hematuria. He had been diagnosed as IgA nephropathy with renal biopsy 12 years ago. When he admitted to our hospital, his blood pressure was 140/80 mmHg, body temperature was 37.2°C, pulse rate was 80 beats per minute. On physical examination there was no abnormality in chest, abdomen and neurological findings. Cardiovascular and abdominal examinations were also normal. However, he had a typical palpable purpuric HSP rash on legs and buttocks for 24 hours and had migratory polyarthritis on arms and legs (Figure 1, 2). His family history was negative for renal diseases as well.

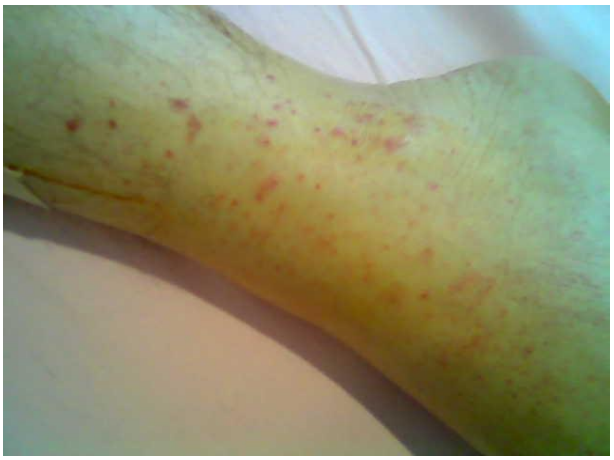

Figure 1: Petechial-purpuric rash and ankle edema. Biopsy revealed leukocytoclastic vasculitis.

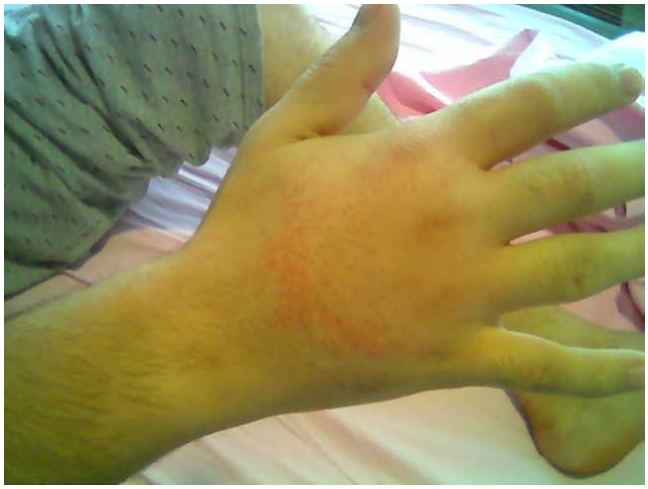

Figure 2: Hyperemia and swelling on the hand due to HSP.

Urinary, biochemical and hematological values on admission, before and after the treatment are shown in Table 1. Urine dipstick test showed mild hematuria and massive proteinuria. Urine and blood cultures were negative. Immunological values are shown in Table 2.

Table 1: Urinary, biochemical and hematological values.

	On admission	Before treatment	After treatment
Urinary laboratory findings			
Protein	(3+)	(3+)	(+)
Glucose	(-)	(-)	(-)
Occult blood	(3+)	(3+)	(+)
RBC (count/HPF)	227	21	15
WBC (count/HPF)	22	50	(-)
Creatinine/protein (mg/mg)	2.7	2.9	1.4
Creatinine clearance (ml/min)	83	58	105
Blood Chemical values			
Glucose (mg/dL)	121	135	99
Blood urea (mg/dL)	54	79	35
Creatinine (mg/dL)	1.4	2.0	1.1
Total protein (g/dL)	7.2	6.0	6.6
Albumin (g/dL)	3.8	2.8	3.9
Sodium (mEq/L)	142	134	141
Potassium (mEq/L)	5.2	4.2	4.4
Chloride (mmol/L)	100	99	106
Calcium (mg/dL)	10.2	8.5	9.7
Inorganic phosphorus (mg/dL)	4.0	4.2	4.3
Aspartate aminotransferase (U/L)	38	24	24
Alanine aminotransferase (U/L)	44	28	38
Hematological laboratory findings			
White blood cell (count/mm^3)	11600	18480	11290
Hemoglobin (gr/dl)	16.2	13.9	14.1
Hematocrit (%)	44.9	39.5	44.0
Platelet (count/mm^3)	340.000	397000	214000
Sedimentation (mm/h)	29	99	35

RBC: red blood cell, WBC: white blood cell.

Table 2: Immunologic findings.

