CASE REPORT

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A Case of Nephrotic Syndrome With Pneumocystis Jirovecii Infection

ABSTRACT
Pneumocystis jirovecii pneumonia (commonly called Pneumocystis pneumonia or PCP) is an opportunistic infection that occurs in immunocompromised individuals. 26 year-old male patient admitted to nephrology department for hypervolemic hyponatremia and consulted to our clinic due to the desaturation. He has been diagnosed with collapsing glomerulonephritis and he was using cyclosporine and prednisolone. Postero-anterior chest X-ray showed a blunt left cardiodiaphragmatic sinus. After ten days the patient's hypoxia deepened. Repeated chest X-ray showed bilateral perihilar heterogeneous opacity. *Pneumocystis jirovecii* was detected in lavage culture. We presented a case of Pneumocystis Jirovecii pneumonia secondary to cyclosporin toxicity because of a rare case.

Keywords: *Pneumocystis Jirovecii*, Collapsing Glomerulonephritis, Nephrotic Syndrome

Pnömosistis Jirovecii Enfeksiyonu Tanısı Alan Nefrotik Sendrom Olgusu

ÖZET
Pnömosistis jirovecii pnömonisi (yaygın olarak Pnömosistis Pnömonisi veya PCP olarak adlandırılır), immün sistemi baskılanmış bireylerde ortaya çıkan fırsatçı bir enfeksiyondur. Nefroloji servisinde hipervolemik hiponatremi nedeni ile yatmakta olan 26 yaşında erkek hasta desatürasyon gelişmesi nedeniyle tarafımıza danışıldı. Hasta kollapsing glomerulonefrit ile takip edilmekte idi ve başvurusunda prednizolon, siklosporin kullanmakta idi. Postero-anterior akciğer grafisinde (PA AC) solda kardiyodiyafragmatik sinüste küntlük mevcuttu. Hastanın yatışının 10. gününde hipoksemisi derinleşti. Tekrar çekilen PA AC'de sağda daha yoğun olmak üzere bilateral perihiler heterojen opasite artışı saptandı. Lavaj kültüründe Pnömosistis Jirovecii üremesi oldu. Siklosporin toksisitesine sekonder gelişen Pnömosistis jirovecii pnömoni olgusunun nadir saptanması nedeniyle olgumuzu sunduk.

Anahtar Kelimeler: Pnömosistis Jirovecii, Collapsing Glomerulonefrit, Nefrotik Sendrom

INTRODUCTION

Pneumocystis jirovecii is a rare opportunistic microorganism. Both humoral and cellular immunodeficiency are important in the development of pneumocystosis. *Pneumocystis jirovecii* can cause lethal pneumonia in children and adults with immunodeficiency secondary to especially malignancy, organ transplantation, corticosteroid therapy, malnutrition and acquired immunodeficiency syndrome (AIDS) patients. We presented our case because of rare cases of pneumocystis jirovecii pneumonia secondary to cyclosporine toxicity.

CASE

A 26 year-old male patient presented with nausea, loss of appetite, face and hand swelling to nephrology clinic. The patient was ex smoker for 1.5 years. He was a professional tennis coach. The patient has a history of treatment with 1 mg / kg methylprednisolone therapy in august 2016 for collapsing glomerulonephritis (GN). December 2016 mycophenolate mofetil (2x500 mg) was added to the treatment. March 2017 cyclophosphamide started for proteinuria and creatinine increasing. Cyclophosphamide-induced allergic symptoms were observed after 2 months of treatment. The patient was using prednisolone 40 mg and cyclosporin 250 mg when he was admitted to the nephrology clinic. Cyclosporine was stopped due to the progression of renal dysfunction, hyperpotassemia and hypertension, as a result of cyclosporin toxicity and the patient was interned. On the 5th day of hospitalization, the patient was consulted to our chest disaese's clinic with hypoxia (fingertip saturation is 75).

