Case Report

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Ascites in a young male: idiopathic FIP1L1-PDGFRA-negative hypereosinophilic syndrome

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Summary

Introduction: Idiopathic hypereosinophilic syndrome is defined as persistently elevated peripheral blood absolute eosinophil count of more than 1.5 × 109/L for at least six months with no obvious secondary cause.

Case Presentation: We report the case of a 26-year-old gentleman of Malay ethnicity who presented to the medical department with a three-week history of abdominal distension associated with dyspepsia and epigastric pain. Physical examination revealed ascites. The complete blood count portrayed peripheral leucocytosis with eosinophilia of 8.84 × 109/L. Parasitic serology was negative. Paracentesis analysis showed exudative ascites with an absolute eosinophil count of 8 × 109/L. He was referred to the haematology department. He was noticed to have bilateral tonsillitis and pruritic skin rash at the legs. There were no palpable lymph nodes or organomegaly. A peripheral blood film showed 44% eosinophils with no excess blasts. Clonal eosinophilic fusion studies did not detect FIP1L1-PDGFRA mutation. JAK2 V617F and BCR-ABL1 mutations were undetected. Serum B12 and tryptase levels were normal. A whole-body computed tomography imaging showed bowel wall thickening at the duodenum, jejunum, ileum, rectosigmoid and splenic flexure. Sections of fragments taken from the endoscopy showed features of eosinophilic gastritis and colitis on histology. Bone marrow biopsy depicted marked eosinophilia. He was started on oral imatinib mesylate 200 mg daily and oral prednisolone 0.5 mg/kg daily which was tapered based on response. He achieved complete remission and is now asymptomatic.

Conclusion: The diagnosis of hypereosinophilic syndrome should be considered in a patient with unexplained ascites. Secondary sinister causes such as malignancy should always be excluded.

Keywords

clinical, haematology (including blood transfusion), hypereosinophilic syndrome, ascites, tonsillitis, eosinophilic gastritis, imatinib mesylate

Lesson

Idiopathic hypereosinophilic syndrome should be considered in a patient presenting with ascites and peripheral blood eosinophilia after excluding secondary causes.

Introduction

Idiopathic hypereosinophilic syndrome (HES) is defined as persistently elevated peripheral blood absolute eosinophil count of more than 1.5×10^9/L for at least six months without any obvious secondary cause. This term was first utilised by Hardy and Anderson to describe patients with significant eosinophilia and eosinophilic cardiopulmonary involvement.[1] HES can cause noticeable repercussions such as thromboembolism, cardiopulmonary dysfunction and neurological sequelae if left untreated.

Case presentation

A 26-year-old previously healthy gentleman of Malay ethnicity presented to the medical department with a three-week history of abdominal distension associated with dyspepsia, epigastric pain and weight loss. He has no significant family history. He is single, a non-smoker, a teetotaller and works as a medical practitioner.

Physical examination revealed a medium built gentleman with a positive abdominal fluid thrill suggestive of ascites. There was no noticeable skin rash.

The complete blood count revealed peripheral leucocytosis with eosinophilia of 8.84×10^9/L. Parasitic serology was negative. Paracentesis analysis showed exudative ascites with an absolute eosinophil count of 8×10^9/L.

He was referred to the haematology department a month later. He was noticed to have bilateral tonsillitis (Figure 1(a)) with pruritic skin rash at the legs (Figure 1(b). There were no palpable lymph nodes or organomegaly.

The laboratory parameters are tabulated in Table 1. A peripheral blood film (Figure 2(a)) showed 44% eosinophils with no excess blasts. Clonal eosinophilic fusion studies did not detect FIP1L1-PDGFRA mutation. JAK2 V617F and BCR-ABL1 mutations were undetected. Serum B12 and tryptase levels were normal. Computed tomography (CT) of the abdomen (Figure 2(b)) showed

Figure 1. Photograph showing (a) bilateral tonsillitis and (b) pruritic crusty rash at the legs.

