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Dr. Tinsae Alemayehu, Assistant Professor of Paediatrics and Child Health, Division of Paediatric infectious diseases, Department of Paediatrics & Child Health, Addis Ababa University. Dr Endale Tefera, Associate Professor of Pediatrics & Child Health, Consultant Pediatric Cardiologist, Department of Pediatrics and Child Health, Addis Ababa

Corresponding Author: Dr. Tinsae Alemayehu, Assistant Professor of Paediatrics and Child Health, Division of Paediatric infectious diseases, Department of Paediatrics & Child Health, Addis Ababa University. Email: tigisttinsae@gmail.com

DILATED CARDIOMYOPATHY IN A CHILD WITHHYPER-IMMUNOGLOBULIN E SYNDROME

Dr T. Alemayehu and Dr E. Tefera

ABSTRACT

Hyper-immunoglobulin E syndrome is a rare primary immunodeficiency. We report a 6-year-old girl diagnosed with hyper immunoglobulin E syndrome and dilated cardiomyopathy. She presented with recurrent pneumonia and chronic eczema since infancy; onychomycosis, eosinophilia, high immunoglobulin E levels, previous treatment for severe infections and dilated cardiomyopathy. She was treated with diuretics, afterload reducers, inotropes, aspirin, steroids and antibiotics. Whether the cardiomyopathy is a co-incidental finding or a result of viral myocarditis due to the recurrent chest infections she had was difficult to conclusively determine.

INTRODUCTION

Hyper-immunoglobulin E (IgE) syndrome is a rare primary immune-deficiency first described in 1966 by Davis et al. Most cases are sporadic (1). Its incidence is about one in 1 million people. Close to 250 cases have been reported, some of which from North and South Africa (2 – 4).

Chipeta et al reported a Zambian infant with recurrent mandibular abscesses, elevated serum IgE, pneumonia, a typical otitis media, thrombocytopenia and typical facies of hyper IgE syndrome (5). Another 8-year-old South African girl was described with chronic eczema, recurrent skin infections and pneumonia, eosinophilia, elevated serum IgE and food allergies (6).

An electronic search of reports from East Africa yielded no results. Cardiovascular abnormalities are occasionally seen in hyper IgE syndrome including aneurysms, pseudo-aneurysms, congenital patent ductusvenosus, and vascular ectasia (7 – 9). We present a 6-year-old girl with eczema since infancy, recurrent respiratory infections, onychomycosis, elevated serum IgE, eosinophilia, food, aeroallergen and inhalant allergies with dilated cardiomyopathy.

Case Report

A 6-year-old girl presented with cough, fast breathing and high grade fever of 3 days. She was on follow-up for generalized eczema and dilated cardiomyopathy and taking topical steroids, diuretics, digoxin and captopril. She is the first child for the family and no sibling or first degree relative was reported with similar problems. Her growth and development was reported to be optimal. The mother reported that the child had marked limitation of physical exertion. She has also had several past admissions for recurrent infections. Her maternal grandfather was reported to be asthmatic. On physical examination, she was in cardio-respiratory distress. Weight was 17 Kg and height was 117 cm. Pulse was 152 beats per

minute and blood pressure was 100/60 mmHg. Her oxygen saturation was 80% on room air. Her teeth showed notching over her lower incisors. She had firm, non-tender bilateral inguinal lymphadenopathy (3 cm by 3 cm). She had flaring, intercostal and subcostal retractions as well as cyanosis. Diffuse wheezing and coarse crepitation's over the right lower thirds lung field were auscultated.

She had engorged neck veins with an active precordium. The point of maximal impulse was at the 6th intercostal space lateral to the mid-clavicular line. She had a S3 gallop and a grade II/VI pan-systolic murmur at the apex with no radiations. The liver was palpable 6 cm below the right costal margin. She had extensive eczematous skin lesions involving the extremities and trunk, sparing the face and scalp. Her thumbnail was partially lost with scales on the remainder part.

Figures 1A & 1B: Skin lesions over the extremities in our patient

Complete blood count (CBC) showed WBCs of 12,000 with 27.9% eosinophil (absolute eosinophil count = 3348) and a platelet count of 439,000.