Parameters	On admission	Parameters	On admission
Immunoglobulin A (g/L)	2.42	C-reactive protein (mg/dL)	**150**
Immunoglobulin E (IU/mL)	1180	HbsAg	(-)
Immunoglobulin G (g/L)	10.7	Anti-HCV	(-)
Immunoglobulin M (g/L)	0.804	Anti-HIV (ELISA)	(-)
Romatoid factor (IU/mL)	(-)	Brucella aglu	(-)
Complement 3 (g/L)	1.48	Gruber-Widal	(-)
Complement 4 (g/L)	0.434	Parvovirus IgM and IgG	(-)
Antinuclear antibodies	(-)	ANCA P	(-)
Anti dsDNA	(-)	Anti-GBMA	(-)
ANCA C	(-)	SM- DNA	(-)

Anti-GBMA:Anti-Glomerular basement membrane antibody.

Immunological evaluation showed: IgG 10.7 g/L (normal range, 7.0-16); IgA 2.42 g/L (normal range, 0.7-4.0); IgM 0.804 g/L (normal range, 0.4-2.3 g/L); IgE 1180 IU/mL (normal range, 0-100); C3 1.48 g/L (normal range, 0.9-1.8); C4 0.434 g/L (normal range, 0.1-0.4). Tests for antinuclear antibody, anti-DNA antibody, anti-neutrophil cytoplasmic antibody (cytoplasmic and perinuclear staining) or anti-glomerular basement membrane antibody were all negative. Ultrasound examination revealed bilateral grade I-II renal parenchymal disease.

His 12 years ago renal biopsy specimen showed moderate proliferative glomerulonephritis without crescent formation. Immunofluorescence study revealed granular staining of IgA (++) and C3 (+) in the capillary wall and mesangial lesions. At this point, a punch biopsy specimen of the skin lesion was obtained. Staining of sections with hematoxylin-eosin revealed perivascular fragmentation of inflammatory cell nuclei and inflammatory infiltrate predominantly perivascular and small vessels of dermis. The infiltrate is consisted of mainly neutrophils. There was evidence of polymorphonuclear leukocyte infiltration throughout the vessel wall. The diagnosis was consistent with leukocytoclastic vasculitis as shown in Figure 3.

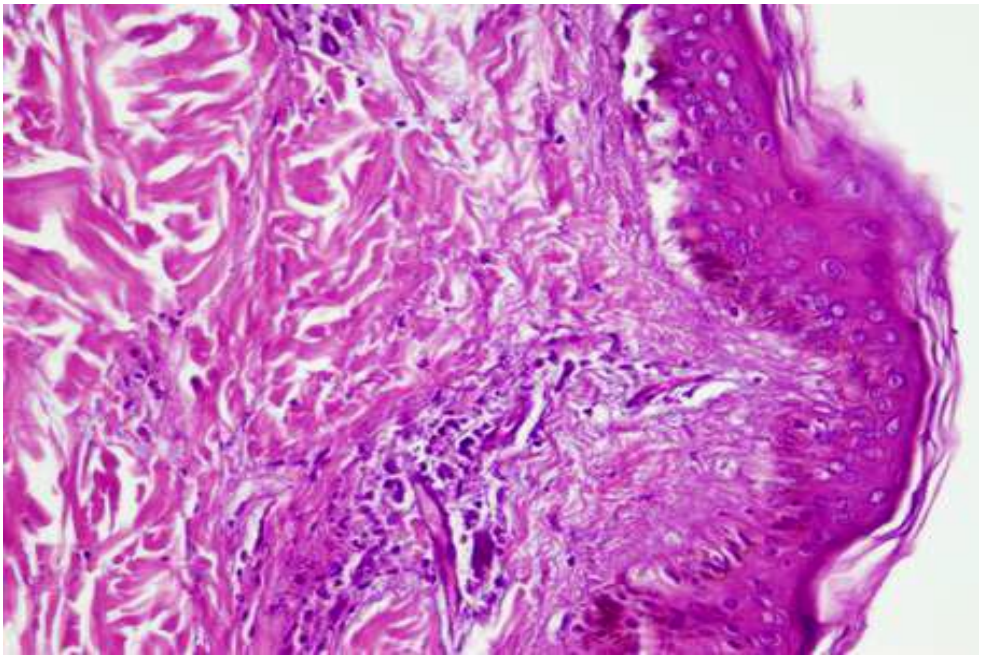

Figure 3: Skin biopsy specimen of the purpuric lesion. Leukocytoclastic vasculitis with infiltration of vessel walls and perivascular area by neutrophils and leukocytoclasis (H&E, X 200).

