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One-lung Ventilation in a Child with Hyper-IgE Syndrome

Arianna De Matteis[1*], Paolo Palma[2], Francesca Stoppa[3], Raffaele Badolato[4], Alessia Scarselli[1], Patrizia D'Argenio[1], Corrado Cecchetti[3], Renato Cutrera[5], Alessandro Inserra[6], Nicola Pirozzi[3], Caterina Cancrini[1]

[1]Unit of Immune and Infectious Diseases, University Department of Pediatrics (DPUO), Bambino Gesù Children's Hospital, Rome, Italy

[2]Research Unit in Congenital and Perinatal Infection, Unit of Immune and Infectious Diseases, University, Department of Pediatrics (DPUO), Bambino Gesù Children's Hospital, Rome, Italy

[3]PICU, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy

[4]Pediatrics Clinic and Institute for Molecular Medicine A. Nocivelli, Department of Clinical and Experimental Sciences, University of Brescia, ASST-Spedali Civili of Brescia, Brescia, Italy

[5]Pneumology Unit - University Hospital Pediatric Department, Bambino Gesù, Children's Hospital, IRCCS, Rome, Italy

[6]Department of Surgery, Bambino Gesù Children's Hospital, Rome, Italy

[*]**Corresponding author:** Arianna De Matteis, Unit of Immune and Infectious Diseases, University Department of Pediatrics (DPUO), Bambino Gesù Children's Hospital, Piazza Sant' Onofrio, Rome, Italy. Tel: +39 3421575545; Email: ari.dematteis@gmail.com

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Abstract

A four years old female affected by AD-HIES was hospitalized for streptococcal right pneumonia with pleural effusion and pneumatocele. Despite multiple antibiotic therapy and Igev she developed massive right hydropneumothorax. Pleural drainage was positioned, and surgical toilette was done. A conservative approach with one-lobe ventilation, chosen in order to allow pleural healing, caused the re-expansion of right lung. STAT3 mutation leads likely to pyogenic pneumonia and to abnormalities in tissue remodeling after surgical intervention, so a conservative approach is recommended. In our case prolonged antibiotic therapy, chest drainage and one lung ventilation allowed to avoid pneumonectomy preserving respiratory function.

Keywords: Hyper-IgE syndrome; One lung ventilation; Pneumococcal pneumonia; Pneumothorax

Text

AD-HIES (Autosomal Dominant Hyper-IgE Syndrome) is a complex primary immunodeficiency, caused by heterozygous mutations in STAT3 (Signal transducer and activator of transcription 3) gene. It displays susceptibility to bacterial and fungal infections, allergic diseases, immunodysregulation and predisposition to develop EBV proliferation. This clinical phenotype derived from a complicated immunodeficiency characterized by hypereosinophilia, high serum IgE and IgD levels, variable alteration in T and B cell phenotype with low Th17 and defective follicular Th cells. STAT3-deficient patients also show abnormalities in multiple systems, including skeletal/dental, connective tissue and central nervous system. Treatment is symptomatic, even if recently Hematopoietic Stem Cell Transplantation(HSCT) has been reported to be a possible therapeutic strategy in STAT3 patient developing lymphoma. Here we reported a child with AD-HIES and severe pneumococcal pneumonia complicated with tension pneumothorax that required multidisciplinary management.

