

Recurrent Swelling of the Lower Limbs (Lymphedema) As a Manifestation of the Idiopathic Hypereosinophilic Syndrome

Feng Yang, Fei Wang, Kedong Li and Maihua Hou*

Department of Dermatology, Nanjing Medical University, China

Volume 1 Issue 1 - 2018

Received Date: 11 June 2018

Accepted Date: 30 June 2018

Published Date: 07 June 2018

2. Keywords

Hypereosinophilic syndrome;
Lower limbs; Swelling

1. Abstract

Hypereosinophilic syndrome is an unexplained disorder characterized by prominent blood and bone marrow eosinophilia and tissue eosinophil infiltration. It can cause damage/dysfunction of multiple organs, mainly involving the skin, heart, lungs, gastrointestinal tract and the nervous system. We present a case of hypereosinophilic syndrome (HES) in a 21-year-old man with recurrent swelling of his lower limbs. This is the first reported case with recurrent swelling of the lower limbs (lymphedema) as a manifestation of HES. All skin lesions rapidly improved following glucocorticoid treatment.

3. Introduction

Hypereosinophilic syndrome (HES) is an unexplained disorder characterized by prominent blood and bone marrow eosinophilia and tissue eosinophil infiltration. HES can cause damage/dysfunction of multiple organs, mainly involving the skin, heart, lungs, gastrointestinal tract and the nervous system [1]. 50 % of patients with HES present with polymorphous skin lesions, including pruritic papules, nodules, urticaria and angioedema [2]. We present a case of HES in a 21-year-old man with recurrent swelling of his lower limbs (lymphedema). After searching all scientific search engines, the authors could not retrieve a similar case in literature.

4. Case Presentation

A 21-year-old male was admitted to our hospital on July 16, 2014 complaining of recurrent swelling of his lower limbs for one year and aggravation for a week, particularly his left leg. The patient started with lower limb erythematous swelling and moderate pruritus that was precipitated by heat. Erythematous lesions and swelling with strong itching relapse on both lower limbs was accompanied by a paroxysmal cough and white sputum, which worsened at night. During that period, there were no cardiac or gastrointestinal symptoms, no fever, no night sweats and no obvious pain or burning sensations in the cutaneous lesions. In a local laboratory examination, his white blood cell count was 25.7×10^9 /L (eosinophils, 17.78×10^9 /L).

On admission, his body temperature was 37°C and his blood pressure was 110/75 mm Hg. Physical examination revealed several smooth, firm enlarged lymph nodes of the neck, groin without apparent tenderness measuring about 1 cm in diameter.

Cardiac and pulmonary auscultation showed no obvious abnormality. The abdomen was soft on palpation without tenderness or rebound tenderness.

Skin examination revealed swelling of both lower limbs, especially the left lower limb, as well as scattered irregularly sized, dark red patches with a wood-like consistency on the swollen lower limbs, with high temperature but no tenderness (Figure 1).



Figure 1: Dark erythematous lesions and significant swelling of both lower limbs, especially the left lower limb.

*Corresponding Author (s): Maihua Hou, Department of Dermatology, The First Affiliated Hospital, Nanjing Medical University, Jiangsu 210029, China, Tel: +86 13776635881; Email: houmaihoa@jsoh.org.cn

Routine blood test results showed a white blood cell count of $29.95 \times 10^9/L$ with over 70% eosinophils at the absolute count of $21.54 \times 10^9/L$. Biochemistry tests revealed uric acid ($459 \mu\text{mol/L}$), lipoprotein a (1107 mg/L), alpha hydroxy butyric acid dehydrogenase (230 U/L), resistance of Streptococcus hemolysin "O" (558.00 IU/mL), and total IgE (577.50 KU/L), with high-density lipoprotein cholesterol (0.77 mmol/L) and low density lipoprotein cholesterol (2.39 mmol/L) declining mildly. No abnormality was found in his urine, coagulation routine, liver or kidneys. The results of sputum culture for several times were negative. The patient was negative for antibodies to tuberculosis, filaria, treponema pallidum and Human Immunodeficiency Virus (HIV). Tests for immunoglobulin (IgA, IgG, IgM), antinuclear antibody series, IFN- γ and complement (C3, C4) revealed no abnormalities. Quantitative DNA of EB virus and cytomegalovirus in the blood was normal. The results of immunoglobulin gene rearrangement and TCR gene rearrangement were negative.

An electrocardiogram (ECG) indicated sinus arrhythmia. Ultrasound examination of the liver, gallbladder, pancreas and spleen showed no abnormalities. Echocardiography showed mild mitral and tricuspid regurgitation. Vascular ultrasound showed thrombosis in his right anterior tibial artery, his left foot dorsal artery and his lower left saphenous vein. CT scans revealed multiple enlarged lymph nodes in the mediastinum, the armpit and the surrounding retroperitoneal and abdominal aorta. A bone marrow aspirate (**Figure 2**),

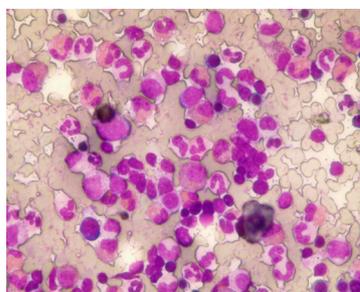


Figure 2: Bone marrow aspirate: A significant proliferation of granulocytes and increased eosinophils. Wright's staining $\times 1000$.

a bone marrow biopsy and a lymph node biopsy (**Figure 3**) showed a great deal of eosinophilic hyperplasia.

