

Case Report

Renal involvement as the first manifestation of hypereosinophilic syndrome: a case report

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Abstract

Idiopathic hypereosinophilic syndrome is characterized by elevated and prolonged blood eosinophilia along with organ system involvement and malfunction. The heart is the most frequently involved organ, and renal participation is extremely rare. Herein, we report on a case of idiopathic hypereosinophilic syndrome with renal involvement as the first manifestation.

Keywords: eosinophils; hypereosinophilia; hypereosinophilic syndrome; renal involvement

Case report

We describe a 73-year-old man who was admitted to our hospital with renal failure but no evidence of proteinuria, haematuria or any other renal signs or symptoms. He had suffered from myocardial infarction 15 years before. He presented a new myocardial infarction 2 years ago and, after an extensive coronary study, underwent a quadruple aortocoronary bypass. After that admission, in every single analysis, blood eosinophilia appeared, but no further studies were done for clarification. Four years before, he had been diagnosed with colon cancer that was treated successfully. He had no other significant health problems until he presented fatigue and symptoms of malaise. He came to the emergency room after being diagnosed with acute renal failure and was admitted to our nephrology department in order to study its aetiology and to initiate adequate treatment.

Clinical history failed to reveal any nephrotoxic drugs or any intercurrent processes that could result in acute renal failure. Physical examination on admission to the nephrology department revealed no abnormalities. Haematologic and biochemical values were as follows: haemoglobin 9.7 mg/dL, leukocytes 10 320/L [21% polymorphonuclears, 28% lymphocytes and 48% eosinophils (4953 eosinophils/L)] and platelets 170 000/L. There were no abnormal cells on the examination of peripheral blood. Glu-

cose was 4.5 mmol/L, urea nitrogen 23 mmol/L, creatinine 659 μ mol/L, creatinine clearance 10 mL/min, potassium 5.3 mmol/L, sodium 134 mmol/L, proteins 95 g/L and albumin 28 g/L. Twenty-four-hour proteinuria and urinary analysis were negative. Hepatic parameters and serum cholesterol levels were normal as well.

We requested a complete microbiological blood study in order to discard hypereosinophilia secondary to infections. Tests for parasitic diseases were negative and HBsAg, HIV antibody, cryoglobulines, ANA, anti-DNA and rheumatoid factor. C3, C4 and factor B complement fractions were also within the normal range. Serum protein electrophoresis showed polyclonal hypergammaglobulinaemia. Serum immunoglobulin G was high (5710 UI/mL) as was immunoglobulin E (796 mg/dL). Serum immunoglobulin A and M were within the normal range. Chest x-rays films showed pulmonary vascular redistribution and an enlarged heart. The abdominal ultrasonographic examination displayed a normal morphology and kidney size. The right renal artery could not be observed and the left renal artery was totally normal without any stenosis. No other abnormalities were found. To rule out multiple myeloma or other lymphoproliferative processes, a bone-marrow aspiration was performed but it was non-productive. Finally, a bone biopsy was performed that showed a moderate eosinophilia without any malignancy. A fine needle aspiration of the abdominal fat was negative for amyloidosis.

Meanwhile, the patient's general condition began to worsen due to oliguria and dyspnoea so a femoral catheter was inserted and he underwent regular haemodialysis every other day. A percutaneous renal biopsy was indicated to identify the aetiology of renal failure. On the day previous to the procedure, the patient suffered from angina pectoris, so treatment with sodium heparin was initiated. After that, hepatic parameters began to be altered as such: amino-aspartate 0.55 μ kat/L, alanine-transferase 0.76 μ kat/L, gamma-glutamine transferase 3.76 μ kat/L, alkaline phosphatases 3.2 μ kat/L and bilirubin 4 μ mol/L. Due to the emergency renal biopsy, while on anticoagulant treatment, a transjugular renal and hepatic biopsy was performed at the Department of Angiovascular Radiology.

