HYPEREOSINOPHILIC SYNDROME: REPORT OF A CASE AND REVIEW OF LITERATURE

H. Moayeri and Z. Oloomi*

Department of Pediatrics, Imam Khomeini Hospital, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Abstract- Idiopathic hypereosinophilic syndrome represents a heterogeneous group of leukoprolifrative disorders associated with prolonged eosinophilia of an undetectable cause with multi organ system dysfunction. It is a rare group disorder in children, most cases are reported in adult age group. We report a child with this syndrome who along with the usual features of the syndrome also had the presentation of cardiac and neurologic complications which did not respond to treatment.

Acta Medica Iranica, 44(4): 285-287; 2006

Key words: Hypereosinophilic syndrome, cardiac complications, neurologic complications

INTRODUCTION

Idiopathic hypereosinophilic syndrome (HES) is a rare condition with organ damage secondary to high eosinophilic counts and marked eosinophilic tissue infiltration (1-3). The eosinophil count exceeds 1500 cells/mm^3 and persists for at least 6 month unless death intervenes. It is rare in children; most cases are reported in women aged between 20 and 50 years (1-3). The clinical presentation is generally insidious but may be acute with sudden cardiac or neurologic involvement. In this article, we report a case of HES who presented with cardiac and neurologic complications.

CASE REPORT

A 3.5 years old male child was admitted in the pediatric ward of Imam Khomeini Hospital, Tehran University of Medical Sciences. He first presented with the complaints of high grade persistent fever along with weakness, nonproductive, non spasmodic cough and tachypnea for a period of 3 months. The child was treated symptomatically as outpatient and became asymptomatic but high grade fever, abdominal distention and tachypnea recurred within a week and he was admitted.

At admission, the child appeared sick with a pulse rate of 120/min, a respiratory rate of 54/minute and a blood pressure of 95/65 mmHg. Anthropometric measurements (height and weight) were normal for sex and age. Auscultation of chest revealed bilateral crepitations and breath sounds in lower right lobe were decreased. Systolic murmur grade III/VI at tricuspid site could be heard. The spleen was palpable 3 cm below the left costal margin and liver 4 cm below right costal margin in the midclavicular line. They were not tender, soft in consistency and had a smooth surface. Other systemic examinations were normal. There was no history of oliguria, dysuria, hematuria, jaundice, skin manifestation, bleeding tendencies, joint pains, worm infestation or allergic disorders. Moreover, there was no history of tuberculosis contact and no history of pica or geophagia. The child was not consuming any medications. There was no history of a similar illness in the family.

Investigations revealed hemoglobin of 7.7 g/dl, WBC of 28000 cell/mm^3 (polymorph 10%, lymphocytes 12%, eosinophils 71%) and platelet

Received: 29 May 2005, Revised: 12 Feb. 2004, Accepted: 6 Aug. 2005

*** Corresponding Author:**
Z. Oloomi, Department of Pediatrics, Imam Khomeini Hospital, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
Tel: +98 21 66927723, Fax: +98 21 66927723
E-mail: h.moayeri@softhome.net

count of 285×10^3/ mm^3. Mean Cell Volume (MCV) was 85 ft and erythrocyte sedimentation rate (ESR) was 12 mm at the end of one hour. Peripheral blood smear examination showed marked eosinophilia with absolute eosinophil count (AEC) of 1988/mm^3.

The bone marrow examination showed myeloid hyperplasia with increased eosinophils and its precursors. Megakaryocyte and erythroid series were normal. No abnormal cells or parasites were seen. Chest radiograph revealed bilateral interstitial infiltration. There was no biochemical evidence of hepatic or renal dysfunction. The Manteau tuberculin skin test result was negative. Ultrasound examination of the abdomen revealed hepatosplenomegaly. Serology for fasciola antibody, hydatoid antibody and toxocara antibody were negative. The immunoglobulin levels were normal (IgG, 1180; IgM, 120; IgA, 77; IgE, 11). Antinuclear antibodies, rheumatoid factor and complement levels were normal. Echocardiographic examination showed mild cardiomyopathy, mild mitral regurgitation and tricuspid regurgitation and an ejection fraction of 50%. Karyotyping was normal. Hematological parameters of parents were normal. Repeated stool examination for ova and cyst were negative for common parasitic infections. Since no cause attributable to hypereosinophilia was found, a diagnosis of idiopathic HES was made. The child was put on prednisolone (2 mg/kg/day) but no clinical improvement occurred. After 3 days of this therapy, hydroxyurea was used for reducing white blood cell count. He suddenly expired because of cardiovascular arrest. Necropsy study showed severe eosinophilic infiltration at both lung and liver (Figures 1and 2).

