Case report

Child Kidney Dis 2015;19:167-170
DOI: http://dx.doi.org/10.3339/chikd.2015.19.2.167

ISSN 2384-0242 (print)
ISSN 2384-0250 (online)

A Case of Hypereosinophilic Syndrome with Bladder Involvement in a 7-Year-Old Boy

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Received: 30 June 2015
Revised: 13 July 2015
Accepted: 3 August 2015

Hypereosinophilic syndrome (HES) is characterized by the presense of hypereosinophilia with evidence of target organ damage. We report a patient diagnosed with eosinophilic cystitis and HES. A 7 year old boy had hematuria, dysuria, and increased urinary frequency for 1 day. Laboratory examinations revealed hypereosinophilia (eosinophils, 2,058/μL), hematuria, and proteinuria. Abdominal sonography revealed diffuse and severe wall thickening of the bladder. The patient was treated initially with antibiotics. However, his symptoms did not improve after 7 days. A computed tomography scan demonstrated severe wall thickening of the bladder and the hypereosinophilia persisted (eosinophils, 2,985/μL). The patient complained of chest discomfort, dyspnea, epigastric pain, and vomiting on hospital day 10. Parasitic, allergic, malignancy, rheumatologic, and immune workups revealed no abnormal findings. Chest X-rays, electrocardiography, and a pulmonary function test were normal; however, the hypereosinophilia was aggravated (eosinophils, 3,934/μL). Oral deflazacort was administered. A cystoscopic biopsy showed chronic inflammation with eosinophilic infiltration. The patient's respiratory, gastrointestinal, and urinary symptoms improved after 6 days of steroids, and he was discharged. The eosinophil count decreased dramatically (182/μL). The hypereosinophilia waxed and waned for 7 months, and the oral steroids were tapered and stopped. This case describes a patient diagnosed with eosinophilic cystitis and HES.

Key words: Hypereosinophilic syndrome, Eosinophilic cystitis, Hypereosinophilia

Introduction

Hypereosinophilic syndrome (HES) is defined as the presence of peripheral blood hypereosinophilia and organ damage or dysfunction attributable to tissue hypereosinophilia, and with exclusion of other disorders or conditions as a major reason for the organ damage. Furthermore, persistent peripheral blood eosinophilia is recorded on at least two occasions with a minimum time interval of 4 weeks (except when immediate therapy is required because of hypereosinophilia-related organ dysfunction)[1]. HES is a multiorgan disorder that can involve the cardiovascular and central and peripheral nervous systems, skin, lungs, gastrointestinal tract, eyes, and urinary system[2]. However, involvement of the urinary bladder is relatively rare. Here, we report a case of HES with bladder involvement in a 7 year old boy.

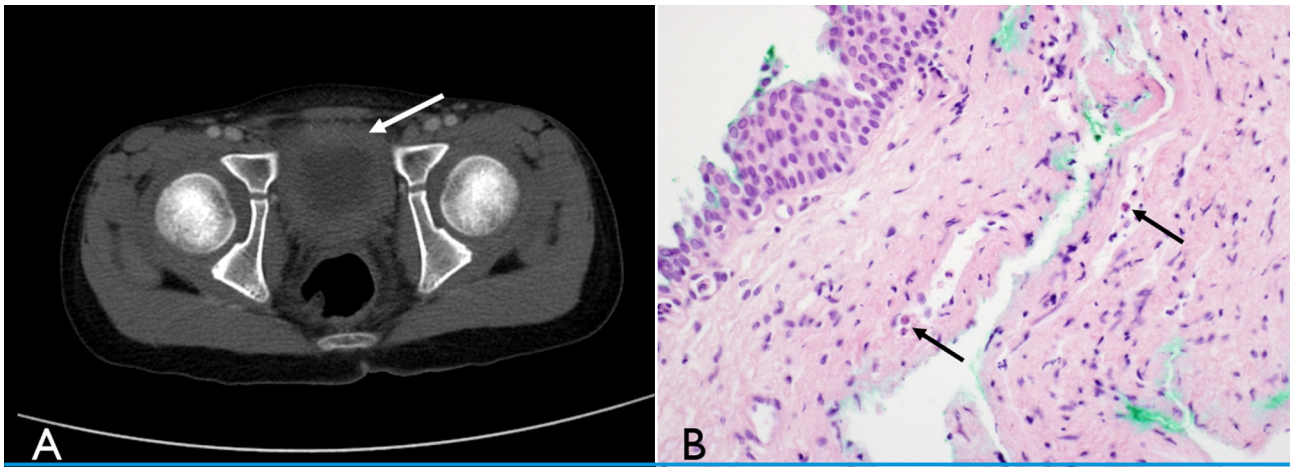

Fig. 1. A. Abdominal computed tomography scan shows severe wall thickening of the urinary bladder (arrow). B. Bladder biopsy shows chronic inflammation and eosinophilic infiltration in the lamina propria and submucosa (arrows) (hematoxylin and eosin, ×200).