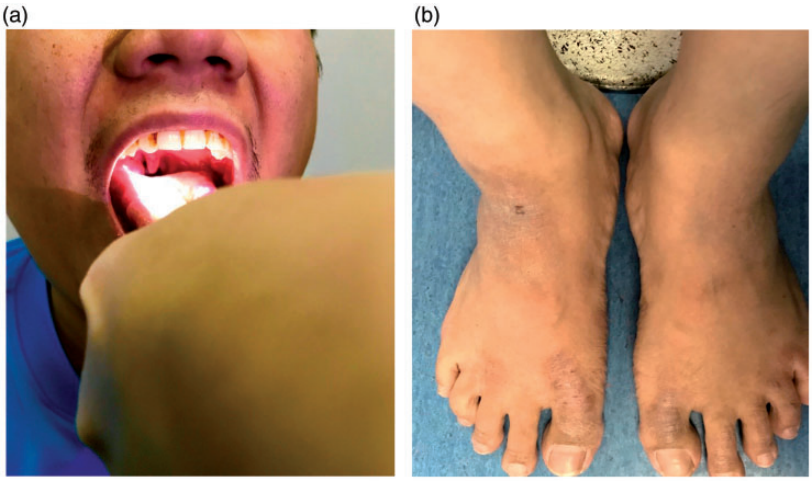


Table 1. Tabulation of laboratory parameters.

Laboratory parameters	Values (unit and normal range)
Haemoglobin	13.5 (31.5–16.5 g/L)
Total white cell count	15 (4–10 × 10^9/L)
Platelet	402 (150–400 × 10^9/L)
Absolute eosinophil count	8.84 (0–0.2)
Absolute lymphocyte count	2.2 (1.5–4.0 × 10^9/L)
Creatinine	80 (40–100 μmol/L)
Albumin	38 (35–50 g/L)
Alanine aminotransferase	28 (0–40 U/L)
Lactate dehydrogenase	160 (90–180 U/L)
Anti-HIV-1,2	Not detected
Toxoplasma IgM, IgG	Negative
Taenia IgM, IgG	Negative
Schistosoma IgM, IgG	Negative
Toxocara IgM, IgG	Negative
Anti-nuclear antibody	Not detected
c-Antineutrophil cytoplasmic antibody	Not detected
p-Antineutrophil cytoplasmic antibody	Not detected

IgM: Immunoglobulin M; IgG: Immunoglobulin G.

bowel wall thickening at the duodenum, jejunum, ileum, rectosigmoid and splenic flexure. Sections of fragments taken from the endoscopy showed features of eosinophilic gastritis and colitis on histology. Bone marrow trephine biopsy showed marked eosinophilia.

A diagnosis of FIP1L1-PDGFRA-negative idiopathic HES was made. He was started on oral imatinib mesylate 200 mg daily and oral prednisolone 0.5 mg/kg daily which was tapered based on response. He has been in complete remission for the past 18 months.