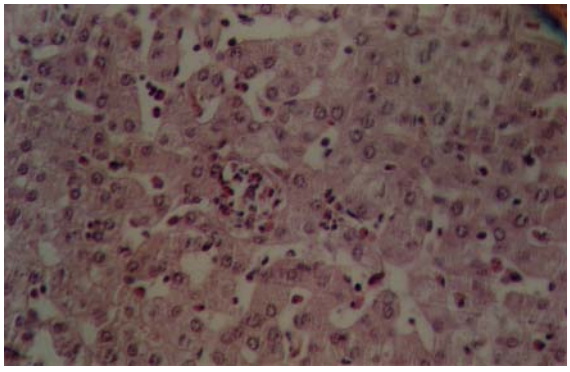

Fig. 1. Sever eosinophilic infiltration in liver tissue.

DISCUSSION

A case of HES was first reported in 1968 by Hard and Anderson but no details were available (1, 4). Chusid and coworkers later used restricted definition and criteria for diagnosis of HES as persistent eosinophilia of more than 1500 cells/mm^3 for at least 6 months or death before 6 months with signs or symptoms of HES, lack of evidence for any recognized cause of eosinophilia and signs and symptoms of multi-organ system involvement (1-5). Fewer than 30 cases have been reported in children below 12 years of age (3). The presentation include: sign and symptoms of multi organ involvement like as weakness, cough, dyspnea, myalgia, rash, fever, rhinitis (1, 6, 7). Any organ may be involved. The characteristic feature of HES in tissue damage related to the release of basic protein, eosinophil peroxidase, cationic protein and eosinophil derived neurotoxin (4). In NIH series hematological involvement was seen in all, pulmonary in 40%, skin in 56%, neurological in 64%, splenomegaly in 45%, hepatomegaly in 35%, cardiovascular in 54% and ocular involvement in 18% (1, 8, 9). In our case the bone marrow, liver, spleen and lung were involved with no peripheral organ damage. The organ involvement was consistent with other reports (2). Myeloproliferative diseases or acute eosinophilic leukemia are considered as differential diagnosis (1). Characteristics of lymphoproliferative include presence of hypogranular, vacuolated eosinophils, presence of Philadelphia chromosome and decreased alkaline phosphatase (1, 5-7). Acute eosinophilic leukemia is of special concern as a differential diagnosis. The conversion of idiopathic HES to

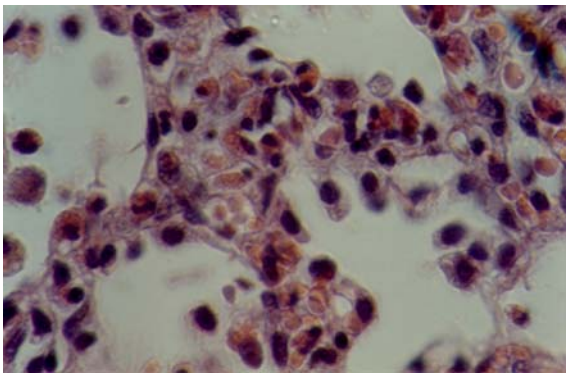

Fig. 2. Sever eosinophilic infiltration in lung tissue.

leukemia is rare. The pulmonary infiltration with eosinophilia syndrome should be kept as a differential diagnosis, especially where there is history of recurrent wheezing or dyspnea.

