

Cytomegalovirus pneumonia in an immunocompetent host with primary ciliary dyskinesia: A case report

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Abstract

Primary ciliary dyskinesia (PCD) is an autosomal-recessive inherited disease caused by mutations in genes involved in ciliary structure and function leading to impaired mucociliary clearance and repeated or chronic, usually bacterial, infections of the upper and lower airways and decreased lung function and bronchiectasis. Cytomegalovirus (CMV) is a DNA virus that usually causes sub-clinical infection and in 10% of the patients causes a mononucleosis-like syndrome. CMV is a causative agent of serious illness in

vulnerable immunocompromised groups such as transplant recipients, patients with immunodeficiency or malignancy and neonates. Life-threatening infection due to CMV, including CMV pneumonia, is not common in immunocompetent patients. In this report we describe a case of an otherwise immunocompetent woman, suffering from PCD, who developed severe CMV pneumonia.

Introduction

Primary ciliary dyskinesia (PCD) is a genetically heterogeneous recessive inherited disease of motile cilia related to respiratory presentations, infertility of males, and laterality defects of organs in approximately 50% of cases. Common respiratory presentations of PCD include chronic rhinosinusitis, chronic serous otitis media, respiratory distress in neonates, bronchiectasis and chronic lung disease [1]. A diagnosis of PCD is made by either biallelic mutations in a known PCD gene or a typical PCD ultra-structural ciliary found by transmission electron microscopy (TEM). Other helpful tests for the diagnosis include nasal nitric oxide (nNO), high-speed videomicroscopy analysis (HSVA), and immunofluorescence (IF) [2,3].

Cytomegalovirus (CMV) is a DNA virus that belongs to the family Herpesviridae. CMV primary infection in immunocompetent patients is usually subclinical and in 10% of the patients a mononucleosis-like syndrome occurring with fatigue, fever, liver function abnormalities and lymphocytosis is present. The spectrum of disease caused by CMV is well studied in certain immunocompromised groups such as transplant recipients, patients with AIDS, patients suffering from malignancy and neonates in whom severe CMV disease can be fatal. On the other hand, life-threatening infection due to CMV, including CMV pneumonia, is rare in immunocompetent patients [4].

We report a case of severe CMV pneumonia in an otherwise immunocompetent patient with PCD.

Case Report

A 23-year-old woman, with a history of primary ciliary dyskinesia, diagnosed five years ago from nasal mucosa biopsy, pre-

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Informed consent: Written consent has been obtained by the patient who this case is referred to.

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sented to our pulmonology department with fever, dyspnea at rest and productive cough over the six last days. She was not receiving any medication.

Clinical examination revealed a febrile patient with crackles on auscultation at all lung fields. Blood pressure was 95/50 mmHg, heart rate was 125 beats per minute, oxygen saturation was 82% on room air and body temperature 37.5°C on admission. Electrocardiography showed sinus tachycardia. Arterial blood gas analysis revealed pO₂ 46 mmHg, pO₂ 39 mmHg, pH 7.49 and HCO₃⁻ 29.2 mmol/L on room air. Chest X-ray showed patchy diffuse infiltrates in both lungs with consolidation in the left middle lung field (Figure 1). Laboratory findings included hemoglobin (Hb) 12.8 g/dL (normal 12-15 g/dL), white blood cells (WBC) 12.97 x 10³/μL (normal 4-11 x 10³ /μL), neutrophils 9.42 x 10³/μL/ 72.6% (normal 2-8 x 10³ /μL, 40-75%), lymphocytes 2.40 x 10³/μL/ 18.5% (normal 1.1-4 x 10³ /μL/20-40%), eosinophils 0.04 x 10³/μL/0.3% (normal 0.04-0.70 x 10³/μL/ 1-6%), monocytes 1.01 x 10³/μL/7.8% (normal 0.10-0.90 x 10³/μL/2-10%), platelets (PTLS) 140 x 10³/μL (normal 150-400 x 10³/μL) and C-reactive protein (CRP) 147 mg/L (normal <6 mg/L). Urinalysis was normal. The other blood biochemistry parameters and thyroid-stimulating hormone (TSH) were normal, with the exception of an elevated serum lactate dehydrogenase (LDH) 633 U/L (normal <225 U/L), elevated aspartate aminotransferase (AST) 83 U/L (normal 4-45 U/L) and elevated alanine transaminase (ALT) 53 U/L (normal 4-45 U/L) (Table 1). The polymerase chain reaction (PCR) tests for influenza A and B and for Coronavirus Disease 2019 (COVID-19) in nasopharyngeal and oropharyngeal samples were performed and were negative. The test for human immunodeficiency virus (HIV) was negative. Urinary antigen tests for *Legionella pneumophila* and *Streptococcus pneumoniae*, serological testing for *Mycoplasma Pneumoniae* and blood cultures were negative. The patient received oxygen therapy with Venturi mask delivering 60% oxygen and intravenous antibiotic therapy with piperacillin-tazobactam and azithromycin empirically. After the first two days

of hospitalisation, fever persisted, accompanied by respiratory deterioration, increase in total peripheral lymphocyte count to 4.37 x 10³ /μL and increase in liver enzymes: AST 1029 U/L (normal 4-45 U/L) and ALT 504 (normal 4-45 U/L). Intravenous moxifloxacin and trimethoprim-sulfamethoxazole were added to her therapy.

