A review of five young infants with pertussis

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Introduction

Pertussis is a worldwide disease that caused significant morbidities and mortalities in children, especially in infants in the pre-vaccine era. Diphtheria-tetanus-pertussis (DTP) vaccine has been available in Hong Kong since the 1950s. Since then, the incidence of pertussis and its associated mortality has dropped dramatically. The annual notification rate of pertussis was reported to range from zero to 15 cases per year from 1989 to 2001.1 2 Only one mortality case involving a 41-day-old infant was reported over the last 35 years.1 However, there has been increasing incidence of pertussis in the last decade in Canada and the United States and it mainly affected adolescents and adults.3-8 This was attributed waning immunity and improved awareness of the diagnosis in adolescents and adults.9 It was also suggested by study done in the Netherlands that antigenic divergence in clinical isolates allowed B. pertussis strains to circulate despite high levels of vaccine uptake.10 The disease was in turn transmitted from these young persons to partially immunised or non-immunised young infants who were more susceptible to develop severe disease. In both the United Kingdom11 and France,12,13 the infant mortality rates from pertussis were reported to be increasing. The current review was undertaken to examine the clinical characteristics of all culture confirmed pertussis cases admitted to the Department of Paediatrics of this hospital from January 2001 to June 2005.

Methods

Records of all culture confirmed paediatric pertussis cases up to 15-year of age admitted to the Department of Paediatrics, Kwong Wah Hospital in Hong Kong in the period from 1 January 2001 to 30 June 2005 were retrieved by the Clinical Management System of the Hong Kong Hospital Authority. Age distribution, clinical characteristics, investigations, treatment, complications, duration of hospitalisation and contact source identification were reviewed.

Results

A total of 5 confirmed cases with positive Bordetella Pertussis culture were identified. All were less than 3-month-old and they presented between March and July. The clinical characteristics of the patients were listed in Table 1.

Apnoea, post-tussive cyanosis, facial flush, vomit and poor feeding were common features (present in 40%, 60%, 40%, 60%, 40% of patients respectively). Fever was not a predominant symptom, being present in only one patient ( transient low grade fever for 1 day ). The classical inspiratory whoop of pertussis was uncommon and was reported in only one patients.

Four of the 5 cases were born full term with normal birth weight and enjoyed good general health before the illness. The remaining case was an otherwise well small-for-date female infant born at full term with a birth weight of 2.2 kg. Two patients received pre-admission antibiotics, i.e. cefaclor. All 5 infants were not yet immunised for pertussis before the illness.

Table 1. Clinical features

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Number of cases (total n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>1-2 month</td>
<td>2</td>
</tr>
<tr>
<td>2-3 month</td>
<td>3</td>
</tr>
<tr>
<td>&gt;= 3 month</td>
<td>0</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>3</td>
</tr>
<tr>
<td>Female</td>
<td>2</td>
</tr>
<tr>
<td>Fever</td>
<td>1 (with low grade fever only)</td>
</tr>
<tr>
<td>Cough duration on admission:</td>
<td></td>
</tr>
<tr>
<td>&lt;= 1 week</td>
<td>2</td>
</tr>
<tr>
<td>1-2 week</td>
<td>2</td>
</tr>
<tr>
<td>2-4 week</td>
<td>1</td>
</tr>
<tr>
<td>Total cough duration:*</td>
<td></td>
</tr>
<tr>
<td>6 week</td>
<td>n=3</td>
</tr>
<tr>
<td>7 week</td>
<td>n=1</td>
</tr>
<tr>
<td>(*1 defaulted follow-up)</td>
<td></td>
</tr>
<tr>
<td>Post-tussive cyanosis</td>
<td>3</td>
</tr>
<tr>
<td>Post-tussive facial flush</td>
<td>2</td>
</tr>
<tr>
<td>Post-tussive vomit</td>
<td>3</td>
</tr>
<tr>
<td>Nasal symptoms</td>
<td>3</td>
</tr>
<tr>
<td>Apnoea</td>
<td>2</td>
</tr>
<tr>
<td>Poor feeding</td>
<td>2</td>
</tr>
<tr>
<td>Duration of hospitalisation</td>
<td>Median: 8 days</td>
</tr>
</tbody>
</table>

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Two out of the 5 cases had household contact history with someone who had recent upper respiratory tract infection (URTI). In one case, both parents suffered recent URTI symptoms but the exact onset dates of symptoms were not documented. In the other case, the elder sister had URTI symptoms 3 weeks prior to the admission of the patient. However, nasopharyngeal specimen for pertussis taken in these suspected source cases (on the 2nd day of admission of the patient) were all negative. Two cases had recent travel history to Mainland China within 10 days prior to onset of symptoms and one case was living in Mainland China and was brought to HK for medical consultation only. Only one infant had lymphocytosis (14.0 x 10^9/L).

