CASE REPORT

Ulcerating Bronchitis Caused by Cytomegalovirus in a Patient with Polymyositis

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Abstract

We herein report a case of cytomegalovirus (CMV) bronchitis in a 62-year-old woman with polymyositis. She presented with respiratory symptoms and CMV antigenemia while undergoing immunosuppressive therapy with methotrexate (MTX) and prednisolone (PSL). Bronchoscopy was performed, which revealed an ulceration of the left main bronchus. A mucosal biopsy confirmed CMV infection, and the patient was diagnosed with CMV ulcerating bronchitis. The administration of ganciclovir improved the lesion, and the CMV antigenemia disappeared. Endobronchial ulceration should be considered in the differential diagnosis of CMV disease.

Key words: bronchitis, bronchial ulcer, cytomegalovirus, endobronchial lesion, ulcerating bronchitis

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Introduction

Cytomegalovirus (CMV) is an opportunistic pathogen observed in immunocompromised patients such as those infected with human immunodeficiency virus (HIV), solid organ recipients, bone marrow recipients and patients with other diseases treated with immunosuppressive therapy. CMV causes a variety of serious diseases (1). CMV-related diseases include pneumonitis, enterocolitis, esophagitis, hepatitis and retinitis. However, little is known about the endobronchial lesions caused by CMV. We herein report a case of ulcerating bronchitis caused by CMV in a patient with polymyositis who was being treated with methotrexate (MTX) and prednisolone (PSL).

Case Report

A 62-year-old woman with polymyositis treated with oral MTX (8 mg/week) and oral PSL (10 mg/day) for eight years presented with fatigue, fever, a dry cough and dyspnea on exertion and was admitted to our hospital. On admission, there were no signs of myalgia or worsening of muscle weakness. A physical examination revealed that the patient’s blood pressure was 102/45 mmHg, her pulse rate was regular at 103 beats/min and her body temperature was 38.0°C. Auscultation of the thorax revealed slight fine crackles in both lungs. Arterial blood gas measurement on ambient air revealed hypocapnia but not hypoxemia (pH: 7.439, PaCO₂: 25.6 torr, PaO₂: 90 torr, HCO₃⁻: 24.1 mEq/L). The laboratory findings revealed mild anemia (WBC: 8,800/μL, hemoglobin: 9.8 g/dL, platelets: 28.5×10⁴/μL) and slightly elevated serum levels of creatine kinase (266 IU/L), AST (40 IU/L), ALT (44 IU/L) and LDH (378 IU/L). The patient’s serum C-reactive protein level was 11.69 mg/dL. Although the plasma β-D-glucan level was within the normal range, an immunoassay of the patient’s blood revealed cytomegalovirus (CMV) antigenemia [C7-horseradish peroxidase (C7-HRP): 96/50000 cells]. Chest radiograph and high resolution computed tomography (HRCT) showed bilateral diffuse ground-glass opacities and nodular opacities (Fig. 1a). It was suspected that MTX-associated pneumonitis, CMV pneumonitis or other respiratory infections were involved. Therefore, the same dose of PSL was continued and MTX was discontinued. Subsequently, bronchoscopy was performed to identify the cause of the manifestations. The
bronchoscopy revealed mucosal edema, flaring and ulceration with thick exudates in the left main bronchus (Fig. 2a). We carefully performed a mucosal biopsy, and the pathological analysis of the specimen revealed the presence of CMV-inclusion bodies (on hematoxylin and eosin staining, Fig. 3a) and CMV-positive cells (on immunohistochemical staining, Fig. 3b). No other pathogens (bacteria, mycobacteria or fungi) were detected and no signs of malignancy were observed. Bronchoalveolar lavage (BAL) of the left lingular segment using 150 mL of sterile saline (recovery rate: 70%) and a transbronchial lung biopsy (TBLB) of the left S3 and S8 regions were also performed. The total cell count in the BAL fluid was 1.76×10^5/mL, and the white blood cell fraction was comprised of 91.0% macrophages, 8.0% lymphocytes, 0.2% eosinophils and 0.8% neutrophils. The cluster of differentiation (CD)4/CD8 ratio was 0.55. The TBLB specimens showed nonspecific and mild lymphocytic infiltration of the alveolar spaces and interstitium. Neither the BAL fluid nor the TBLB specimens were found to have CMV-inclusion bodies or CMV-positive cells upon immunohistochemical staining. A polymerase chain reaction (PCR) assay for detecting *Pneumocystis jirovecii* in the BAL fluid was negative, and no evidence of any other pathogens was observed in the specimens. Based on these findings, we made a definitive diagnosis of ulcerating bronchitis caused by CMV. However, we could not make a diagnosis of pulmonary involvement. At the time of the diagnosis of CMV ulcerating bronchitis, the patient did not have any symptoms suggestive of the involvement of other organs usually associated with CMV, such as retinitis, esophagitis, gastritis or enterocolitis. The patient was treated with intravenous ganciclovir (250 mg every 12 hours), and her condition and symptoms gradually improved. Three weeks after the initiation of ganciclovir, the CMV antigenemia disappeared (C7-HRP: 0/50000 cells) and the HRCT abnormalities also completely resolved (Fig. 1b). Repeated bronchoscopy showed considerable improvement of the endobronchial lesion. In particular, the ulcerated lesion in the left main bronchus was replaced with normal mucosa while only demonstrating slight scarring. 