Case report

A 7 year old boy with a 1-day history of hematuria, dysuria, and increased urinary frequency was admitted to the hospital. He had mild lower abdominal pain. The patient had no significant medical or family history, such as asthma or atopic dermatitis. A physical examination revealed tenderness in the suprapubic area and right costovertebral angle. A laboratory investigation revealed hemoglobin of 13.5 g/dL; white blood cell count of 12,180/μL (eosinophils, 2,058/μL), and a platelet count of 430,000/μL. C-reactive protein level and erythrocyte sedimentation rate were in the normal range. A urinalysis showed proteinuria and hematuria (10–29 red blood cells/high power field). No dysmorphic red blood cells were detected. The results of urine cultures, including an adenovirus culture, were not specific. Chest and abdominal X-rays were normal. Abdominal sonography revealed diffuse and severe wall thickening of the urinary bladder, suggesting cystitis. A kidney dimercaptosuccinic acid scan was normal. A voiding cystourethrogram showed only a minimal grade 1 vesicoureteral reflux on the right side. We suspected hemorrhagic cystitis initially, so the patient was treated with empirical antibiotics (cefotaxime and gentamicin). The urinalysis and urine culture were negative after 7 days; however, the patient's symptoms had not improved. Increased urinary frequency, incontinence, and urgency persisted, although anticholinergic medication (oxybutynin chloride 5 mg/day) was added on hospital day 5. Computed tomography (CT) urography showed severe wall thickening of the bladder on hospital day 8 (Fig. 1A). A repeat blood investigation revealed a white blood cell count of 9,630/μL (eosinophils, 2,985/μL). The patient complained of chest discomfort, dyspnea, epigastric pain, vomiting, increased urinary frequency and urgency, incontinence, and dysuria on hospital day 10, but he had no fever. Levels of the creatine kinase-myocardial band, troponin T, IgE, and eosinophil cationic protein were within normal ranges. The findings of another immunological study (IgG, IgA, IgM, and lymphocyte subsets) were not specific. The following results were all negative: multiple allergosorbent test for common allergens, human immunodeficiency virus Ag, antineutrophil cytoplasm antibody, antinuclear antibody, and a stool analysis for ova and parasites. The follow-up chest X-ray was normal (Fig. 2). Electrocardiography showed normal sinus rhythm, and a pulmonary function test was not specific after salbutamol nebulizer therapy (forced vital capacity [FVC], 94%; forced expiratory volume in 1 sec [FEV_1], 109%, and FEV_1/FVC, 97%). Another blood analysis revealed a white blood cell count of 11,470/μL (eosinophils, 3,934/μL). Investigations of peripheral blood morphology were repeatedly nonspecific, except the hypereosinophilia. Because the patient's systemic symptoms remained aggravated, oral deflazacort (2 mg/kg/day) was administered beginning on hospital day 12. A cystoscopic bladder wall biopsy was performed after 3 days of steroid therapy and showed infiltration of eosinophils and mild chronic inflammation in the lamina propria and submucosa (Fig.

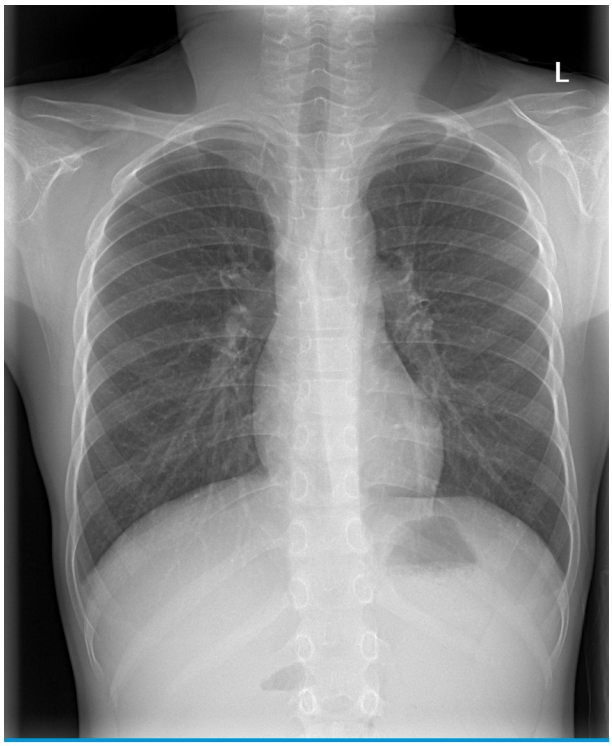

Fig. 2. Chest X-ray showed no specific findings on hospital day 10.

1B). The patient's respiratory, gastrointestinal, and urinary symptoms had improved after 6 days of steroids, and he was discharged. The eosinophil count decreased dramatically (182/μL). After discharge, the steroid was tapered for about 1 month. However, the patient redeveloped dysuria and increased urinary frequency, and his eosinophil count increased (1,048/μL). The steroid dose was tapered gradually, depending on the blood analysis results, and stopped over 7 months. No bladder wall thickening was detected on abdominal sonography after 1 year. The patient has been followed for the last 2.5 years and is doing well.

