Recurrent hemoptysis with *Penicillium marneffe* and *Stenotrophomonas maltophilia* in Job's syndrome

Bosco HM Ma MBChB¹, Calvin SH Ng MD FRCS Edin CTh¹, Rebecca KY Lam MBChB², Song Wan MD PhD¹, Innes YP Wan MBChB FRCS Edin CTh¹, Tak Wai Lee MBChB FRCS Edin¹, Anthony PC Yim MD FRCS Eng Glas Edin¹

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Pulmonary infection caused by the opportunistic organisms *Penicillium marneffe* and *Stenotrophomonas maltophilia* in patients with Job's syndrome is rare and not well documented. The case of a 30-year-old man with Job's syndrome who developed recurrent pneumonia and lung abscesses caused by *P. marneffe* and *S. maltophilia*, complicated by massive hemoptysis, is described. Bronchial artery embolization was successful in controlling the hemoptysis; however, the infection proved fatal despite appropriate antimicrobial therapy. A brief review of the literature on Job's syndrome and its associated infective pulmonary manifestations is also presented.

Key Words: Embolization; Hemoptysis; Job's syndrome; *Penicillium marneffe*; *Stenotrophomonas maltophilia*

CASE PRESENTATION

A 30-year-old man was admitted to hospital for the management of massive hemoptysis. He had a long history of childhood cutaneous infections and recurrent pneumonia complicated by empyema, and thoracic and pulmonary abscesses that required prolonged intravenous antibiotics and surgical decortifications. His family history was unremarkable. A previous sweat test was negative. Further investigations revealed marked eosinophilia and grossly elevated serum immunoglobulin (Ig) E levels of 2510 IU/L (normal range 0 to 100 IU/L), but normal IgA, IgG and IgM levels, which led to the clinical diagnosis of Job's syndrome. Despite prophylactic oral antibiotics (predominantly ampicillin-based), he suffered from further bouts of severe pneumonia with massive hemoptysis and the subsequent development of a large right upper lobe cavitating abscess that required lobectomy. Interestingly, the abscess culture grew *Stenotrophomonas maltophilia*, which was successfully treated with sulperazone (cefoperazone and sodium sulbactam).

During the current admission 10 years later, he again presented with dyspnea and life-threatening hemoptysis. Multiple scars were noted from previous skin abscesses of the face and limbs, as well as from bilateral thoracotomy incisions. Breath sounds were reduced bilaterally, especially over the right side. A complete blood panel revealed leukocytosis (white blood cell count $16.4 \times 10^9/L$ [normal range $4 \times 10^9/L$ to $11 \times 10^9/L$]), predominantly neutrophils (85.1%) and eosinophils (9.5%). A chest radiograph showed consolidative changes and cavitations over the right lower zone. Computed tomography

Hémoptysie récurrente avec *Penicillium marneffe* et *Stenotrophomonas maltophilia* dans le syndrome de Job

L'infection pulmonaire opportuniste causée par *Penicillium marneffe* et *Stenotrophomonas maltophilia* chez des patients atteints du syndrome de Job est rare et peu documentée. Les auteurs décrivent ici le cas d'un homme de 30 ans atteint du syndrome de Job ayant présenté une pneumonie et des abcès pulmonaires récurrents à *P. marneffe* et *S. maltophilia*, compliqués par une hémoptysie massive. L'embolisation de l'artère bronchique a été réalisée avec succès et a permis de maîtriser l'hémoptysie. Toutefois, l'infection s'est révélée fatale malgré l'administration d'une antibiothérapie appropriée. Les auteurs présentent en outre une brève revue de la littérature sur le syndrome de Job et les manifestations infectieuses pulmonaires qui y sont associées.

revealed multiple pneumatoceles (Figure 1), the largest being 5.5 cm in size, with fluid levels in the right lower lobe. Urgent angiography was performed and two culprit hypertrophic bronchial arteries supplying the right main and right lower lobe bronchi (Figure 2A) were successfully occluded by microsphere embolization (500 μ m to 700 μ m) (Figure 2B), with subsequent resolution of hemoptysis. In addition, percutaneous drainage of the dominant lung abscess was performed. Both sputum and abscess fluid cultures grew *Penicillium marneffe*, which produces a characteristic soluble red pigment at 30°C (Figure 3). The patient was treated with amphotericin B and the prophylactic antibiotic cefepime. Despite appropriate antifungal and antibiotic therapy, his contralateral lung also rapidly became infected and he finally succumbed to respiratory failure.

DISCUSSION

The term Job's syndrome was coined in 1966 by Davis et al (1), who described a rare condition characterized by recurrent staphylococcal skin infections, sinusitis, otitis media and pulmonary infections. Other clinical manifestations described since then include candida endocarditis, keratitis and corneal perforation, craniofacial and dental abnormalities, and skeletal deformities (2). Pulmonary complications such as recurrent pneumonia, pneumatocele formation and lung abscesses caused by bacterial and fungal infections are also common (3-7) (Table 1).