Two patients, one had concurrent influenza A infection, had desaturation that required oxygen supplement in the paediatric intensive care unit (PICU). Of these, one had frequent desaturations associated with apnoeas, but no mechanical ventilatory support was needed. In the other case, the patient had frequent and severe post-tussive desaturation with SpO₂ down to 60% and was admitted to PICU for close observation with oxygen supplement. Serious complications like pneumonia, seizure, cerebral haemorrhage, subconjunctival haemorrhage, or cardiopulmonary failure did not develop in the 5 cases.

Four of the 5 cases received standard treatment of 2 weeks oral erythromycin and one of the case received 5 days oral azithromycin. The duration of hospital stay ranged from 4 days to 24 days and the median duration was 8 days. The durations of hospital stay in the 2 PICU cases were 15 days and 7 days respectively. The patient with the longest hospital stay of 24 days was a case with frequent transient post-tussive cyanosis and mild desaturation with marked parental anxiety. All patients were discharged without sequelae. One patient had defaulted follow-up after discharge. The remaining four were followed up till most of the cough subsided and the total cough duration ranged from 6 weeks to 7 weeks.

Inhaled bronchodilator (ipratropium 4 puff q6h prn via aerochamber) was given to 2 cases with mild wheeze noted on physical examinations that improved after bronchodilator 1.5% NaCl nasal drops was given to 2 of the cases for relief of nasal blockage.

Discussion

This review summarised the clinical characteristics of culture positive paediatric pertussis cases in our hospital from January 2001 to June 2005. Pertussis is a notifiable disease in Hong Kong. In the corresponding period of the study from 1 January 2001 to 30 June 2005, a total of 74 cases were notified. The annual incidence in each year were listed as followed: 15 cases in 2001, 23 cases in 2002, 5 cases in 2003, 10 cases in 2004 and 21 cases in first half of 2005. Under-diagnosis was generally believed to be common, especially in adolescents and adults who may present only as prolonged cough. It is a common misconception amongst medial practitioners that pertussis was an early childhood disease. It is noteworthy that inspiratory whoop is uncommon amongst infants and the current case series reconfirms this observation. High index of suspicion is required for the diagnosis as a significant number of cases do not have typical clinical features.

The low total case number in this study could also be related to the variable sensitivity of pertussis culture from nasopharyngeal specimens. Culture is the golden standard for diagnosis of pertussis due to the high specificity. However, the reported sensitivity ranged from 3% to 52% and the yield was affected by 1) technique and culture method 2) timing of culture 3) previous pertussis vaccination with higher culture positive rates in non-immunised patients (25% vs 52%) 4) recent antibiotics. The isolation rate was highest within the first 3 weeks of cough. All specimens for cultures in this review were taken within 3 week of onset of cough. As with other many infectious disease, polymerase chain reaction (PCR) is emerging as a new diagnostic tool for pertussis with sensitivity similar to that of culture. One study by Loeffelholz et al reported sensitivity up to 93.5% and specificity of 97.1%. Pertussis PCR is currently not available in Hong Kong as a routine service.

The incidence of pertussis was reported to be increasing in the United States, Canada, particularly in adolescents and adults. Infant mortality rates from pertussis was also increasing in both the United Kingdom and France. The case mortality rate in the US was 0.2% overall and 0.8% in cases younger than 6-month-old, while in Canada it was reported to be 1.0% for cases younger than 6-month-old. White cell count and pneumonia were reported to be independent predictors of fatal outcome in the multivariate model (Lynda, 2003). The reported incidence of pertussis in Hong Kong remained low from 0-15 cases per year from 1989 to 2001. The cases number ranges from 23 in 2002 to 15 in 2003 and 10 in 2004. Although 2005 witnessed 32 cases of pertussis, a longer surveillance was needed to see if it was indeed a rising trend or just the cyclical epidemic peaks that occurred every 2-5 years as part of the disease characteristic. The case fatality rate in Hong Kong was not reported. The only mortality case reported in the last 35 years was a 41-day-old female infant who contracted the disease.
from his father and died of complication of pneumonia in October 1997.7