A patient with HES who has no organ dysfunction or symptoms despite high AEC needs no treatment except for a close follow up at 3 to 6 monthly intervals (2, 4, 6). The symptomatic patients should be treated with prednisolone therapy until clinical improvement occurs and then the dose should be tapered (1, 4, 5, 10). Symptomatic patient non responsive to steroids should be offered chemotherapeutic agents. Common chemotherapeutic drugs used include hydroxyurea, vincristine, 6 mercaptopurine, busulfan and chlorambucil. Hydroxyurea because of absence of leukemogenic effect and oral administration is used frequently. Interferon alpha and cyclosporine have also been found to be useful in HES (11). Imatinib mesylate is a promising drug in the treatment of idiopathic HES with response seen as early as one week after starting treatment, although further data are awaited for its use in the pediatric population (11).

Long term prognosis of patients with idiopathic HES contributes to be rather poor with 40% reported mortality at 10 years (11). Although mortality of HES is high, adhesive medical treatment can result in significant clinical improvement. The most common mode of mortality in HES is damage to heart and CNS by eosinophilic infiltration. Thrombectomy in thrombo-embolism, endocardial resection in endocardial fibrosis and valve replacement in severe regurgitation of mitral and tricuspid valve can be life saving (2, 3). NIH published a follow up of 50 patients diagnosed and treated over 11 years, with variable survival rates depending on the major organ involved. Patients with cardiovascular complications had a low survival rate. In conclusion, HES represents an emergency in children and it may be complicated by vital organ involvements. Our case highlights the importance of through screening in a symptomatic patient with marked eosinophilia.

REFERENCES

1. Fauci AS, Harley JB, Roberts WC, Ferrans VJ, Gralnick HR, Bjornson BH. NIH conference. The idiopathic hypereosinophilic syndrome. Clinical, pathophysiologic, and therapeutic considerations. Ann Intern Med. 1982 Jul; 97(1):78-92.
2. Alfaham MA, Ferguson SD, Sihra B, Davies J. The idiopathic hypereosinophilic syndrome. Arch Dis Child. 1987 Jun; 62(6):601-613.
3. Spry CF. The hypereosinophilic syndrome. In: Wearherall DJ, Ledingham JGG, Warell DA, eds. Oxford Text Book of Medicine. 3rd ed. Oxford: Oxford Medical Publication. 1996. p. 3610-3613.
4. David P, Schenlein, Woiff SM. Ensinophilia and hypereosinophilic syndrome. In: Hoffmann R, Benz JE, Hattil Js, eds. Hematology Basic Principles and Practice. 2nd ed. New York: Churchill Livingstone; 1995. p. 784-791.
5. Wardlaw AJ, Kay AB. Eosinopenia and eosinophilia. In: Beutler E, Lichtman MA, Coller BS, Kipps JT, eds. William's Hematolology. 5th ed. New York: McGraw Hill. 1995. p. 844-851.
6. Weller PF, Bubley GJ. The idiopathic hypereosinophilic syndrome. Blood. 1994 May 15; 83(10):2759-2779.
7. Schooley RT, Flaum MA, Gralnick HR, Fauci AS. A clinicopathologic correlation of the idiopathic hypereosinophilic syndrome. II. Clinical manifestations. Blood. 1981 Nov; 58(5):1021-1026.
8. Bhatnagar S, Patwari AK, Narayan S, Lalit S, Anand VK. Idiopathic hypereosinophilic syndrome. Indian Pediatr. 1999 Aug; 36(8):824-827.
9. Jameson MD, Segraves SD. Idiopathic hypereosinophilic syndrome. Postgrad Med. 1988 Dec; 84(8):93-96.
10. Bass DA. Eosinophilic syndrome. In: Wyngaarden JB, Smith LK, eds. Cecil Text Book of medicine. 17th ed. Philadelphia: W. B. Saunders Co; 1985. p. 1011-1022.
11. Ault P, Cortes J, Koller C, Kaled ES, Kantarjian H. Response of idiopathic hypereosinophilic syndrome to treatment with imatinib mesylate. Leuk Res. 2002 Sep; 26(9):881-884.