Computerized tomography (CT) of the chest and abdomen were performed. Chest CT revealed enlarged mediastinal lymph nodes, pleural effusion in both lungs, cylindrical bronchiectasis in lower lobes, in right middle lobe and in lingula, consolidation in the left lower lobe and patchy diffuse ground glass opacities with "crazy paving" pattern in both upper lobes (Figures 2 and 3) Abdomen CT showed hepatomegaly, perihepatic effusion and pericholecystic edema. The patient underwent upper abdomen ultrasonography which revealed hepatomegaly with heterogeneous appearance of the liver, without focal abnormalities and without intrahepatic or extrahepatic bile duct dilation. In addition, the patient underwent echocardiography with normal ejection fraction and valve function.

At the fourth day of hospitalisation the patient presented with further respiratory deterioration with diffuse bilateral infiltrates in all lung fields (Figure 4), was intubated and admitted to intensive care unit. Serological testing for Epstein Barr virus (EBV) was positive with IgG 46 U/mL (normal <9 U/mL) and IgM 41 U/mL (normal <9 U/mL) and serological testing for CMV was positive with IgG 31.7 Units (normal <9 Units) and IgM 199 Units (normal <45 units). Previous antibiotic therapy was stopped and the patient received therapy with ceftazidime, colmycin and gancyclovir. Bronchoscopy was performed and bronchial washings and bronchoalveolar lavage were obtained from lingula and lower left lobe. Cytological and microbiological examination of bronchial washing and bronchoalveolar lavage (BAL) was negative. Respiratory virus panel test in BAL for detection of human respiratory viruses by use of multiplex PCR was performed and was negative. CMV quantitative PCR in blood was performed revealing 2.8 x 10³ U/L (1.7

Table 1. Laboratory data on admission.

Serum parameters	Patient's data
Urea (10-50 mg/dL)	30
Creatinin (0.5-1.5 mg/dL)	0.9
Glucose (60-100 mg/dL)	97
Na (135-148 mEq/L)	135
K (3.5-5.3 mEq/L)	4
AST (5-45 U/L)	83
ALT (5-45 U/L)	53
GGT (5-45 U/L)	35
ALP (42-128 U/L)	75
LDH (135-225 U/L)	633
Albumin (3.5-5.1 g/dL)	3.5
Proteins (6.5-8.5 g/dL)	7.4
CRP (<6 mg/L)	147
Ht (37-45%)	38.1
Hb (12-15 g/L)	12.8
PTLS (150-400 x 10 ³ /μL)	140 x 10 ³
WBC (4-11 x 10 ³ /μL)	12.97 x 10 ³

Na: sodium; K, potassium; AST, aspartate aminotransferase; ALT, alanine transaminase; GGT, gamma-glutamyl transferase; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Ht, hematocrit; Hb, hemoglobin; PTLS, platelets; WBC, white blood cells.



Figure 1. Chest radiography on admission showing patchy diffuse infiltrates in both lungs with consolidation in the left middle lung field.

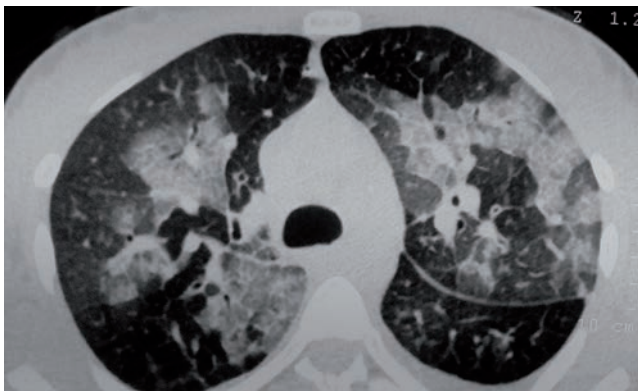


Figure 2. Chest computerized tomography showing ground glass opacities with “crazy paving” pattern in both upper lobes.

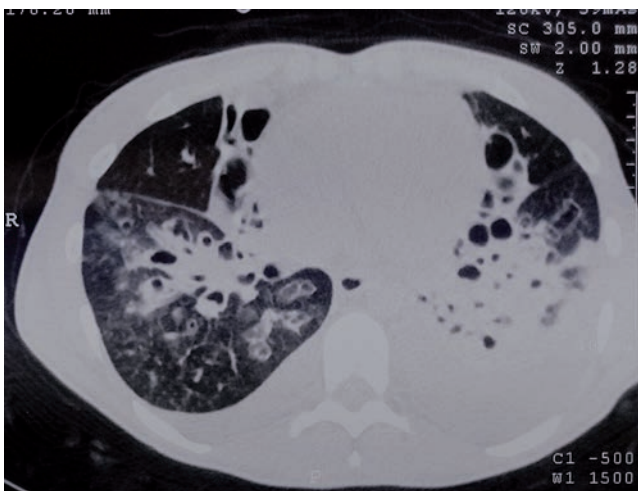


Figure 3. Chest computerized tomography showing pleural effusion in both lungs, cylindrical bronchiectasis in lower lobes and consolidation in the left lower lobe.