Based on these clinical and pathological features, the patient was diagnosed with IgA nephropathy with overlapping HSP nephritis and migratory asymmetric polyarthritis. Treatment with oral fluocortolone at a dose of 60 mg/day was started. Anti-hypertensive and nephroprotective therapy by using enalapril 10 mg/day was administrated orally. Following the treatment, clinical symptoms were rapidly abated. Three weeks after the beginning of these treatments proteinuria decreased from 2.9 to 1.4 gr/day and his renal functions improved. During follow-up, 3 weeks later rash and arthritis resolved.

DISCUSSION

Here we reported a patient with IgA nephropathy nowadays presented with HSP nephritis and migratory polyarthritis. When IgA nephropathy was diagnosed around 12 years ago, he did not show any abnormalities other than hematuria and proteinuria. To the best of our knowledge, there was no case of overlapping IgA nephropathy and HSP nephritis with migratory polyarthritis.

Henoch-Schonlein purpura nephritis might be proposed to be related to IgA nephropathy as the morphologic and immunopathologic features are similar in two conditions. The exact pathogenic mechanisms of HSP and IgAN have not been fully identified yet.

Urinary tract infections are commonly associated with hematuria and cause other symptoms like dysuria and urgency. In our case kidney stones and neoplasm were ruled out by ultrasound; urinalysis and culture did not show an infection as the cause of hematuria. Furthermore, red blood cells in urine were dysmorphic under microscopy, suggesting glomerular hematuria. Episodes of gross hematuria are characteristic of some glomerular diseases such as IgA nephropathy. Our patient had a history of hematuria and proteinuria and diagnosed as IgA nephropathy 12 years ago.

The most common symptom of HSP is characteristic skin rash. In HSP rash is typically symmetrical and seen on hips, feet, in the extensor surfaces of elbows and sometimes in other parts of the body (arms and body).[13] In the feet, gluteal region and lower extremities of our patient, there were petechial, purpuric rash. During follow up, similar rash on both hands were observed. Palpable purpuric lesions may usually be seen in bacteriemia[14] or systemic vasculitides.[15] The concurrent appearance of gross hematuria, proteinuria and palpable purpura strongly suggested a systemic process such as HSP. Therefore, there is a reasonable presumption that the appearance of purpura and gross hematuria were suggestive of HSP nephritis in this patient. The purpura, in spite of suggesting of HSP, might also indicate a systemic disease with renal involvement such as polyarteritis, lupus or cryoglobulinemia.[16] The serological tests for autoimmune antibodies were all negative (Table 2). The slight positivity for cryoglobulins has been reported in HSP[14], but in this cases complement was in the normal range and had no antibodies against hepatitis C virus, usually associated with cryoglobulinemia. The purpuric lesions, gross hematuria and the history of abdominal pain led us to perform a biopsy of the affected skin area. In this respect light microscopy revealed small blood vessels of the dermis with a perivascular infiltrate mainly consisting of mononuclear and polymorphonuclear cells. Immunofluorescence showed deposits of IgA, characteristic of HSP.

Joint involvement is the second most common clinical manifestation especially in childhood HSP. The incidence of joint involvement decreases with advancing age. HSP associated arthritis can affect a single joint or multiple joints. It is usually oligoarticular and nondestructive. Oligoarticular form involves large joints such as the ankle and knee, but more rarely wrist, elbow and the fingers may be affected. When two or more joints are affected symmetrical involvement is frequent. Migratory polyarthritis is relatively rare in childhood. Pain in HSP respond well to non-steroidal anti-inflammatory agents.[13,17]

It is reported that in patients with IgA nephropathy, HSP in later years may present with arthritis and arthralgia.[18] Unlike other cases, in our case joint symptoms such as arthritis / arthralgia were asymmetric and migrating. There was swelling and tenderness in the patient's soft tissue around the affected joints. During follow-up we observed migrating arthritis and arthralgia in both ankles, knees, elbows, wrists, fingers and toes. Sondike SB has identified a case with gastrointestinal ulcer, cholecystitis and severe hypoalbuminemia secondary to HPS and joint symptoms similar to our case.[19]

Hypertension typically occurs as part of acute HSP nephritis, with impaired renal function, and often with oliguric hypervolaemia. In our cases hypertension was also noted, but this condition was disappeared with enalapril treatment.

CONCLUSION

In summary our case is the first to identify HSP with skin, kidney and joint involvement in an adult male with IgA nephropathy. Purpura and migratory polyarthritis may be important symptoms of HSP in a IgAN patients. HSP and IgAN may probably be different clinical manifestations of the same disease with common pathogenesis.

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