The mode of inheritance appears to be autosomal dominant with incomplete penetrance, although most cases are sporadic in nature (2,8,9). Neutrophil chemotactic defect and T cell

¹Department of Surgery; ²Department of Microbiology; Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, NT, Hong Kong SAR, China
Correspondence: Dr Calvin SH Ng, Division of Cardiothoracic Surgery, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong SAR, China. Telephone 852-2632-2629, fax 852-2637-7974, e-mail calvinng@surgery.cuhk.edu.hk

Figure 1) Computed tomography scan revealing multiple pneumatoceles with fluid level. The largest one is 5.5 cm in size (in the right lower lobe)

Figure 2) A Pulmonary angiogram showing two hypertrophic bronchial arteries supplying the right main (black arrow) and right lower lobe bronchi (white arrow). **B** The hypertrophic arteries were occluded following microsphere embolization

dysfunction are thought to be the underlying deficiencies in Job's syndrome. Raised serum IgE levels and eosinophilia, which are diagnostic of Job's syndrome, are in fact not the principal

Figure 3) Sputum culture at 30°C produced a mold. Identification was aided by the formation of a soluble red pigment that diffused into the agar

cause because IgE production involves T cell stimulation and the ability of B cells to class switch into IgE production. The humoral immune system is dependent on cell-mediated immunity. Individuals with humoral immunodeficiency are prone to recurrent infections by pyogenic agents, especially encapsulated bacteria, such as *Haemophilus influenzae*, *Streptococcus pneumoniae* and staphylococci (8). Interferon-gamma, a lymphokine that enhances neutrophil respiratory burst and bactericidal activity, has also been found to be at significantly lower levels or undetectable in patients with Job's syndrome. Recombinant human interferon-gamma was demonstrated to enhance neutrophil chemotactic response in Job's syndrome (10). Furthermore, antihistamines (ie, H_2 receptor antagonists) such as cimetidine, have been suggested

TABLE 1
Summary of the literature of pulmonary involvement in patients with Job's syndrome

Pulmonary involvements	Treatment and outcome	Patient age, years/sex	Author (reference)
<i>Staphylococcus aureus</i> pneumonia complicated by empyema	Antibiotics and thoracostomy	11/male	Lui and Inculet (14)
Recurrent right lower lobe abscesses	Antibiotics and lobectomy		
Right upper lobe pneumatocele and right spontaneous pneumothorax	Thoracostomy complicated by bronchopleural fistula, necessitating right upper lobectomy	19/male	Schamberger et al (15)
Right middle and lower lobe pneumatoceles	Conservative		
Right lower lobe abscess with <i>Aspergillus fumigatus</i> colonization	Antibiotics and thoracostomy		
	Right lower lobectomy		
Right lower lobe pneumonia and pneumatocele caused by <i>Staphylococcus aureus</i> , <i>Haemophilus influenzae</i> , <i>Aspergillus fumigatus</i> and <i>Candida albicans</i>	Antibiotics and antifungals	11/female	Santambrogio et al (5)
	Right lower lobectomy		
Recurrent <i>Pseudomonas aeruginosa</i> and <i>Staphylococcus aureus</i> pneumonia	Antibiotics	30/male	Hall (6)
<i>Aspergillus</i> left upper lobe abscess	Left upper lobectomy		
	Amphotericin B and itraconazole		
Disseminated pulmonary candidiasis and septicemia	Antibiotics and antifungals	23/female	Yilmaz (3)
	Succumbed to respiratory failure		
Right and left lower lobe pneumonia and empyema	Antibiotics and thoracostomy	10/male	Jhaveri (4)
Left lower lobe pneumonia complicated by hydropneumothorax	Antibiotics and thoracostomy		
	Residual multiple pneumatoceles		
	Succumbed to respiratory failure		
Right upper lobe and left lower lobe pneumonia and empyema	Antibiotics and thoracostomy	2/female	Connolly (7)
Right lower lobe pneumonia and life-threatening hemoptysis	Embolization with polyvinyl ethanol		
Pulmonary angiogram: Pseudoaneurysm from a hypertrophic bronchial artery			

as another possible treatment to enhance neutrophil chemotactic ability (11).

Pulmonary pathogens that have been commonly associated with Job's syndrome include *Staphylococcus*, *Pseudomonas*, *Aspergillus* and *Candida* species (Table 1). Of interest, our patient's lung abscesses were caused by the atypical organisms *P. marneffe* and *S. maltophilia*. The associations of these two organisms with Job's syndrome have not been well documented in the English literature. *P. marneffe* was discovered in 1956 as a naturally occurring sylvatic fungus within numerous bamboo rat species endemic to southeast Asia and southern China. It commonly causes respiratory, cutaneous and systemic infections in immunocompromised patients, especially those with AIDS or receiving renal and bone marrow transplantation (12). In contrast, *S. maltophilia* is an aerobic Gram-negative bacillus and an infrequent pathogen in humans. It is known to be a frequent colonizer in the hospital setting, in irrigation solution and in intravenous fluids. The organism is also associated with respiratory tract infection in immunocompromised patients, particularly those with cystic fibrosis (13). *S. maltophilia* is usually resistant to multiple anti-

microbial agents – the most effective agents are cefepime and trimethoprim with sulfamethoxazole. In our case, both amphotericin B and cefepime were administered to account for both organisms.

The other challenge is the management of severe hemoptysis in the immunocompromised patient. Bronchial artery embolization (BAE) is quickly becoming a popular, less invasive approach for the treatment of hemoptysis. However, its clinical efficacy for infective causes of hemoptysis in immunocompromised patients, such as Job's syndrome, is not well documented. Only one other case of a successful BAE for massive hemoptysis from pneumonia and bronchial artery pseudoaneurysm (in a 2-year-old girl with Job's syndrome) is reported in the English literature (7). In the past, lung resections in Job's syndrome were reserved for uncontrolled pneumonia and pulmonary abscess rather than hemoptysis (3-7) (Table 1). One should also consider that the risk of postoperative infective complications and bronchopleural fistula would be significantly higher in the immunocompromised patient. BAE remains the initial treatment of choice for this select group of patients presenting with hemoptysis.

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