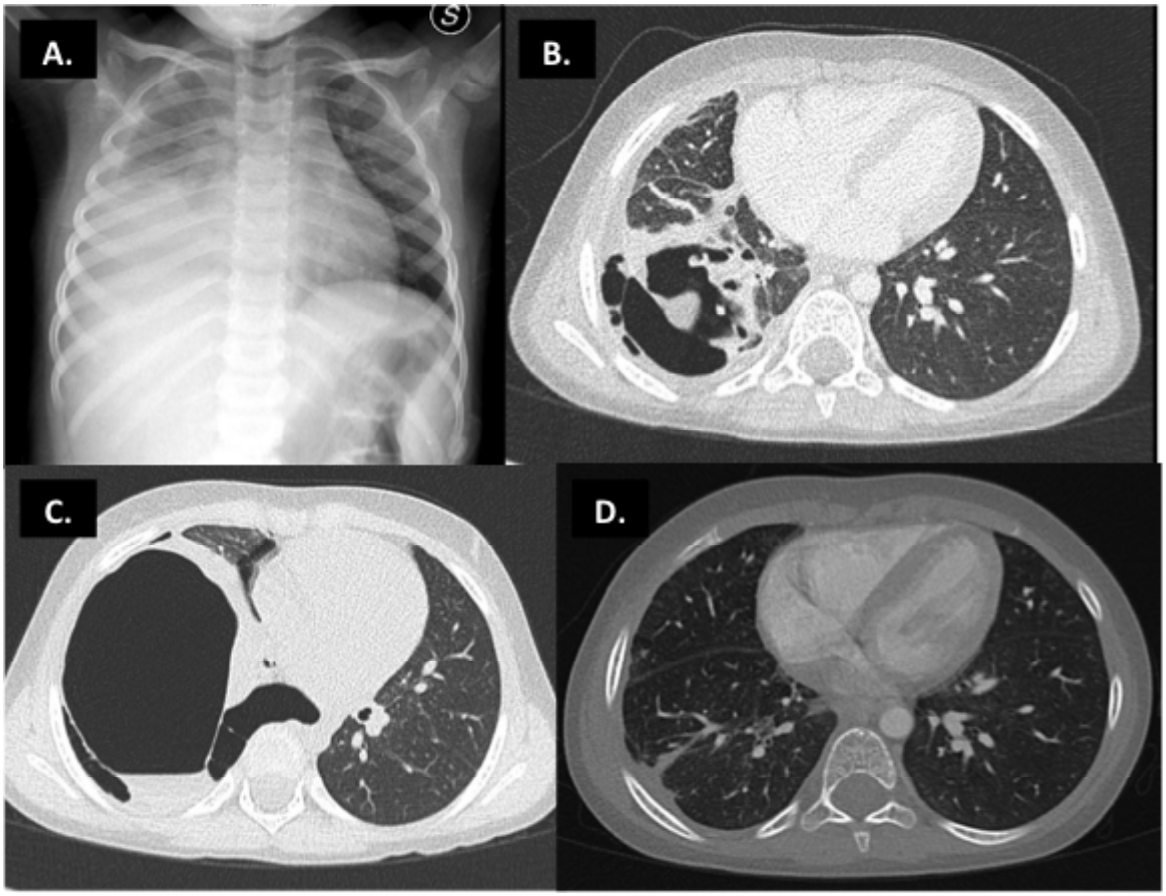
A three-years old child came to our attention due to refractory dermatitis since first months of life, recurrent upper respiratory infections and dysmorphic facial features. Her family history was not relevant. Hematological and immunological investigations revealed normal counts of polymorphonuclear neutrophils and eosinophils. IgE level was significantly elevated (> 5000 KU/L), with normal IgG, IgM and IgA levels but incomplete specific

response to pneumococcal vaccine after booster. However specific responses after pneumococcal and measles vaccinations were absent. A reduction of memory B and naïve T cell subsets was found, while *in vitro* lymphocyte proliferation to OKT3 and PHA as well as B lymphocyte proliferation, differentiation and Ig production upon CpG were normal (Table): low levels of IL-17 were detected as reported in these patients. Diagnosis of hyper-IgE syndrome was confirmed by genetic analysis that revealed the presence of heterozygous mutation in STAT3 gene (R382Q). It's the most prevalent mutation affecting DNA-binding domain, related to recurrent cold skin abscesses and pneumonia, lung cyst formation, eczema and recurrent upper respiratory infection.

