Case 9

The patient was a 5½-week-old male who was transferred to our institution with a 10-day history of choking spells. The child's spells began with repetitive coughing and progressed to his turning red and gasping for breath. In the prior 2 days, he also had three episodes of vomiting in association with his choking spells. His physical examination was significant for a pulse of 160 beats per min and respiratory rate of 72/min (both highly elevated). The child's chest radiograph was clear. There was no evidence of tracheal abnormalities. His white cell count was 15,500/μl with 70% lymphocytes. The culture from the nasopharyngeal swab is seen in Fig. 1.

1. What was the organism infecting this child?

2. Why are specimens from the nasopharynx the specimens of choice in the diagnosis of this infection? Other than culture, what other methodology can be used to identify the presence of this pathogen in a specimen?

3. Why did this patient have a predominance of lymphocytes?

4. Were this child's clinical course and chest radiograph consistent with his infection? Explain your answer.

5. What is the epidemiology of this infection, and how might it be prevented?

6. The drug of choice to treat this infection is erythromycin. Clinically, the cough may persist for some time following therapy with erythromycin. Give possible reasons why a cough may persist in the face of erythromycin therapy.

Figure 1

9 Case Discussion

1. This child had a classic presentation for whooping cough, whose etiologic agent is *Bordetella pertussis*. The "mercury-like" colonies seen in Fig. 1 are typical of this organism.

2. *B. pertussis* specifically binds to ciliated epithelial cells. This binding is mediated by filamentous hemagglutinin (FHA), an important virulence factor of this organism. Since the nasopharynx is lined with ciliated epithelial cells, culture of this site has a higher yield than culture from any other specimen source. In addition to culture, many laboratories perform PCR (polymerase chain reaction) to demonstrate the presence of *B. pertussis* in nasopharyngeal specimens. Advantages of PCR in comparison with culture include the rapidity with which the diagnosis can be established (hours, compared with days for traditional culture) and the fact that the organism, because it is so fastidious, may be very difficult to recover in culture, particularly if the specimen is not processed immediately.

3. *B. pertussis* produces a variety of virulence factors, including pertussis toxin. In earlier literature, pertussis toxin was described as many different entities, usually on the basis of a particular biological activity. One of the terms used to describe it was "lymphocytosis-promoting factor" because >50% of the peripheral white blood cells in mice injected with it were observed to be lymphocytes (the normal proportion is approximately 25%). Clinically, lymphocytosis, often as high as 70 to 80%, is routinely seen in patients with whooping cough and is a distinguishing characteristic of this infection.

4. Yes. This child's presentation is typical of whooping cough. This infection is usually limited to the upper airways, and pneumonia due to either *B. pertussis* or secondary bacterial agents is unusual. Therefore, normal chest radiographs are common.

Children with whooping cough often have paroxysms of coughing. The term "paroxysm" means a sudden recurrence or intensification. Children often cough repeatedly, and when they gasp for breath, the sound of this inspiration is the "whoop" of whooping cough. Because of repetitive coughing and resulting disruption of breathing, the children will have abnormal oxygen exchange and will often turn red and sometimes blue. The repetitive coughing may also result in vomiting or choking on respiratory secretions. All of these signs were seen in this child.

5. This disease is spread from person to person via respiratory secretions. No animal vector or reservoir has been identified. Young children, especially those under 2 months of age, are at increased risk for developing *B. pertussis* infection. At the age of 2 months a series of pertussis vaccinations is begun. Immunity increases with increasing numbers of doses of the vaccine, but the efficacy of the vaccine even after the entire series is probably no better than 90%. The disease is most severe in children under 6 months.

Recently a new pertussis vaccine was approved by the Food and Drug Administration to replace the whole-cell pertussis vaccine for use in primary childhood immunization series. A number of adverse effects have been associated with the whole-cell vaccine, ranging from pain and erythema at the injection site and associated fever to persistent crying and, rarely, seizures. The new vaccine, which is acellular, contains five pertussis components including the two major pertussis virulence factors, FHA and pertussis toxoid. This vaccine is more efficacious than the whole-cell vaccine, with significantly fewer postvaccination adverse reactions. This is important because, in the past, press reports of adverse reactions following vaccination with whole-cell *B. pertussis* vaccine resulted in decreased *B. pertussis* vaccination rates. When vaccination rates declined, the rates of infection increased, especially in children less than 1 year of age, the patient population most vulnerable to this organism. Since adverse effects are low and efficacy is high with the acellular vaccine, it is hoped that vaccination rates with this new vaccine will rise and that outbreaks resulting from poor vaccine compliance will no longer occur.

6. Although erythromycin is active against *B. pertussis,* the damage that the *B. pertussis* tracheal cytotoxin causes, ciliostasis and death of the tracheal epithelial cells, is not reversed by the administration of an antibiotic. Thus the cough persists. Another possible reason why the cough may persist in the setting of erythromycin use is patient noncompliance, since erythromycin is often associated with gastrointestinal intolerance. Bacterial pneumonia, an occasional complication of pertussis, must also be considered in a persistent cough, particularly if the patient worsens clinically.

Finally, the possibility that the organism is resistant to erythromycin must be considered. *B. pertussis* isolates have been recently identified in Arizona that are resistant in vitro to erythromycin, with a minimum inhibitory concentration (MIC) of greater than 64 μg/ml. The MIC of erythromycin against *B. pertussis* usually ranges from 0.02 to 0.1 μg/ml. Resistant isolates have not been previously reported.

References

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