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CASE REPORT

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Intrapleural therapy for pleural infection from bronchopleural fistula in an adult with hyper-IgE syndrome

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Abstract

We presented the case of an adult patient with hyper-IgE syndrome (HIES) who was admitted acutely with a large hydropneumothorax from lung consolidation, a bronchopleural fistula and pleural infection. He has had recurrent pulmonary and skin infections since childhood and longstanding pneumatoceles. He was treated with systemic antibiotics and chest tube drainage. Administration of two doses of low-dose intrapleural therapy (1 mg tissue plasminogen activator and 5 mg deoxyribonuclease) allowed complete evacuation of his residual loculated pleural fluid, aided resolution of his infection without provoking a significant air leak and avoided the need for surgery.

KEYWORDS
broncho, empyema, fibrinolytic, hyper-IgE, pleural, pleural

INTRODUCTION

Hyper-IgE syndrome (HIES) is a rare immunodeficiency that can arise from mutations of various (but most commonly STAT3 or DOCK8) genes resulting in broad defects in immunity and possible connective tissue, skeletal and vascular defects. Recurrent cutaneous and pulmonary infections are common from early childhood. One report of DOCK8 deficient-HIES patients found that <50% survived to age 20.[1] Hence most literature centres on paediatric cohorts.

Respiratory complications especially pneumonia (80% of patients), lung abscess, bronchiectasis, and resultant pneumatoceles represents a major cause of morbidity. Pleural infection/empyema has been reported only in paediatric patients. Poor post-operative healing in HIES patients make surgical drainage the last resort.

We present an adult patient with HIES who developed pleural infection from an underlying bronchopleural fistula and was successfully treated with intrapleural tissue plasminogen activator (tPA)/deoxyribonuclease (DNase) therapy without needing surgery.

CASE REPORT

A 27-year-old male with confirmed STAT3-HIES (exon 20 mutation, c.1867 T > C) presented with a two-day history of right-sided pleuritic chest pain and dyspnea, following a week of productive cough.

He was diagnosed with HIES in early childhood and had recurrent skin abscesses and pneumonias. As a 1-year-old, he underwent a left thoracotomy/decortication for an empyema. He has had spinal osteomyelitis and discitis and underwent bilateral corrective surgery for talipes equinovarus in childhood. Into adulthood, he was frequently hospitalized for recurrent, predominantly cutaneous, infections. He has longstanding bilateral parenchymal cysts and cylindrical bronchiectasis. His compliance with long-term prophylactic co-trimoxazole and itraconazole therapies was variable. He works as a barber and does not smoke.

At presentation, he was apyrexial, tachypneic (30/min) but not hypoxic and had clinical signs of a right pleural effusion. He had eczematous skin and multiple scars from prior skin abscesses and surgeries. Blood tests revealed a neutrophilic leukocytosis (16×10^9/L) and an elevated C-reactive