All of the cases in this review were less than 3-month-old, comparable with previous reported Hong Kong data that most cases (91%) involved infants less than 6-month-old.1 In another study done in Taiwan that included both inpatients and outpatients, the percentage of case less than 3-month-old was 34.8% while less than 1-year accounted for 52.2%. Another small peak (24%) occurred in those aged 5- to 9-year-old.20 In a large prospective general practice population study of 500 consecutive case of pertussis, cases less than 1-year-old contributed to only 3.3% of all the cases while the peak incidence was noted in 3-year-old.21 It might be related to the difference in index of clinical suspicion and diagnostic criteria. Moreover, disease is generally more serious in young children17 with higher hospitalisation rates and complication rates in patients less than 1-year-old.20 This difference in severity accounted for the different percentage of infants cases in reported series, depending on the population studied.

For the sex distribution, 3/5 (60%) of the cases in our study were male. The total number of cases was too small to draw any conclusion. Previous study showed that pertussis affected females more22 and the difference was more prominent in adults (68% vs 32%).17 However, another study by Ulrich et al16 showed equal sex distribution for pertussis in children (49.3% in male vs 50.7% in female).

Complication like pneumonia, seizure, cerebral haemorrhage, subconjunctival haemorrhage, and cardiopulmonary failure were absent in the current cases and there was no mortality. This was similar to that reported from the UK. A higher complication rates were reported by others. Vesselinova-Jenkins et al found 8.3% of their cases developed pneumonia, 7% convulsions and 22% hospitalisation.24 Lin et al reported 28.3% to have developed pneumonia, 2.2% convulsions, 2.2% cardiopulmonary failure.18 Another study however found a much lower rate of complications and a hospitalisation rate of 2.8% only.25

Immunity from pertussis vaccine is not life long and is likely to wane after 3 years and disappears after 10 to 12 years.1,16,23 Passive protection from placental transfer of maternal antibodies to young infants apparently does not occur in pertussis in contrast to many other infectious diseases.23 This renders young infants who have not yet completed the 3 doses of pertussis vaccine most vulnerable to the disease.

Because of waning immunity, protection to an adolescent or adult depends very much on the administration of booster doses and background boosting of vaccine-induced immunity through repeated exposure to wild strains The role of adolescents and adults in transmitting pertussis to infants was well documented.20-23 Herd immunity played an important role in disease control and to prevent death and morbidities in those young vulnerable infants. Improved disease control could be achieved by one of the following means: i) universal adult immunisation, or ii) selective immunisation of mothers and close family contacts of newborns, or iii) selective immunisation of health care workers, or iv) selective immunisation of child care workers, or v) selective immunisation of adolescents, or vi) preschool booster at 4-6 years of age and vii) reinforcement and/or improvement of current infant and toddler immunisation strategies.34 Different strategies would be appropriate to different countries depending on in the current vaccination programmes and disease incidence. Currently only Australia, Austria, Canada, France and Germany have incorporated an adolescent booster dose into the immunisation programme.35 In Hong Kong, there is no definite reported rising trend of pertussis whilst the immunisation rate in young infants exceeds 95%. Case fatality remained very low.

Antimicrobial agents given early during the catarrhal stage may ameliorate the disease but after cough becomes established, antimicrobial agents may not have beneficial effect on the course of illness but they are still recommended in order to limit the spread of the disease to others. Drugs of choice include erythromycin estolate (40-50 mg/kg/day orally in 4 divided doses for 14 days) or azithromycin dihydrate (10-12 mg/kg/day orally in daily dose for 5 days) or clarithromycin (15-20 mg/kg/day orally in 2 divided doses for 7 days). There was an association noted between orally administered erythromycin and infantile hypertrophic pyloric stenosis in young infants <2 weeks of age while the risk with azithromycin and clarithromycin is unknown. Pencillins and first/second-generation cephalosporins are not effective treatment for pertussis. Trimethoprim-sulfamethoxazole is another treatment alternative (trimethoprim 8 mg/kg/day and sulfamethoxazole 40 mg/kg/day in 2 divided doses).30

In summary, pertussis that warrants hospitalisation in our hospital affects mainly those young infants who have not been immunised. The most prominent features apart from severe cough are post-tussive cyanosis, post-tussive vomiting and apnoea.

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