

CASE REPORT

Acquired Immune Deficiency Syndrome in Differential Diagnosis of Hyper-IgE-Immunoglobulinemia: Pediatric Case Report

by Manolya Acar,¹ Murat Sutcu,¹ Ozge Umur,² Hacer Akturk,¹
Selda Hancerli Torun,¹ Zeynep Tamay,³ Nuran Salman,¹
and Ayper Somer¹

¹Pediatric Infectious Diseases and Clinical Immunology, Istanbul University Faculty of Medicine, Istanbul, Turkey

²Pediatrics Istanbul, Istanbul University Faculty of Medicine, Istanbul, Turkey

³Pediatric Allergy, Istanbul University Faculty of Medicine, Istanbul, Turkey

Correspondence: Murat Sutcu, Istanbul University Faculty of Medicine, Pediatric Infectious Diseases and Clinical Immunology, Millet St. 34093, Fatih, Istanbul, Turkey. Mob: 0905308793344. Tel: 0904142000/32566. E-mail <sutcu13@yahoo.com>.

ABSTRACT

Acquired immune deficiency syndrome can be encountered with hypereosinophilia and hyperimmunoglobulin E (hyper-IgE) values, though these levels are rarely so high to be compared with hyperimmunoglobulin E syndrome. A 9-year-old boy presented with the complaint of fatigue, weakness, weight loss and generalized pruritic rash lasting for a year. He had frequent respiratory tract infections, wheezing episodes and urticarial skin lesions before that. On admission, he was cachectic and he had generalized lymphadenopathy, hepatosplenomegaly, oral moniliasis and pruritic rash all over his body. Laboratory evaluation revealed marked lymphopenia and hypergammaglobulinemia with extremely high IgE values (IgE: 59 300 kU/l). He was diagnosed with stage 4 human immunodeficiency virus (HIV) infection and started on antiretroviral treatment. In conclusion, HIV infection can be presented with increased IgE values.

KEYWORDS: acquired immune deficiency syndrome, hyperimmunoglobulin E, child.

INTRODUCTION

Hyperimmunoglobulin E (hyper-IgE)-immunoglobulinemia is oftenly attributed to hyperimmunoglobulin E syndrome (HIES), as serum IgE level above 2000 IU/ml is a strong indicator of HIES [1]. Although many other clinical conditions such as allergic diseases, parasitic worm infestations, inflammatory conditions,

primary immune deficiency syndromes, malignancies and acquired immune deficiency syndrome (AIDS) are related with increased serum IgE levels, it is uncommon to manifest with such high values [2]. Herein, we report a 9-year-old boy presented with extremely high serum IgE levels who was then diagnosed with AIDS.

CASE REPORT

A 9-year-old boy presented to our outpatient clinic with the complaint of fatigue, weakness, weight loss and generalized pruritic rash, which had appeared a year ago. In history, he was born in Uzbekistan as a fifth child from a healthy father and a mother with the diagnosis of rheumatoid arthritis. At one year of age, he had been operated for inguinal hernia and given erythrocyte suspension which he had been sick since then, as their parents signified. He had visited several clinics for recurrent wheezing and skin rash, and was given antiasthmatic medication together with local antihistaminic solutions. He got worse in the last year, and lost 7 kg within 2 months.

On admission, he was cachectic and seemed exhausted. He weighted 18 kg (z score -2.95), and his height was 123 cm (z score -0.89). He had oral moniliasis and generalized pruritic rash all over his body (Fig. 1). Hepatosplenomegaly and generalized multiple mobile lymphadenopathies <1 cm in diameter were encountered. Respiratory sounds were coarse, and no crackles were heard on auscultation. Cardiovascular and neurologic system examinations were normal.

On laboratory evaluation, white blood cell count was $6100/\text{mm}^3$ (neutrophil $3900/\text{mm}^3$, lymphocyte $605/\text{mm}^3$), mean hemoglobin level was 10.6 g/dl and platelet level was $268\,000/\text{mm}^3$. He had hypergammaglobulinemia with extremely high serum IgE levels (IgG: 1506 g/dl , IgA: 810 g/dl , IgM: 182 g/dl , IgE: $59\,300\text{ kU/l}$). Peripheral blood smear examination revealed hypereosinophilia (22.3%) together with hypochromic microcytic anemia. Liver transaminases, renal function tests, serum electrolyte levels and C-reactive protein values were within normal limits. His clinical findings in addition to



Fig. 1. Profound cachexia and generalized pruritic rash.

lymphopenia and marked hypergammaglobulinemia raised the suspicion of human immunodeficiency virus (HIV) infection. Anti-HIV test and confirmation Western blot were reported as positive. HIV RNA was $4\,378\,407$ copies/ml with CD4 being 1%. He was diagnosed with stage 4 HIV infection/AIDS according to World Health Organization criteria and started on antiretroviral treatment (ART), including lamivudine, zidovudine and lopinavir/ritonavir combination. Echocardiographic examination and central nervous system magnetic resonance imaging were normal. Skin prick testing with a standard battery of common aeroallergens including house dust mite, weed and tree pollens, mold and animal dander was evaluated as negative. He was consulted to dermatology clinic, and his generalized rash was diagnosed as scabies because tiny burrow lesions were identified. Local 5% permethrin solution was applied to his skin lesions. With proper treatment, his lesions disappeared in time and viral load achieved to undetectable levels. At that time, serum IgE levels decreased to 978 kU/l with serum eosinophil ratio of 0.2%.