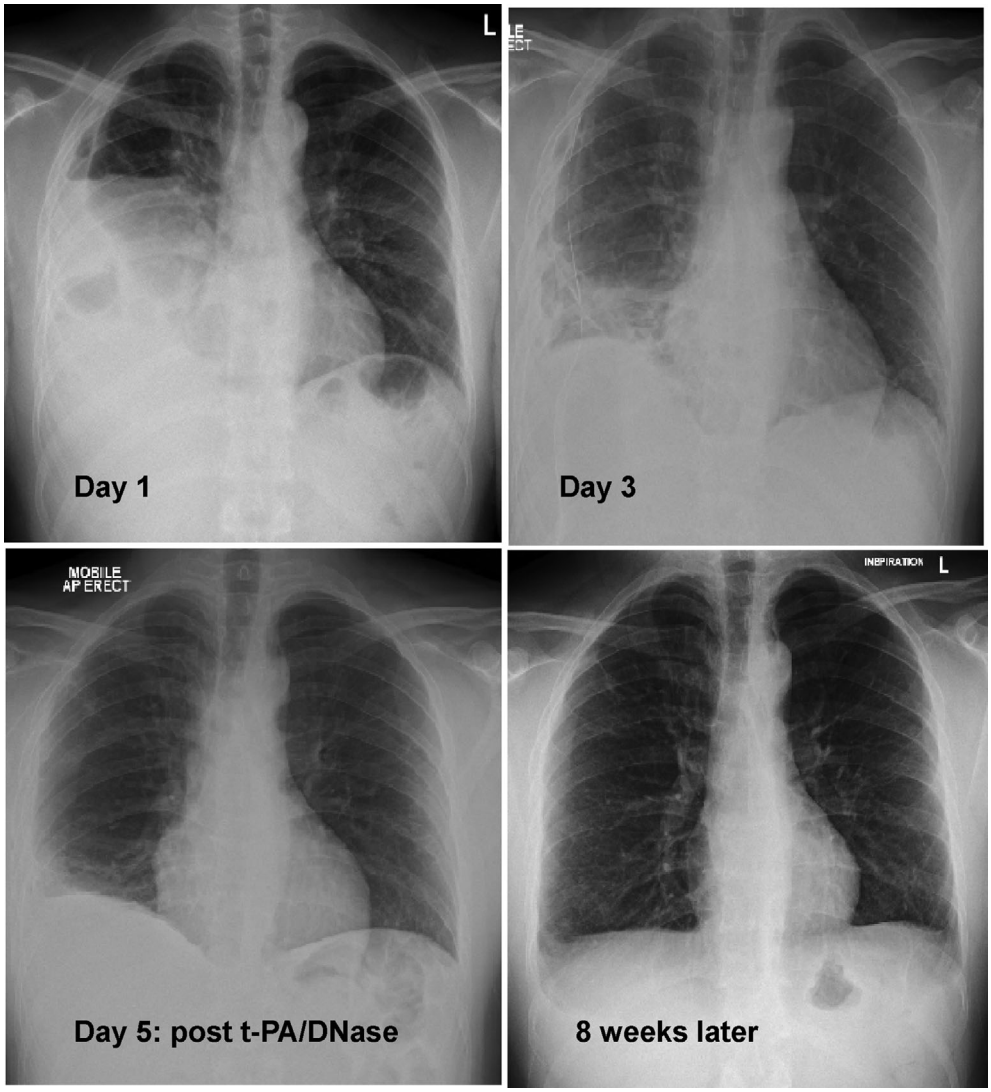

FIGURE 1 **Day 1**: patient attended ED and chest tube was inserted for right hydropneumothorax which drained 1200 mL of fluid. **Day 3**: Chest radiograph and bedside ultrasound confirmed residual right postero-basal loculated pleural effusion. Intrapleural tPA/DNase therapy was initiated. **Day 5**: Complete resolution of the right pleural effusion after two doses of tPA/DNase and removal of another 650 mL of fluid. **Eight weeks later**: Patient was asymptomatic with a near normal chest radiograph at follow-up.

protein (CRP, 144 mg/mL) level. Nasopharyngeal swab for SARS-CoV-2 RNA was positive but there was no radiological evidence of COVID pneumonitis. Chest x-ray revealed a large right pleural effusion with an air-fluid level (Figure 1). The fluid was echogenic and multiseptated on ultrasonography. Computed tomography confirmed a right-sided hydro-pneumothorax, pleural enhancement, bilateral pneumatocoeles (Figure 2) and a bronchopleural fistula within the right lower lobe, likely from a ruptured lung abscess/pneumatocele.

Empirical intravenous piperacillin/tazobactam and oral azithromycin was initiated. An 18-Fr intercostal catheter was inserted under ultrasound guidance and showed no evidence of air leak when connected to underwater seal drainage. Over 12 h, 1200 mL of turbid fluid was drained. Although no organisms were cultured, the fluid analyses were consistent with pleural infection: pH 7.1, glucose 2.0 mmol/L, LDH 2850 U/L, protein 65 g/L and abundant polymorphic leukocytes on microscopy. Sputum culture showed *Streptococcus pneumoniae*.

He clinically improved but CRP remained elevated (133 mg/mL) 2 days after tube thoracostomy. Repeat imaging confirmed a moderate-size residual pleural fluid collection (Figure 1). Intrapleural tPA (Alteplase 1 mg) with DNase (5 mg) was commenced. After two doses, a further 650 mL of pleural fluid was drained with complete radiological clearance of the effusion (Figure 1). CRP decreased to 67 mg/mL. There was no evidence of air leak after a trial of clamping of the chest tube before its removal. He was discharged home with two further weeks of piperacillin/tazobactam, followed by 2 weeks of oral amoxycillin/clavulanic acid.