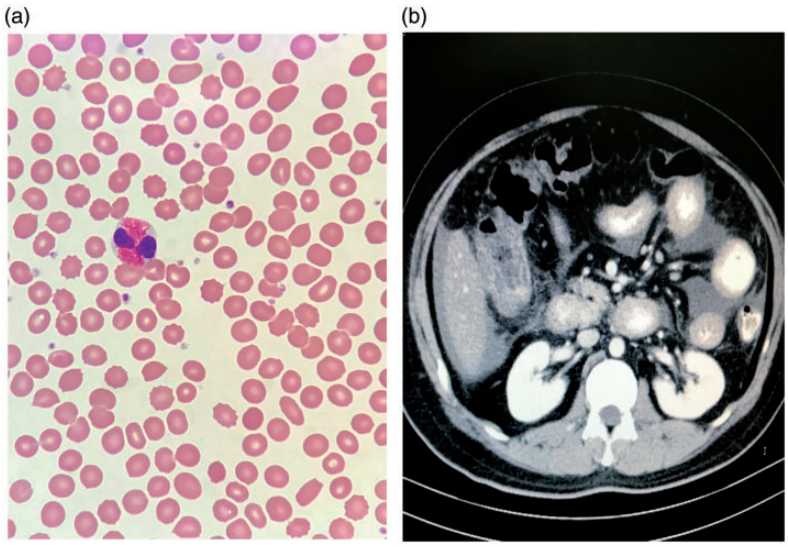
Discussion

Our case illustrates a young man who presents with eosinophilic ascites secondary to FIP1L1-PDGFRA-negative idiopathic HES. Eosinophilic ascites has been reported in 14% of patients with idiopathic HES.[2] Secondary causes such as helminth, protozoan, fungal, viral infections, T-cell lymphomas, immunodeficiency states and IgG4-related diseases should be excluded. Other differential diagnoses for idiopathic HES-associated-eosinophilic ascites include eosinophilic gastroenteritis (EGE), myeloproliferative HES, lymphocyte-variant HES, overlap HES, familial HES, systemic mastocytosis and idiopathic HES.[2]

EGE is typically organ-specific. EGE histology usually reveals more than 50 eosinophils per high-power-field in the lamina propria with large numbers of eosinophils present in the muscularis and serosa.[2] When EGE is present with eosinophilic infiltration of other bodily systems, the diagnosis of idiopathic HES should be considered.

Myeloproliferative-HES (m-HES) is usually characterised by splenomegaly, elevated levels of serum

Figure 2. (a) Peripheral blood film showing eosinophilia and (b) abdomen computed tomography showing bowel wall thickening.



B12 and serum tryptase and the presence of myeloid precursors in the bone marrow.[2] Interstitial deletion in chromosome 4q12 resulting in active fusion tyrosine kinase, FIP1L1-PDGFRA is seen in m-HES and responds well to imatinib mesylate therapy.[3]

Chronic eosinophilic leukemia – not otherwise specified (CEL-NOS) is characterised by the presence of clonal cytogenetic or molecular abnormalities such as DNMT3A, TET2, ASXL1 with a blast count of 2–19% in the peripheral blood and 5–19% in the marrow.[4] BCR-ABL1, PDGFRA, PDGFRB and FGFR1 are usually absent in CEL-NOS.[4] CEL with PDGFRA mutation has an excellent prognosis whereas CEL associated with FGFR1 mutations often progress to acute eosinophilic leukemia.[4] It is challenging to differentiate FIP1L1-PDGFRA-negative idiopathic HES from CEL-NOS, but the former has a more favourable prognosis with a longer median survival.[4]

Lymphocyte-variant HES (L-HES) is characterised by the presence of aberrant CD3-/CD4+ T-cell population and TCR gamma-delta rearrangements on flow cytometry.[5] Patients with L-HES have predominant skin and soft tissue symptoms.

HES patients with PDGFRA positivity should be treated with corticosteroids (prednisolone 0.5 mg/kg daily) and imatinib mesylate (100–400 mg daily).[6] Higher dose of steroids (oral prednisolone 1 mg/kg daily) is frequently required in cardiac involvement to prevent myocardial necrosis and heart failure.[6] Patients frequently relapse within months of imatinib discontinuation. FIP1L1-PDGFRA molecular testing should be performed every 3–6 months to monitor for relapsed disease as molecular relapse often precedes haematological relapse by 2–3 months.[7] PDGFR-negative HES usually requires higher doses of imatinib and responds slowly. Hydroxyurea, interferon-alpha, nilotinib or dasatinib can be used as second-line agents if imatinib and steroids fail to control the disease.

Organ-specific EGE shows a 90% response rate to corticosteroids.[7] Usually, oral prednisolone with an initial dose of 0.5–1.0 mg/kg daily is used. Some patients may require long-term low-dose steroids as they frequently relapse once steroids are discontinued.[7]

Higher doses of corticosteroids (prednisolone 0.5–1 mg/kg daily) are required in L-HES.[8] Interferon-alpha is a second-line agent used if the patient is unable to tolerate higher doses of steroids. Patients with L-HES should be monitored judiciously for development of T-cell lymphomas.

Novel agents such as humanised monoclonal anti-IL5 antibodies, mepolizumab and benralizumab may show promise in HES.[9]

Conclusion

The diagnosis of HES should be considered in a patient who presents with unexplained ascites by assessing the ascitic fluid and peripheral blood for the presence of eosinophilia. Other clinically important causes such as malignancy must always be excluded before a diagnosis of idiopathic HES is established.

Declarations

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