Case Report

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Hyper Eosinophilia with Hereditary Angioedema (HAE): Case Report

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Abstract

Background: Hyperesinophilia (HES)with Hereditary angioedema (HAE), is a rare disease characterized by peripheral blood eosinophilia > 1500/mcl (> 1.5 × 10^9/L) persisting ≥ 6 months and the presence of end-organ damage. Hereditary angioedema is a lifelong illness characterized by recurrent swelling of the skin, intestinal tract, and, the upper airway. It results from insufficient activity of the C1-inhibitor protein, leading to disturbances in the kallikrein/bradykinin pathway.

Case presentation: We reviewed a case of Hypereosinophilia with hereditary angioedema (HAE) in 7-year-old boy who was referred from another hospital in Coimbatore for further management. He had elevated absolute eosinophilic count & elevated IgE. Bone marrow aspiration and biopsy were done which showed increased eosinophil. Stool for ova/ cyst was negative. He was initiated on oral prednisolone (10mg), pantaprozole (20mg) & dexamethasone (50mg).

Conclusion: Hereditary angioedema (HAE) is a genetic condition that poses a threat to life; this condition necessitates rapid diagnosis and treatment to control acute attacks and avert potentially lethal complications, especially when swelling impacts the airway, and can despite recent developments in treatment options, a child quality of life can be significantly affected.

Keywords: Hyperesinophilia, Hereditary angioedema, Protein C1-inhibitor, Kallikrein/ bradykinin, Bone marrow, Biopsy.

INTRODUCTION

Eosinophils are derived from myeloid progenitors in the bone marrow, through the action of three hematopoietic cytokines: granulocyte macrophage colony-stimulating factor (GM-CSF), interleukin-3 (IL-3), and interleukin-5 (IL-5). Of these three, only IL-5 is specific for eosinophil differentiation. The main functions of Eosinophils include host defence, inflammation modulation, and tissue destruction.[1]

Recent developments in the understanding of the underlying pathogenesis have demonstrated that hyper eosinophilia may arise from either the primary involvement of myeloid cells or the occurrence

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of an interstitial chromosomal deletion on 4q12, which is result from the *FIP1L1-PDGFRA* fusion gene (F/P^+ variant) or increased interleukin (IL)-5 production by a clonally expanded T cell population (lymphocytic variant), most frequently characterized by a $CD3^-CD4^+$ phenotype.[2]

The increased number of eosinophil's inflames tissues and causes organ damage. The heart, lungs, skin, oesophagus, and nervous system are most often affected, but any organ can be sustaining damage. Eosinophilic pneumonia arises as a consequence of lung tissue damage caused by activated eosinophil's. The substances and chemical mediators like cytokines, Leukotriene & Toxic granule product are released by activated macrophages, damage the tissues and contribute to the disease pathology[3]. The most prevalent type of hereditary angioedema (HAE) results from a lack of C1 esterase inhibitor (C1-INH-HAE), though HAE can also manifest with normal C1-INH levels. Angioedema is characterized by self-limiting tissue swelling resulting from intermittent increases in vascular permeability, which are triggered by the release of bradykinin (BK) and/or other cell–derived mediators. Typically, the recurring swellings are limited to the skin and/or the upper respiratory, gastrointestinal, and genitourinary systems.[4] (Fig. 1)

