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Case Report

Internal Medicine Section

A Case of Erythroderma Secondary to Hypereosinophilia

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ABSTRACT

Hypereosinophilic syndrome (HES) is a myeloproliferative disorder characterised by marked peripheral eosinophilia and end organ damage attributable to eosinophilia without secondary cause. Early recognition and treatment are essential to prevent morbidity and mortality. Cytoreduction with Steroids, Hydroxyurea and Imatinib are the main stay of treatment. Molecular studies like Fip1-like-1 fused with platelet derived growth factor receptor alpha (FIP1L1-PDGFRα) etc., are recommended in view of therapeutic implication. In this paper we report a rare case of HES developing in a lady 6 months after surgical removal of lymphangioma of spleen, which in itself is rare.

Keywords: Adrenal insufficiency, Cytoreduction, Lymphangioma of spleen, Tissue eosinophilia

CASE REPORT

A 67-year-old female was admitted to our emergency in altered sensorium with generalized erythroderma and patchy hair loss. She underwent splenectomy for lymphangioma [Table/Fig-1] six months before. Clinical examination showed erythroderma, sacral edema, mucosal dark pigmented lesions, patchy hair loss and madarosis. Basic laboratory investigations showed anaemia (Haemoglobin-7.3 gm/dl), leucocytosis (White blood cell count-19,000/c.mm) with hypereosinophilia (Absolute eosinophil count : 11,768/c.mm) and thrombocytosis (5,08,000/c.mm).

She had severe hypoalbuminemia (albumin - 1.9 gm/dl) probably secondary to loss of protein through skin. Anti-nuclear antibody (ANA), anti-double stranded DNA (anti-Ds DNA) and anti-neutrophil cytoplasmic antibody (ANCA) were negative. In the absence of any significant history of atopy, allergic disorders, or parasites to explain her high eosinophil counts she was submitted to a work up for primary hypereosinophilia and any associated end organ damage. In view of high Vitamin B12 levels (16,680ng/L) and hypereosinophilia, there was a strong suspicion of myeloproliferative disorders. Molecular genetic work up showed absence of Fip1-like-1 fused with platelet derived growth factor receptor alpha (FIP1L1-PDGFRα) and BCR-ABL mutation. Bone marrow biopsy showed scanty marrow with eosinophilia [Table/Fig-2].

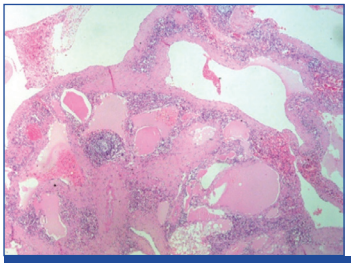
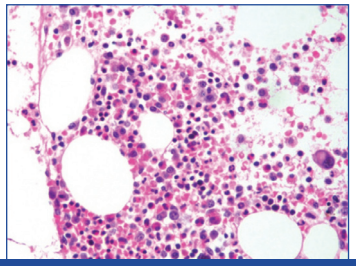
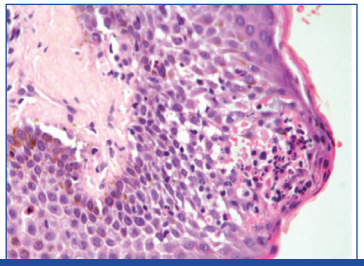
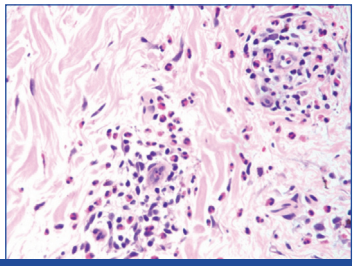
T-cell receptor rearrangement studies were done and primary cutaneous T cell lymphoma was ruled out. A skin biopsy showed subcorneal eosinophilic collection with spongiotic dermatitis [Table/Fig-3] and dermal eosinophilia [Table/Fig-4], representing tissue damage secondary to hypereosinophilia. In view of persistent electrolyte abnormalities with hyponatremia and hyperkalemia, she was evaluated for adrenal insufficiency.

A short synacthen test did not show appropriate increase in cortisol levels despite the administration of ACTH. Hence, a diagnosis of primary hypoadrenalism was made and she was started on adequate replacement doses of steroids. CECT scan of the abdomen showed normal adrenals. Adrenal failure was suspected to be due to eosinophil infiltration. However, a biopsy of adrenal gland was not done. She was started on Hydroxyurea 500mg once daily and Prednisolone 1mg/kg/day. She improved after starting medications. She was doing well 6 months post treatment and was subsequently lost to follow-up.