Chest X-ray showed gross cardiomegaly (cardiothoracic ratio 65%) with some degree of lung congestion. Electrocardiography showed sinus rhythm with a rate of 150 beats per minute, left atrial and left ventricular enlargement and nonspecific repolarization abnormalities. Echocardiography showed dilated left ventricle with markedly reduced systolic function (30% by M-mode estimation), dilated left atrium and minimal mitral and tricuspid regurgitation. Serum IgE levels ranged between 1500 IU/ml (at presentation) and 9404 IU/ml (late infancy). Lymph node biopsy showed dermatopathic lymphadenopathy while a skin biopsy revealed psoriasis form dermatitis consistent with chronic spongioticeczematous dermatitis.

She showed a high level sensitization for dates, mango and nuts (food panel), for the mite species *Dermatophagoides Pteronyssinus* and *DermatophagoidesFarinae* (aeroallergen panel) and for desert palm pollens (inhalant panel). Work-up for a possible primary immuno-deficiency started from measuring CBC and serum immunoglobulin (Ig) levels which were normal barring the marked eosinophilia and elevated serum IgE level. Hence, defects of antibody production were ruled out. Advanced T cell defect tests could not be done but absolute lymphocyte counts were normal. Typical clinical features of DiGeorge syndrome were absent with a normal serum calcium level. Wiskott-Aldrich syndrome was ruled out because of normal or high platelet counts. Eosinophilia and elevated IgE are not features of chronic granulomatous disease.

The other phagocyte disorders mismatched her presentation. Serum C3 & C4 complement

levels were low, 48 mg/dL and 12.8 mg/respectively. Though these are insufficient for screening for complement deficiencies, a high IgE and eosinophilia speak against them. Our patient exhibited recurrent upper and lower respiratory infections, episodes of severe cardiac and gastrointestinal infections, chronic eczema since infancy, onychomycosis, eosinophilia and markedly elevated IgE levels pointing to hyper IgE syndrome being her primary immune-deficiency. She was managed with intranasal oxygen, intravenous antibiotics, diuretics, afterload reducers, digoxin and aspirin. Co-trimoxazole prophylaxis and topical Beclomethasone were given upon discharge. On follow up she was reported to have improved exercise capacity, decreased cough and orthopnea and overall feeling.

DISCUSSION

Hyper-immunoglobulin E syndrome is characterized by defective neutrophil chemotaxis and increased IgE. The autosomal dominant form is related to mutations in the signal transducer and activator of transcription 3 (STAT 3) gene which causes defective Th17 function (10). The various clinical features include high serum IgE, skin abscesses, recurrent pneumonias, retention of primary teeth, scoliosis, easily occurring fractures, eosinophilia, characteristic facies (prominent forehead, deep-set eyes, a broad nasal bridge, mild prognathism), midline facial anomalies, newborn rash, eczema, frequent upper respiratory tract infections, candidiasis, recurrent life-threatening infections, hyper-extensibility of joints, lymphoma and onset of symptoms early in life (1).

Our patient presented with many of the aforementioned features. Serum IgE was elevated to 55 times the normal values with eosinophilia. She had more than 3 admissions for severe pneumonia. She is on follow-up for eczema since infancy. She had onychomycosis of her finger nails. Her past history is marked for frequent flus and treatment for acute pericarditis and dysentery. Her diagnostic score for hyper IgE syndrome according to the USA National Institutes of health (NIH)scoring was 45 (Diagnosis is unlikely for scores less than 20; indeterminate for scores between 20 and 40 and suggestive of hyper IgE syndrome for scores greater than 40) (1).

Genetic confirmation and work-up of family members were not possible to do in our facility. Cardiovascular abnormalities are occasionally seen in hyper IgE syndrome. Aneurysms with some leading to myocardial infarction, pseudoaneurysms, congenital patent ductusvenosus, and vascular ectasia have been reported (7 – 9). The pericarditis was diagnosed 3 months prior to presentation after she complained of cough of 10 days' duration followed by difficulty of breathing.

There were no other past episodes of pericarditis which could be linked to the dilated cardiomyopathy (diagnosed at age 3 years). There were also no signs of nutritional deficiencies which might be related to the cardiomyopathy. Definitive cure is not available for hyper IgE syndrome. Prophylactic antimicrobials are a cornerstone of management (6).

CONCLUSIONS

We report a child with Hyper Immunoglobulin E syndrome in combination with dilated cardiomyopathy. Whether the cardiomyopathy is a co-incidental finding or a result of viral myocarditis as part of the recurrent chest infections she has had was difficult to conclusively determine".

CONFLICT OF INTERESTS

The authors declare no conflicts of interests.

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