Discussion

We report a patient who was diagnosed with eosinophilic cystitis and HES. He initially had urinary symptoms followed by various clinical manifestations of HES, persistent peripheral blood hypereosinophilia and bladder tissue damage.

HES is uncommon in children, and the incidence is not well characterized. Consensus criteria for HES were proposed in 2012. HES is defined as the presence of hypereosinophilia (absolute eosinophil count > 1,500 cells/μL for ≥ 1 month) and/or findings of tissue hypereosinophilia. The diagnosis of HES includes evidence of eosinophil-mediated target organ damage and excludes all other potential causes of hypereosinophilia[2]. The original proposed definition was the presence of peripheral blood eosinophilia > 1,500 cells/μL for > 6 months; however, this is less consistently embraced today because of the ability to rapidly evaluate eosinophilia. Moreover, some patients should be treated more rapidly to minimize organ damage[3]. The hypereosinophilia of our case was not longer than 6 months. However, the patient showed hypereosinophilia and eosinophil infiltration in the mucosa and submucosa of the bladder wall. Although the eosinophilic infiltration into bladder tissue at admission was not striking, it may have been due to prior steroid treatment because of his systemic HES symptoms. Furthermore, the steroid therapy was not terminated in the short-term after discharge because of the recurrent bladder symptoms and peripheral blood eosinophilia. The steroid therapy was tapered gradually and stopped over 7 months, depending on blood analysis results and urinary symptoms.

HES can cause multiple organ damage, and clinical manifestations of HES are characterized by dermatologic, pulmonary, gastrointestinal, cardiac, ocular, and neurologic symptoms. Badr et al.[4] reported a 16 year old girl who presented with chest pain, palpitations, dyspnea, and vomiting. She was diagnosed with eosinophilic pericardial effusion and HES with restrictive cardiomyopathy. Eosinophilic cystitis associated with HES is a very rare disorder, and only a few cases have been reported[5]. Hosoki et al.[6] reported eosinophilic cystitis, gastritis, enteritis, and pulmonary nodules in an 8 year old patient with HES, who had diarrhea, abdominal pain, and general fatigue. Laboratory data showed marked eosinophilia. An abdominal CT scan showed a markedly thickened bladder wall. Only a high-dose steroid was effective (oral prednisolone 2 mg/kg/day), and cyclosporine was added to treat recurrent abdominal pain. In particular, Dorna et al.[7] reported a similar case to ours. An 8 year old girl presented with a history of dysuria, increased urinary frequency, and suprapubic pain. She had only urinary symptoms and was treated with oral prednisolone (1 mg/kg/day). The patient was diagnosed with eosinophilic cystitis and idiopathic HES. In our case, a 7 year old boy initially showed gross hematuria, dysuria, and increased urinary frequency.

Peripheral blood eosinophilia persisted and other systemic symptoms of HES, including dyspnea, chest pain, epigastric pain, and vomiting developed subsequently. No other secondary cause for hypereosinophilia was identified in this patient.

No standard HES therapy guidelines exist, but corticosteroids are considered the most useful medication for treating HES. A multicenter retrospective study reported that 81% (163 of 188) of patients with HES were initially treated with corticosteroids. Among them, 85% of patients experienced a partial or complete response 1 month after initiating treatment[5]. The recommended dose of prednisone is 0.5–1 mg/kg daily until clinical improvement and a reduction of the eosinophil count, and then a tapering regimen is required. Hydroxyurea is the most commonly used second-line agent in a steroid non-responder. Hydroxyurea should not be used alone, but is beneficial in combination with a corticosteroid or interferon (IFN)-α[8]. IFN-α was reported in 1990, and controls the disease in patients refractory to corticosteroids and hydroxyurea[9]. Vincristine, cyclophosphamide, and etoposide also have hematologic benefits[3]. In this case, the patient was treated with antibiotics, anticholinergics, and corticosteroids. The patient had a good response to steroid therapy and did not need further second-line agents. One study reviewed nine cases of patients diagnosed with eosinophilic cystitis and with definite or probable HES. Of the nine patients, seven (78%) received steroid therapy and four (44%) developed a recurrence[10]. The patient in our study also had recurrent urinary symptoms, and peripheral blood eosinophils increased after tapering the steroid for 1 month. However, these symptoms were controlled successfully by oral steroid therapy for 7 months. In general, patients with idiopathic HES who respond well to steroid therapy or have elevated IgE levels have a good prognosis; however, untreated idiopathic HES has an 80% mortality rate at 3 years[11]. Our patient responded well to oral steroids and has been doing well after the 2.5 year follow-up.

We report a rare case of eosinophilic cystitis with HES in a 7 year old boy. The patient initially developed urinary symptoms and hypereosinophilia and then displayed pulmonary, cardiac, and gastrointestinal symptoms with a persistently elevated absolute eosinophil count. He was treated effectively with oral steroid therapy for > 6 months. In conclusion, eosinophilic cystitis can be the first clinical manifestation of HES in children and peripheral blood eosinophilia should be carefully followed up in patients with nonspecific systemic symptoms.

Conflicts of Interest

The authors declare no conflicts of interest.

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