DISCUSSION

Chusid et al., first defined hypereosinophilic syndrome (HES) based on fourteen cases in 1975 [1]. Over a period of time the definition for HES changed due to advancement in molecular studies and new therapeutic interventions. HES is defined as peripheral eosinophilia (>1500 cells/cmm) with end organ damage due to tissue eosinophilia and absence of secondary cause for eosinophilia. HES is sub classified as per pathogenesis as primary or neoplastic, secondary or reactive, idiopathic, specific syndrome associated with hypereosinophilia and hypereosinophilia of undetermined significance [2]. Our patient had HES with severe peripheral eosinophilia and end organ damage in the form of erythroderma. She had a prior splenectomy for lymphangioma which was probably coincidental.

HES is a rare disease with heterogenous presentation. The main organs involved are skin, lungs, intestine, heart and kidneys. The most serious complication of HES is cardiac involvement, which can lead to myocardial fibrosis, chronic heart failure and death. In the current case, the patient had severe peripheral eosinophilia with erythroderma, the dermal involvement being proven by histopathological examination. Adrenal involvement

[Table/Fig-1]: Lymphangioma of the spleen. **[Table/Fig-2]:** Bone marrow showing eosinophilia. **[Table/Fig-3]:** Skin biopsy showing subcorneal eosinophilic collection with spongiotic dermatitis and dermal eosinophilia. **[Table/Fig-4]:** Skin biopsy showing dermal eosinophilia.

was suspected to be due to eosinophilic infiltration, since no other cause was found.

The aetiology of hypereosinophilia can be primary or secondary. Tests to rule out secondary causes were negative in the current case (Stool routine, antinuclear antibodies, anti-neutrophil cytoplasmic antibody, HIV ELISA etc.,). High B12 levels is said to be an indirect indicator of myeloproliferative disorder. However, BCR-ABL and Fip1-like-1 fused with platelet derived growth factor receptor alpha (FIP1L1-PDGFRα) mutations were negative. Bone marrow studies were done which showed hypereosinophilia. Even though every effort needs to be made to obtain necessary diagnostic studies, including blood work, imaging studies and biopsies of affected tissue before initiating therapy, treatment should not be delayed. Patients presenting with potentially life threatening complications as in the current case manifesting as severe erythroderma, marked eosinophilia should be treated with high dose corticosteroids, while awaiting a definitive diagnosis. The patient received high dose steroids with which she showed significant clinical improvement.

Subsequently, she was started on hydroxyurea for cytoreduction. Many treatment options are available currently for HES. Steroids are the mainstay of treatment. Hydroxyurea and Interferon alpha are useful in steroid refractory HES [3]. A number of cytotoxic therapies are available for the treatment of HES. Apart from hydroxyurea, other drugs like Cladribine and Cytarabine have been used for management of steroid refractory HES [4]. Response to Imatinib, a tyrosine kinase inhibitor in FIP1L1-PDGFRα positive patients almost reaches 100%. Resistance to Imatinib has been observed in few cases [5]. Imatinib activity at the molecular level in HES remains unclear [6]. Low dose Imatinib (100mg/day) has resulted in haematological and molecular remission in most of the patients [7].

Monoclonal antibodies are now emerging therapy in the treatment of HES. Use of anti IL-5 monoclonal antibody Mepolizumab can result in corticosteroid-sparing for patients negative for FIP1L1-PDGFRα mutation [8]. Alemtuzumab(anti CD-52 antibody) is another monoclonal antibody useful in relapsed and refractory cases [9].

Allogeneic stem-cell transplantation is a potentially curative therapy for refractory HES [10]. Bone marrow transplantation is an option for those patients with FIP1L1-PDGFRα positive but resistant to Imatinib therapy. Patient follow-up must be done periodically with complete blood count plus absolute eosinophil count to monitor the extent of eosinophilia and development of end organ damage.

CONCLUSION

We report a case of idiopathic hypereosinophilia in an elderly female with end organ damage manifesting as erythroderma and adrenal insufficiency. All cases of hypereosinophilia need to be evaluated for primary bone marrow disease after excluding the secondary treatable causes. Extensive end organ damage needs to be treated immediately with high dose steroids following which a cytoreductive therapy can be instituted. Tyrosine kinase inhibitors are becoming the main stay of therapy in primary eosinophilia with FIP1L1-PDGFRα positivity.

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