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Idiopathic Hyper-Eosinophilic Syndrome (IHES) Presenting with Peripheral Neuropathy: A Case Report

Nadir Zafar Khan, Syed Ahmed Ali Hasan, Muhammad Qasim Zia, Ehtesham Khalid, Mona Aziz, Zafar Iqbal

Department of Neurology, Shaikh Zayed Postgraduate Medical Institute, Lahore.

SUMMARY

A 40 years old man presented with excruitiating pain and numbness in all 4 extremities and pain epigastrium . After thorough investigations he was diagnosed as a case of idiopathic hypereosinophilic syndrome (IHES) and successfully treated with oral prednisolone, following which the patient is doing well.This case is being reported as IHES presenting with peripheral neuropathy is rarely seen.

INTRODUCTION

Eosinophilia is a common entity in tropical countries as Parasitic infestations are frequently seen. There exists a large list of causes for eosinophilia from mild (500 to <1,500/cmm) to moderate (1,500 to < 5,000/cmm), but severe degree (> 5,000/cmm) of persistent eosinophilia is a rare entity. Idiopathic hyper-eosinophilic syndrome presenting with peripheral neuropathy is an extremely rare presentation.

CASE REPORT

A 40 years old man with no known co-morbid condition attended by different outpatients clinic with complains of pain and numbness in all four extremities and pain epigastrium along with low grade fever, nocturnal dry cough, anorexia, and colicky abdominal pain with altered bowel habits for 6 months. Investigations revealed Total leukocyte count 20, 000/cmm, Neutrophil 68% Eosinophil 41%, Lymphocyte17% Monocyte 7%, ESR 70 mm/1st hr. Other investigations revealed no abnormality. Patient was treated with repeated courses of albendazole (400 mg) without any improvement. One month later, he was admitted in neurology unit with difficulty in walking.

Examination revealed vitals pulse 70/min. regular, Blood pressure 120/80 mmHg, mild pallor, clubbing, mild hepatomegaly; Central nervous system (CNS) examination showed marked wasting of all four limbs, bulk and tone reduced .Power 4/5 proximally and 2/5 distallyin lower limbs, ankles reflexes were absent , fasciculation in lateral calf, sensory impairment up to ankles and wrists, planters response were absent bilaterally. Examination of other systems did not reveal any abnormality.

Investigations: Hb 10.4 gm/dl, MCV 76.7 fl, MCH 24.8 pg/cell, MCHC 32.3 g/dl, RBC 4.20 million/umm, platelet count 2.95 lacs/umm, peripheral smear shows normocytic, normochromic picture , TLC 23,000/cmm, N 32% E 56% L 10% (absolute eosinophil count 12,880/cmm) (Fig. 1), ESR 70, C-reactive protein 48 mg/l. Serum albumin 2.67 g/dl and protein electrophoresis shows increase alpha-1 and alpha-2 fraction suggestive of an inflammatory process, CT abdomen shows picture suggestive of pyelonephritis rest of the study normal RA factor positive, TIBC 425 µg%, Serum iron 38 µg%, Urine for routine and microscopic examination revealed protein (+); Urine for Bence Jones protein negative LDH 307 U/l, LFT, sugar, urea, creatinine , electrolytes, amylase, lipase were within normal limits. Examination of stool did not reveal any ova, parasites, or cysts. HIV 1, 2-ve, HbsAg and anti HCV negative, ANA, C-ANCA and P-ANCA negative, serum B 12 ,Folate,C3, C4 Anti Transglutaminase IgA and IgG within normal limit with normal thyroid status, Chest X-Ray shows Normal study. Ultrasound abdomen showed mild hepatomegaly. Echocardiography –Ejection Fraction

40% Dilated Left ventricle with moderate Left Ventricle systolic function. Marked segmental wall motion defects. Upper Gastrointestinal endoscopy shows esophageal candidiasis and biopsy from 2nd part of duodenum shows mild to moderate degree of chronic nonspecific Duodenitis. Colonoscopy shows two areas of superficial ulceration one in splenic flexure and other in transverse colon, biopsy taken from ulcer shows lamina propria infiltrated with inflammatory cells.

Nerve conduction study reveals:

- Motor — reduced compound action potentials of bilateral median and tibial nerves with absent F-wave response .
- Sensory — mildly reduced sensory nerve action potentials of both upper limbs and mod. Reduction in lower limbs.
- Conclusion — mixed sensory and motor polyneuropathy.

