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BRIEF REPORT

Patrick Ray
Yannick Lefort
Catherine Beigelman
Jean-Francois Finet
Bruno Riou

Two cases of acute respiratory failure due to carcinomatous lymphangitis in HIV patients

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P. Ray (✉) · B. Riou
Emergency department, GH
Pitié-Salpêtrière,
Assistance Publique - Hôpitaux de Paris,
47–83 boulevard de l'hôpital, 75013 Paris,
France
e-mail: patrick.ray@psl.ap-hop-paris.fr
Tel.: +33-1-42177242
Fax: +33-1-42177263

Y. Lefort
Medical and Surgical Intensive care unit,
Place du 11 Novembre,
17108 Saintes, France

C. Beigelman
Radiology, GH Pitié-Salpêtrière,
Assistance Publique - Hôpitaux de Paris,
Paris, France

J.-F. Finet
Anatomopathology, GH Pitié-Salpêtrière,
Assistance Publique - Hôpitaux de Paris,
Paris, France

Abstract In HIV-infected patients, acute respiratory failure is usually due to infectious pneumonia. In this report, we describe two cases of acute respiratory failure in HIV patients with clinical presentation suggesting infectious pneumonia. In both cases, the clinical condition deteriorated and death occurred after several days despite therapy. In both cases bronchial biopsies confirmedbronchogenic carcinoma responsible for carcinomatous lymphangitis.

Keywords Human immunodeficiency virus · Carcinomatous lymphangitis · Acute respiratory failure

Introduction

Pulmonary complications are frequent in acquired immunodeficiency syndrome (AIDS) patients, with pneumonia as the leading cause, mainly *Pneumocystis carinii* pneumonia (PCP). HIV infection and concomitant pulmonary malignancies have been reported as Kaposi's sarcoma (KS) or bronchogenic carcinoma [1]. To our knowledge, these are the first descriptions of carcinomatous lymphangitis presenting as acute respiratory failure (ARF) in HIV patients.

Case reports

Case 1

A 57-year-old man was admitted to the emergency department because of dyspnea. The patient had been HIV seropositive for 9 years, presumably due to homosexual contact. He had pneumocystis pneumonia and took daily prophylaxis with cotrimoxazole. Therapy with zidovudine and lamivudine had been stopped by the patient just before hospitalization. The last CD_4 cell count was $209\times10^3/\mu$l. He had a 70-pack per year smoking and alcohol ingestion history.

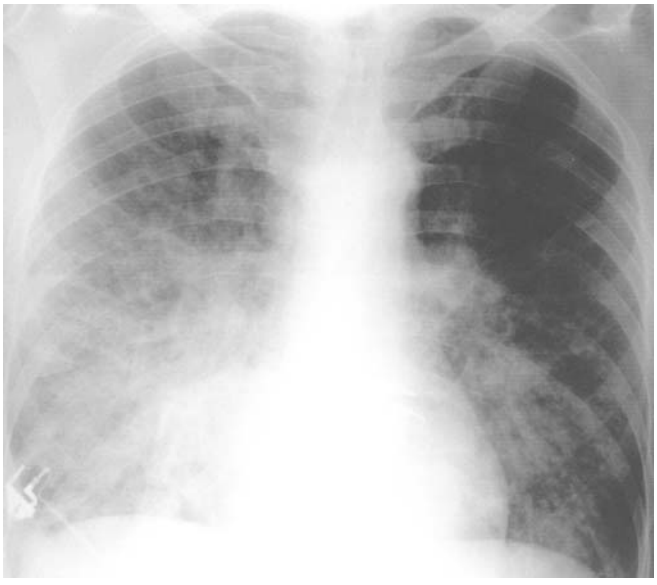

Fig. 1 The chest X-ray demonstrated bilateral predominant right peribronchovascular infiltration, and ground glass opacities located on the lower half of the right lung with a paracardiac opacity. A nodular pattern better seen on the lower part of the left lung was also observed. There was no significant pleural effusion nor mediastinal enlargement

The patient reported weight loss over the last 2 months, with productive cough, dyspnea, and fever. No sweating or shivering was noted. The first chest X-ray (Fig. 1) showed right dominant peribronchovascular infiltration with ground glass opacities and nodular pattern. Bronchoscopy was refused and the patient given clarithromycine for 10 days, but worsened.

Two weeks later, the patient had orthopnea. His temperature was 36.8 °C, pulse rate (PR) was 103/min, blood pressure (BP) was 114/64 mmHg and respiration rate (RR) was 25/min. Physical examination revealed cachexia, bilateral ronchi, and suspected hepatic mass. Lymphadenopathy (1.5 cm) was detected in the subclavicular area.

