Case Report

Tuberculosis in a case of hyper immunoglobulin E syndrome

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Abstract

Hyper immunoglobulin E syndrome (HIES) is a rare primary immunodeficiency disorder characterized by elevated serum IgE, dermatitis, and immunodeficiency that predisposes to multiple skin and lung infections. The most frequent pathogen responsible for infections in these patients is *Staphylococcus aureus.* Tuberculosis (TB) in patients with HIES is an uncommon finding, and there are only a few reports of mycobacterial infections in known cases of HIES. We present a case of abdominal TB that developed in a 15-year-old boy who also had HIES.

Keywords: Hyper immunoglobulin E syndrome, rare primary immune deficiency, tuberculosis

Introduction

Hyper immunoglobulin E syndrome (HIES) is a rare primary immunodeficiency disorder characterized by elevated serum IgE, dermatitis, and recurrent skin and lung infections.[1] Three genetic etiologies of hyper IgE have been identified: STAT3, DOCK8, and TYK2. Association with TYK2 deficiency has shown some reported cases of hyper IgE with disseminated nontuberculous mycobacterial (NTM) infection.[2] Microbial cultures of recurrent pulmonary infections show *Staphylococcus aureus*, *Streptococcus pneumonia*, and *Haemophilus influenzae* more commonly while nontuberculous mycobacteria are secondary pathogens in pulmonary infections.[3] Tuberculosis (TB) has been rarely reported in children with HIES with sporadic report of miliary TB.[4] We present a child with HIES who developed abdominal TB.

Case Report

A 15-year-old boy who had been previously diagnosed to have HIES in view of recurrent skin pustules with dermatitis and elevated serum IgE (IgE = 3943 IU/ml [normal = 10–180 IU/ml]) along with skin biopsy suggestive of lymphomatoid papulosis presented with recurrent abdominal pain and fever 3 months ago. Ultrasound (USG) of the abdomen showed multiple mesenteric lymphadenopathy, and Mantoux test was positive (25 mm). He was started on four drugs for antituberculous therapy consisting of isoniazid (H), rifampicin (R), ethambutol (E), and pyrazinamide (Z) for 2 months and then HR as continuation phase. However, the child stopped antituberculosis treatment (ATT) after taking it only for 3 months. He had no loss of weight or appetite. He then again had pain in the abdomen and presented to us for further management. On examination, his weight was 24 kg, height was 134 cm, and he had pallor and papular dermatitis all over the skin. On systemic examination, he had mild tenderness in the periumbilical region. Investigations showed hemoglobin of 8.9 mg/dl, white blood cell count of 8100/cumm (58% polymorphs, 35% lymphocytes, 5% eosinophils, and 2% monocytes), erythrocyte sedimentation rate of 77 mm at the end of 1 h, and platelets of 238,000/cumm. USG of the abdomen showed multiple mesenteric lymph nodes with largest being 1.6 cm × 1.4 cm. His urine showed albuminuria with microscopic hematuria. A repeat serum IgE

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was elevated (8856 IU/L). HIV ELISA was negative. He was started on four drugs for ATT (HRZE), and urine was obtained for *Mycobacterium tuberculosis* culture. He is currently on follow-up.

Discussion

HIES has two basic forms - autosomal dominant and autosomal recessive.

Natural human immunity to mycobacteria group relies on the functional interleukin-12/23-interferon-gamma integrity of macrophages connecting to T-lymphocytes/natural killer cells. Patients with severe forms of primary immunodeficiency diseases have more profound immune defects involving this circuit, as seen in severe combined immunodeficiency, complete DiGeorge syndrome, X-linked hyper IgM syndrome, CD40 deficiency, chronic granulomatous disease, and HIES.[5] TB has not been reported commonly in patients with HIES. A study shows that NTM infections are more common in HIES patients with structural airway disease. In the absence of predisposing airway changes, NTM infections were not found in HIES patients, suggesting that susceptibility to pulmonary NTM in HIES may be more related to airway than immune dysfunction. An alternate explanation is the severity of immune dysfunction, through recurring infections, predisposes both to the severity of the structural lung disease and NTM disease.[2] Our patient was diagnosed to have abdominal TB based on the presence of mesenteric nodes, a positive Mantoux test, and previous response to anti-TB therapy. We do not have bacteriological confirmation of TB as the lymph node biopsy was not undertaken in our patient. Our patient did not have previous recurrent chest infections which could predispose to structural lung disease and thus he did not have pulmonary TB.

The diagnosis of HIES can be made based on a combination of clinical and laboratory findings for both types of HIES. An elevated level of serum IgE is a virtually universal finding in these patients. Clinically, patients usually present with recurrent skin and lung infections, in the form of abscesses, dermatitis, or pneumonia. A strong clinical suspicion followed by laboratory investigations points to a diagnosis of HIES. Mutational analysis helps distinguish between the two forms of HIES.[6] Our patient had clinical features of skin involvement and elevated IgE levels with recurrent skin infections suggestive of HIES. We have not been able to do mutation analysis in our patient due to nonavailability of test.

Therapy of HIES remains largely supportive. Antibiotic prophylaxis with trimethoprim-sulfamethoxazole is frequently used as prophylaxis against recurrent respiratory infections. Treatment of skin conditions such as eczema and skin infections is an important component of HIES management. While there is no established guideline for the treatment of TB in primary immunodeficiencies, a case report of disseminated NTM in a patient with HIES mentions that treatment with standard combination therapy for TB for a period of 12 months is indicated.[7] Another case report of miliary TB in HIES was successfully treated with first-line ATT drugs.[4] The role of interferon-gamma, granulocyte-colony stimulating factor, or other immune modulators in HIES is unproven. Bone marrow transplantation (BMT) is curative for autosomal-recessive HIES with DOCK8 deficiency and it is recommended. Autosomal-dominant HIES patients do well with intensive therapy and supportive care, and BMT is not recommended for those individuals.[6] Our patient was started on ATT and was subsequently lost to follow-up.

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Conflicts of interest

There are no conflicts of interest.

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