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Focal segmental glomerulosclerosis in a patient with hypereosinophilic syndrome

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ABSTRACT

Background: Renal complication in hypereosinophilic syndrome (HES) is rare, with literature scarcely reporting association of this syndrome with glomerular involvement. While the direct effect of eosinophilic infiltration in tissues has been linked to histological damage of the HES, other mechanisms may account for renal involvement too.

Case Presentation: We present a case of a 17-year-old male patient, with progressive edema, contact reactive erythematous skin lesions, acute kidney injury, nephrotic syndrome and progressive eosinophilia. His bone marrow biopsy revealed moderate hyperplasia with severe eosinophilia and atypical lymphocytes. His renal biopsy revealed glomeruli, enlarged in volume with mesangial expansion and hypercellularity and segmental thickening of capillary loops. Likewise, some glomeruli showed peripheral hyalinosis with synechiae to Bowman's capsule. Tubules showed cloudy swelling, mild tubular atrophy and hyaline cylinders. Interstitial area showed infiltrated lymphomononuclear cells, focal with no evidence of eosinophils. Blood vessels were unaltered. Immunofluorescence identified glomeruli with granular mesangial IgM deposition. After corticosteroid treatment, eosinophilia and creatinine values regress to normal range.

Conclusions: While our case may suggest the coexistence of two unrelated diseases, further studies are required to assess the pathophysiology of glomerular involvement in HES. Given the possibility that mechanisms other than the direct effect of eosinophils are involved in certain patients

Case Report

Implication for health policy/practice/research/medical education:
Hypereosinophilic syndrome (HES) is a uncommon disease with rare glomerular involvement. While the direct effect of eosinophilic infiltration in tissues has been linked to histological damage of the HES, this case raises a possible new physiopathological mechanism for an uncommon association

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1. Background

Hypereosinophilic syndrome (HES) is a disease characterized by an eosinophil count of over 1500 eosinophils/mm^3 on at least two different occasions, with evidence of tissue hypereosinophilia or organ damage associated with hypereosinophilia (1,2). It is generally diagnosed by exclusion, with an estimated prevalence of 0.36 to 6.3 patients per 100 000 population. It usually occurs between the ages of 20 and 50 and is more common among men (1,2).

The disease may be primary, secondary, or idiopathic (1,2). Secondary causes include parasitic or fungal infections, neoplasms, blood diseases, allergic diseases, and autoimmune diseases. Skin, nervous system, lungs,

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and the heart are organs most often involved. Heart disorder is the main cause of death (1,2).

While a case has been reported in which the kidney is the first organ to be involved (3), renal involvement is generally rare, while the disease itself being uncommon (2). Kidney involvement is related to vascular disorder, interstitial nephritis, electrolyte disturbances, Charcot-Leyden crystals or glomerular diseases (2). Few cases of HES with glomerular lesions have been reported in medical literature (4-11).

We describe a case of HES with nephrotic syndrome secondary to focal segmental glomerulosclerosis.

2. Case Presentation

A 17-year-old male patient with no significant clinical history, with progressive edema associated with dyspnea and general discomfort referred to the hospital. Physical examination revealed anasarca. A week after admission to the hospital, contact reactive erythematous skin lesions was detected.

His initial serum creatinine was 2.9 mg/dL. Urine test values were as follows: leukocytes 14/hpf, red cells 27/hpf, blood ++, glucose +++ and epithelial cells 36/hpf. Initial urine protein was 7.46 g/d. Two weeks later, a second urine protein revealed a proteinuria of 21 g/d. Likewise, total cholesterol was 210 mg/dL, HDL-C 28.9 mg/dL, LDL-C 122 mg/dL, and triglycerides 291 mg/dL, as well as plasma hemoglobin was 14.8 g/dL, leukocytes 7740/mL, platelets 243000/mL, and eosinophils 851/mL. Nine days after admission, eosinophilia had significantly increased to 2031/mL and then 4905/mL.

Examination of stool for parasites was negative. Serology tests for hepatitis B and C, toxoplasmosis, rubella, cytomegalovirus, ANA, anti–DNA, ANCA/MPO and proteinase 3 (PR3) were negative. Serum C3 and C4 components of the complement system were within normal ranges. Likewise, echocardiogram, chest X-ray, abdominal CT and pelvic CT were normal.

