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HYPERIMMUNOGLOBULINEMIA E SYNDROME: CLINICAL CASE REPORT

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ABSTRACT

Hyperimmunoglobulinemia E Syndrome (HIES) is a medical condition that can be sporadic or inherited. It consists of multiple overlapping primary immunodeficiencies and is characterized by a classic triad of elevated immunoglobulin E (IgE) levels, recurrent pneumonias, and skin abscesses. The prevalence of this pathology is 1/1,000,000 live births.

Objective: To describe the clinical case of a patient with Hyper IgE Syndrome who presented in adolescence with skin and respiratory conditions.

Methodology: observational-descriptive study with the report of a clinical case whose discussion was accompanied by pertinent bibliography on the subject. Articles were searched in scientific databases such as PubMed, Elsevier and Springer, taking into account only those articles in English and Spanish, with years of edition after 2018, and that belong to quartiles 1-4. In this work, we report the case of a 22-year-old male patient who was admitted to the pulmonology clinic with a productive yellowish cough of one month accompanied by dyspnea, after performing diagnostic imaging tests, bronchiectasis was obtained as findings, so the etiological investigation of the same was initiated and after this the diagnosis of Hyperimmunoglobulinemia E Syndrome was made.

Keywords: Hyperimmunoglobulinemia/ Immunoglobulin E/ pulmonary/ bronchiectasis

INTRODUCTION

Hyperimmunoglobulinemia E syndrome (HIES) was first described by Davis and Wedgwood in 1966 in two girls suffering from recurrent staphylococcal abscesses, pneumonia, andeczemaA neonatal-onset study was characterized in 1972 by Buckley, who found that these abscesses and chronic eczema were associated with exceptionally high serum IgE concentrations (1,2). This pathology It has an incidence of less than 0.001% and a prevalence of 1 to 9 cases per 1,000,000 inhabitants, in addition,

it maintains a male-female ratio of 1:1, has been reported in different ethnic groups and is likely to appear in subsequent generations within the same family (1,3)

This immunodeficiency is of unknown etiology, with multisystem impact, caused by dominant mutations in the gene encoding the transcription transducer and activator protein (STAT-3), thus generating a deficit of Th17 cells, thus explaining the susceptibility of these patients to infections (4,5).

This syndrome is a primary immunodeficiency disorder characterized by a triad of increased immunoglobulin E, skin lesions and infections in the respiratory system causing pneumatoceles and bronchiectasis, these being the main particularities through which a diagnosis can be achieved since recurrent pneumonia and abnormal scarring lead to severe destruction of the lung parenchyma (6,7). It is classified into two types: I (autosomal dominant: irregularity in various organs) and II (autosomal recessive: directly affects the immune system, high levels of IgE, infections in the respiratory system and skin) (8).

HIES is difficult to diagnose since not all patients show obvious characteristics, as a result of this, doctors can confuse HIES with common lung infections, which is why reaching the diagnosis is a challenge, in addition, the treatment for these patients currently requires multidisciplinary management and the prognosis is still to be investigated in its entirety.

CASE REPORT

A 25-year-old male patient with a history of pneumonia complicated with empyema at the age of 6 years, during his childhood and adolescence with a history of recurrent eczema in the upper limbs, recurrent boils in the frontal region and submental abscesses. At the age of 14 years, he presented a new picture of pneumonia complicated with empyema requiring admission to the Intensive Care Unit (ICU) and osteomyelitis of the dorsal spine due to *Staphylococcus aureus.*

She was referred to the Pulmonology Department by the Internal Medicine Department because she presented with a productive yellowish cough of one month of evolution accompanied by dyspnea MMRC 1. On physical examination saturating 90% of the ambient air, on auscultation wheezing in the right lung field and preserved vesicular murmur in both lung fields. A chest X-ray was performed, which showed a cavitary lesion in the right lung field, for which a chest computed tomography (CT) scan was requested (Figure 1).