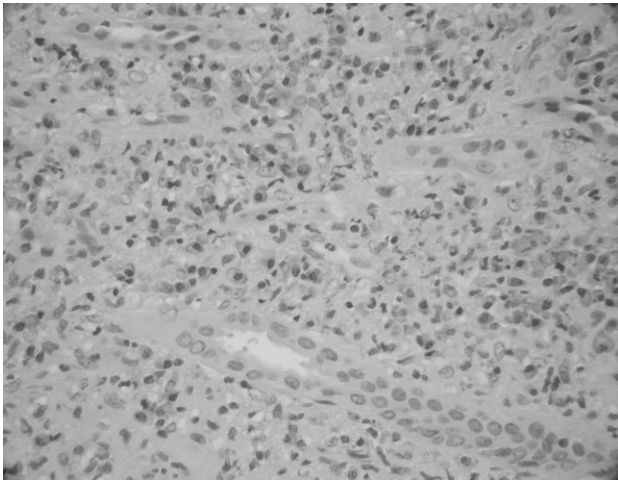


Fig. 1. Kidney—tubular atrophy and the presence of eosinophils in the interstitium. H&E 40×

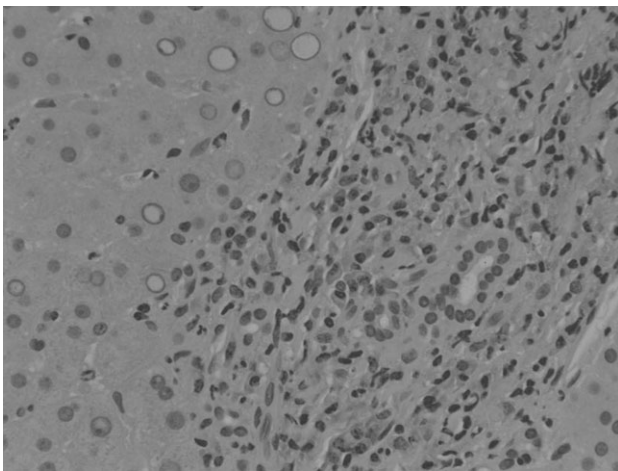


Fig. 2. Liver—expanded porta's space with plasmatic cells and eosinophils. H&E 40×

The hepatic biopsy (Figure 2) displayed mild acute hepatitis with some chronic lesions and a huge number of eosinophils. The renal biopsy (Figure 1) showed severe chronic tubulointerstitial nephritis with intense eosinophilia and no evidence of malignancy. There was only one glomerulus without any kind of immunoglobulin deposition.

Based on the clinical course and histological findings, the diagnosis of idiopathic hypereosinophilic syndrome with renal involvement as the first manifestation was made; steroid therapy was then initiated at a dose of 1 mg/kg/day of oral prednisone.

After treatment with corticosteroids for 24 h, eosinophilia on peripheral blood dramatically reduced to 10% and there was a rapid improvement in his clinical condition. Five days after prednisone initiation, urinary output reappeared, renal function ameliorated and haemodialysis was withdrawn. He was discharged a few days later, and the steroids were tapered gradually when he became asymptomatic. Three months later, renal function remained stable

with a serum creatinine of 262 $\mu\text{mol/L}$, normalized hepatic parameters and normal blood eosinophil count. The dose of steroids was reduced to 15 mg/day. To date, there is no evidence of any other organ involvement. In the outpatient clinica, the dose of steroids was reduced to 5 mg/day due to the improvement of renal parameters (serum creatinine was 190 $\mu\text{mol/L}$ and urea was 9 mmol/L). A few months after this steroid reduction, the total count of eosinophils rose to 4660/L (38%) and renal biochemical parameters had worsened as well, serum creatinine was 265 $\mu\text{mol/L}$ and urea 14 mmol/L. Hepatic parameters stayed within the normal range. So we decided to increase the dose of steroids again. Three weeks later, eosinophilia on peripheral blood reduced to 130 eosinophils/L (1.1%) and creatinine had improved to 194 $\mu\text{mol/L}$ again.

