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Atypical presentation of *Legionella* pneumonia among patients with underlying cancer: A fifteen-year review☆

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Summary *Background:* Immunocompromised patients, especially those receiving treatment with corticosteroids and cytotoxic chemotherapy are at increased risk for developing *Legionella* pneumonia.
Objective: The aim of this study was to determine clinical and radiographic characteristics of pulmonary infection due to *Legionella* in persons undergoing treatment for cancer and stem cell transplant (SCT) recipients.
Methods: Retrospective review of *Legionella* cases at MSKCC over a fifteen-year study period from January 1999 and December 2013. Cases were identified by review of microbiology records.
Results: During the study period, 40 cases of *Legionella* infection were identified; nine among these were due to non-pneumophila species. Most cases occurred during the summer. The majority [8/9, (89%)] of patients with non-*pneumophila* infection had underlying hematologic malignancy, compared to 18/31 (58%) with *Legionella pneumophila* infections. Radiographic findings were varied-nodular infiltrates mimicking invasive fungal infection were seen only among patients with hematologic malignancy and hematopoietic stem cell transplant (SCT) recipients and were frequently associated with non-*pneumophila* infections (50% vs 16%; $P = 0.0594$). All cases of nodular *Legionella* pneumonia were found incidentally or had an indolent clinical course.

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Conclusions: Legionella should be considered in the differential diagnosis of nodular lung lesions in immunocompromised patients, especially those with hematologic malignancy and SCT recipients. Most cases of nodular disease due to *Legionella* are associated with non-*pneumophila* infections.
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Introduction

Patients undergoing treatment with cytotoxic chemotherapy are known to be at a higher risk for developing *Legionella* pneumonia.[1,2] Although *Legionella pneumophila*, specifically serogroup 1, is the most commonly recognized species,[3] several non-*pneumophila Legionella* types can cause pulmonary infections in severely immunosuppressed patients.[4–6] The clinical and radiographic features of *Legionella* are mostly indistinguishable from other bacterial pneumonias with lobar consolidation described as the most common radiographic finding.[7] Isolated case reports of *Legionella* pulmonary infection with atypical radiographic presentation have previously been described among immunocompromised hosts.[8–11]

Evaluation of atypical pulmonary infiltrates in immunocompromised hosts, especially SCT recipients, is a frequently encountered problem in clinical practice that can pose a diagnostic and management dilemma for clinicians. Invasive diagnostic procedures such as flexible bronchoscopy and lung biopsies are often necessary to make a definitive diagnosis. While this is the favored approach, frequent occurrence of thrombocytopenia, coagulation abnormalities, and frail health status of patients can preclude the performance of these procedures. Recognizing the atypical presentation of common infections in specialized patient populations would be useful when few diagnostic options exist.

The aim of this study was to characterize the clinical and radiographic presentations of *Legionella* pneumonia among patients undergoing treatment for cancer and stem cell transplant recipients.

Methods

Retrospective review of all cases of *Legionella* pneumonia diagnosed at Memorial Sloan Kettering Cancer Center (MSKCC) over a fifteen-year period, from January 1, 1999 to December 31, 2013. MSKCC is a 471 bed tertiary care cancer center in New York City with 19,000 annual admissions and 122,000 patient-days. Cases were identified by review of microbiology records for results of *Legionella* urinary antigen via enzyme immunoassay tests (BinaxNOW® *Legionella*), lower respiratory tract bacterial cultures (sputum, bronchoalveolar lavage, lung tissue, and pleural effusion) and/or serological testing specific for *L. pneumophila* and non-*pneumophila* antibodies. Culture for *Legionella* species was routinely performed on all respiratory samples during the study years using Buffered charcoal yeast extract (BCYE) and BCYE selective (BCYE w/PAV) culture media while the urinary antigen and serology tests were only done on request from the ordering physician. Electronic medical records were reviewed to obtain information on demographic and clinical characteristics, treatment, and outcomes. All radiographic findings at the time of diagnosis were reviewed and characterized by MSKCC radiologists. Additional review of all cases with nodular infiltrates was performed by MSKCC radiologist (A.P.).

Statistical analysis

Categorical variables were compared using the chi-square or Fisher's exact test. Continuous variables were compared using the Mann—Whitney—Wilcoxon rank-sum tests. Statistical analyses were performed with SAS version 9.4 (SAS Institute, Cary, NC). All reported *P* values are two-sided. A *P* value $\leq$0.05 was considered statistically significant.

The MSKCC Institutional Review Board waived the need for informed consent.

Results

During the fifteen-year study period, 40 cases of microbiologically confirmed *Legionella* pneumonia were identified at MSKCC. No *Legionella* outbreaks occurred during the study period, and none of the cases were hospital-acquired. *Legionella* infections showed a seasonal pattern with most cases (53%) diagnosed between July and September (Fig. 1).

Microbiologic characteristics

The causative organism for 31/40 (77.5%) cases was *L. pneumophila*; 9 cases were due to non-*pneumophila* species. The latter group included the following species — *Legionella micdadei* (4 cases); *Legionella jordanis* (2 cases); and one case each of *Legionella maceachernii* and *Legionella bozemanii*. A single case was identified based on serological titers for non-*pneumophila* (1:1024) and compatible clinical illness. Sputum cultures were obtained in this case but did not yield any growth. Majority of cases (8/9) due to *non-pneumophila* species occurred in patients with hematologic malignancy or SCT recipients.

Co-infection was diagnosed in a single case; *Aspergillus ustus* was isolated along with *L. pneumophila* on biopsy of lung nodule in a SCT recipient. In all other cases, *Legionella* species was the only infecting organism identified.

Radiographic features

The radiographic presentation of *Legionella* pneumonia varied among the cohort. Among the 40 cases, eight presented with solitary or multiple nodules; the remaining 32 cases displayed a mix of non-nodular lung abnormalities including lobar consolidation (20/32; 63%), ground glass opacities (5/32; 16%), and patchy infiltrates (4/32; 13%). Para pneumonic pleural effusions were identified in two cases.

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