

A rare case of idiopathic hypereosinophilic syndrome [IHES] presenting with generalized body swelling

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Introduction

Idiopathic hypereosinophilic syndrome (IHES) is a rare disorder with unexplained, non-reactive over production of eosinophils along with multiorgan dysfunction. IHES has a multitude of cutaneous manifestations as the dominant presenting symptom. We report a rare case of IHES, where the patient presented with unusual, generalized body swelling and thickened indurated skin. According to our knowledge similar cutaneous presentation has not been reported in the literature.

Case report

A 66-year-old diagnosed patient with ischemic heart disease presented with generalized, body swelling and intense itching for 6 months duration. The systemic inquiry was unremarkable except for pain and weakness of his both upper and lower limbs. Exami-

nation revealed generalized edema with some degree of pitting only on extremities. The skin was thickened and indurated. Scratch marks and excoriated papules were seen all over the body (Figure 1, 2). In all limbs, proximal muscle power was 3/5 with vague sensory impairment. Other systemic examination was unremarkable.

Blood counts revealed severe eosinophilia ($25 \times 10^9/l$) with normal hemoglobin and platelets: no abnormal cells in the blood picture. Skin histology showed marked dermal eosinophil infiltration with lymphocytes and histiocytes. The gastrointestinal biopsy also demonstrated eosinophil infiltration. Bone marrow biopsy revealed reactive eosinophilia without malignant transformation. FIP1L1 gene analysis was negative. Nerve conduction and electro-myography were compatible with mono neuritis multiplex. 2D-ECHO cardiogram showed good cardiac status with an EF of 60%.



Figure 1.



Figure 2.

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The rest of the serological, endocrinological, and imaging investigations were unremarkable. Parasitic, malignant, and allergic causes of hypereosinophilia were ruled out.

Diagnosis of IHES made. Treatment started with high-dose oral prednisolone, hydroxyurea, and imatinib. Following a good response in the initial few months, the patient developed severe congestive heart failure with high troponin I. 2D-ECHO cardiogram showed global hypokinesia with (EF 15%). Unfortunately, the patient passed away.

Discussion

IHES is a rare, underdiagnosed multisystem disorder that is characterized by persistent marked eosinophilia, presence of eosinophil-related target organ damage with the exclusion of other causes of hypereosinophilia. IHES is classified into primary (neoplastic), secondary (reactive) and idiopathic variants¹.

Primary IHES includes eosinophilic leukemia and individuals with FIP1L1-PDGFR α , PDGFR β , FGFR1 gene mutation etc. Most of these mutant products activate tyrosine kinase which ultimately leads to unconditional cell proliferation causing clinical disease. Secondary IHES is characterized by clonal proliferation of T cells with Th2 cytokines, particularly IL5. Idiopathic IHES is diagnosed in patients whose underlying pathogenesis for IHES remains unknown¹.

Clinical manifestations of IHES are highly variable and greatly depend on the involved target organ. Target organ damage is either due to direct eosinophil infiltration or by cytotoxic substances released by eosinophils (eosinophil cationic protein, eosinophil derived neurotoxin, eosinophil peroxidase, free oxygen radicals, etc.)². Although virtually any tissue or organ can be affected by IHES, commonly affected organs are the heart, lungs, skin and nervous system⁵.

Cardiac involvement evolves in three stages: namely, early necrotic stage involving the endo-myocardium which is often asymptomatic but can present as acute heart failure, thrombotic stage, and finally fibrotic stage which gives rise to irreversible restrictive cardiomyopathy².

As this patient's initial 2D ECHO was normal and suddenly presented with acute severe cardiac failure, he could have developed acute necrotic myocardial damage.

Neurological manifestations may involve either the central nervous system or the peripheral nervous system. Proposed mechanisms of these changes are due to direct cellular infiltration, cellular damage due to eosinophil-derived neurotoxin, or due to thrombosis etc.². Our patient also had mono neuritis multiplex which is compatible with the diagnosis.

IHES patients show multitudes of cutaneous manifestations like urticaria, angioedema, erythematous pruritic papules and nodules, vasculitis-like lesions and rarely fibrotic skin changes etc. More than 50% of hypereosinophilic syndrome patients have cutaneous manifestations at the time of presentation. However, its pleomorphic nature often delays the diagnosis.

Our patient presented with an unusual pattern of severe generalized body swelling with thickened indurated skin which resembles anasarca. This is not reported in the literature. Thickened skin could be due to a profibrotic environment made by eosinophils releasing TGF beta, which leads to increased collagen synthesis and extracellular matrix deposition. Vascular damage and leakage caused by eosinophil-related toxic mediators could have contributed to the generalized body edema seen in our patient.

Our patient was treated with high dose oral prednisolone, imatinib, and hydroxyurea^{1,2}. Even though he had a good response initially, with tapering off oral prednisolone he developed severe congestive heart failure. Studies have shown that in some proportion of patients imatinib causes adverse cardiac outcomes especially during the initial period of therapy^{3,4}. To minimize this, we need to combine it with high-dose corticosteroids and then taper corticosteroids slowly.

References

1. Jean L, Bologna, Julie V. Schaffer, Cerroni L. *Dermatology* – fourth edition.
2. Florence ER, Goldman M, Cogan E. Hypereosinophilic syndromes. *Orphanet Journal of Rare Diseases* 2007, article number 37.
3. Pardnani A, Reeder T, Porrata L F. Imatinib therapy for hypereosinophilic syndrome and other eosinophilic disorders. *Blood* 2003; **101**: 3391 -7.
4. Pitini V, Arrigo C, Azzarello D. Serum concentration of cardiac troponin T in patients with hyper eosinophilic syndrome treated with imatinib is predictive of adverse outcomes. *Blood*; 2003: 3456-7.
5. Vikram K, Mahajan, Singh R, Karaninder S. Idiopathic hypereosinophilic syndrome: A rare cause of erythroderm. *Journal of Dermatological Case Reports* 2014: 108-14.