White blood cell (WBC) count was of 2,900/mm^3 with 58% of neutrophils, and platelet count was 139,000/μl. Serum electrolyte, renal, and liver tests were within normal ranges. LDH was 1,753 UI/l. C-reactive protein was 81 mg/l. PaO_2 was 54 mmHg while breathing room air, pH 7.51, and $PaCO_2$ 38 mmHg. Clear worsening of the radiographic lesions was observed.

The patient was admitted to the intensive care unit (ICU). Bronchoscopy and bronchoalveolar lavage were performed, showing inflammatory mucosa associated with bronchial obstruction of the right middle lobe. Amoxicilline, erythromycin, and cotrimoxazole were started. Blood culture and *Legionnella pneumophila* urinary antigen as cultures for mycobacteria, fungi, viral agents, and opportunistic bacteria remained negative. BAL fluid did not reveal cytological abnormality.

Because of worsening, mechanical ventilation was started. Another bronchoscopy was performed, and multiple endobronchial biopsies showed carcinomatous lymphangitis of poorly differentiated adenocarcinoma. Echography revealed three hypoechogenic hepatic lesions. Despite antimicrobial agents and steroids (methylprednisolone at a dosage of 1 mg/kg twice a day), acute respiratory distress syndrome (ARDS) developed. He died 5 days after admission. No autopsy was performed.

Case 2

A 42-year-old man was admitted for dyspnea. He was an intravenous drug and alcohol abuser and had a 30-pack per year smoking history. For 9 years, he had been receiving antiretroviral treatment and primary prophylaxis with TMX-SMX for HIV infection. The CD_4 cell count was unknown before admission. Seven years before this, he had pneumonia but chest X-ray was normal 6 months before admission.

Ten days before admission, he complained of dyspnea, fever, cough, and night sweats. The first chest X-ray revealed a left hilar mass with adjacent nodular Kerley lines, mediastinal enlargement, and patchy alveolar consolidation. Pneumonia was suspected and amoxicilline/clavulanate, erythromycin, and TMP-SMX were started. 4 days later, respiratory failure appeared.

At admission in the ICU, fever was 39.2 °C, RR was 38/min. BP was 130/70 mmHg and PR was 125/min. Thoracic examination revealed bilateral crackles, clubbing, and use of accessory respiratory muscles. The patient also complained from headache without nuchal rigidity. WBC was 20,000/mm^3. LDH level was 549 UI/l. The others laboratory tests were within the normal range, especially central nervous system fluid analysis. Blood cultures and Legionnella urinary antigen remained negative. First endoscopy showed normal bronchi. BAL identified 10^4 CFU/m, of *E. Coli*. No alveolar hemorrhage was observed. Despite active antimicrobial therapy (cefotaxime and amikacine), fever persisted and respiratory condition deteriorated. Mechanical ventilation was instituted after failure of non-invasive ventilation. The thoracic CT scan performed 1 week later (Fig. 2) revealed left stenosis of the upper lobe bronchus, hilar mass surrounding the pulmonary artery, and distal consolidation. There were also bilateral mediastinal and hilar lymphadenopathy, metastatic nodules, ground glass densities and consolidation in dependent regions with left pleural effusion. Another bronchoscopy was performed, confirming left upper bronchus extrinsic compression. Bronchial biopsy demonstrated carcinomatous lymphangitis with a poorly differentiated adenocarcinoma. BAL cultures for bacteria, mycobacteria, fungi, and viral agents remained negative. The patient developed ARDS and died 9 days after admission. The family refused autopsy.

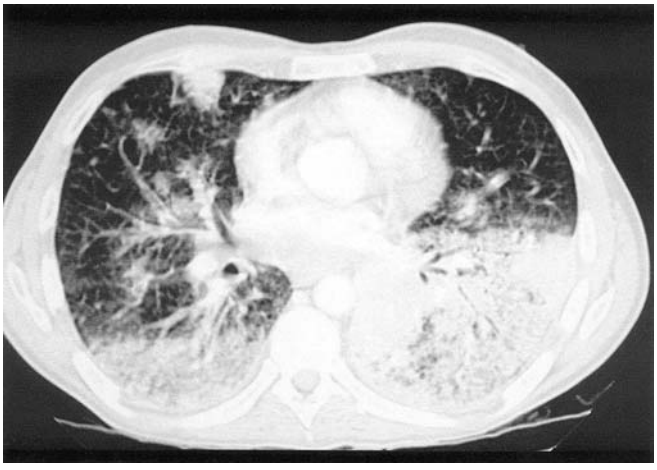

Fig. 2 The CT scan showed pulmonary metastatic nodules, but also ground glass densities in dependent regions predominantly on the left side, with a small left pleural effusion