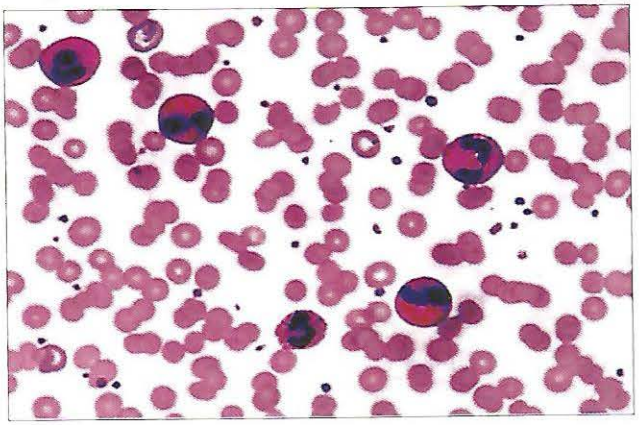

Fig. 1. Peripheral smear.

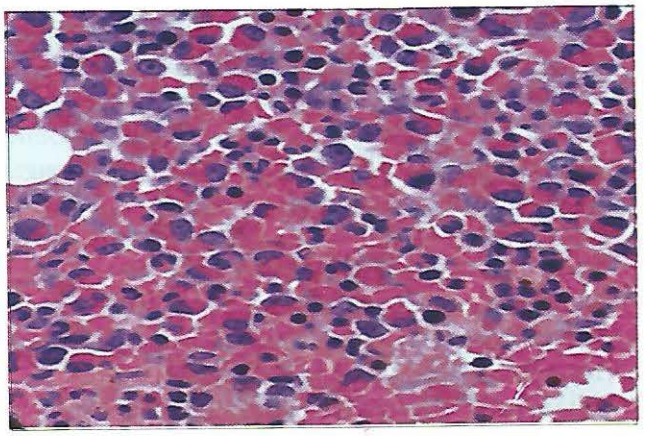

Fig. 2. Bone marrow biopsy

Skin biopsy shows perivascular chronic inflammatory cell infiltration with no evidence of vasculitis; bone marrow aspiration and biopsy (Fig. 2) shows hyper cellular marrow, increased erythropoiesis, increased megakaryocyte, no blast cell or any evidence of eosinophilic leukaemia.

The patient was provisionally diagnosed as IHES and treated with tab. prednisolone 60 mg/PO daily alongwith Mecobalamin and Gabapentine and he started showing improvement on follow up he gained weight ,Echo shows 60% ejection Fraction (previously 40%). Further investigations shows TLC 11500/cmm, E2%. The patient was subsequently followed-up for 12 months without any recurrence of symptoms and signs.

DISCUSSION

IHES was identified by Hardy and Anderson in 1968[1]. Hyper-eosinophilic syndrome varies from an asymptomatic phenomenon to a life threatening multi system disease4. It is recognized on the basis of eosinophil count > 1,500/cmm for a period of > 6 months duration and multi organ involvement (*i.e.*, heart, lung, kidneys, GIT, CNS, skin, musculoskeletal, etc.) in the absence of eosinophilic blast cells in peripheral blood or bone marrow, and absence of other causes of eosinophilia.

IHES is diagnosed by exclusion of other causes of eosinophilia (Table 1) and also by following the diagnostic criteria (Table 2).

The exact incidence of HES is hard to determine because it is a diagnosis of exclusion. It is a rare condition, although numerous reports exist in the literature. At the national Institute of Health between 1971 and 1982, 50 cases of HES were diagnosed and followed up[2]. The disease is rare in children. Internationally HES is rare and the exact incidence is uncertain.

The course of HES varies from relatively indolent to fulminant and rapidly fatal. The prognosis of HES has improved significantly since definition of HES and the development of imatinib. Ultimately, the mortality associated with HES is due to malignant transformation of myeloid or lymhoid cells into a frank eosinophilic leukemia[3].

Table 1: Common causes of eosinophilia.

1.	Parasitic infestation – Filariasis, strongyloides, trichinosis, etc.
2.	Allergic diseases – Asthma, hay fever, serum sickness, eczema, etc.
3.	Drugs – Iodides, aspirin, sulfonamide, penicillin, etc.
4.	Vasculitic disease and collagen vascular diseases – rheumatoid arthritis, polyarteritis nodosa, Churg- Strauss syndrome, Wegener's granulomatosus, etc.
5.	Blood diseases – CML, lymphoma, All – M4 E0, etc.
6.	Solid tumors – Lung, stomach, pancreas, ovary, uterus, etc.
7.	Hypereosinophilic syndrome – Loeffler's syndrome, tropical pulmonary eosinophilia, Loeffler's endocarditis, eosinophilic leukemia, and idiopathic hypereosinophilic syndrome.

