Opportunistic bacterial, viral and fungal infections of the lung

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Abstract

Opportunistic infections are a major cause of morbidity and mortality in severely immunocompromised patients, such as those receiving chemotherapy or biological therapies, patients with haematological malignancy, aplastic anaemia or HIV infection, and recipients of solid-organ or stem cell transplants. The type and degree of the immune defect dictate the profile of potential opportunistic pathogens; T-cell-mediated defects increase the risk of viral (cytomegalovirus, respiratory viruses) and *Pneumocystis jirovecii* infections, whereas neutrophil defects are associated with bacterial pneumonia and invasive aspergillosis. However, patients often have combinations of immune defects, and a wide range of other opportunistic infections can cause pneumonia. Importantly, conventional non-opportunistic pathogens are frequently encountered in immunocompromised hosts and should not be overlooked. The radiological pattern of disease (best assessed by computed tomography) and speed of onset help to identify the likely pathogen(s); radiological imaging can subsequently be supported by targeted investigation including the early use of bronchoscopy in selected patients. Rapid and expert clinical assessment can identify the most likely pathogens, which can then be treated aggressively, providing the best opportunity for a positive clinical outcome.

Keywords *Aspergillus*; *Crypotococcus*; fungi; immunocompromised host; *Nocardia*; opportunistic infections; pneumonia; viruses

Key points

- Knowledge of the immune defect helps to narrow down the potential pathogens
- Computed tomography of the chest is better than radiographs at defining the radiological pattern of disease in immunocompromised hosts
- In selected patients, early bronchoscopy increases the yield of microbiological identification of a potential pathogen
- Prolonged high-dose glucocorticoids (>20 mg/day for >21 days) predispose to *Pneumocystis jirovecii* pneumonia (PJP)
- Biological agents are associated with specific immune defects that increase the risk of opportunistic lung infections (e.g. tumour necrosis factor-α inhibitors and risk of mycobacterial disease, endemic fungi and *Legionella pneumophila*; anti-CD20 drugs and mycobacterial disease, cytomegalovirus pneumonitis and PJP)
- Due to the increase in azole resistance of *Aspergillus fumigatus*, combination of an azole with an echinocandin antifungal agent is recommended in immunocompromised hosts with severe invasive pulmonary aspergillosis
- A travel history is important to identify infections caused by endemic fungi

Introduction

Opportunistic infections occur when a loss of established innate or adaptive immune responses allows an organism that is normally weakly virulent to cause infection. The type and degree of immune defect dictate which potential opportunistic pathogens are likely (Table 1). Opportunistic lung infections are a major cause of morbidity and mortality for patients immunocompromised because of HIV infection, haematological malignancy, aplastic anaemia or chemotherapy treatment, or who are recipients of solid-organ or stem cell transplants, and also can complicate treatment with the new biological therapies for inflammatory conditions. Immunocompromised patients also have an increased risk of infections caused by more conventional pathogens, which should be considered in the differential diagnosis. Expert clinical assessment with early diagnosis and aggressive treatment are required for a positive outcome. Computed tomography (CT) is more sensitive than plain chest radiography for defining the predominant pattern(s) of lung involvement. Combined with knowledge of the patient's immune status (loss of T-cell or antibody-mediated immunity, or defects in neutrophil-mediated immunity), this can often identify the most likely pathogens. This article provides a concise overview of the most common opportunistic lung infections.

Bacteria

Conventional bacterial pathogens

Although the risk of opportunistic infection is high in immunocompromised patients, most pneumonias are related to the more

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Type of immune defect according to disease/treatment and range of commonly associated pathogens

Immune disorder	Causes	Typical microorganisms
Neutrophil disorders		
Neutropenia	Drugs (chemotherapy, azathioprine, methotrexate, carbimazole, sulphonamides)	Gram-positive bacilli (*Staphylococcus aureus*, streptococci)
	Leukaemia	Gram-negative bacilli
	AIDS	Fungi (*Aspergillus* spp., *Candida* spp., non-*Aspergillus* filamentous fungi)
	Felty's syndrome	
	Aplastic anaemia	
	Early HSCT	
Neutrophil chemotaxis	Diabetes mellitus	*Staph. aureus*
	Cirrhosis	Streptococci
	Sarcoidosis	*Candida* spp.
	Drugs (glucocorticoids, amphotericin B)	Zygomycosis
Neutrophil phagocytosis	Chronic granulomatous disease	*Staph. aureus*
	Myeloproliferative disorders	*Nocardia* spp.
	Inherited phagocyte defects	Gram-negative bacilli
		Fungi (*Aspergillus* spp., *Candida* spp., non-*Aspergillus* filamentous fungi)
T-cell-mediated immunity	AIDS	Herpesviruses,
	Lymphoma	Respiratory viruses
	HSCT	*Pneumocystis jirovecii*
	Solid organ transplantation	Endemic mycoses, e.g. *Histoplasma capsulatum*, *Cryptococcus*
	Drugs (T-cell-depleting antibodies, glucocorticoids, ciclosporin, tacrolimus)	Parasites (*Strongyloides*, *Toxoplasma*)
		Mycobacteria
		Nocardia
		Legionella pneumophila
B-cell-mediated/antibody deficiency	Multiple myeloma	Encapsulated bacteria (e.g. *Streptococcus pneumoniae*, *Haemophilus influenzae*)
	Plasmapheresis	Herpesviruses
	Drugs (anti-B-cell therapies)	
	HSCT	
	Chronic lymphocytic leukaemia	
	Lymphoma	
	Multiple myeloma	
Other		
Complement deficiency	Congenital	Encapsulated bacteria (e.g. *Strep. pneumoniae*, *Haem. influenzae*)
	Acquired (systemic lupus erythematosus, anorexia nervosa)	*Staph. aureus*
Asplenia	Splenectomy	Encapsulated bacteria (e.g. *Strep. pneumoniae*, *Haem. influenzae*)
	Sickle cell disease	*Staph. aureus*

HSCT, haemopoietic stem cell transplantation.

Table 1

conventional bacterial pathogens. These are particularly common after a viral illness. They usually present similarly to pneumonia in immunocompetent individuals[1] with fever, respiratory symptoms, focal consolidation and rapid rises in inflammatory markers. The major risk factors are neutropenia, antibody deficiencies and high-dose corticosteroids. The organisms involved are more diverse than those seen in conventional pneumonia and are more likely to be resistant to first-line antibiotics. They include both Gram-positive (*Streptococcus pneumoniae*, *Staphylococcus aureus*) and Gram-negative (e.g. *Pseudomonas aeruginosa*, *Proteus* species, *Escherichia coli*, other enteric pathogens) organisms.

Mycobacteria

Reactivation of latent tuberculosis occurs in patients with T-cell immune defects. *Mycobacterium tuberculosis* cultures and