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CASE REPORTS

Diffuse Large B-Cell Lymphoma and Job's Syndrome: A Case Report

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ABSTRACT

Job's syndrome or hyperimmunoglobulin E syndrome (HIES) is a rare primary immunodeficiency. Characterized by recurrent pulmonary and skin infections with elevated IgE serum level, this syndrome has been considered a risk factor for lymphoma. Although the majority of cases were diagnosed in childhood, there are still a few cases that were diagnosed in adulthood. It is necessary to recognize these two conditions since the treatment for lymphoma patients with HIES should be adjusted and needs a thorough care. Here we present a case of diffuse large B cell lymphoma in a patient with symptoms of HIES diagnosed during chemotherapy.

Keywords: hyper-immunoglobulin E syndrome, Job's syndrome, non-Hodgkin's lymphoma, DLBCL.

INTRODUCTION

Job's syndrome or hyperimmunoglobulin (Ig) E syndrome (HIES) is a rare primary immunodeficiency characterized by immunodeficiency and somatic features, such as eczema, *Staphylococcus aureus*-induced skin abscesses, recurrent pneumonia with pneumatoceles, *Candida* infections, skeletal/connective tissue defects, and elevated IgE serum levels (>2000 IU/mL) (1, 2). Skin abscesses lack inflammation signs such as warmth, redness and tenderness, so they are called "cold" abscesses (2). The prevalence of HIES is lower than 1:1,000,000 (1). HIES is usually inherited in an autosomal dominant form, and occasionally in the recessive form (2).

Since 1987, this syndrome has been considered a risk factor for cancer, particularly lymphoma (3). There are many reports on Job's syndrome cases developing lymphoma (2-5).

Here we present a case of diffuse large B-cell lymphoma (DLBCL) with symptoms of HIES emerged during chemotherapy, and we review the relevant literature. ❑

CASE PRESENTATION

A 57-year-old woman came to our outpatient clinic with a chief complaint of having a swollen neck. She did not feel comfortable in her neck. Other lymph node enlargements were also found on her axilla and inguinal region. She had fever, night sweat, losing weight, and decreased appetite.

She was examined by computed tomography (CT) scan, which revealed lymphadenopathy (Figure 1). Biopsy was performed and the result showed diffuse large B-cell lymphoma (DLBCL). Immunohistochemistry confirmed the diagnosis of DLBCL).

The patient was given chemotherapy with a full dose of R-CHOP regimen (rituximab plus cyclophosphamide, doxorubicin, vincristine, pred-

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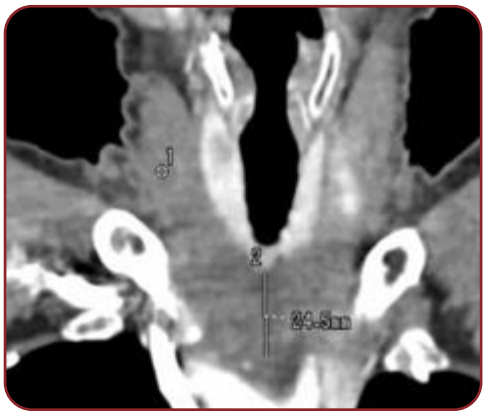

FIGURE 1. Neck CT scan showing lymphadenopathy

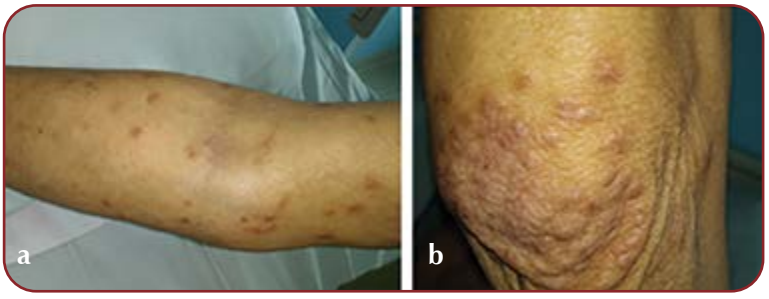

FIGURE 2. Nodular rashes in patient's arm (a) and leg (b)

nisone) for six cycles *per* three weeks. After two cycles, the tumor showed good response against chemotherapy.

After two cycles of chemotherapy, she complained of having urticarial and nodular rashes in extremities, trunk, and even scalp. The patient had a history of recurrent skin infections in the past. She was evaluated by a dermatologist and an immunologist. A high level of IgE was found (9,000 IU/mL). Further evaluations showed no eosinophilia or specific allergen, negative viral hepatitis infection (B and C), negative tuberculosis, and also negative HIV infection. After being assessed as hyperimmunoglobulin E syndrome, she was given topical symptomatic treatments (antibiotics). Complaints were alleviated.

