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Early infantile pertussis; increasingly prevalent and potentially fatal

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Abstract We report nine cases of severe early pertussis in infants less than 7 weeks of age. Clinical features at this age are atypical and may be confused with more common illnesses such as bronchiolitis. All were very difficult to manage. Ventilation was required for apnoeas in five cases, seizures in two or respiratory failure in two. Complications included hypotension in seven cases, pulmonary hypertension in one, pneumothoraces in two, seizures in five and co-infection in five. Two cases were referred for extracorporeal membrane oxygenation and six died. Infection was confirmed either at post mortem or by culture from pernasal swabs. The mother or other close family members were symptomatic at the time and thought to be the source of infection.

Conclusion The nine cases suggest a significant resurgence of the infection, which may be fatal in early life. If reporting continues to increase, the immunisation schedule will need to be reviewed and secondary transmission prevented where possible, to protect this vulnerable pre-immunisation group.

Key words Immunisation · Infantile · Pertussis · Vaccination

Abbreviations *ECMO* extracorporeal membrane oxygenation · *HFOV* high frequency oscillatory ventilation · *RSV* respiratory syncytial virus

Introduction

Vaccination against pertussis has led to a significant decline in morbidity and mortality. However, young infants remain susceptible and may present with atypical symptoms compared to older children. Making the diagnosis in early infancy requires the awareness that the organism continues to circulate and how it may present. Management of severe cases is difficult and death is not uncommon. We report our recent experience of nine cases of severe early infantile pertussis from the mid Trent region of England, UK, where the incidence is rising.

Summary of cases

The nine cases were managed on the paediatric intensive care units in Nottingham (eight beds) and Derby (four beds) in the mid Trent region of England, UK. The region has approximately 60,000 live births per year. Six cases presented within a 10-month period over the winter months of 1997. The most recent case presented in March 1999. Seven of the infants were male. All were healthy term deliveries presenting between 2 and 6 weeks of age, i.e. before their first immunisation. Table 1 summarises the clinical course and complications of the nine cases.

Case 7 was atypical. He had been unwell for 4 weeks before admission, but the majority had been unwell for less than 4 days. All presented with a history of poor feeding and cough. The cough was described as paroxysmal in five cases. Additional symptoms included apnoeas (five cases), fever (four cases), vomiting (two cases) and seizures (three cases). Typically cough, anorexia and poor feeding were noticed first, suggesting an upper or lower

Table 1 Clinical course and complications

Case	WCC $\times 10^9/l$ (% lymphocytes)	Reason for intubation	Admission to intensive care (days)	Intermittent positive pressure ventilation (h)	Complications and co-infection	Outcome	Contacts
1	69.1 (25)	Seizure	2	27	Seizures, hypotension	Died	Mother
2	63.0 (61)	Apnoea	3	10	Pneumothoraces, hypotension, rhinovirus	Died	Mother, father, brother
3	69.5 (30)	Apnoea	3	15	Hypotension, RSV, <i>S. aureus</i>	Died	Cousins
4	32.5 (87)	Apnoea	6	168	<i>Pseudomonas</i> , Coronavirus	Alive	Brother
5	58.2 (42)	Apnoea	1	700, 173 ECMO, 120 HFOV	Pneumothorax hypertension, hypotension, seizures	Alive	Sister
6	95.3 (25)	Respiratory failure	1	168	Hypotension, seizures, brain damage	Died	Mother, father, siblings
7	62.5 (56)	Respiratory failure	48	41	Oedema, hypotension	Died	Mother, brother
8	89.0 (17)	Apnoea	5	9	Seizures, pulmonary hypertension, hypotension, hypoglycaemia, adenovirus	Died	Mother, brother
9	41.4 (74)	Seizures	26	216	Seizures, <i>S. aureus</i>	Alive	Mother, siblings

respiratory tract infection. Fever and or vomiting were cause for further concern in these very young infants. Increased respiratory distress, apnoeas and seizures quickly followed, leading to admission and eventually intubation, which was required very shortly after presentation in two cases.

Presenting during the bronchiolitis season, the first four cases seen were initially thought to be bronchiolitis or bronchopneumonia and were treated as such, with oxygen and fluids to maintain hydration. In case 3, respiratory syncytial virus (RSV) was isolated early on from the admission nasopharyngeal aspirate. However, all infants received broad spectrum antibiotics either because of their age, the severity of their symptoms or their negative RSV status. Pernal swabs were not considered in the first three cases. The total white cell count and total lymphocyte count were very high in all cases. The percentage of neutrophils was greater than lymphocytes in five cases.