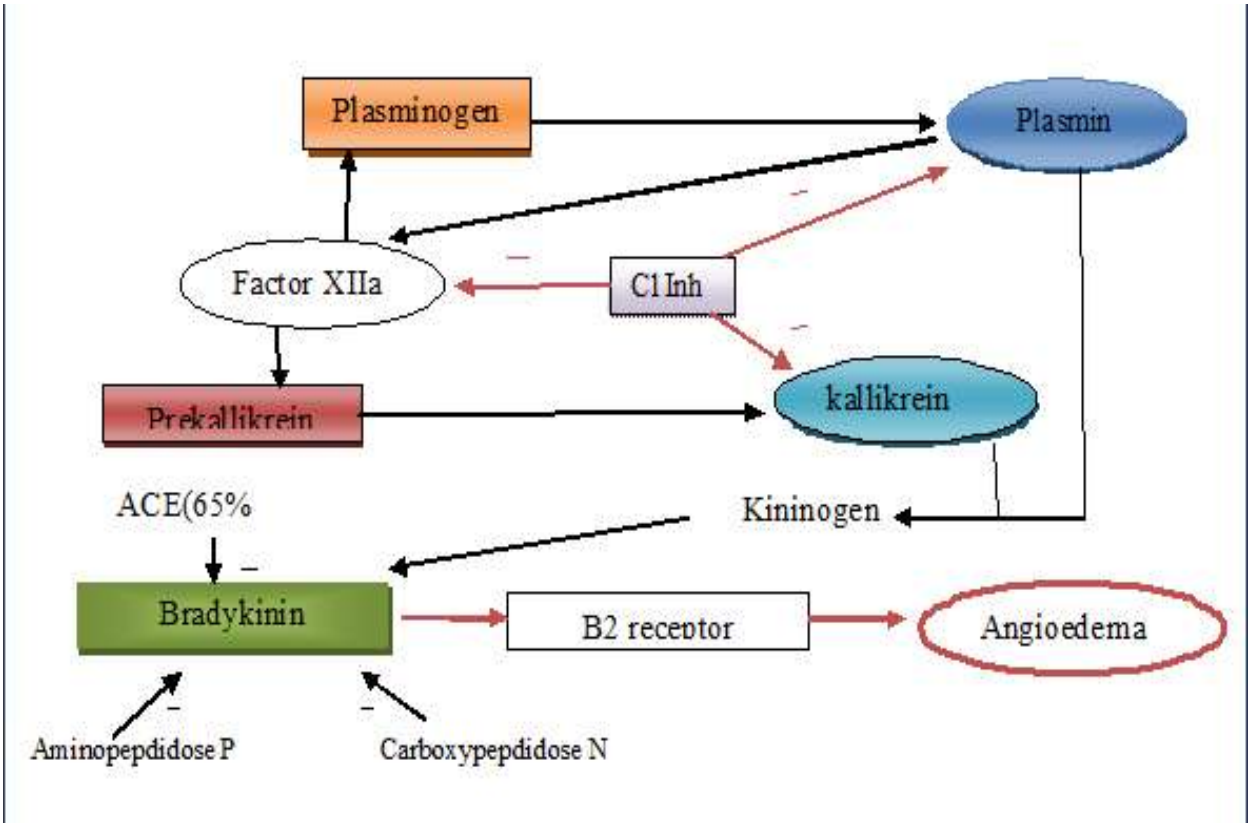

Fig. 1: Shows HAE Mechanism

CASE REPORT

A 7 year old boy admitted in paediatric medical ward and presented with the complaints of rashes on face, hand and headache, giddiness for 4 days constipation for 3 days. After admission the detailed history was collected. There was no family history of atopy or eosinophilia.

He was apparently normal till three years of age. He had a history of recurrent soft tissue swelling, migratory in nature with a symmetric involvement of lower limb, scrotum, abdomen & trunk, he was admitted in medical ward. The laboratory investigation showed that his Absolute eosinophilic count was 5800(cells/mcl) *(fig. 2), (Table 1)* He was diagnosed with hyper eosinophilic syndrome with cutaneous involvement (eosinophilic fasciitis / cellulitis) and was noted to have spontaneous resolution of swelling with fall in eosinophil count without any specific treatment. He was advised to do biopsy in case of recurrent swelling but lost to follow up in view of Covid pandemic and treated on OPD basis.

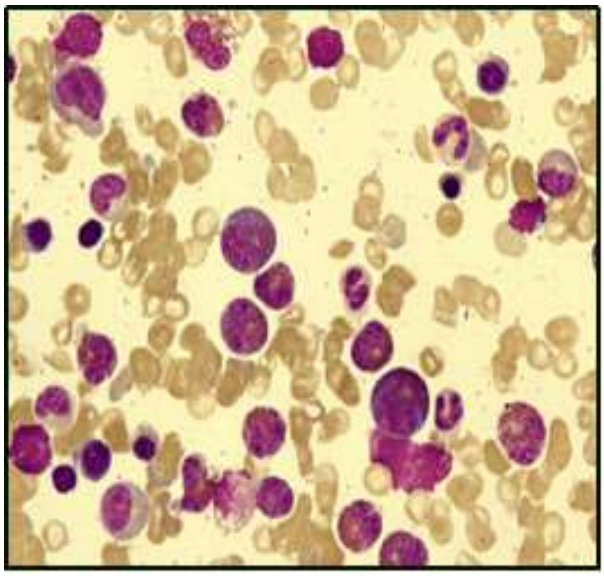

Fig. 2: Shows increased eosinophil count in blood

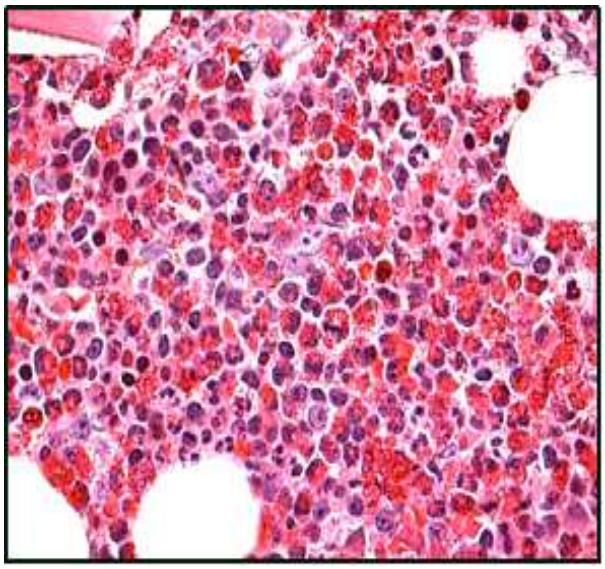

Fig. 3: Bone marrow aspiration and biopsy were done which showed increased eosinophil count

