A case of hypereosinophilic syndrome with colonic obstruction: An unusual complication

Sir,

Hypereosinophilic syndrome (HES) is characterized by hypereosinophilia (HE) and organ damage,[1,2] which affects men more commonly than women.[3] The disease can be detected incidentally, but more often presents either insidiously or acutely with cardiac, neurological, cutaneous, pulmonary, or gastrointestinal manifestations, with cardiac involvement being a major cause of morbidity and mortality in patients.[1,3] Early identification and aggressive therapy are of paramount importance in decreasing the morbidity and mortality associated with this condition. It is also important to study the clinical variants to determine if they are prognostically important in the face of the modern therapy for this disease.[2]

A 34-year-old male, presented with complaints of low grade intermittent fever, breathlessness on exertion, and dry cough of 3 weeks duration. Clinically, he had bilateral wheeze. Investigations revealed eosinophilia (absolute eosinophil count [AEC] - 2100/cubic millimeter [cu mm]), stool for parasitic ova/cysts was negative; peripheral blood smear for microfilaria and filarial antigen were negative; and chest radiograph revealed bilateral reticulonodular opacities [Figure 1a]. He was diagnosed as a case of peripheral eosinophilia with pulmonary infiltrates and treated empirically with diethyl carbamazine and antihelmenthics. There was no response and investigation revealed worsening of eosinophilia (AEC - 15918/cumm). His metabolic and biochemical parameters were normal, Serum ANCA, Aspergillus fumigatus-specific Immunoglobulin E, viral markers and sputum for eosinophils were normal. High-resolution computed tomography of the chest showed extensive areas of ground glass and centrilobular nodular opacities involving all lobes of both lungs along with fine reticulations and inter lobular septal thickening [Figure 1b]. Bone marrow aspirate and biopsy showed hypercellular marrow, increase in eosiophilic series with increase in eosinophilic myelocytes and metamyelocytes, with hyper lobulated eosinophils. Fiber optic bronchoscopy was normal, and bronchoalveolar lavage cytology showed predominant eosinophils.

Two-dimensional echocardiography showed thickened and fixed posterior mitral leaflet with doming of anterior
mitral leaflet with grade 2/3 mitral regurgitation. Based on these evidences, he was diagnosed with a case of HES with pulmonary and cardiac involvement and was started on steroids (prednisolone 1 mg/kg). His symptoms and chest radiograph showed significant improvement after 2 weeks of steroids, but eosinophilic leucocytosis persisted (max AEC - 31980/cumm). While on steroids, he developed colicky pain in the left iliac fossa. Ultrasonography of the abdomen revealed dilated and thickened peristaltic bowel loops, sigmoidoscopy showed normal recto-sigmoid, and rectal biopsy revealed eosinophilic infiltration in the intervening lamina propria suggestive of eosinophilic colitis. FIP1L1-platelet derived growth factor receptor alpha (PDGFRA) gene rearrangement was positive.

In view of HES with multisystem involvement and positive PDGFRA-FIP1L1 gene rearrangement, and no response to steroids, he was treated with tyrosine kinase inhibitors (TKI) and steroids were tapered and stopped. He responded well to treatment and became asymptomatic over a period of 2–3 weeks and eosinophilia also resolved. Two months later, he developed recurrence of pain abdomen in left iliac fossa and constipation. Barium enema of rectum and sigmoid colon [Figure 1c] showed dilated, descending colon with multiple, tight, short-segment stricture with preserved mucosal pattern. Repeat colonoscopy showed an extrinsic bulge noted at sigmoid – descending colon junction and a stricture near splenic flexure [Figure 1d], which was nonnegotiable. He underwent left hemicolectomy with end-end anastomosis. Surgery was uneventful, and he recovered well after the surgery. HPE of colon showed nonspecific colitis with short-segment stricture, and preserved mucosal pattern. (d) Colonoscopic view showing stricture with preserved mucosal pattern

Figure 1: (a) Chest radiograph posteroanterior view showing bilateral reticulonodular opacities in mid and lower zones. (b) High-resolution computed tomography scan of the chest showing ground glass and centrilobular nodular opacities, fine reticular opacities, and interlobular septal thickening involving both lungs. (c) Contrast radiograph of the abdomen (Barium enema) showing dilated, descending colon with short segment stricture, and preserved mucosal pattern. (d) Colonoscopic view showing stricture with preserved mucosal pattern

HE in the peripheral blood is defined as an AEC > 1500 cells/µL on two examinations separated in time by at least 1 month and/or pathologic confirmation of tissue HE. A HES is defined by the association of HE (as defined above), with eosinophil-mediated organ damage and/or dysfunction, provided other potential causes (such as an allergic drug reaction or parasitic infection) for the damage have been excluded. Most patients are diagnosed between the ages of 20 and 50 years. A retrospective multicenter series of 188 patients reported the frequency of specific symptoms at presentation as dermatologic - 37%, pulmonary - 25%, gastrointestinal - 14%, cardiac - 5%, asymptomatic, and incidentally detected - 6%. In our case, patient had the involvement of lungs, heart, and colon. Even though his respiratory symptoms got relieved with steroids, he developed eosinophilic colitis whilst on therapy. Detection of PDGFRA-FIP1L1 gene rearrangement changed the management as he was switched to imatinib, which halted the disease process. TKI is the treatment of choice for patients with FIP1L1-PDGFRα - rearranged HES, since almost all patients achieve and maintain complete hematologic, clinical and molecular remissions. Chronic treatment is well tolerated, and responses are stable over time at doses as low as 100 mg daily.

The presence of FIP1L1-PDGFRα gene dysfunction is associated with high fibrogenic potential and can cause liver fibrosis, renal fibrosis, and myocardial fibrosis. Platelet-derived growth factors (PDGFs) exert their biological effects through the binding and activation of two receptor tyrosine kinases, PDGFR a and b. Ligand binding to PDGFRA/b on the cell surface induces receptor oligomerization and tyrosine phosphorylation, activating a number of downstream signal transduction pathways, including Ras/MAP kinases, PI3 kinase/AKT, and PLC/ PKC pathways. The ureters and digestive tract are radially patterned tubes composed of concentric layers of connective tissue and smooth muscle surrounding a specialized epithelium and a luminal space. Cells lining the lumen express hedgehog signals to regulate mesenchymal proliferation and patterning. Increased PDGFRA signaling affects stromal fibroblasts, which become hyperplastic and generate fibrotic overgrowths. Our patient, in due course of time developed descending colon fibrosis leading to colonic obstruction, requiring left hemi colectomy in spite of disease in remission.

The stricture formation in the descending colon in our patient could be explained due to fibrosis, which led to colonic obstruction. Colonic obstruction secondary to HES has not been reported in the literature. This may be the index case of HES with colonic obstruction requiring surgical intervention which had a favorable outcome.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have...
given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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