Five cases suffered increasing respiratory distress for a further 1 to 5 days before intubation was required. Ventilation was required for recurrent apnoeas (five cases), seizures (two cases) and respiratory failure (two cases) (Table 1). Cases 7 and 9 initially stabilised in oxygen only. However, case 7 had a rapid deterioration late in his illness, presenting with respiratory failure and hypotension, while case 9 required intubation for frequent seizures. All cases required ventilation with high pressures and desaturations were common. Thick tenacious secretions were a constant feature and were very difficult to manage. Co-infection was found in four cases and may have contributed to their poor respiratory status. Their X-rays showed hyperinflation and collapse consolidation. In two infants pneumothoraces developed. In seven cases, inotropic support was necessary. Case 8 had significant problems with pulmonary hypertension and suprasystemic right ventricular pressures, despite the use of pulmonary vasodilators. Cases 2, 3 and 8 had fatal rapid deteriorations after intubation. Cases 1 and 5 were so difficult to ventilate that extracorporeal membrane oxygenation (ECMO) was arranged.

Case 1 died before transfer. Case 5 went on to require prolonged respiratory support with ECMO and high frequency oscillatory ventilation (HFOV). Intensive care support was withdrawn in case 6 after EEG, cranial ultrasound and clinical examination revealed extensive cerebral damage. Five infants had seizures as part of their illness. Six of the nine cases died and a post mortem was performed in four cases. In three cases, the diagnosis was only made at post mortem. The other cases were diagnosed from pernasal swabs. At post mortem, pulmonary findings were similar, revealing widespread mucus plugging and extensive mucosal damage. Of note, there was severe depletion of lymphocytes from the thymus, lymph nodes and spleen. Incidentally, case 8 was found to have a secondary atrial septal defect and polysplenia.

Discussion

As pertussis related morbidity has declined so has awareness and reporting, even in the event of death [9]. Diagnosis was made only at post mortem in three of our cases because of short illnesses characterised by rapid clinical deterioration. The typical features of mid childhood, which clinicians remember, are not the same as those in the non-immunised very young infant, in whom diagnosis may be delayed. Pertussis was not the first diagnosis considered at presentation in the first of our cases, particularly during a bronchiolitis epidemic. The symptoms reported did suggest possible respiratory infection; bronchiolitis or bronchopneumonia being most likely. However, the important differentiating symptom of a paroxysmal cough was reported in only five of the nine cases and should not be considered as pathognomic in infancy. No patients developed an inspiratory whoop. Apnoeas secondary to respiratory infection are common in this age group but seizures are unusual in this context. They should serve as a useful diagnostic clue, as they are a significant and well recognised complication of pertussis encephalopathy. The total white cell counts and lymphocyte counts were very high in all of these severe cases and were useful indicators of probable pertussis. We found that the percentage of neutrophils may be greater than that for lymphocytes. In the later cases the above features were recognised immediately as neonatal pertussis, allowing earlier confirmation of the presence of pertussis from pernasal swabs.

Intubation and ventilation were necessary because of apnoeas, seizures or respiratory failure. It has been suggested that ventilation is straightforward in the majority requiring intubation [4]. This was not true in our cases or in the experience of others [5]. Thick secretions, patchy collapse consolidation combined with hyperinflation, pulmonary hypertension and co-infection made ventilation very difficult. Broad spectrum antibiotics (including erythromycin), mucolytics, steroids (dexamethasone)

methasone and hydrocortisone), bronchodilators and surfactant were tried with no apparent benefit. Case 5 would not have survived without ECMO. Unfortunately six of our patients died. In this series and in others death was associated with age, co-infection and multisystem involvement [10]. Five patients had seizures, suggesting encephalopathy, and five had evidence of respiratory co-infection.

The possible source of the pertussis infection is shown in Table 1. These close family members all had recent illnesses with a prolonged cough. In case 3 the contacts (two cousins) had been notified as probable pertussis cases. Unfortunately, even when pertussis was considered in the contact family members, no pernasal swabs were taken. Reporting has increased recently despite good current local and national vaccination uptake [8]. However protection is temporary and *Bordetella pertussis* continues to circulate, often silently [6] amongst those who have been vaccinated. In addition there is now a cohort of young adults whose parents declined vaccination because of concerns about possible adverse effects (encephalopathy), who are susceptible to primary infection and may pass infection on to their own infants. With the help of our local public health laboratory service we attempted to trace the immunisation records of the parents thought to be contacts. Unfortunately we were unable to find documentary evidence of their immunisations.

A significant resurgence of pertussis has been predicted [2]. It is unclear why so many severe cases have occurred in such a small area, although a smaller group has been reported in the London area [8]. The susceptible infant may be at increasing risk from an increasing population of unprotected adults or poorly protected siblings. If this series is followed by others, or by increased reporting in other age groups then, methods of improving protection to the susceptible infant must be reconsidered. The importance of maintaining high vaccination rates at the earliest possible age cannot be overstated [3]. However, neonatal vaccination does not provide adequate protection [1]. Furthermore, it has been suggested that the change to an accelerated programme of vaccination in the UK (2, 3 and 4 months)

may be responsible for the increase in cases [8] by leading to shorter immunity in siblings. The vulnerable newborn, may be at risk from all family members in whom pertussis has been forgotten or not been considered likely. If newer acellular vaccines are acceptable, then boosting in early childhood and adolescence may help reduce secondary transmission of pertussis to newborn babies [7]. These cases serve to remind us that pertussis continues to circulate and how difficult to manage it can be when spread to young infants, in whom it may be fatal.

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