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Case Report

Hypereosinophilia presented as thromboembolic event: a rare manifestation

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ABSTRACT

Eosinophilia refers to peripheral blood absolute eosinophil count above the ULN, normal range of AEC is 0.05-0.5× 109/l (1-6%). Hyper eosinophilia refers to AEC above 1.5×109/l. Hypereosinophilia can affect multiple organs and can cause cardiomyopathy, gastroenteritis, cutaneous lesions, pneumonitis, and neuritis. In addition, some patients develop thromboembolic complications. We are presenting a case who presented to us with thromboembolic complication later diagnosed as hypereosinophilia with Bone marrow showing myeloid associated eosinophilia (Primary eosinophilia).

Keywords: Eosinophilia, Deep vein thrombosis, Pulmonary embolism, Thromboembolism

INTRODUCTION

Eosinophilia refers to peripheral blood absolute eosinophil count above the ULN, normal range of AEC is 0.05-0.3×109/l (1-6%). Hyper eosinophilia refers to AEC above 1.5×109/l. The underlying cause of eosinophilia should be sought and possible eosinophilic associated end organ damage should be evaluated.

There are numerous causes of eosinophilia which are divided into 3 categories primary, secondary (reactive) and idiopathic. Secondary eosinophilia is by far the most common cause of eosinophilia that include allergic disorder (asthma, Hay fever, rhinitis, atopic dermatitis, non-allergic dermatologic cause such as wells syndrome (eosinophilic cellulitis), drug induced eosinophilia, infectious diseases– tissue invasive helminths, vasculitis disorder (polyarteritis nodosa, eosinophilic granulomatosis with polyangitis). Primary eosinophilia is clonal/neoplastic proliferation of eosinophils. Diagnosis of clonal eosinophilia requires morphologic, cytogenetic or molecular evidence of a myeloid neoplasm. Idiopathic hypereosinophilic syndrome (HES) is a diagnosis of exclusion in patient who are thoroughly investigated without cause being found and defined as AEC 1.5×109/l or more with end organ damage. Eosinophilia in peripheral blood is less known condition to promote a hypercoagulable state that may favor venous thrombosis.[1] An unprovoked thromboembolic event should be recognized as possible manifestation of eosinophilic associated tissue damage.

Here, we are describing a patient who came to us with deep vein thrombosis and later diagnosed as myeloid neoplasm associated eosinophilia and during hospital stay on day 4 developed massive pulmonary thromboembolism from which patient could not be revived in spite of best available treatment.

CASE REPORT

A 34-year-old female presented with insidious onset pain and swelling in right lower limb since last 10 days, which progressed rapidly from foot to thigh. There was no history of prolonged immobilization, any surgery, major trauma, drug intake, allergy or any other risk factor or family history of inherited thrombophilia. She has history

of low-grade fever on and off since 10 days. On physical examination, she was conscious and oriented to time, place and person with BP- 118/80 mm Hg, PR-88 bpm, regular. Pallor was present. Chest examination revealed bilateral clear and equal vesicular breath sound. No organomegaly and lymphadenopathy was found on examination. There was edema in her right lower limb extending upto groin with Homan's sign positive.

On laboratory evaluation, complete hemogram revealed Hb-7.6 gm/dl, markedly elevated total leucocyte count-75,400 cells/mm3 with marked eosinophilia- 62% and AEC- 42,748 cells/mm3. In view of unilateral limb edema color doppler ultrasonography of right lower limb was done which revealed echogenic material in right common femoral, superficial femoral, visualized part of deep femoral and popliteal vein with loss of compressibility on probe compression. On color Doppler there was no flow suggestive of thrombosis. Proximally, the thrombus was extended into right external iliac vein. The diagnosis of acute DVT was made and patient was started on inj LMWH subcutaneously.

Work up was done for eosinophilia to know the cause, which revealed negative result for ova and cyst in stool, test for parasites in serum was also negative. Serum IgE was mildly raised. Bone marrow aspiration and biopsy was done showing cellular marrow, with increased M:E ratio, erythropoiesis– normo to megaloblastic, myeloid hyperplasia with myeloid cells seen in all stages of maturation and increase in eosinophils and eosinophilic precursors. Blast< 5% of total nucleated cells. Impression given as eosinophilic myeloid reaction.