At clinic review 2 weeks after stopping antibiotics, he remained systemically well (CRP 1.1 mg/mL) with no fever. Chest radiograph showed no pleural effusion but a small

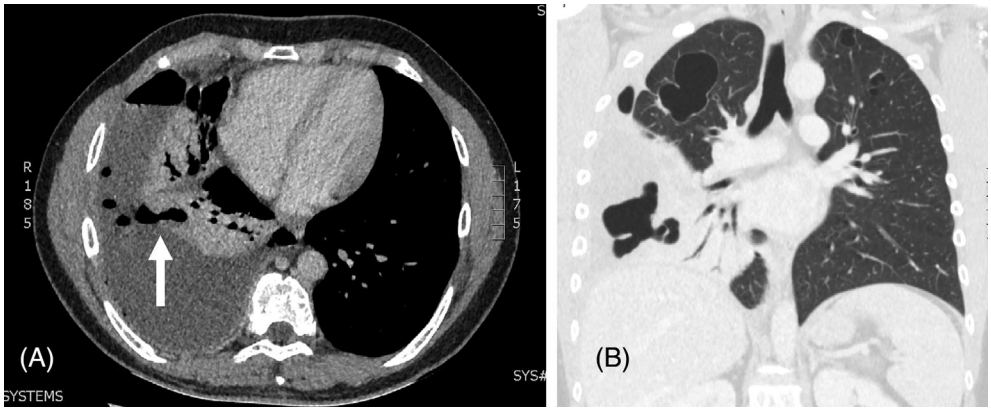

FIGURE 2 (A) Chest computed tomography scan performed on the day of admission showed a large hydropneumothorax. A breach of the visceral pleura was seen with direct communication between the lung cavity/pneumatocele and the pleural space (arrow). Air bubbles were within pleural fluid suggested multiple loculations. (B) The coronal view showed bilateral longstanding pneumatoceles.

loculated pneumothorax which resolved spontaneously on subsequent x-ray 8 weeks after discharge. He remained well with no residual respiratory symptoms.

DISCUSSION

We reported the first case of pleural infection in an adult HIES patient, and the successful use of low-dose intrapleural tPA/DNase therapy in this high-risk setting.

Isolated cases of empyema complicating paediatric HIES patients have been reported. Data for pleural infection in adults with HIES is lacking, presumably because of the limited survival.

Individuals with HIES are prone to pyogenic infections from early childhood and throughout life; over 90% suffer from recurrent pneumonias, usually from *Staphylococcus aureus* or *Streptococcus pneumonia*.[2] Systemic inflammatory response to infection/pneumonia is diminished, likely from impaired inflammatory cytokine signalling, delaying presentations.[2] This may explain why our patient remained apyrexial and systemically well despite his significant pleuropulmonary infection.

In HIES, impaired clearance of infection and abnormal tissue remodelling may lead to formation of lung abscess and pneumatoceles (found in 70% of cases, including our patient). These may rupture and cause empyema and were the likely events underlying our patient's presentation.

Our patient received standard management of pleural infection including systemic antibiotics and tube thoracostomy. Intrapleural tPA/DNase therapy has an established role to help evacuate infected pleural fluid collections and can reduce the need for surgical drainage to <5%.[3] The radiographic evidence of a bronchopleural fistula posed potential risks in applying intrapleural tPA/DNase therapy in our patient, but the absence of air leak after drain insertion suggested the fistula was either closed or small. HIES patients have high risks from surgery, in part from impaired tissue healing.[4] Successful treatment with tPA/DNase avoided surgery, and associated complications, for our patient.

The optimal dose of tPA in intrapleural therapy has not been determined. In a randomized trial, use of 10 mg tPA (with DNase) was efficacious.[3] Our dose de-escalation series showed that lower tPA doses (5 and 2.5 mg) were similarly effective.[5] In high risks cases, such as ours, a 'test' dose of 1 mg tPA (with 5 mg DNase) was justifiable, and indeed provided complete radiological clearance of the pleural collection after two doses, which facilitated early hospital discharge.

AUTHOR CONTRIBUTIONS

All authors contributed to writing, editing and approval of the final manuscript.

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CONFLICT OF INTEREST STATEMENT

Y. C. Gary Lee is an Editorial Board member of Respirology Case Reports and a co-author of this article. They were excluded from all editorial decision-making related to the acceptance of this article for publication. The other authors have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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