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CME article

Necrotising pneumonia in children

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EDUCATIONAL AIMS

- To describe the pathophysiology of lung necrosis
- To highlight recent changes in pneumococcal and staphylococcal disease and their implications for therapy
- To discuss recent changes in the aetiology and epidemiology of necrotic pneumonia in children
- To provide a practical guide to the management of children with necrotising pneumonia

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SUMMARY

Necrotising pneumonia remains an uncommon complication of pneumonia in children but its incidence is increasing. Pneumococcal infection is the predominant cause in children but Methicillin resistant *Staphylococcus aureus* (MRSA) and Panton-Valentine leukocidin (PVL) staphylococcal infection are also important causes of severe necrotising pneumonia. Clinical features of necrotic pneumonia are similar to those of an uncomplicated pneumonia except that the patient is clinically much more unwell and has usually failed to respond adequately to what would normally be considered as appropriate antibiotics. Pleural involvement is frequent. Initial management is similar to that for non-complicated pneumonia with careful attention to fluid balance and adequate analgesia required. Some patients will need intensive care support, particularly those with PVL-positive staphylococcal infection. Broad-spectrum antibiotics should be given intravenously, with the exact choice of agent informed by local resistance patterns. Pleural drainage is often required. Despite the severity of the illness, outcomes remain excellent with the majority of children making a full recovery.

INTRODUCTION

Necrotizing pneumonia is a severe form of lung disease associated with the formation of abscesses and cavitation within the lung parenchyma, and usually, but not always significant pleural involvement.

AETIOLOGY

Many insults can cause acute lung necrosis, but the great majority of cases in children are related to infection. Bacterial infection is the most common, especially *Streptococcus pneumoniae* and *Staphylococcus aureus*, a list of causative organisms is given in Table 1. Other organisms including *Mycoplasma pneumoniae* and adenovirus can cause serious disease with chronic and even fatal consequences. It should be remembered that infection is frequently culture negative and modern culture negative techniques may be required to determine the precise aetiology. This review will concentrate on infectious causes.

The important non-infectious causes to consider are listed in Table 2. The most common of these to consider in paediatric practice is aspiration of food contents, which is frequently complicated by secondary bacterial infection.

EPIDEMIOLOGY

Necrotising pneumonia is an ancient condition, and previously a major cause of death in both adults and children. The clinical features may well have first been described by Hippocrates and later in some detail by Laennec in 1826.[1]

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Table 1
Infections associated with necrotising pneumonia

Bacterial:	Viruses:	Fungi*:
Streptococcus pneumoniae	Influenza	*Aspergillus spp.*
Staphylococcus aureus	Adenovirus	*Candida spp.*
Streptococcus mitis spp.	Herpes group including -Cytomegalovirus (CMV), Varicella-Zoster, Epstein-Barr Virus (EBV)	*Histoplasma capsulatum*
Streptococcus pyogenes (Group A Streptococcus)		*Coccidioides spp.*
Mycoplasma pneumoniae		*Blastomyces spp.*
Pseudomonas spp.		*Cryptococcus neoformans*
Fusobacterium spp.		

* A primary fungal cause is very rare in immunocompetent individuals but must be considered in immunosuppressed or immunodeficient patients.

The complications of bacterial pneumonia were major killers of all age groups prior to the era of antibiotics and modern surgical techniques. A high proportion of those dying in the great pandemics of influenza such as that in 1919 will have died from complications related to the subsequent bacterial pneumonia. As primary bacterial pneumonia became less common in the 20th century, so the more severe necrotising forms of the disease also decreased, at least partially as a consequence of the widespread introduction of antibiotics.

The problem had become very uncommon in the antibiotic era but the incidence of complicated disease has again increased over the last two decades.[2] The mechanisms responsible for these changes vary according to the causative organism, but are complex and still incompletely understood.