Figure 1. (a) High resolution chest computed tomography obtained on admission showed bilateral diffuse ground-glass opacities and nodular opacities. (b) High resolution chest computed tomography obtained after the administration of ganciclovir treatment revealed the pulmonary abnormalities to be completely resolved.

Figure 2. (a) Bronchoscopy performed before treatment showed mucosal edema, flaring and ulceration with thick exudates in the left main bronchus. (b) Bronchoscopy performed after ganciclovir treatment revealed that the ulcerated lesion in the left main bronchus was replaced with a normal mucosa while only demonstrating slight scarring.
venous ganciclovir and immunoglobulin, and his symptoms were consistent with malignant lymphoma (9). The patient was treated with intra-arterial ganciclovir and immunoglobulin. Analysis of ganciclovir improved the patient’s pulmonary function, and the patient’s symptoms as well as the bronchial ulcer are suggestive of a diagnosis of CMV pneumonitis.

In conclusion, we have herein described a case of ulcerating bronchitis caused by CMV in a patient with polymyositis. When CMV-related disease is suspected in immunocompromised patients who present with common respiratory symptoms, such as a dry cough and dyspnea on exertion, clinicians should thus be aware that ulcerating bronchitis is one possibility in the differential diagnosis of CMV-related diseases and CMV pneumonitis.

The authors state that they have no Conflict of Interest (COI).

References


To date, no relapses of CMV bronchitis or development of any other CMV-related diseases have been observed.

Discussion

CMV-related diseases are common complications in immunocompromised patients and have a variety of clinical manifestations (1). CMV pneumonitis, in particular, is a relatively frequent and potentially serious complication (2-6). With regard to respiratory complications other than pneumonitis, small airway lesions such as bronchiolitis obliterans have been reported to be associated with CMV infection in lung transplant and bone marrow recipients (7, 8). However, little is known about the endobronchial lesions caused by CMV. To date, only one other case has been reported. This was a case of ulcerating bronchitis diagnosed on PCR for CMV using bronchial washing in a patient with polymyositis (9). The patient was treated with intra-venous ganciclovir and immunoglobulin, and his symptoms successfully resolved. These findings and the patient’s clinical course supported a diagnosis of CMV ulcerating bronchitis; however, there was no pathological confirmation. In the present case, the diagnosis was histopathologically confirmed by the presence of both CMV-inclusion bodies (detected on immunohistochemical staining) and CMV-positive cells (detected on immunohistochemical staining) in a biopsy specimen. Therefore, this is, to the best of our knowledge, the first reported case of ulcerating bronchitis caused by CMV with evidence of pathology, CMV antigenemia and the patient’s clinical course.

The pulmonary involvement observed in the present case was suspected to be CMV pneumonitis or MTX-associated pneumonitis; however, we could not make a definitive diagnosis. MTX-associated pneumonitis is a serious and unpredictable side-effect of the administration of MTX (10) with a reported prevalence of 0.3-7.5% (11). Treatment for MTX pneumonitis includes discontinuation of MTX therapy and systemic administration of a corticosteroid. In the present case, a diagnosis of MTX-associated pneumonitis could not be completely ruled out because a clinical improvement was observed after the discontinuation of MTX. However, the presence of CMV antigenemia and the fact that the administration of ganciclovir improved the patient’s pulmonary symptoms as well as the bronchial ulcer are suggestive of a diagnosis of CMV pneumonitis.

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