She continued chemotherapy until six cycles, with tight monitoring, and prophylaxis against infection. The final evaluation was conducted with Positron Emission Tomography-Computed Tomography (PET-CT) scan. The result was a complete response. The IgE levels were lowered to 1000 IU/mL. ❑

DISCUSSIONS

We report the case of a patient with diffuse large B-cell lymphoma (DLBCL) who presented with signs of hyperimmunoglobulin E syndrome (HIES) during chemotherapy. Previous reports of HIES patients with DLBCL are summarized in Table 1 (1, 2, 4, 6-8), all of them being diagnosed as having DLBCL with HIES at ages ranging from 17 to 48 years old. They were diagnosed with HIES before presentation with DLBCL manifestations. In our case, the patient has not been diagnosed with HIES before DLBCL was established and she was 57 years old at the time she received the diagnostic of BLBCL with HIES.

The common immunological signs of HIES are chronic eczematoid eruption, recurrent cutaneous and pulmonary bacterial infections, and mucocutaneous candidiasis. Bacterial infections are predominantly due to *Staphylococcus aureus*, and barely *Streptococcus pneumonia* and *Haemophilus* sp. Other infectious manifestations, including sinusitis, otitis, gingivitis, dental abscess, septic arthritis, and osteomyelitis, are also common (9). The classic immunologic triad of HIES, which are

TABLE 1. Summary of previous reports of HIES patients with DLBCL

Age of HIES diagnosis	Age of lymphoma diagnosis	Gender	Site of DLBCL	IgE level (IU/mL)	Citation
nr	46 years old	Male	Cervical LN	8,127	Nester et al. (6)
Childhood	20 years old	Male	Groin LN	11,655	Huber et al. (7)
Early childhood	22 years old	Male	L2 vertebra, spleen	53,480	Leonard et al. (4)
17 months	17 years old	Male	Inguinal LN	3,870	Wallet et al. (8)
Early childhood	44 years old	Male	Inguinal LN	2,000-4,500	Belada et al. (1)
15 years old	48 years old	Male	Parotid	4,000	Kumánovics et al. (2)
57 years old	57 years old	Female	Cervical LN, axilla LN, inguinal LN	9,000	Present

HIES=hyper-immunoglobulin E syndrome; DLBCL=diffuse large B-cell lymphoma; IgE=immunoglobulin E; nr=not reported; LN=lymph node

recurrent staphylococcal cutaneous abscesses, recurrent airway infections, and elevated serum level of IgE (4, 10), are generally found in 85% of patients over eight years old (10). In other case presentations, an IgE serum level that exceeds 2,000 IU/mL (10 times the normal limit) was suggested as an appropriate threshold in establishing a definitive diagnosis (10, 11). However, in 20% of cases, the IgE level may decrease with age, thus a normal IgE level should not exclude the presence of HIES in an adult person (10). In addition, patients with HIES are prone to develop autoimmune disease and malignancies (4, 9). It is estimated that patients with HIES have 259-fold increases in relative risk of lymphoma development compared to general population (4). The increased risk of lymphoma in patients with HIES could be caused by immunodeficiency, immune surveillance impairment, or transformed function of mutant STAT3. Mutant STAT3 would stimulate cell proliferation and survival that would lead tumorigenesis.

In our case, the patient had a history of recurrent cutaneous infections with an elevated IgE serum level. Moreover, she was diagnosed as having DLBCL as well. These were enough reasons to establish the diagnosis of HIES.

Most of HIES patients are diagnosed in childhood as they get recurrent infections. Nevertheless, there is a case reported an undiagnosed HIES until adulthood when getting multiple systemic fungal infections (12). Our patient was evaluated for HIES after developing a generalized cutaneous lesion subsequently to two cycles of full dose chemotherapy for DLBCL. The previous conditions of recurrent skin infection had not been considered part of a primary immunodeficiency. Skin infection was thought to be the infectious complication of lymphoma treatment. As reported by Belada *et al* (1), the critical issue in treatment of HIES patients with lymphoma is serious immunodeficiency as well as history of pulmonary and skin infections with colonization of multi-resistant microbes. It is not recommended to give dose-intensive treatment to these patients because of a high risk of severe infectious complications (1). Our patient had developed infectious complication though she was only given a full dose of the treatment. Intensive supportive care was indeed needed concurrently with chemotherapy. As the skin lesion was ameliorated, the next cycles were continued, certainly with maximal caution. Therefore, it is important to consider the possibility of HIES in lymphoma patients, since it is necessary to give them a tailored therapy and thorough supportive care. ❑

CONCLUSION

Job's Syndrome or HIES is a rare primary immunodeficiency prone to malignancy development, particularly a lymphoma. The symptoms of HIES may be similar to those of other immunodeficiencies, but they should be considered in lymphoma patients. The simultaneous presence of both conditions affects the required treatment and caution should be considered. ❑

Conflicts of interest: none declared.
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