Table 2: Diagnostic criteria for IHES

1.	Eosinophils > 1,500/mm3 for at least 6 months duration.
2.	Reactive causes of eosinophilia excluded.
3.	Known eosinophilic disease entities excluded.
4.	Evidence of eosinophilic end organ damage.
5.	Clonal eosinophilic disorder excluded.

Survival statistics vary. A review of 57 patients with advanced disease had a mean survival rate of 9 months and 3 year survival rate of 12%; in another analysis of 40 patients ,the 5 year survival rate was 80 % and the 10 year survival rate was 42%. A study from NIH in 1982[2] noted a mean duration of disease of 4.8 years (range 1–24 yr). How newer treatments, such as cyclosporine, have affected mortality and morbidity is unclear.

No racial predilection is recognized. Male predominance (4-9:1 ratio) has been reported in historic series, but this is likely to reflect the quasi-exclusive male distribution of a sporadic hematopoietic stem cell mutation found in recently characterized disease variant.

A study from NIH[2] of 50 patients reported that the mean age of onset was 33 years .In 70 % of patients, the onset of disease occur between 20-50 years. Although rare, this disease HES does occur in children. A review in 1987[4] from Wales found 18 published reports of HES in children younger than 16 years .The incidence seems to decrease in elderly person.

In our case, the patient was a 40 year old man with involvement of central nervous system and gastrointestinal system presenting with Peripheral neuropathy and epigastric pain. We primarily suspected it to be a case of eosinophilic gastroenteritis (EGE), but since it is associated with H/O allergy to food or milk, commonly presents in the 3rd to 5th decade, involves only stomach and small intestine, with eosinophilic infiltration, Endoscopy showed this was not the case. As the patient had multisystem involvement without any definite cause, it was diagnosed as IHES. Regarding cardiovascular involvement, it is a common feature in IHES.

For development of cardiac symptoms, disease duration is usually more than 10 months, and early institution of steroid may normalize the cardiac findings to some extend[5]. In our patient after giving steroids Ejection Fraction improved to 60% (from 40% previously) In early cases. However, endomyocardial biopsy to confirm the cardiac involvement, was not possible in our setting. Bone marrow biopsy shows an increase in all stages of eosinophilic differentiation, but there are no diagnostic characteristics[6], and the same also holds true for biopsy of the affected site[6]. For confirmation of diagnosis, tissue biopsy is not required[6].

Treatment with oral prednisolone 1 mg/kg/day for 2 weeks followed by alternate day for 3 months shows clinical improvement, but eosinophil counts rarely normalise[5]. Patients may also be treated with low dose steroids for many years[6]. If no clinical improvement is achieved after 3 months treatment additional hydroxyurea, interferon alpha, cyclosporine, or etoposide may be added[5]. We gave oral prednisolone 60 mg /day with mecobalamin and gabapentine .patient showed marked improvement in his functional status ,gained weight.

Complications

Because HES is a multi system disease, the complications depend on the organs involved. Cardiac involvement which may lead to Congestive heart failure. Three types of neurological complications occur: thromboembolic, primary CNS dysfunction and peripheral neuropathies.

Prognosis of HES is good, with approximately half of patients alive 14 years after diagnosis. The main cause of death are thromboembolic disease, central nervous damage and leukemia. Generally once an effective treatment has been found. Patient continues for many years with small fluctuation in their symptoms that are usually easily managed by temporary increase in steroid dose[6].

Consultations

HES is multi system disorder. It is often hard to diagnosis because its symptoms are not specific. Consultation from all medical specialties can be helpful in making diagnosis. In particular, consultation wit a neurologist, cardiologist, a hematologist and a dermatologist can be helpful.

CONCLUSION

IHES can present with peripheral neuropathy along with other systemic involvement. For control of eosinophil count. Treatment With oral low dose steroid is effective and patient can survive long term without disability.

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The Authors:

Nadir Zafar Khan,
Associate Professor
Department of Neurology,
Shaikh Zayed Hospital, Lahore.

Syed Ahmed Ali Hasan,
Senior Registrar
Department of Neurology,
Shaikh Zayed Hospital, Lahore.

Muhammad Qasim Zia,
Trainee Registrar
Department of Neurology,
Shaikh Zayed Hospital, Lahore.

Ehtesham Khalid,
Trainee Registrar,
Department of Neurology,
Shaikh Zayed Hospital, Lahore.

Mona Aziz
Assistant Professor
Department of Haematology,
Shaikh Zayed Hospital, Lahore.

Zafar Iqbal
Professor
Department of Medicine,
Shaikh Zayed Hospital, Lahore.

Address for Correspondence:

Nadir Zafar Khan,
Associate Professor
Department of Neurology,
Shaikh Zayed Postgraduate Medical Institute,
Lahore.