Revista ARACÊ
ISSN: 2358-2472

# ASSOCIATION BETWEEN HYPER-IGE SYNDROME AND SWYER-JAMES-MACLEOD SYNDROME IN A PEDIATRIC PATIENT: A CASE REPORT

https://doi.org/10.56238/arev6n3-317

**Submission date:** 10/25/2024 **Publication date:** 11/25/2024

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## ABSTRACT

Introduction: Hyper-IgE Syndrome, also known as Job's Syndrome, is a rare immunological condition characterized by elevated levels of immunoglobulin E (IgE), which is associated with recurrent skin and lung infections, as well as skeletal abnormalities. Since its initial description in 1966, this syndrome has challenged clinical management, especially due to the persistence of skin abscesses and Staphylococcus aureus infections. Swyer-James-MacLeod Syndrome, or Hyperlucent Lung, is a lung condition associated with respiratory infections in childhood, which results in changes in pulmonary vascularization and ventilation. This study aims to explore the relationship between these two syndromes in a pediatric patient. Objective: To document and discuss the care path of an eight-year-old child diagnosed with Hypergammaglobulinemia E and Hyperlucent Lung Syndrome, contributing to the understanding of the interactions between these rare conditions. Methods: This study consists of a descriptive case report based on the retrograde analysis of the medical records of L.F.C., a patient treated at a university hospital. The analysis included clinical, laboratory and imaging information, as well as therapeutic interventions performed. Data were collected systematically, ensuring the inclusion of information on recurrent infections and the manifestations associated with each syndrome. Clinical evaluation included a detailed physical examination and laboratory tests to quantify immunoglobulin levels. Imaging tests, such as chest CT scans and lung scans, were performed to assess for the presence of hyperlucency and perfusion changes. Results: L.F.C. had a history of recurrent infections, including twelve episodes of pneumonia, with complications such as septicemia and pleural effusions. Cultures of cutaneous abscesses identified Staphylococcus aureus, corroborating the infectious profile of hyper-IgE. The patient's IgE levels exceeded 2000 U/mL, and pulmonary hyperlucency was confirmed by tomography. Treatment included antibiotics and corticosteroids in high doses. Conclusion: This case illustrates the complexity and interconnection between Hyper-IgE Syndrome and Swyer-James-MacLeod Syndrome, highlighting the importance of a comprehensive diagnostic approach and clinical surveillance in children with a history of recurrent infections. Early detection of pulmonary complications and appropriate therapeutic interventions are crucial to minimize long-term impacts on respiratory health and quality of life. This study contributes to the understanding of the interactions between these rare syndromes and reinforces the need for more research to explore their associations.

**Keywords:** Hyper-Ige Syndrome. Swyer-James-Macleod syndrome. Hypergammaglobulinemia E. Recurrent Infections. Paediatrics.

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ISSN: 2358-2472

## INTRODUCTION

Hyper-IgE Syndrome, also known as Job's Syndrome, is a rare immunological condition that was first described in 1966 and characterized by abnormally high levels of immunoglobulin E (IgE), associated with recurrent skin and lung infections, as well as skeletal and connective tissue abnormalities. This complex clinical picture poses a challenge for treatment, especially due to the presence of "cold" skin abscesses that become persistent and are often associated with *Staphylococcus aureus* infections (Davis et al., 1966). Since the first reports, researchers have sought to better understand this syndrome, which significantly impacts the quality of life of patients and has high rates of morbidity and mortality due to recurrent infections and the resulting complications (Freeman et al., 2007; Hafsi & Badri, 2019).

The manifestation of Hyper-IgE occurs in two main forms: autosomal dominant and autosomal recessive. The dominant form is usually more severe and may include skeletal changes, while the recessive form is often associated with autoimmune diseases. In both, however, there is a consistent pattern of recurrent infections, including sinusitis, pneumonia, and otitis media, which often begin in the first months of life. These persistent infections can significantly compromise lung function and, in the long term, predispose the patient to irreversible tissue damage, including bronchiectasis and other lung structural abnormalities (Sowerwine et al., 2012; Chamlin et al., 2002).

