Summary: We illustrate 2 cases of pneumonia associated with Bordetella pertussis infection in 72-year-old and 61-year-old patients with cancer receiving myelosuppressive therapy after hematopoietic stem cell transplantation. Bacterial infections are a significant cause of morbidity and mortality in patients with cancer, and those receiving hematopoietic stem cell transplant, solid organ transplant, or myelosuppressive therapy are at increased risk. The infection was detected and the 2 patients had good outcomes following azithromycin treatment. Pertussis, also known as whooping cough, is a contagious respiratory illness that has become a public health challenge due to decreased immunity of the pertussis vaccine. Therefore, it is critical to recognize pertussis early in the course of the disease.

Introduction
The lung is one of the most frequently involved organs in a variety of complications in the immunocompromised host.\(^1\) Among the pulmonary complications that occur in persons who are immunocompromised, infection is the most common and is associated with high rates of morbidity and mortality.\(^1\) The most commonly encountered type of infection is bacterial in origin.\(^2\) Before the development of vaccines, Bordetella pertussis infection was a significant threat among immunocompetent hosts.\(^3\) Bordetella vaccination has significantly reduced the number of infections, but immunity appears to be short lived.\(^4\) In addition, a large portion of the population remains susceptible to infection from \textit{B pertussis}.\(^5\) We present 2 cases of \textit{B pertussis} infection that led to pneumonia in patients with cancer. The medical staff members at our institution were up to date on their vaccinations, and no secondary cases of pertussis were reported.

Case Reports
Case 1
A woman aged 72 years with metastatic ovarian cancer who was receiving chemotherapy with intrathecal methotrexate, gemcitabine, and carboplatin presented with a 12-day history of productive cough with yellow sputum and shortness of breath associated with the coughing spells. She had tried a cough suppressant with minimal relief. She denied fever, chills, sweats, hemoptysis, ill contacts, and recent travel.

Her vital signs were within normal limits, and findings on physical examination were significant for crackles heard throughout the lung fields. Her white blood cell count was 4,910/µL with a normal differential. The patient denied receiving pneumocystis prophylaxis in the past and tested negative for \textit{Pneumocystis jiroveci}.

The result from a nasopharyngeal swab sent for a respiratory viral polymerase chain reaction (PCR) panel was positive for \textit{B pertussis}. PCR testing was negative for adenovirus, \textit{Chlamydia pneumoniae}, coronavirus, metapneumovirus, rhinovirus, enterovirus, influenza types A and B, \textit{Mycoplasma}, parainfluenza virus types 1 to 4, and respiratory syncytial virus. Computed tomography (CT) of the chest showed dependent areas of subpleural consolidation and patchy, ground-glass opacities (Fig 1).

She was discharged home with a 5-day course of oral azithromycin (250 mg daily). Repeat PCR testing 1 week later was negative for \textit{B pertussis}. She reported improvement of her symptoms 3 weeks later.

Case 2
A man aged 61 years admitted to our hospital with a 5-year history of chronic lymphocytic leukemia and a matched, unrelated donor stem cell transplantation 12 days prior complained of a 1-day history of nonproductive cough, sore throat, and fatigue. He denied fever, chills, shortness of breath, hemoptysis, nausea, vomiting, ill contacts, and recent travel.

His vital signs were all within normal limits. Finding on physical examination was remarkable for coarse breath sounds heard across the left lung fields. His white blood cell count was 560 µL, absolute neutrophil...
count was 190 µL, and lymphocyte count was 200 µL. The patient was receiving pneumocystis prophylaxis and tested negative for *P jiroveci*.

The result from a nasopharyngeal swab sent for a respiratory viral PCR panel was positive for *B pertussis*. PCR testing was negative for adenovirus, *C pneumoniasae*, coronavirus, metapneumovirus, rhinovirus, enterovirus, influenza types A and B, *Mycoplasma*, parainfluenza virus types 1 to 4, and respiratory syncytial virus. Radiography of his chest showed an interval increase in opacification of the perihilar lungs. CT of his chest demonstrated patchy, bilateral airspace disease and ground-glass nodularity, which was greatest in the left lower lobe and bilateral small pleural effusions (Fig 2). Rapid strep testing was negative, and blood cultures did not show any growth after 3 days.

He was treated with a 7-day course of oral azithromycin (250 mg daily) and was followed-up in the clinic. He reported complete resolution of his symptoms 2 weeks later. Repeat PCR testing for *B pertussis* performed on day 26 was negative.

**Discussion**

*B pertussis*, a gram-negative aerobic, pleomorphic coccobacilli, is known to cause whooping cough, which is a respiratory tract infection characterized by paroxysmal cough.6-9 *B pertussis* is transmitted by large droplets produced during coughing, sneezing, or talking. These droplets generally travel fewer than 3 feet and can be deposited on mucosal surfaces of susceptible individuals.10 *B pertussis* belongs to the *Bordetella* genus, which now includes 9 species, and *B pertussis*, *B parapertussis*, and *B bronchiseptica* are the 3 most studied.11

Infection is initiated by the attachment of *B pertussis* to the cilia of epithelial cells of the upper respiratory tract. Evasion of host defenses is facilitated by adenylate cyclase toxin (CyaA) and pertussis toxin.12 CyaA enters the neutrophils and catalyzes the excessive production of cyclic adenosine monophosphate, which intoxicates the cells such that phagocytosis is compromised. Similar to CyaA, pertussis toxin adversely affects phagocytosis and inhibits the migration of lymphocytes and macrophages to areas of infection.12 Local tissue damage of the ciliated epithelial cells may be due to tracheal cytotoxin, dermonecrotic toxin, and perhaps CyaA.12

Although *B pertussis* mainly causes pulmonary issues, it has been documented to be associated with otitis media,13 encephalopathy,14 bacteremia,15 hemolytic uremic syndrome,16-18 infantile hypertrophic pyloric stenosis,19 multiple sclerosis, amyotrophic

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Fig 1. — Computed tomography of the chest showing dependent areas of subpleural consolidation and patchy, ground-glass opacities.