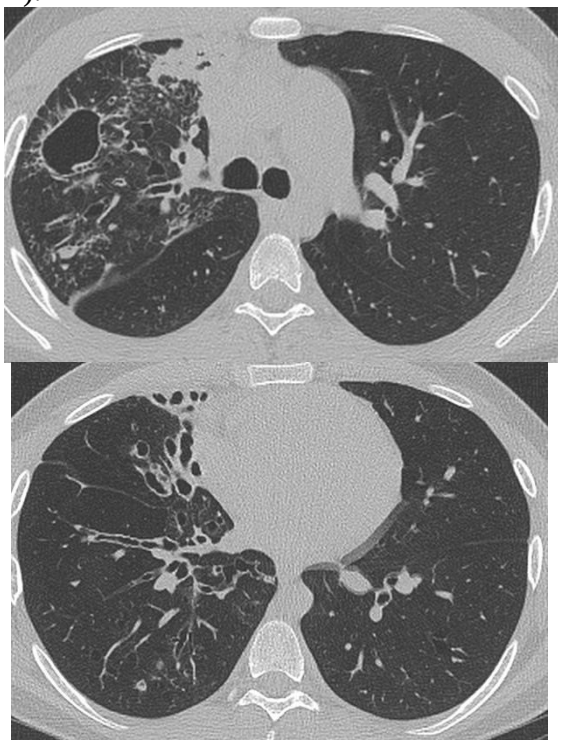

Fig 1: Compressive axial tomography (CT) sagittal multiplanar reconstruction. Retrieved from the HVCM Imaging System

The CT scan reported: cylindrical bronchiectasis and localized variations in the right upper lobe, middle lobe and lower lobes of right predominance; marked peribronchial thickening was observed. Small area of condensation in the anterior segment of the right upper lobe. Cavitary image with drainage bronchus in the right upper lobe. No mediastinal lymphadenopathy.

After this, it was decided to admit the patient to hospital and bronchoscopy with alveolar lavage of the right upper segment was performed. Growth of multisensitive *Serratia marcescens* and *Staphylococcus aureus* is observed in bronchoalveolar lavage cultures. Antibiotic therapy was started for 14 days with levofloxacin and clindamycin with a good clinical response, finally due to persistent cough, an inhalation corticosteroid (Fluticasone) was added to the medication at a dose of 250 mcg 1 puff every 12 hours.

In view of the diagnostic doubt and as part of the etiological investigation of bronchiectasis, serological tests, rheumatogram and immunoglobulins were requested, within which an IgE of 2500 IU/ml was obtained (normal range <= 100 IU/ml)

Finally, due to the history of recurrent infections, both of the skin and at the respiratory level accompanied by high levels of IgE, a diagnosis of Hyperimmunoglobulinemia E Syndrome was established as the cause of bronchiectasis, so it was decided to refer to the Hematology service, after the assessment of the patient by this service, suggests starting treatment with immunoglobulin G at a dose of 30 g every 4 weeks and prophylactic doses of cotrimoxazole 3 times a week.

At the end of the multidisciplinary management established by the Pulmonology and Hematology services, the patient showed a clear improvement in both pulmonary function and radiological function (Figure 2), so it was decided to discharge the patient with follow-up by outpatient consultation.

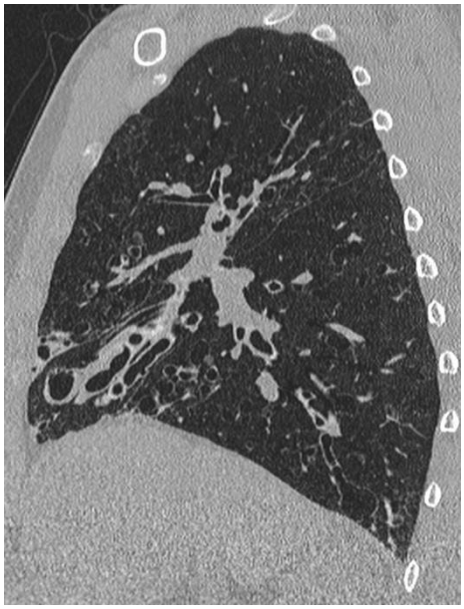

Fig 2: Computed Axial Tomography (CT)
Retrieved from the HVCM Imaging System

The CT scan reported: decreased peribronchial thickening remaining in the middle lobe. The area of condensation described in the previous study is not visible. The cavity in the upper lobe decreased in size in the contemporary study.

EVOLUTION

Currently, at 25 years of age, the patient is in good general condition, persists with skin lesions, however, he does not present new respiratory exacerbations and continues to receive monthly immunoglobulin G at a dose of 600 mg/kg and is being monitored by the corresponding services.

DISCUSSION

Hyperimmunoglobulinemia E syndrome is an uncommon primary immunodeficiency, characterized by a triad of elevated IgE levels, eczema, and skin and lung infections, which result in structural damage to the lung and decreased lung function, these manifestations according to Kasuga et al. (9) are quite common during childhood. mentioning that, before 18 months, practically all patients with this pathology have eczematous dermatitis of papulo-pustular morphology type folliculitis, frequently impetiginized by *Staphylococcus aureus*, on the face, neck, shoulders, armpits and trunk, so that cutaneous manifestations are usually the first clinical finding to establish the diagnosis of this pathology, which is what happened with the patient in the clinical case At the age of 6, he presented with skin lesions and complicated pneumonia (9,10).