	Value at diagnosis	Normal value
White blood cells (10^3/µL) - Neutrophils - Lymphocytes - Eosinophils - Monocytes - Basophils	5.73 2.09 2.75 0.17 0.38 0.09	5.50-15.00 1.65-8.25 2.20-8.55 0.00-1.05 0.19-1.65 0.00-0.22
Lymphocyte subset (#/µL / %) - CD3+ - CD4+ - CD8+ - CD19+ - CD16+CD56+	 2123/77.2% 1152/41.9% 693/25.2% 324/11.8% 280/10.2%	 1578-3707/59.7-77.6 870-2144/31.1-47.4 472-1107/16-26.9 434-1274/12.9-29.2 155-565/4.8-16.2
Immunoglobulin - IgG (mg/dl) - IgA (mg/dl) - IgM (mg/dl) - IgE (kU/L)	 1059 167 198 >5000	 463-1710 27-173 62-257 <100
Anti-Pneumococcus ab (mg/L)	27*	>35
T phenotype (%) - CD4+CD45RA+ - CD4+CD45RO+ - CD8+CD45RA+ - CD8+CD45RO+	 25.1 16.8 14.1 11.1	 53-86 9-26 69-97 4-16
B phenotype (%) - $IgM^{hi}CD38^{hi}$ (Transitional) - CD27- (Mature) - CD27+ (Memory) - IgM- $CD38^{hi}$ - (Plasmacell)	 20.9 61.2 4.5 13.4	 3.1-12.3 62.9-92.2 7.8-31.7 0.6-4
*Absence of response after booster dose of pneumococcal conjugated vaccine		

Table: Immunological examination at diagnosis.

At 4 years old she was hospitalized for pneumonia. Laboratory findings revealed neutrophilia, lymphopenia and an increase in inflammatory markers. Chest X-ray showed right lower lobe opacity associated with pleural effusion (Figure A), promptly treated by intravenous Piperacillin/tazobactam, subsequently associated with Meropenem and Vancomycin; due to the persistence of pleural effusion a chest drainage was positioned. During hospitalization therapy with monthly endovenous immunoglobulin (Igev) was started. After the evidence of Streptococcus pneumoniae by real time Polymerase Chain Reaction (PCR) made on pleural effusion intravenous therapy with Linezolid and Rifampicin was started, determining a progressive clinical improvement. Chest CT (Computer Tomography) showed the persistence of right lower lobe consolidation associated with cystic lesion and multiple bronchopleuralfistula (Figure B). Later her clinical conditions deteriorated with fever, severe dyspnea, chest pain and retches associated with massive right hydropneumothorax evidenced by chest CT (Figure C). Microbiological examination confirmed the persistence of *Streptococcus pneumoniae* in pleural effusion. Antibiotic therapy with Linezolid and Levofloxacin was started; pleural drainage was positioned and later surgical toilette with closure of main bronchopleural fistula was done without reduction of pleural air collection. In view of the several pneumatoceles and of the bronchopleural fistula surgical resection and talc pleurodesis were considered but excluded in order to avoid more likely severe complications in these patients with immune dysregulation. Thus, the option of one-lobe ventilation was attentively considered by multidisciplinary team and successfully performed. Pre-extubation chest CT showed re-expansion of right lung (Figure D). Due to prolonged immobilization and thrombophilic predisposition determined by mutation of Methylenetetrahydrofolate reductase (MTHFR) gene, she presented thrombosis of left ilio-femoral vascular axis, necessitating anticoagulant therapy, and a sepsis by *Candida tropicalis* likely treated with Liposomal Amphotericin B and Caspofungin.



Figures(A-D) A. Chest radiograph. Right lower lobe opacity associated with pleural effusion. **B.** Chest CT, pulmonary window. right lower lobe consolidation associated with cystic lesion and bronchopleural fistula. **C.** Chest CT, pulmonary window. Right hydro-pneumothorax with left shift of mediastinum and with collapsed and dislocated right lung. **D.** Chest CT, pulmonary window. Re-expansion of right lung.

She was dismissed after three months of hospitalization in fairly good clinical condition and she continued therapy with Fluconazole for 9 months. Currently she is 7 years old and she continues prophylaxis with subcutaneously immunoglobulin (Igsc) has mild cutaneous infection and upper respiratory infection.