Fig 2. — Computed tomography of the chest demonstrating patchy, bilateral airspace disease and ground-glass nodularity (greatest in the left lower lobe).
lateral sclerosis,01 cerebral ataxia,21 and Wegener granulomatosis.22

Cough is one of the most common complaints among patients with *B pertussis* infection.23 Diagnosis can be made by PCR assay because it is a rapid, efficient, and specific technique with superior sensitivity compared with that of culture.24-26

Five other cases have been cited in the literature of pertussis in patients with cancer and a mix of hematological malignancies and solid tumors (Table).15,27-30 It is worthy of note that these cases were published prior to the advent of PCR assay and several were based on culture of the organism from extrapulmonary sources (eg, blood, empyema fluid).15,27-30

The recommended antimicrobial agents for the treatment or chemoprophylaxis of pertussis in patients who are immunocompromised or immunocompetent are azithromycin, clarithromycin, and erythromycin.31 Trimethoprim/sulfamethoxazole can also be used.32 Erythromycin, clarithromycin, and azithromycin are preferred for the treatment of pertussis in persons who are at least 1 month of age.31 For infants younger than 1 month of age, azithromycin is preferred for postexposure prophylaxis and treatment because azithromycin has not been associated with infantile hypertrophic pyloric stenosis, unlike erythromycin.33,34 Azithromycin should be used with caution because it is associated with prolongation of the QT interval.35 For patients allergic or intolerant to these agents, doxycycline or levofloxacin is an alternative option (rather than no treatment).35 If symptoms do not improve after a trial of macrolides, then resistance should be suspected.36,37

Use of vaccination against *B pertussis* has been well studied.38 The diphtheria, tetanus, and acellular pertussis (DTaP) vaccine is indicated only for children younger than 7 years of age.38 However, the adult tetanus, diphtheria, and acellular pertussis (Tdap) vaccine is a 3-dose series with high tetanus and pertussis content that may be more immunogenic in recipients of hematopoietic stem cell transplantation, so it should be considered as the initial vaccination for this patient population, regardless of age.38 Furthermore, Suzuki et al30 suggested that acellular pertussis vaccine can be considered for patients after receiving hematopoietic stem cell transplantation, even if they are adults or older than 7 years of age.

### Conclusions

We presented 2 patients who had good outcomes following azithromycin treatment. Due to the advent of and availability of polymerase chain reaction–based diagnostic testing, the rate of *Bordetella pertussis* infection among patients who are immunocompromised and have cancer is expected to increase.39 Such test-

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**Table. — Studies of *Bordetella pertussis* Infection in Patients With Cancer**

<table>
<thead>
<tr>
<th>Study</th>
<th>Age, y</th>
<th>Sex</th>
<th>Malignancy</th>
<th>Symptoms</th>
<th>Source of Culture/PCR</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>72</td>
<td>F</td>
<td>Ovarian cancer</td>
<td>Productive cough, Shortness of breath</td>
<td>Pharynx PCR assay</td>
<td>Azithromycin</td>
<td>Improved</td>
</tr>
<tr>
<td>Case 2</td>
<td>61</td>
<td>M</td>
<td>Chronic lymphocytic leukemia</td>
<td>Nonproductive cough, Sore throat, Fatigue</td>
<td>Pharynx PCR assay</td>
<td>Azithromycin</td>
<td>Improved</td>
</tr>
<tr>
<td>Florax27</td>
<td>16</td>
<td>M</td>
<td>ALL</td>
<td>Nonproductive cough</td>
<td>Pharynx PCR</td>
<td>Roxithromycin</td>
<td>Symptoms resolved after 2 mo of treatment</td>
</tr>
<tr>
<td>MacLean29</td>
<td>—</td>
<td>—</td>
<td>Bronchogenic lung cancer</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Senturk28</td>
<td>64</td>
<td>F</td>
<td>Non–small-cell lung cancer</td>
<td>Dyspnea, Chest pain</td>
<td>Empyema PCR assay</td>
<td>Erythromycin 2 mg/d</td>
<td>Improved</td>
</tr>
<tr>
<td>Suzuki30</td>
<td>10</td>
<td>M</td>
<td>ALL</td>
<td>Dry cough, Sleep disturbances</td>
<td>Plasma serum PCR assay</td>
<td>Cephalosporin, Clarithromycin</td>
<td>Poor</td>
</tr>
<tr>
<td>Troseid15</td>
<td>63</td>
<td>M</td>
<td>Multiple myeloma</td>
<td>Cough, Hoarseness, Fever</td>
<td>Blood culture</td>
<td>Clarithromycin</td>
<td>Poor</td>
</tr>
</tbody>
</table>

ALL = acute lymphoblastic leukemia, F = female, M = male, PCR = polymerase chain reaction.
ing can be easily done via a nasopharyngeal swab. The literature is scant regarding pertussis in adults — and this is particularly true among those with cancer — due to the historical difficulty of accurate diagnostic testing.59

References