Among the pulmonary complications related to Hyper-IgE, Swyer-James-MacLeod Syndrome, or Hyperlucent Lung Syndrome, stands out, a rare lung condition characterized by unilateral hyperlucency, which can be identified through imaging tests, such as chest X-ray or CT scan. This syndrome, discovered in 1953, is frequently associated with recurrent respiratory infections in childhood, which interfere with normal parenchymal development and pulmonary vascularization, resulting in areas of hypoperfusion and impaired ventilation. Thus, patients with this condition have a lung with reduced vascularization, which contributes to a hyperlucent appearance and, often, to bronchiectasis in the affected lung (Miguel et al., 2014; Machado et al., 2019; Turcu et al., 2018).

The relationship between Hyper-IgE and Hyperlucent Lung syndromes is still little explored in the medical literature, but some evidence suggests a link between recurrent respiratory infections and pulmonary structural changes. The presence of frequent and difficult-to-treat infections in patients with hyper-IgE can cause an exacerbated inflammatory response, which can cause damage to the lung parenchyma. Over time, these lesions may

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ISSN: 2358-2472

predispose to the development of the pulmonary hyperlucency characteristic of Swyer-James-MacLeod Syndrome, resulting in permanent structural damage that alters ventilation and local perfusion (Santana et al., 2018; Mehra et al., 2017).

The association of these two conditions in a single patient not only brings complexity to clinical management, but also raises important questions for understanding the interaction between the immune system and lung development in individuals with primary immunodeficiencies. Case studies such as this one are valuable to the medical community, as they help to identify potential causal relationships and explore the underlying pathophysiological mechanisms. The detailed description of clinical manifestations, imaging findings, and treatment strategies can help in the understanding and differential diagnosis of these pathologies, contributing to a more assertive and individualized management for patients with these complex clinical conditions (Garg et al., 2011; Abdulla et al., 2017; Damle et al., 2012).

In addition, the clinical variability of Swyer-James-MacLeod Syndrome, which can present asymptomatically to conditions with severe respiratory symptoms, adds a diagnostic challenge for health professionals. The presence of the diagnostic triad of unilateral pulmonary hyperlucency, decreased ventilation, and perfusion is essential for the confirmation of the syndrome. Patients may benefit from conservative therapeutic approaches, such as chest physiotherapy and the use of inhaled corticosteroids, but in severe cases, surgical interventions may be considered (ABATE et al., 2014; DALTRO et al., 2011; Sulaiman et al., 2009).

This case study, by reporting the concomitant occurrence of Hyper-IgE and Hyperlucent Lung in a child, offers valuable insights for the understanding of these rare diseases and contributes to the advancement of clinical practices aimed at the management of immunocompromised pediatric patients. The analysis of the manifestations and clinical evolution described highlights the importance of rigorous and multidisciplinary follow-up, aiming to optimize quality of life and reduce the long-term impacts of respiratory infections and complications associated with Hyper-IgE syndrome (Scullin et al., 2022; DE NARDI et al., 2023; Couillard et al., 2021).

## METHODS

This study consists of a descriptive case report, based on the retrograde analysis of the medical records of a patient treated at a university hospital. The objective is to

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ISSN: 2358-2472

document and discuss the care path of an eight-year-old child diagnosed with two rare conditions: Hypergammaglobulinemia E and Hyperlucent Lung Syndrome. The analysis includes clinical, laboratory and imaging information, as well as therapeutic interventions performed throughout the service.

The medical records were reviewed in search of relevant data that could elucidate the patient's clinical history, including main complaints, history of recurrent infections, results of laboratory and imaging tests, and interventions performed. Data were collected systematically, ensuring the inclusion of information on skin and lung infections, as well as manifestations associated with each syndrome.

The clinical evaluation included a detailed physical examination, where we sought to identify signs of active infections, skin lesions, and respiratory compromise. Laboratory tests were performed to quantify the levels of immunoglobulins, including IgE, IgG, IgA, and IgM, which are crucial for the diagnosis of Hyper-IgE Syndrome. In addition, imaging tests, such as chest computed tomography and lung scintigraphy, were performed to assess the presence of hyperlucency and changes in pulmonary perfusion.

To protect the patient's privacy, names and any identifiers that could reveal his identity were omitted. The study was approved by the Research Ethics Committee of the Federal University of Triângulo Mineiro, under opinion number 5,434,194. The patient and his/her legal guardian signed the terms of assent and free and informed consent, respectively, ensuring compliance with the ethical guidelines established for health research.