STAT3 has a significant impact on development Th17 cells, which are critical in the clearance of fungal and extracellular bacterial infections. Bronchial epithelial cells were more dependent on Th17 cytokines (IL-17 and IL-22) for the production of antibacterial factors. Despite immunization with antipneumococcal conjugated vaccine our patient does not have a specific response and developed a severe pneumococcal infection with complications. Considering the inability to produce specific antipholisaccarides response, due to defective IL-10 and IL-21 signaling which are related to a reduction of B memory cells predisposing to bacterial infection and to a lower response to vaccine in these patients Igev prophylaxis should be strongly considered at the diagnosis. Complications associated with pulmonary infections are one of the most common causes of death in patients with HIES. Late diagnosis leads to significant impairment of patients' respiratory function and reduces the chances for normal development in child. The optimal clinical management of lung parenchymal abnormalities in AD-HIES is not yet known. Authors demonstrated that lung surgery in this syndrome is associated with high complications, such as persistence of bronchopleural fistula and severe pleural effusion difficult to manage. Abnormal activation of cytokine signaling, and an increasing risk of chronic inflammation triggered by invasive proceedings should be considered to limit surgical options that should be considered only in the setting of severe symptoms. In our case we have chosen a conservative approach, based on prolonged antibiotic therapy, chest drainage and one lung ventilation. This invasive technique, mainly used during thoracic surgery in oncologic patients, never described in literature for AD-HIES patients, determined a complete resolution of the pneumothorax avoiding the risk of surgical intervention and preserved respiratory function.

Nowadays the treatment for AD-HIES include aggressive medical or surgical management for infections and prophylactic antibiotic and Ig therapy. HSCT are reported only in few cases and outcomes are mixed. It has been demonstrated that HSCT in AD-HIES patients with lymphoma can restore immunological alterations and might delayed or halted the other abnormalities of the syndrome.

It is reasonable to consider early HSCT as therapy in severe AD-HIES, in order to prevent some of the serious complications and to improve the quality of life, even if pulmonary defects determined by infections could not be restored.

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Conflict of Interest

The other authors have no conflicts of interest to disclose.

Clinical Trial Registration

None.

References

1. Chandesris MO, Melki I, Natividad A, Puel A, Fieschi C, Yun L, et al. (2012) Autosomal dominant STAT3 deficiency and hyper-IgE syndrome: molecular, cellular, and clinical features from a French national survey. Medicine (Baltimore) 91: e1-19.

2. Farmand S, Sundin M (2015) Hyper-IgE syndromes: recent advances in pathogenesis, diagnosis and clinical care. Curr Opin Hematol 22: 12-22.

3. Freeman AF, Renner ED, Henderson C, Langenbeck A, Olivier KN, Hsu AP, et al. (2013) Lung parenchyma surgery in autosomal dominant hyper-IgE syndrome. J ClinImmunol 33: 896-902.

4. Gennery AR, Flood TJ, Abinun M, Cant AJ (2000) Bone marrow transplantation does not correct the hyper IgE syndrome. Bone Marrow Transplant 25: 1303-1305.

5. Jhaveri KS, Sahani DV, Shetty PG, Shroff MM (2000) Hyperimmunoglobulinaemia E syndrome: pulmonary imaging features. Australas Radiol 44: 328-330.

6. Jończyk-Potoczna K, Szczawińska-Popłonyk A, Warzywoda M, Bręborowicz A, Pawlak B (2012) Hyper Ig E syndrome (Job syndrome, HIES) - radiological images of pulmonary complications on the basis of three cases. Pol J Radiol 77: 69-72.

7. Liu JY, Li Q, Chen TT, Guo X, Ge J, Yuan LX (2011) Destructive pulmonary staphylococcal infection in a boy with hyper-IgE syndrome: a novel mutation in the signal transducer and activator of transcription 3(STAT3) gene (p.Y657S). Eur J Pediatr 170: 661-666.

8. Patel NC, Gallagher JL, Torgerson TR, Gilman AL (2015) Successful Haploidentical Donor Hematopoietic Stem Cell Transplant and Restoration of STAT3 Function in an Adolescent with Autosomal Dominant Hyper-IgE Syndrome. J ClinImmunol 35: 479-485.

9. Nester TA, Wagnon AH, Reilly WF, Spitzer G, Kjeldsberg CR, et al. (1998) Effects of allogeneic peripheral stem cell transplantation in a patient with job syndrome of hyperimmunoglobulinemia E and recurrent infections. Am J Med 105: 162-164.