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RESEARCH **CASE REPORT**

The Effectiveness of Omalizumab in the Treatment of Hyper-IgE Syndrome: A Case Report

Raneem Nsour[1*], Aseel Al-Khatib[1], Rama Shannak[1], Ammar Daoud[2]

ABSTRACT

BACKGROUND - Hyper-immunoglobulin E (IgE) syndrome (HIES) is a rare primary multisystem immunodeficiency disorder with an incidence of one case per million population. It is characterized by elevated serum IgE levels, dermatitis, recurrent skin and lung infections, skeletal abnormalities such as scoliosis, and distinctive facial features. Moreover, the clinical manifestations may include vascular, dental, joint, and brain abnormalities. Treatment for HIES predominantly targets symptom relief. Omalizumab, a monoclonal antibody, works by inhibiting the binding of free IgE to receptors on effector cells, consequently reducing the release of inflammatory mediators and alleviating some cutaneous and respiratory symptoms of HIES. To date, according to our understanding, no treatment protocol for HIES patients exists in Jordan. To fill this gap, we report our experience using omalizumab and intravenous immunoglobulin (IVIG) in treating the first documented case of HIES in Jordan.

CASE PRESENTATION - We present the case of an 18-year-old male patient who had been diagnosed with HIES since infancy. The patient had been subjected to multiple treatment trials, but none proved effective. In our treatment protocol, 150 mg of omalizumab was administered subcutaneously every 2 weeks, later increasing to 300 mg. Following this treatment, the eczema symptoms and eosinophil count showed a marked reduction. The patient's IgE level decreased from 21,800 IU/ml in 2011 and 2,039 IU/ml in 2019 to 764 IU/ml in 2022, with treatment commencing in the latter year.

CONCLUSION - The combined use of omalizumab and IVIG therapies demonstrated efficacy in reducing the elevated IgE levels and symptom severity in our patient. There is a need for more case studies to report clinical findings in the management of HIES.

KEYWORDS - Job's syndrome, HIES, Omalizumab, IVIG

[1] Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan

[2] Department of Internal Medicine, Faculty of Medicine, Jordan University of Science and Technology, Irbid 22110, Jordan.

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Corresponding Author:
Raneem Nsour

Faculty of Medicine, Jordan University of Science and Technology,
Irbid, Jordan

Email: rjnsour185@med.just.edu.jo

INTRODUCTION

Hyper-immunoglobulin E (IgE) syndrome (HIES) is a rare primary multisystem immunodeficiency disorder with an incidence of one case per million population. It is characterized by a triad of findings: increased serum IgE level, recurrent skin infection, and pneumonia. The diagnosis of HIES is based on clinical and laboratory findings, with elevated eosinophil and IgE levels of >1,500/ml and >2,000 IU/ml, respectively, being the most common. Blood leukocyte count and the levels of serum immunoglobulins, including IgM, IgG, and IgA, are frequently normal but can be deficient in some cases[1].

STAT3 mutation is the dominant cause of HIES and is characterized by musculoskeletal abnormalities (scoliosis, retained primary teeth, and hyperextensibility), pulmonary abnormalities (recurrent pneumonias resulting in bronchiectasis and pneumatocele), vascular abnormalities, and eczematoid dermatitis [2]. Omalizumab, a humanized recombinant monoclonal antibody that inhibits the binding of IgE to its receptor, which is found on the surface of mast cells and basophils, was used as a treatment for chronic urticaria, atopic dermatitis, mastocytosis, HIES, bullous pemphigoid, Netherton syndrome, urticarial vasculitis, Churg-Strauss syndrome, and toxic epidermal necrolysis[3]. In our study, we aimed to report the effectiveness of omalizumab therapy combined with IVIG for the treatment of HIES as this patient had tried various regimens without success due to intolerance.

In this case report, the clinical presentations, imaging findings, and clinical features are outlined in accordance with the CARE guidelines.