DISCUSSION

HIV-related atopy has already been reported with a prevalence between 10 and 52% in pediatric series. In addition, HIV/AIDS patients have hypereosinophilia and increased total IgE levels, although the prevalence of allergic diseases and laboratory values are not correlated all the time [3, 4]. Although a high frequency of increased total IgE has been reported in pediatric HIV studies, none of them reports such an extremely high value as in our case [5, 6]. Our patient had several wheezing episodes, atopic eczema and nonspecific urticarial lesions before admission. But these symptoms were not such severe to require hospitalization. The other immunoglobulin series were also increased, which was consistent with the idea of polyclonal B-cell activation-induced hypergammaglobulinemia.

A correlation between increased IgE levels and decrease in the number of the CD4^+ cells has been described. The hyper-IgE-immunoglobulinemia and hypereosinophilia are related with the severity of the disease and attributed as indicators of poorer prognosis [5]. In addition, blood eosinophilia can cause organ damage secondary to release of multiple toxic

products. Any tissue or organ may be affected in the body, although the most common complications arise from the nervous system, skin, heart and lungs [7]. In our case, initial blood eosinophil ratio was 22.3% and serum IgE value was as high as 59 300 kU/l (normal <100 kU/l). These values were compatible with low CD4 ratio (1%). Although he was presented as stage 4 disease, fortunately, central nervous system and cardiac involvement were not obvious. After he was started on ART, serum eosinophil and IgE values decreased gradually (0.2% and 978 kU/l, respectively). However, because of patient's incompatibility, his viral load and CD4 counts fluctuated in time. In last patient visit, total IgE and CD4 ratio were 1172 kU/l and 27%, respectively.

Scabies, the disease caused by the mite *Sarcoptes scabiei*, can be a presenting feature in children with HIV infection, especially in the ones with CD4 counts <150 cells/ μ l [8]. Although positive correlation was reported between total IgE and severity of manifestations, such an extremely high value is out of the ordinary [9]. Dermatologic evaluation confirmed the diagnosis of scabies in our patient. His pruritic skin lesions resolved completely with the effect of ART and local permethrin therapy.

In our case, when we faced with such an extremely high IgE value, we considered HIES as an initial diagnosis. But characteristic findings of HIES, such as coarse phenotypic appearance, teeth abnormalities, skeletal deformities or history of recurrent skin abscesses, were not consistent with our patient. In addition, the hallmarks of AIDS including wasting syndrome, hepatosplenomegaly, lymphadenopathy,

presence of lymphopenia together with hypergammaglobulinemia were prominent and led us to perform HIV testing.

In conclusion, although such an IgE level is exceptionally high, it is relevant to emphasize the collaboration of HIV infection with increased IgE values, and evaluate the patients for possible diagnosis of AIDS.

REFERENCES

1. Ochs HD, Notarangelo LD. (2010). Williams hematology: Chapter 82. In: Immunodeficiency Diseases. 8th edn. New York: McGraw-Hill Medical. ISBN 9780071621519.
2. Lin RY. Chronic diffuse dermatitis and hyper-IgE in HIV infection. *Acta Derm Venerol* 1988;68:486–91.
3. Linhar LS, Traebert J, Galato D, *et al.* Allergic diseases in subjects under 18 years living with HIV. *Allergy Asthma Clin Immunol* 2014;10:35.
4. Vanker A, Rhode D. Human immunodeficiency virus and allergic disease. *J Allergy Clin Immunol* 2009; 22:168–72.
5. Secord EA, Kleiner GI, Auci DL, *et al.* IgE against HIV proteins in clinically healthy children with HIV disease. *J Allergy Clin Immunol* 1996;98:979–84.
6. Wright DN, Nelson JRRP, Ledford DK, *et al.* Serum IgE and human immunodeficiency virus (HIV) infection. *J Allergy Clin Immunol* 1990;85:445–52.
7. Roufosse FE, Goldman M, Cogan E. Hyper eosinophilic syndromes. *Orphanet J Rare Dis* 2007;2:37.
8. Cruz CR, Carvalho VO, Santos RV, *et al.* Laboratorial atopy markers in children with human immunodeficiency virus. *Mem Inst Oswaldo Cruz* 2010;105:293–8.
9. Abd El-Aal AA, Hassan MA, Gawdat HI, *et al.* Immunomodulatory impression of anti and pro-inflammatory cytokines in relation to humoral immunity in human scabies. *Int J Immunopathol Pharmacol* 2016;92:188–94. 0394632015627464.