Two weeks after admission, a bone marrow biopsy revealed moderate hyperplasia with severe eosinophilia and atypical lymphocytes, which was diagnosed as HES. An ultrasound-guided renal biopsy was conducted. Of 23 glomeruli, none of which were globally sclerosed (Figure 1). Glomeruli were found to be enlarged in volume with mesangial expansion and hypercellularity with segmental thickening of capillary loops. Five glomeruli showed peripheral hyalinosis with synechiae to Bowman's capsule. Tubules showed cloudy swelling, mild tubular atrophy (5%), and hyaline cylinders. Interstitial area showed infiltrated lymphomononuclear cells, focal (5%) with no evidence of eosinophils. Fibrosis was not detected. Blood vessels were unaltered.

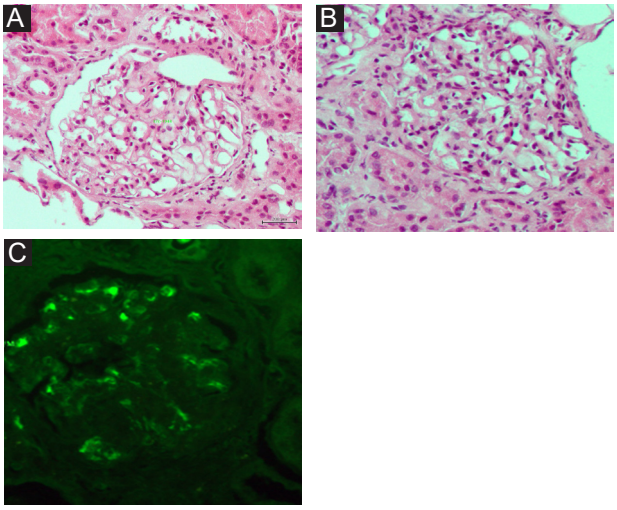

Figure 1. (A) Glomerulus enlarged in size with mild mesangial expansion and occasional rigid capillary loops (H-E 20x). **(B)** Glomerulus enlarged in size with mild mesangial expansion and a peripheral hyaline area, as well as adhesion to Bowman's capsule (H-E 40x). **(C)** Immunofluorescence: granular gesangial IgM deposition.

Immunofluorescence study showed granular mesangial IgM deposition. The histological findings were consistent with focal segmental glomerulosclerosis classic variant without specification.

Association between HES and focal segmental glomerulosclerosis was deemed probable. Then three pulses of methylprednisolone were administered, followed by prednisone 70 mg daily, calcium carbonate 500 mg tid, atorvastatin 40 mg qd, losartan 50 mg bid, and furosemide 80 mg bid. A week after, eosinophilia and creatinine values regress within normal range (185/mL and 0.86 mg/dL respectively). Urine protein was reduced by 50% and general clinical improvement was observed.

3. Discussion

While the histologic findings in some case reports of glomerular involvement in HES patients have been scarcely specific (12), membranous glomerulonephritis (4,5), IgA nephropathy (6), focal segmental glomerulonephritis (7), immunotactoid glomerulonephritis (8), endocapillary proliferation (9), and crescentic glomerulonephritis with deposition of immune complexes have also been identified (10,11).

The pathophysiology of renal involvement in a HES patient has been scarcely studied. However, it is thought to be similar to histologic involvement by HES on other organs by mass effect due to the proportion of eosinophils and eosinophil cytotoxicity (2). In fact, these reports are characterized by eosinophilic infiltration in renal biopsy, which does not occur in our patient (2-12). While focal segmental glomerulosclerosis and HES may be two coexisting diseases—yet unrelated in our patient—

the low proportion of cases reported in the literature of glomerular involvement of HES, compels us to consider the possibility of physiopathological mechanisms not yet known may account for such coexistence. Immune mechanisms may well be involved in certain patients, as suggested by the finding of deposition of immune complexes, such as IgM in our case, as has been reported previously in a patient with endocapillary proliferation associated with HES (9). Other authors have identified Ig deposition of IgG, IgA and C3 (4,6,10), however, deposition of immune complexes have not always been found in renal biopsies of involved patients (7).

The prognosis of HES has improved, with a 5-year survival rate of 70% to 90% (9). However, treatment of glomerular involvement in a HES patient is not standardized, but assuming renal involvement involves severity of disease while in such cases, high-dose corticosteroids with uneven responses were administered (2,7,9). The satisfactory corticosteroid treatment response in our patient might suggest an association between both diseases.

4. Conclusions

While our case may suggest the coexistence of two unrelated diseases, further studies are required to assess the pathophysiology of glomerular involvement in a HES patient, given the possibility that mechanisms other than the direct effect of eosinophils are involved in certain patients.

Authors' contribution

Authors contributed to the manuscript equally.

Conflicts of interest

The authors declare that they have no conflicting interest.

Ethical considerations

Written informed consent was obtained form the patient's parents for publication of this report.

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