CASE PRESENTATION

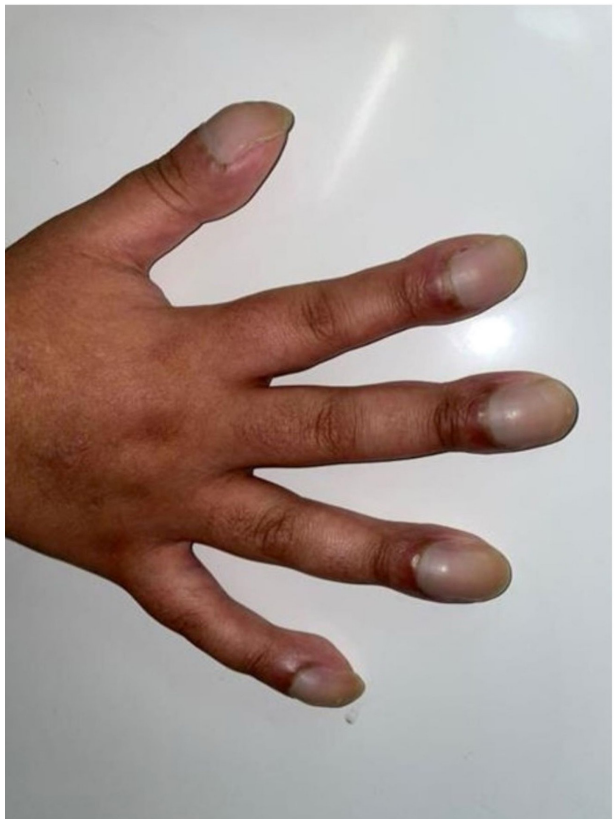
Our patient was an 18-year-old man with no consanguinity reported by his parents. He was born at full term via cesarean delivery for an unknown cause. The family reported that he had a scalp injury at birth, which took months to heal, but had no delay in the separation of the umbilical cord ruling out other causes of immunodeficiencies. At the age of 2 years, the patient started to experience a recurrent chest infection and severe eczema, and it was during this period that he was diagnosed with HIES. At the age of 5 years, his IgE level increased from 140 IU/ml to 21,800 IU/ml, and he had high eosinophils percentage of 33 before the initiation of treatment.

In January 2022, the patient was evaluated at the Immunology Services of the Royal Medical Services and was diagnosed with chronic lung disease characterized by multicystic bronchiectatic changes; chronic eczema that was resistant to conventional therapy; and classical features of HIES, which included stunted growth, skeletal deformities, osteochondroma of the tibia, osteopenia, scoliosis, and joint hypermobility.

However, laboratory tests indicated lymphopenia and eosinophilia, with no signs of anemia. Currently, the patient is on a regimen that includes methotrexate (20 mg weekly), prophylactic fluconazole (due to recurrent fungal infections), Bactrim, mycophenolate mofetil (500 mg twice daily), and prednisolone (25 mg daily) as maintenance therapy.

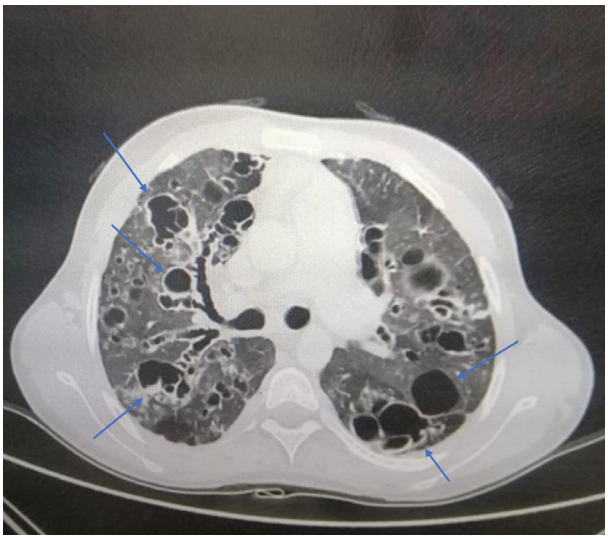
Clinically, our patient had several HIES complications, including characteristic facial features such as facial asymmetry, deep-set eyes, a broad nose, abnormal teething, and prominent skin pores. In addition, his chronic lung disease led to digital clubbing (Figure 1).