The collected data were organized and analyzed qualitatively, aiming at a discussion that could contribute to the understanding of the interactions between Hypergammaglobulinemia E and Hyperlucent Lung Syndrome, in addition to assisting in the clinical management of similar cases.

## RESULTS

L.F.C., an eight-year-old patient, was treated at a university hospital with a main complaint of recurrent infections. On the day of the consultation, the patient exhibited signs of sinusitis, with purulent discharge in one of the ears. In the anamnesis, it was identified that the patient suffered from ear infections since he was three months old, having contracted chickenpox at five months. The clinical history reveals that the child developed pyoderma, laryngitis, otitis and sinusitis recurrently, often accompanied by yellow-green

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ISSN: 2358-2472

phlegm. In addition, L.F.C. presented with chronic eczema on the scalp, characterized by desquamation and the presence of fistulas, as well as frequent episodes of tonsillitis.

The patient recorded a total of twelve episodes of pneumonia, of which three resulted in pleural effusion and one culminated in septicemia. Among the various respiratory infections, L.F.C. also presented episodes of sinusopathy and ozenous rhinitis, always with secretions with a foul odor. The presence of recurrent abscesses on the scalp, which are difficult to treat, was confirmed by cultures that identified *Staphylococcus aureus*. The patient also had three documented episodes of urinary tract infections and four episodes of arthritis, often followed by cellulitis.

On physical examination, the patient presented constant pruritus in the flexor and extensor regions, with hyperchromic lesions that occasionally presented meliaceous secretion and a scaly process on the scalp, also characterized by intense pruritus. At the age of seven, L.F.C. suffered bilateral pneumonia that evolved into an acute abdomen, resulting from a spontaneous perforation of the rectum, resulting in severe septicemia and requiring three subsequent corrective surgeries.

Pulmonary evaluation revealed bilateral diffuse thick rales, with a large amount of secretion, predominant expiratory wheezing on the left, and fine rale on the right. The respiratory rate was elevated, around 52 breaths per minute, with intercostal and furcula retraction, in addition to prolonged expiratory time. Lung scintigraphy showed decreased perfusion and ventilation in the left lung.

A chest CT scan revealed the presence of subpleural bullae at the base of the right lung and hyperlucency of the left lung. Planigraphy showed the presence of pneumatoceles at the base of the right lung, whereas ear tomography revealed chronic otitis media with mastoiditis on the left. Regarding laboratory tests, the immunoglobulin count showed IgG at 1670 mg/dL, IgA at 228 mg/dL, IgM at 226 mg/dL, and IgE at 2130 mg/dL.

Based on the elevated IgE levels and the clinical picture presented, the patient was diagnosed with Hyper-IgE syndrome. In addition, the pulmonary hyperlucency observed on chest CT scans corroborated the diagnosis of Swyer-James-MacLeod syndrome. The treatment instituted included the use of antibiotics and corticosteroids in high doses, aiming to control infections and relieve the symptoms associated with the syndromes diagnosed.

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## DISCUSSION

Hyper-IgE Syndrome, as demonstrated in the case of L.F.C., is a rare immune condition that is characterized by recurrent infections, affecting multiple systems, especially the skin and lungs. The patient, with twelve episodes of pneumonia throughout his clinical history, presents a pattern consistent with the existing literature, which indicates a high rate of morbidity associated with this condition (Freeman et al., 2007). The worsening of respiratory infections is often caused by Staphylococcus aureus, which was identified in the patient's skin abscess cultures, corroborating the infectious profile characteristic of hyper-IgE (Chamlin et al., 2002). Cutaneous manifestations, including chronic eczema and pyoderma, are commonly seen in children with this syndrome, reflecting the complexity of the interactions between immune deficiencies and the clinical presentation of patients (Hafsi & Badri, 2019).