Table 1: Shows complete blood test value in each hospital admission

Complete Blood Cell Count	Reference value	First Visit	Second Visit	Third Visit
Absolute Esinophil Count	80-360 µl	510µl	362 µl	946 µl
Hemoglobin	10.7-14.7g/dl	12.5g/dl	12.61g/dl	12.8g/dl
PCV	33-45%	36.2%	37.6%	39.4%
Total Wbc Count	50014500Cells/cumms	6400Cells/cumms	9040cells/cumms	8600cells/cumms
Poly Morphs	45-75%	28%	42.19%	26.%
Lymphocytes	20-40%	63%	43.35%	62%
Monocytes	2-10%	1.0%	9.01%	1.0%
Eosinophils	2-6%	8%	6.2%	11%
Basophils	0.0-1.0%	0.0%	0.25%	0.0%
Total Rbc Count	3.7-5.7 mil/microliter	5.01 mil/microliter	4.82 mil/microliter	5.45 mil/microliter
MCH	23-31 pg/cell	24.94pg/cell	26.24pg/cell	23.4pg/cell
MCHC	32-36 g/dl	34.4 g/dl	33.5 g/dl	32.4 g/dl
MCV	72-88 μm^3	72.4 μm^3	78.1 μm^3	72.2 μm^3
RDW	11.5-14.5%	17.4%	16.4%	15.1%
Platelet Count	150000-521000 cells/µl	240000 cells/µl	239900 cells/µl	312000 cells/µl
Neutophil	1-2.5	0.4	0.95	0.5

Table 2: Shows immunoglobulin value

Biochemistry	Child Value	Reference Value
Immunoglobulins IGA	240	41 to 297mg/dl
Immunoglobulins IGE	13760	Upto 90IU/dl
Immunoglobulins IGG	1873	600 to 1300 mg/dl
Immunoglobulins IGM	65	40 to 160mg/dl

He developed sharp chest pain on right side for 3 weeks, moderate and intermittent fever lasted for 1 week and again admitted in pediatric medical ward. Child was evaluated by pediatrician, Hematologist, pathologist, dermatologist, ophthalmologist. On physical examination the child was having left side strabismus.

At admission the child had absolute eosinophil count of around 1500 (cells/mcl). Bone marrow

aspiration and biopsy were done which showed increased eosinophil and no abnormal cells. Subsequent complete blood count done showed falls in eosinophil count. Stool for ova/cyst was negative. Immunoglobulin profile done showed elevated IgE and mildly elevated IgG *(Fig. 3 & Table 2)* ANA (antinuclear antibody test) was negative. USG & CT Thorax was suggestive of moderate pleural effusion on right side & gallbladder sludge.

Diagnostic pleural tap was done and pleural fluid analysis was suggestive of exudative effusion with 82 percentage eosinophil. The child was diagnosed with Eosinophilic pneumonia and work up for TB Negative, Mild positive for C-ANCA (Anti neutrophil cytoplasmic antibody). Workup to rule out hereditary is done. C4 level are normal and C1 esterase level is high.

During hospital stay child developed high grade fever spikes followed by vesiculopapular skin rash on hand and feet and oral ulcers. He was initiated on oral prednisolone (10mg), pantoprazole (20mg). Then he was also empirically started on tablet dexamethasone (50mg). Simultaneously parental counselling was conducted.

DISCUSSION

HES is a rare, diverse illness that can cause multiple tissue and organ damage in addition to an inexplicable persistent eosinophilia. It is divided into three categories: idiopathic, primary (clonal), and secondary (reactive) HES. HES is most frequently caused by infections and drug reactions.[5]

In this case review the child presented with primary symptoms of rashes on face, hand and recurrent soft tissue swelling of lower limb, scrotum, abdomen & trunk followed by pulmonary and gastrointestinal involvement. Hyper-IgE syndrome was suspected in child because of the very high IgE level. C4 level are normal and C1 esterase level is high.

This case report is similar with a case of 10 yrs old boy admitted in the medical ward Aarhus University Hospital, Aarhus N, Denmark, the main symptoms exhibited by the child were a severe itching and a widespread papulonodular skin rash. The child did not exhibit a heightened vulnerability to skin infections or occurrences of invasive infections. No skeletal abnormalities were present, nor were there any characteristic facial features associated with hyper-IgE syndrome.[5]

The Goal of HES Management is to lower eosinophil levels in the blood and tissues, thereby preventing tissue damage–especially in the heart. Standard HES treatment includes glucocorticosteroid medications such as prednisone, and chemotherapeutic agents such as hydroxyurea, chlorambucil and vincristine. Interferon-alpha may also be used as a treatment. This drug requires administration through frequent injections.[6]

This case, Initially the child was noted to have spontaneous resolution of swelling with fall in eosinophil count without any specific treatment and they failed to follow up the treatment due to Covid pandemic. After which experienced recurring symptoms, which led to hospitalization. Following the administration of steroid medication Prednisolone 20 mg/day & T. Dexamethasone 50 mg, peripheral blood hyper eosinophilia reverted to a low level.

CONCLUSION

Early identification and intervention for children with HES may be made easier by regular follow up. Steroid management and early detection are crucial to avert major complications. Sensitizing the parents and child about prevention of infection is imperative.

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