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Casi clinici

Case reports

Pneumocystis jiroveci pneumonia (PCP) misdiagnosed as pandemic influenza H1N1 in a renal transplant patient

Polmonite da Pneumocystis jiroveci (PCP) diagnosticata erroneamente come influenza da H1N1 in un paziente trapiantato di rene

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INTRODUCTION

Pandemic influenza is of particular concern in transplant patients. However, there is a significant overlap in the symptoms of respiratory infections and distinguishing the pathogen which causes the symptoms could be difficult in the absence of sensitive diagnostic assays such as PCR [1]. Here, we report a case of *Pneumocystis jiroveci* pneumonia (PCP) in a renal transplant patient which was initially misdiagnosed as pandemic influenza H1N1.

CASE

A 40-year-old man was admitted to hospital with cough, fever, fatigue and dsypnea. He had received a renal transplant from a cadaveric donor seven months previously and was on tacrolismus, prednisolone and mycophenolate mofetil therapy. Physical examination and laboratory investigations were unremarkable except for high lactate dehydrogenase levels. Computerized tomography of the chest showed patchy ground glass opacity throughout both lungs. Oseltamivir 150 mg/day and intravenous levofloxacin 750 mg/day were started with a diagnosis of possible pandemic influenza H1N1 involving the lower respiratory tract. Despite antiviral and antibacterial therapy, the patient did not improve and bronchoscopy was performed five days later. Bronchoalveolar lavage (BAL) fluid culture did not yield any bacteria and acid-fast staining was negative. Microscopy and PCR of the BAL fluid was positive for *P. jiroveci*. 1,3-beta-D-glucan (Fungitell, Associates of Cape Cod, cut-off 80 pg/mL) was positive in serum (>523 pg/mL) and BAL fluid (277 pg/mL). He was treated with intravenous trimethoprim-sulfamethoxazole (TMP-SMX) 15 mg/kg/day and prednisolone 40 mg twice a day initially. His symptoms improved rapidly and at the eighth day of therapy he was discharged with oral TMP-SMX which was completed to three weeks. The dose of prednisolone was lowered after the first week of the therapy and tacrolismus was added. At the start of therapy for PCP, lymphocyte subgroup analysis was performed which showed a low number of CD4 (+) T-lymphocytes (173 cells/mL). The patient remained on TMP-SMX 160/800 mg twice a week for secondary prophylaxis for an additional six months.

DISCUSSION

From 1 November 2009 to 31 December 2009, 234 patients were hospitalized with influenza-like illness in our clinic. Although the diagnosis was confirmed in 80 patients with PCR, the remaining patients improved with supportive therapy including oseltamivir [2]. Thirty-seven of the 80 PCR confirmed cases had pneumonia. Twenty-eight of the patients had bilateral, predominantly basal, patchy alveolar opacities, while 11 patients had unilateral consolidations [2]. Bronchopneumonia, interstitial pneumonia and adult respiratory distress syndrome have

been reported in several case series from the Mediterranean region [3, 4]. However, the misdiagnosis of serious illness during the first months of the flu pandemic was highlighted.

Diagnosis of pandemic influenza according to case definitions resulted with diagnostic delay in patients with falciparum malaria, neutropenic fever, meningococcal meningitis, dengue fever, salmonellosis, acute coronary syndrome and metastatic gastric carcinoma [5, 6]. To our knowledge, this is the first case with PCP which was initially misdiagnosed as influenza in a renal transplant setting. Due to the lack of the sensitivity of influenza case definitions, attending physicians should cautiously explore alternative diagnoses particularly in patients with severe co-morbid diseases.

PCP occurs in 5-15% of solid organ transplant recipients receiving standard immunosuppression without PCP prophylaxis. In general, anti-Pneumocystis prophylaxis is recommended for all solid organ transplant recipients for at least 6-12 months post-transplant [7]. In our patient, PCP prophylaxis was terminated one month prior to his admission despite a low CD4 (+) T-cell count. Based on data from HIV patients, the CD4(+)T-lymphocyte count can provide a guide to the duration of prophylaxis. Co-infections such as cytomegalovirus pneumonia is of concern in patients with PCP [8]. Although there are no specific clinical and laboratory findings for PCP, diagnosis is usually based on the microscopic detection of cysts in respiratory specimens, such as sputum and BAL specimens which is strongly related to the observer's skills and experience. The detection of 1,3-beta-D-glucan (BDG), a cellwall component of *P. jiroveci* in the serum, is a promising method for diagnosis. The sensitivity and specificity of BDG detection with the Fungitell assay for PCP were 100 and 96.4% in serum samples from 28 patients with HIV infection or a haematological malignancy, respectively [9]. In our patient, serum BDG was higher than 523 pg/mL which is the upper cut-off value for the commercial kit (Fungitell, Associates of Cape Cod) and BDG in BAL was three times higher than the positive threshold.

In conclusion, PCP should be borne in mind by physicians dealing with respiratory infections, particularly in transplant patients.

Key words: Pneumocystis jiroveci, PCP, pandemic influenza H1N1, misdiagnosis

SUMMARY

Respiratory infections are of particular concern in transplant patients. However, there is a significant overlap in the symptoms caused by different pathogens. Here, we report a case of *Pneumocystis jiroveci* pneumonia (PCP) in a renal transplant patient which was initially misdiagnosed as pandemic influenza H1N1. The patient did not improve under oseltamivir treatment and bronchoscopy was performed five days later after hospitalization. PCP was diagnosed by microscoping evaluation of bronchoalveolar lavage (BAL) fluid. Besides, BAL and serum of the patient yielded a large amount of 1,3-beta-D-glucan, a cellwall component of medically important mycoses including *P. jiroveci*. The patient was successfully treated with intravenous trimethoprim-sulfamethoxazole. Due to the lack of sensitivity of influenza case definitions, the attending physicians should be careful about alternative diagnoses particularly in transplant patients with severe respiratory infections.

RIASSUNTO

Le infezioni respiratorie destano particolare preoccupazione nei pazienti sottoposti a trapianto. Nel presente articolo viene presentato un caso di polmonite da Pneumocystis jiroveci (PCP) insorta in un paziente sottoposto a trapianto renale e inizialmente diagnosticata come influenza pandemica da H1N1. Il trattamento con oseltamivir non ha determinato miglioramento del paziente e dopo cinque giorni di ospedalizzazione è stata eseguita una broncoscopia. La PCP è stata diagnosticata mediante valutazione microscopica del lavaggio broncoalveolare (BAL). Inoltre, sia nel BAL che nel siero del paziente è stata riscontrata una quantità elevata di 1,3-beta-D-glucano, una componenete del cell wall di micosi clinicamente rilevanti, quale quella da P. jiroveci. Il paziente è stato trattato con successo con trimetoprim-sulfametossazolo somministrato per via endovenosa.

In assenza di una definizione appropriata di caso di influenza, sarebbe opportuno considerare con attenzione la possibilità di diagnosi alternative, in particolare nei pazienti trapiantati affetti da gravi infezioni respiratorie.

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