Based on clinical and laboratory evaluation patient diagnosed as DVT with myeloid associated eosinophilia. Patient was than treated with corticosteroid with Hydroxyurea and planned for further workup of myeloid associated eosinophilia which include FISH panel for FIP1L1-PDGFRA, PDGFRB, BCR-ABL and JAK-2 V617F. But on same day (day 4 of admission) patient developed sudden onset shortness of breath with tachypnea, tachycardia followed by altered sensorium. She was in hypotension, ECG showing Sinus tachycardia, 2D Echo showing RV dysfunction with McConnell's sign present. Patient expired due to massive thromboembolism.

DISCUSSION

This patient presented with acute onset proximal right lower limb deep vein thrombosis who developed pulmonary thromboembolism and later on found to have primary eosinophilia. Eosinophilia has multiple etiology and require a thorough workup to diagnose underlying pathology for proper management and prevention of complication. Secondary (reactive) eosinophilia should be excluded first in all cases and in patient with AEC >1500/mm3 with no obvious cause found, a hematological neoplasm with clonal eosinophilia should be considered. Clonal eosinophilia includes eosinophilia associated with AML, MDS, CML, mastocytosis and MDS/MPN overlap. Myeloid neoplasm associated eosinophilia also include the WHO MPN subcategory of Chronic eosinophilic leukemia-Not otherwise specified (CEN-NOS) & WHO myeloid malignancy subcategory referred as myeloid/lymphoid neoplasm with eosinophilia and rearrangement of platelet derived growth factor receptor (PDGFR α, β) or Fibroblast growth factor receptor 1 (FGRA1) or PCM1-JAK2.[2] For evaluation of Clonal eosinophilia, test for FIP1L1-PDGFRA, PDGFRB by FISH or nested RT-PCR to be done. Serum tryptase estimation is needed if differential diagnosis includes CEL or systemic mastocytosis. BM aspiration, trephine biopsy and cytogenetic analysis need to be done accordingly. End organ damage should be assessed using chest radiography and/or CT thorax, echocardiography, serum troponin and pulmonary function test.

In this report, patient presented with DVT and hypereosinophilia. Hypercoagulability due to hypereosinophilia has previously been reported but mechanism not properly understood. Eosinophils release toxic cationic proteins which include eosinophil cationic protein, eosinophil derived neurotoxin, major basic protein, eosinophil peroxidase and platelet activating factor. These granular proteins may promote platelet activations and also inhibit anticoagulation activity of thrombomodulin.[3-5]

Treatment of eosinophilia depend on underlying cause. For secondary eosinophilia identify underlying cause and treat accordingly. Urgent treatment is needed in patient presented with high AEC with end organ damage. High dose corticosteroids are the mainstay of emergency treatment, start with 1mg/kg/day of methylprednisolone intravenously or oral prednisolone 0.5-1 mg/kg/day for 1-2 weeks. Corticosteroid can be slowly tapered over period of 2-3 months to lowest possible maintenance dose to maintain response.[6,7] Corticosteroid can inhibit the production of inflammatory mediators such as eosinophilic cationic proteins, major basic protein, eosinophilic peroxidase and eosinophil derived neurotoxin, which are thought to cause hypercoagulability.[8] Primary (clonal) eosinophilia with FIP1L1-PDGFRA are highly sensitive to Imatinib and a starting dose of 100 mg daily should be commenced and titrate accordingly.[9] Eosinophilia with PDGFRB rearrangement or an ETV6-ABL2 fusion gene are responsive to 400mg Imatinib daily.[10] Neoplasm associated with ETV6-FLT3 may be responsive to sunitinib or sorafenib. Patient with other hematological neoplasm with clonal eosinophilia should have treatment directed at management of the neoplasm. If there is organ damage or dysfunction relating to the eosinophilia, treatment with corticosteroid should also be given. Patient with idiopathic HES should also be treated with steroid and those who do not respond should be given immunomodulatory drugs (cyclosporine, azathioprine),

monoclonal Ab (mepolizumab– anti IL-5, alemtuzumab– anti CD52).

CONCLUSION

we have presented a case of DVT with pulmonary thromboembolism with hypereosinophilia and Bone marrow suggestive of myeloid neoplasm associated eosinophilia but we could not able to perform cytogenetic and FISH panel due to early demise of patient. Eosinophilia is a risk factor and precipitating factor for DVT and pulmonary thromboembolism. It is necessary for physician to keep thromboembolic complication in mind while dealing with patient of eosinophilia.

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