Figure 1. Digital clubbing and finger enlargement



Moreover, on high-resolution chest computed tomography, bilateral diffuse extensive cystic, varicoid and bronchiectatic changes with wall thickening and air fluid were observed, indicating bronchiectasis with a mosaic perfusion pattern. In addition, multiple well defined variably-sized thick-walled cavity lesions were seen representing pneumatoceles (Figure 2).

Figure 2. Chest computed tomography image showing pneumatocele and bilateral diffuse cystic and bronchiectatic lung changes with a mosaic perfusion pattern.



In April 2022, the first dose of omalizumab was administered as 2 IV injections, each of 150 mg, followed by 4 months of 0.4g/kg IVIG only. This regimen significantly reduced the IgE levels to 750 IU/ml and resulted in a decrease in the frequency of exacerbations and hospital admissions. However, 3 months later, the drug became unavailable, which led to an increase in IgE level to 32,800 IU/ml.

This case report was limited by the unavailability of a STAT3 mutation test in our institution. However, a JAK2 mutation test was performed, with a negative result. Moreover, no other workup was done for bronchiectasis such as cystic fibrosis, but the patient did not have baseline asthma with allergic bronchopulmonary aspergillosis as we did a fungal culture and smear which turned out negative.

DISCUSSION

As a rare disease with high treatment costs and resource requirements, HIES poses many challenges for both the patient and the healthcare system. Given the ambiguity in diagnostic criteria, the wide range of symptoms, and with clinical molecular genetic testing as the only precise diagnostic method readily available, the National Institutes of Health grading system and a thorough medical history taking can only aid in diagnosis [4].

As it inhibits free IgE receptors from binding to the surface of mast cells, omalizumab has been demonstrated to contribute to the reduction of itchiness, IgE levels, and eosinophil count, without adverse side effects and has been successfully used to treat asthmatics with blood IgE levels between 30-700 IU/ml and minimize their need for steroid medication. Patients with IgE levels of more than 700 IU/ml, as in our patient who has IgE level of 764, found that omalizumab had similar clinical effects to those shown in those with IgE levels between 30 and 700 IU/ml in terms of controlling asthma symptoms and reducing the requirement for systemic corticosteroids[5]. In earlier studies using omalizumab to treat Hyper-IgE syndrome, atopic dermatitis and eczema were the predominant symptoms in the majority of patients. Following treatment with various omalizumab doses, the skin lesions gradually came under control, and IgE levels dropped in most patients [6].

The clinical response can be monitored by therapy response markers such as total serum IgE levels, that showed significant decrease after administration of omalizumab. Basophil levels were also investigated, patients who were treated with Omalizumab experienced an increase in basophil count.

Although C-reactive protein (CRP) is not thought to be a main biomarker for omalizumab treatment response, recent research has revealed that CRP may be elevated in hyper IgE as a result of mast cell activation. Following omalizumab therapy, there was a noticeable drop in CRP levels[7].
We used omalizumab as part of our patient's medical therapy after receiving Institutional Review Board (IRB) approval to evaluate its clinical efficacy. However, no funding was provided, leading to the main issue with this medication, which is its excessive cost and restricted availability of Omalizumab in Jordan. This forced us to stop the administration of omalizumab to our patient.

CONCLUSION

HIES is a hereditary immunodeficiency disorder characterized by recurring boils, sinus and lung infections, and severe rash that appears during infancy, with high IgE levels. In our study, we aimed to investigate the effectiveness of omalizumab for the treatment of HIES. In addition, we administered intravenous immunoglobulin as an adjunct therapy, as it has been proven effective for alleviating increased IgE levels and severe symptoms in HIES. To give significant evidence, however, additional case studies, research and long-term follow-up are still necessary to establish the clinical efficacy of Omalizumab in HIES.

INFORMED CONSENT

Human subjects: Consent was obtained by all participants in this study. Faculty research committee issued approval 140-2022. this is a notification email from electronic research proposal system please note that your proposal number: 140-2022 has been approved by faculty research committee.

AUTHOR CONTRIBUTIONS

RN drafted the manuscript, data collection and lead team supervisor.

RS and AK drafted the manuscript and data collection

AD revised the manuscript and treated the patient.

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