Discussion

Despite PCP prophylaxis and improvement in antiretroviral therapy, respiratory diseases are still frequent in AIDS patients. Whatever the CD_4 cell count [2, 3], infection remains the leading cause of ARF and mortality is still around 40—50% [4, 5]. Because of its high incidence, PCP was suspected in both patients. The second hypothesis was severe community-acquired pneumonia, especially due to *S. pneumoniae*, *Haemophilus influenzae* or *Legionnella pneumophila* [6]. In both cases bronchoscopy with BAL was first performed. Thus, because of radiological presentation and worsening, despite wide antimicrobial therapy including TMP-SMX, pulmonary malignancies were suspected and bronchial biopsies were performed, as recommended [7].

Kaposi's sarcoma usually affects homosexual men [8], is the commonest malignancy associated with AIDS, and is a cause of ARF [1, 8, 9]. The first patient was homosexual but had no extra pulmonary KS lesion. In both patients, endobronchial KS has not been observed and BAL did not reveal alveolar hemorrhage. Thus, this hypothesis was very unlikely. Other malignant lesions associated with AIDS have been reported [10, 11, 12]. Lymphomas have been described as either part of a disseminated disease or as primary pulmonary involvement. However, thoracic imaging was not suggestive of pulmonary lymphoma [11].

Despite several reports of bronchogenic carcinoma in AIDS patients [9, 12], increased incidence is still debated. Median age of patients is around 40 years. Most of them are smokers or intravenous drug abusers, like our patients. Among the lung cancers, adenocarcinoma is the most frequent, followed by epidermoid carcinoma and small-cell lung cancer. Most of these patients had generalized cancer, but ARF has never been reported as a manifestation of carcinomatous lymphangitis in AIDS patients. In one prior report, this has been described in association with PCP [13]. This 35-year-old, male, drug abuser complained of rapid weight loss, dyspnea, and fever. Radiographic evaluation revealed ground grass opacities and left mediastinal mass. PaO_2 was 56 mmHg and LDH was 693 UI/l. BAL showed PCP and bronchial biopsies revealed carcinomatous lymphangitis due to poorly differentiated adenocarcinoma. PCP was the main cause of dyspnea because the patient initially improved with steroids and TMX-SMX, and died several months later [13].

As expected in our patients, histology revealed adenocarcinoma. In the case of carcinomatous lymphangitis, the tumor can be of extra-pulmonary origin. No autopsy was performed. However, primary lung cancer was strongly suggested by the endoscopic bronchial aspect in the first case, and CT scan with mediastinal adenopathy and metastatic nodules in the second. We concluded that both patients had primary pulmonary cancer with carcinomatous lymphangitic.

In non-HIV patients, ARF related to lung cancer is due to massive hemoptysis, pulmonary embolism, pneumonia, and other factors [14]. However, ARF due to carcinomatous lymphangitis has also been rarely reported [15].

In these two cases, clinical and radiological presentation was highly suggestive of pneumonia but carcinomatous lymphangitis was the main cause of ARF. In the second case, a bronchial stenosis could have initially worsened ARF. However, the negative second BAL with active antimicrobial therapy demonstrated control of infection.

No study has reported on a large series of lymphangitic carcinoma, with the emphasis on recent investigations or treatment with steroids. Several procedures have been proposed, but there is no preferred procedure of choice between CT scan or bronchoscopy with either BAL, bronchial or transbronchial lung biopsy [16, 17, 18, 19]. In one study of chronic diffuse infiltrative lung disease, a CT scan associated with clinical and radiological findings could make a correct diagnosis of lymphangitic carcinoma in 92% of cases [19]. In a recent study, transbronchial lung biopsy and BAL were proposed to determine the etiology of pulmonary infiltrates in mechanically ventilated patients because of thei safety and diagnosis yield. However, lymphangitic carcinoma was not present [20]. An analysis of 530 cases revealed that multiple transbronchial lung biopsy (more than five) had a diagnosis yield in LC of 68% of cases [18].

Physicians should be aware that, in the HIV patient, carcinomatous lymphangitis could present as ARF and mimic pulmonary infection. When lymphangitic carcinoma is suspected, CT scan and multiple bronchial or transbronchial biopsy or both should be considered, although no well-defined strategy has yet been validated.

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