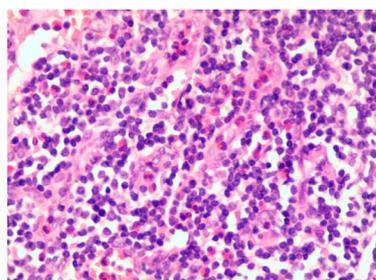


Figure 3: Lymph node biopsy: Reactive hyperplasia accompanied by eosinophilia. HE $\times 400$.

Histology of a lesional specimen showed dense eosinophilic infiltration, a lymphatic dilatation in the dermis, eosinophil emboli in the lumens (**Figure 4**), and positive staining for D2-40 in lymphatic vessels. The FIPILT-PDGFR α fusion gene was negative. Based on the sustained eosinophilia, cutaneous manifestations and exclusion of secondary causes, a diagnosis of HES was made.

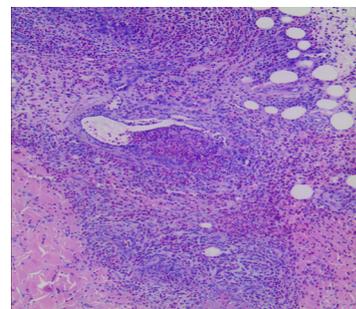


Figure 4: Histology of lesional specimen: Massive eosinophilic infiltration in the dermis, around subcutaneous fat, blood vessels and collagen. Eosinophil emboli in the lumens HE $\times 200$.

The patient was then treated with 40 mg methylprednisolone along with anticoagulants (warfarin, low molecular heparin) and an antiplatelet (aspirin), which led to a dramatic reduction in his peripheral blood eosinophilia (at the absolute count of $0.63 \times 10^9/L$) and clearance of his skin rash in the first week of treatment. Thus far, follow-up has been consistent.

5. Discussion

Hypereosinophilic syndrome (HES) is a disease characterized by the following: (a) a persistent absolute eosinophil count (AEC) of $>1500 \text{ cells/uL}$ documented on two occasions at least 1 month apart and/or pathologic confirmation of tissue hypereosinophilia, (b) evidence of eosinophil-mediated organ damage or dysfunction, and (c) other potential causes of the damage have been ruled out [3-8]. In our case, bone marrow biopsy and lymph node biopsy both indicate hypereosinophilia. Owing to dense eosinophilic infiltration and lymphatic dilation in the dermis, erythematous lesions and swelling relapse on both lower limbs. Meanwhile, we have excluded potential causes of the damage such as malignant lymphadenoma. Accordingly, our case fulfilled those diagnostic criteria of HES. Treatment of HES is generally aimed at long-term reduction of eosinophil levels in the blood and tissues to avoid end-organ damage, minimizing damage from the end products of eosinophil metabolism. Corticosteroid is the first-line therapy for FIP1L1-PDGFR α -negative HES, and is very effective for reducing levels of peripheral eosinophils. In this case, our patient presented recurrent nonpitting edema of lower limbs as well as scattered irregularly sized, dark red patches with a wood-like consistency on the swollen lower limbs. The skin lesions were tough, and the biopsy was difficult to conduct. This lesion should be differentiated with venous thrombosis. The latter often pre-

sents acute painful edema with soft skin and could subside after prolonged elevation of the affected limb. After the treatment with glucocorticoid, our patient's eosinophil counts normalized within 3 days, the swelling of the lower extremities and his skin rash disappeared in the first week. The clinical improvement strongly suggests that our patient had an excellent response to glucocorticoid and that the lymphatic emboli resulted from mechanical obstructions by increased eosinophil counts. When the eosinophil counts rapidly returned to normal, the emboli disappeared quickly. Thus, we assume that eosinophil emboli can be relieved spontaneously and are sensitive to glucocorticoid, which is associated with the characteristics of the lymphatic system, such as a higher water content than the plasma, without platelets or other blood coagulation factors. Further, the lymphatic system is a regulator of tissue fluid. A great number of eosinophils appeared in the patient's blood, bone marrow and lymph nodes, resulting in hematological and lymphatic system embolism. Therefore, the patient still requires a long-term follow-up to monitor the risk of progressing to eosinophilic leukemia.

References

1. Klion A. Hypereosinophilic syndrome: current approach to diagnosis and treatment. *Annu Rev Med.* 2009;60:293-306.
2. Carlesimo M, Fidanza L, Mari E, Feliziani G, Narcisi A, De Marco G, et al. Wells syndrome with multiorgan involvement mimicking hypereosinophilic syndrome. *Case Rep Dermatol.* 2009;1:44-8.
3. Valent P, Klion AD, Horny HP, Roufosse F, Gotlib J, Weller PF, et al. Contemporary consensus proposal on criteria and classification of eosinophilic disorders and related syndromes. *J Allergy Clin Immunol.* 2012;130(3):607-12.
4. Park SM, Park JW, Kim SM, Koo EH, Lee JY, Lee CS, et al. A case of hypereosinophilic syndrome presenting with multiorgan infarctions associated with disseminated intravascular coagulation. *Allergy Asthma Immunol Res.* 2012;4(3):161-4.
5. Rothenberg ME, Klion AD, Roufosse FE, Emmanuel Kahn J, Weller PF, Uwe Simon H, et al. Treatment of patients with the hypereosinophilic syndrome with mepolizumab. *N Engl J Med.* 2008;358(12):1215-28.
6. Park YM, Bochner BS. Eosinophil survival and apoptosis in health and disease. *Allergy Asthma Immunol Res.* 2010;2(2):87-101.
7. Kobayashi M, Komatsu N, Kuwayama Y, Bandobashi K, Kubota T, Uemura Y, et al. Idiopathic hypereosinophilic syndrome presenting acute abdomen. *Intern Med.* 2007;46(10):675-8.
8. Ferguson GT, Starkebaum G. Thromboangiitis obliterans associated with idiopathic hypereosinophilia. *Arch Intern Med.* 1985;145(9):1726-8.