PATHOPHYSIOLOGY

The term necrotising refers to the death of cells or groups of cells and implies permanent cessation of their integrated function, although this does not mean that significant clinical and structural recovery may not occur. Most necrosis in the context of the lung parenchyma is of the liquifactive or colliquative form. Necrosis by organisms causing putrefaction results in the production of foul-smelling gas and brown, green or black discolouration of the tissues is referred to as gangrene. The term pulmonary gangrene was coined to describe this type of disease in the 1940s. Hseih *et al*[3] have emphasised the distinction between necrosis referring to the pathology whereas gangrene refers to the pathophysiological mechanism involved, although the terms are often used inter-changeably in clinical practice.[3] This group has also demonstrated that thrombosis of intrapulmonary blood vessels may well be of critical importance in mediating the pathophysiology of this group of conditions.[3,4]

These changes are additional to the features of lobar pneumonia which classically are associated with complete clinical and radiological resolution over time. The consequences of necrosis are ultimately destruction of the normal lung architecture, which is replaced by cavities which are surrounded by a wall of variable thickness. The cavity is usually not in continuity with the conducting airways and is filled with either gas or liquid pus.

Table 2
Important non-infectious causes of necrotising pneumonia

Aspiration of foods contents
Chemotherapeutic agents including Bleomycin, Cyclophospamide
Crohn's disease
Graft versus host disease
Inhalation of chemicals including hydrocarbons, kerosene, mineral oils, furniture polish and turpentine
Inhaled foreign body
Meconium aspiration syndrome
Psoriasis
Sickle cell disease
Smoke inhalation
Toxic shock syndrome
Systemic lupus erythematosis
Wegener's granulomatosis and other necrotising vasculitides

Pneumococcal disease

A dramatic increase in paediatric empyema was first reported from the West Midlands, UK in 1997[5] and this phenomenon has since been confirmed by many centres across the globe.[6–11] Barriers to understanding the cause or causes of this problem in the UK have been that most cases are culture negative, presumably because of antibiotics in primary care and hospital prior to obtaining pleural fluid for culture, and the fact that blood cultures are usually negative even in antibiotic naïve patients with invasive bacterial disease.[12] Other countries with presumably higher rates of positive bacterial culture disease subsequently demonstrated that most of this disease was pneumococcal in origin.[8] This was then confirmed for culture negative disease with the advent of pneumococcal PCR and other molecular detection techniques, and of this most disease was shown to be due to serotype 1 disease using serotype specific ELISAs.[13,14]

There are approximately ninety disease-causing pneumococcal serotypes, and different serotypes are recognised to cause different patterns of disease. Individual serotypes vary in properties including their propensity to cause disease in different organs, their virulence and invasive potential, ability to colonise the nasopharynx and likelihood of expressing genes responsible for conferring antibiotic resistance.[15] There are also considerable geographical differences in the relative prevalence of individual serotypes and how these change over time.[16,17] The factors responsible for determining temporal changes in the relative prevalence of individual serotypes are incompletely understood. There are considerable "secular" changes which probably reflect Darwinian competition for ecological space between pneumococcal serotypes and between pneumococci and other organisms.[18] In addition there are other recognised influences including selection pressure from antibiotic use, and more recently from the introduction of conjugate pneumococcal vaccines.[19]

The first commercially available conjugate pneumococcal vaccine Prevenar© was introduced into the routine infant vaccine schedule in the USA between 2000 and 2001. The first commercially available version of this vaccine contained antigen for serotypes 4, 6B, 9 V, 14, 18C, 19F and 23F which were the seven most common causes of culture positive pneumococcal disease prevalent in the USA at the time.[20] Introduction of the vaccine was associated with an initial rapid reduction in the incidence of pneumonia and complicated disease in both immunised patients and the general population, presumably as a consequence of increased herd immunity.[21] Unfortunately some of these benefits were short lived and there followed an increase in severe invasive pneumococcal disease related to serotypes not present in the seven valent vaccine, especially 19A disease.[22,23] 19A disease is notable for being particularly associated with a severe, virulent necrotising pneumonia which is often associated with resistance to multiple antibiotics.[24]