Figure 4. Chest radiography showing with diffuse bilateral infiltrates in all lung fields.

X10³ copies/mL) and the diagnosis of CMV respiratory infection was made. BAL was examined for owl’s eye cells, that were not present. Administration of colmycin and ceftazidime was stopped.

The patients after four days of intubation presented with improvement, was extubated and received therapy with high flow nasal oxygen. CMV target organs including eyes, thyroid gland and liver were examined without abnormal findings in fundoscopy, thyroid gland ultrasonography and upper abdomen ultrasonography respectively. A new CT of the chest showed great improvement in radiological findings with mosaic attenuation without consolidation or opacities and without pleural effusions. The patient had gradually complete recovery after a therapy with gancyclovir with a total duration of three weeks. Administration of gancyclovir was stopped when CMV DNA in peripheral blood was not detectable.

Furthermore, the patient was checked for any types of immunodeficiency. The subpopulations of lymphocytes were normal, the ranges of immunoglobulins and complement components were increased and the test for HIV was negative.

Discussion

The case we described is original for two reasons. The first reason is that CMV pneumonia is not frequent in immunocompetent hosts [4]. Klemola *et al.* reported two cases of cytomegalovirus (CMV) infection associated with pneumonia in previously healthy hosts [5]. Manian and Smith reported a case of CMV pneumonia in an immunocompetent host whose clinical condition improved with gancyclovir intravenous therapy [6]. Halimi *et al.* described a case of CMV infection in an immunocompetent woman with pulmonary and hepatic involvement [7]. Nine cases of severe pneumonia due to CMV in non-immunocompromised hosts were described by Eddleston *et al.* in a review reporting 34 cases of severe CMV infection [8]. McCormack *et al.* described a case of severe CMV pneumonia with myocardium and liver involvement in an immunocompetent host [9]. Karakelides *et al.* reported a case of cavitory lesion of the lung with a diagnosis of CMV pneumonia, based on the presence of CMV inclusions in the cells examined from transbronchial biopsy and from the resection of the lesion [10]. Abgueuen *et al.* described two cases of severe CMV pneumonia in non-immunocompromised patients complicated by deep venous thrombosis and pulmonary embolism [11]. Severe community-acquired pneumonia due to CMV in immunocompetent adults has been described by Cunha *et al.* Barclay *et al.* [12,13]. Ii *et al.* described a previously healthy 73-year-old man with CMV infection presented with bilateral pneumonia, hepatitis and orchitis, diagnosed by finding CMV inclusions in the alveolar and bronchial cells [14]. Back *et al.* described a CMV infection with encephalitis, myocarditis and pneumonia while Teixidor *et al.* described a case of pneumonia, pancreatitis and encephalitis due to CMV in immunocompetent hosts [15,16].

Our case is original for a second reason. To our knowledge, the current report is the first to described severe CMV pneumonia in a patient with PCD. In patients with PCD, several bacterial microorganisms are associated with the development of pulmonary infections. However, in these patients, the role of viruses as causative agents of pneumonia has not been investigated [17]. Alanin *et al.* in their study investigated the bacterial flora in non-chronic and chronic infections in the lower airways of patients with PCD and found that *Haemophilus influenzae* was the most frequent microorganism while other common pathogens were *P. aeruginosa*,

Streptococcus pneumoniae, *Moraxella catarrhalis* and *Staphylococcus aureus* [17]. Wijers *et al.* in their review summarised the microorganisms that cause lung infections in patients with PCD and made the comparison with patients with cystic fibrosis (CF). According to their review, in contrast to CF, *Haemophilus influenzae* is the pathogen most frequently found in patients with PCD in adolescents and in early adulthood while *P. aeruginosa* is also common, especially in adults. Other bacterial species frequently discovered from sputum samples of patients with PCD include *S. aureus*, *S. pneumoniae*, atypical Mycobacteria, *Ralstonia species*, *Moraxella catarrhalis*, and *Achromobacter xylosoxidans* [18]. Roden *et al.* in their study determined the prevalence and susceptibility of the most common respiratory microorganisms in PCD patients and concluded that *Haemophilus influenzae* was the most common pathogen followed by *S. aureus*, *Moraxella catarrhalis* and *P. aeruginosa* and atypical mycobacteria were cultured from two patients [19]. Recently, Sakhaee *et al.* described a child with PCD who developed bilateral pneumonia due to mimivirus diagnosed by positive for mimivirus PCR of sputum and BAL. This case is the first to describe viral pneumonia in a patient with PCD [20].

Conclusions

In conclusion, severe CMV pneumonia is a rare clinical entity in non-immunocompromised hosts. In addition, it is the first time that CMV is mentioned as causative agent of severe pneumonia in a patient with PCD. Clinicians should be aware of the potential role of CMV and other viruses as responsible microorganisms for severe pneumonia in patients with PCD.

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