Discussion

Eosinophilia can cause many lesions in different organs and tissues as a result of eosinophil cytotoxic properties. The HES is characterized by a maintained overproduction of eosinophils with organic involvement. The diagnosis of idiopathic HES is based on Chusid's criteria, which are as follows: marked eosinophilia [absolute eosinophil count (AEC) $>1500 \times 10^6/\text{L}$], chronic course (>6 months), exclusion of other evident aetiologies for eosinophilia and signs or symptoms of eosinophil-mediated tissue injury [1]. The aetiology of the HES has yet to be clarified. In some instances, tumours are one of the multiple causes of secondary eosinophilia. Our patient had surgery for a carcinoma of colon, but there are no reports in the medical literature implicating this kind of tumour. Otherwise, the absence of relapse of the tumour at the time of diagnosis makes it improbable. HES has to be distinguished from reactive hypereosinophilia in parasitic infections, allergic diseases and haematological diseases [2].

HES occurs at any age, though most cases occur between 20 and 50 years of age and it affects men more frequently than women (9:1). The beginning of the disease is generally asymptomatic, being discovered by chance. Our case reflects this; he therefore had had blood eosinophilia for two years prior to admission to our nephrology Department with renal insufficiency and blood eosinophilia.

In previous reported cases of idiopathic hypereosinophilic syndrome, renal involvement is poorly described. In some articles, most patients present late during the course of idiopathic hypereosinophilic syndrome with ischaemic renal changes secondary to thromboembolism from endomyocardial disease [3,4]. Another cause of renal disease associated with increased blood eosinophils is cholesterol atheroembolism, but this complication has been reported in elderly patients with advanced atherosclerosis and is frequently associated with thrombocytopenia and low serum complement. There are some cases in the literature that presented as a MPO-ANCA-positive crescent and immunotactoid glomerulonephritis with immunoglobulin G, M and A and complement deposits in glomeruli. The mechanisms implicated in renal involvement are similar to those implicated in damaged tissue in other organs, such as eosinophil cytotoxicity, mass effect due to eosinophilic

infiltrates and thromboembolic events secondary to cardiac damage. Another described affection is nephrotic syndrome due to membranous glomerulopathies complicated with renal vein thrombosis and thrombotic microangiopathy [5–8].

To our knowledge, this is the first documented case of severe eosinophilic interstitial nephritis as the only structural renal damage associated with hypereosinophilic syndrome. There is an article describing the case of a patient affected by hypereosinophilic syndrome associated with kidney insufficiency, specifically eosinophilic interstitial nephritis. However, the eosinophilic interstitial nephritis was not so severe as in our case and it was associated with arteriolar glomerulitis with vasculitis [9].

Although mortality is high, aggressive medical treatment can result in significant clinical improvement. Steroids are the treatment of choice for idiopathic hypereosinophilic syndrome with progressive organ damage, but the dose should be lowered as soon as there is any evidence of response. When there is no response, other possibilities of treatment are possible, according to new published articles. This additional therapy consists of oral hydroxyurea, vincristine, immunosuppressant agents such as cyclosporine A, antimetabolite drugs such as methotrexate and colchicine; interferon-alpha at high doses; tyrosine kinase inhibitors such as imatinib mesylate that selectively inhibits a series of protein tyrosine kinases, including BCR-ABL, platelet-derived growth factor receptor alpha (PDGF-RA) and platelet-derived growth factor receptor beta (PDGFRB) or a drug similar to imatinib mesylate, nilotinib, which is a competitive inhibitor at the ATP-binding site of BCR-ABL, and it has been demonstrated that it is more potent than imatinib. Allogeneic stem cell transplantation has also been used as one of the final options as well as monoclonal antibodies such as anti-IL5 (mepolizumab) or anti-CD52 (CAMPATH). [10–12].

Despite renal pathology in idiopathic hypereosinophilic syndrome being extremely rare, in recent years some cases have appeared describing different types of renal involve-

ment. The diagnosis must be made in time in order to initiate treatment promptly and obtain a complete recovery in renal function. Our patient could serve as an example, having had a very good response to corticosteroid therapy such that he could be withdrawn from haemodialysis.

Conflict of interest statement. None declared.

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