The diagnosis of Hyper-IgE syndrome in L.F.C. was substantiated by elevated serum IgE levels, which exceeded 2000 U/mL, a value that is widely accepted as indicative of the condition (Davis et al., 1966). The prevalence of Hyper-IgE syndrome is considered rare, and the detection of similar cases is essential for advancing knowledge about its complex clinical manifestations and implications for clinical management. The high incidence of infections and complications in childhood requires an aggressive and multidisciplinary therapeutic approach, often involving the use of high-dose antibiotics and corticosteroids, as adopted in this case, in order to control infections and alleviate associated symptoms (Sowerwine et al., 2012; Santana et al., 2018). This approach is essential, since persistent infections can result in chronic complications that significantly compromise the patient's quality of life.

The association of Hyper-IgE Syndrome with Swyer-James-MacLeod Syndrome observed in this case is particularly remarkable. It provides a valuable perspective on the interactions between recurrent respiratory infections and pulmonary structural changes. The pulmonary hyperlucency identified in L.F.C. through imaging tests emphasizes the importance of radiological screening in the evaluation of children with frequent pulmonary infections (Machado et al., 2019). This unilateral hyperlucency can be interpreted as a chronic inflammatory response that, over time, leads to a remodeling of the lung parenchyma and a decrease in vascularization, corroborating previous findings that associate respiratory infections with permanent structural changes (Turcu et al., 2018; Abate et al., 2014). This interaction suggests that Hyper-IgE Syndrome may be a significant

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factor in the pathogenesis of Hyperlucent Lung Syndrome, a hypothesis that deserves to be further investigated in future studies.

Imaging findings, such as reduced perfusion and ventilation in the left lung, are defining features of Swyer-James-MacLeod Syndrome, where inadequate development of pulmonary vascularization results in hyperlucency and respiratory functional impairment (Miguel et al., 2014; Mehra et al., 2017). Early identification of pulmonary alterations in patients with Hyper-IgE may facilitate more effective therapeutic interventions, such as respiratory physiotherapy and corticosteroid administration, which have the potential to minimize the progression of pulmonary complications (Daltro et al., 2011; Sulaiman et al., 2009).

In addition, the clinical variability of Swyer-James-MacLeod Syndrome, which can present asymptomatically or with significant respiratory symptoms, poses a diagnostic challenge for healthcare providers. This asymptomatic presentation can result in late diagnosis and complications that may become irreversible, reinforcing the need for a high index of clinical suspicion, especially in pediatric patients with a history of recurrent infections (Damle et al., 2012; Scullin et al., 2022). The characterization of the clinical manifestations and the analysis of the imaging findings in this case are therefore fundamental to guide the clinical management of patients with these rare conditions.

However, this study also has limitations that should be considered. First, this is an isolated case report, which restricts the generalization of the findings to a larger population. In addition, the analysis was based on retrospective clinical data, which may be subject to reporting bias and incompleteness. Future prospective, multicenter studies are needed to validate the observed associations and further explore the mechanisms underlying the interactions between Hyper-IgE Syndrome and Swyer-James-MacLeod Syndrome. Documenting additional cases and conducting controlled studies will allow for a better understanding of the clinical implications of these syndromes, which may ultimately lead to improvements in treatment strategies and management of pediatric patients with these conditions.

## CONCLUSION

The case report of L.F.C. illustrates the complexity and interconnection between Hyper-IgE Syndrome and Swyer-James-MacLeod Syndrome, highlighting how recurrent lung infections in childhood can significantly contribute to the development of chronic lung

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changes. The patient had a rich clinical history of respiratory and skin infections, characterizing a typical hyper-IgE profile, which culminated in severe episodes, such as pneumonia and septicemia. The diagnosis was corroborated by elevated IgE levels and radiological findings that showed pulmonary hyperlucency, confirming the association with Swyer-James-MacLeod syndrome.

These findings emphasize the importance of a comprehensive diagnostic approach and ongoing clinical surveillance in children with a history of recurrent infections. Early detection of pulmonary complications and the implementation of appropriate therapeutic interventions are crucial to minimize the long-term impacts on the respiratory health and quality of life of these patients. In addition, this study contributes to the understanding of the interactions between these rare conditions, suggesting that hyper-IgE may play a central role in the pathogenesis of lung abnormalities such as hyperlucency, a topic that deserves further investigation in future research.

In summary, the documentation of cases such as that of L.F.C. is essential to improve knowledge about Hyper-IgE Syndrome and its association with Hyperlucent Lung Syndrome, stimulating better information in the medical community and the promotion of more effective clinical management for patients affected by these complex conditions.

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