Mayne et al. (11) in their study entitled Hyper IgE syndrome: atopic dermatitis as first manifestation: Case report, mentions the association with negative dominant mutations in the STAT3 gene, which is responsible for participating in the signaling of cytokines, growth factors and hormones, the consequence of the loss of function of this gene concludes in the interruption of the differentiation of T helper lymphocytes 17 (11,12).

Cedano et al. (13) mention that human keratinocytes and bronchial epithelial cells are deeply dependent on the synergistic action of Th17 lymphocytes for the production of antistaphylococcal factors, including neutrophil-recruiting chemokines and antimicrobial peptides, thus losing the ability to act against bacteria such as *Staphylococcus aureus* and fungi such as *Candida albicans*, answering why bacterial infections occur selectively in the skin and lungs of patients with HIES (13).

The diagnosis of this pathology is based on clinical findings, laboratory tests that in most cases include elevated levels of eosinophilia in approximately 90% of patients and markedly high levels of IgE, which is what could be observed in the patient's laboratory tests, in addition genetic tests can be used to confirm this syndrome if they are available. Shimizu et al. (14) mentions that the diagnosis is usually late because the infections are usually afebrile and without signs of inflammation, however, Toribio et al (15) allege that recurrent pneumonia is the most frequent pulmonary manifestation and with which a diagnosis can be initiated, since these lesions evolve with irreversible damage. causing lesions such as pneumatoceles and pulmonary bronchiectasis, which is what happened with the patient in the aforementioned clinical case, where we observed that the chest CT scan reported bronchiectasis that were the basis for initiating the diagnostic investigation of HIES (14,15).

Currently, there is no specific treatment for these patients and only symptomatic treatments are used, however, the initial management is broad-spectrum empirical antibiotic therapy covering MRSA and high-dose intravenous immunoglobulin (IVIG) replacement (15). This treatment coincides with the management given to the patient, since antibiotic therapy was started in a timely manner and after diagnosis, intravenous immunoglobulin therapy was started at a dose of 30 g each month.

Regarding prophylactic treatment, it is important to mention the adequate moisturization of the skin with emollient creams, antihistamines and topical corticosteroids; regarding skin and respiratory infections, cotrimoxazole (2.5 mg/kg of the trimethoprim component twice a day) can be used since it has been shown to be useful in reducing the annual incidence of infections and in turn, It seems to increase the survival of patients, however, several studies mention that since there have been no controlled trials on the duration and frequency of prophylactic treatment, this depends on the doctor

and the patient's condition; At present, the patient in the clinical case has continued to use cotrimoxazole 3 times a week and has not presented new skin lesions (15,16).

Finally, the management of these patients should be carried out in conjunction with a multidisciplinary team, since these patients usually have comorbidities and can develop multiple complications and cause death, so the prognosis is uncertain and is totally dependent on early diagnosis and adequate and timely treatment, as is the case of the patient. who has had a good evolution and continues to comply with their treatment. Currently, research has been mentioned on the use of bone marrow transplantation in order for these hematopoietic precursors to regulate the alterations caused by the altered immune response, in addition, another therapeutic option under study is lung transplantation, however, it is feasible only in those cases in which the patient is immunologically stable and does not present any infection (14,16).

CONCLUSION

In conclusion, Hyperimmunoglobulinemia E Syndrome is a rare primary immunodeficiency, characterized by elevated levels of IgE and skin and lung infections, which end in both functional and structural damage to the lungs, resulting from a mutation associated with the STAT3 gene.

It is important to bear in mind that this pathology is uncommon so it is necessary to determine the different clinical manifestations that these patients present from childhood and even from breastfeeding, in some cases patients do not present any symptoms and the diagnosis is reached incidentally, however, most begin with cutaneous and respiratory manifestations from an early age, as is the case in question.

Therefore, HIES is still a diagnostic challenge in the health environment due to its high complexity, therefore, it is necessary to establish a comprehensive and multidisciplinary management to treat patients suffering from this pathology, therefore, it is necessary that both medical staff and researchers continue to study the different possible diagnostic and therapeutic methods for the different complications suffered by these patients. All this with the aim of improving their quality of life.

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