The patient was suffering from shortness of breath and chronic unproductive cough in the system interrogation. His physical examination, fever 36ºC, blood plessure 150/90 mm/Hg, decrase bilateral subscapular respiratory soundsand , +++/+++ pretibial edema. His laboratory examination was white blood cell count 9,3 10^3/Ul, neutrophil count 8,9 10^3/Ul . CRP 0,6 mg/dl. Moderate hypoxemia was detected (Ph:7,42 PO2:53 mmHg PCO2:35,4 mmHg, HCO3:23,6 mEql/L). The alveolar-arterial gradient was elevated (52,75).

Posteroanterior chest X-ray (PA AC) showed that; left cardiodiaphragmatic sinus was blunt. Diuretic therapy was given considering that desaturation was secondary to hypervolemia. Fluconazole and ampicillin-sulbactam treatment were given for oral candidiasis and pneumonia in six days. Due to high fever, the antibiotherapy was changed to piperacillin-tazobactam 3x2,25gr, trimethoprim-sulfamethoxazole (TMP-SMZ) 2x800mg (for prophylaxis), acyclovir 1x800mg. The patient's hypoxemia was deepening and repeated X-ray showed heterogeneous opacity has increased of bilateral perihilar, more intense on the right (Figure 1).

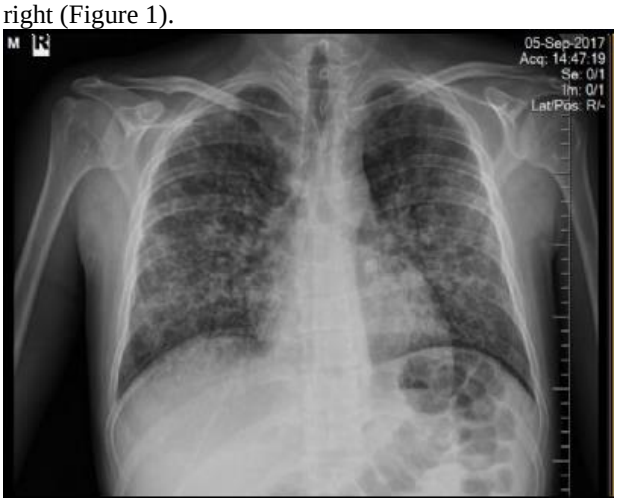

Figure 1. Heterogeneous opacity increase of bilateral perihilar, more intense on the right

High-Resolution Computerized Tomography (HRCT) was performed. Bilateral pulmonary alveolar frosted glass densities and consolidation areas, bilateral pleural effusion and widespread free circulation within the abdomen were observed (Figure 2).

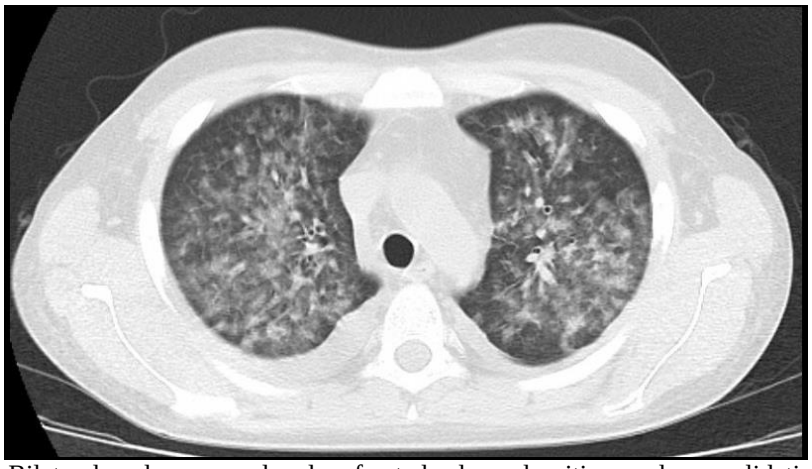

Figure 2. Bilateral pulmonary alveolar frosted glass densities and consolidation areas, bilateral hemorrhagic pleural effusion.

Bronchial lavage was taken with bronchoscopy on patient who could not give sputum. *Pneumocystis jirovecii* was detected in lavage culture. In the cytology reactive bronchial epithelium in a degenerated appearance on the serofibrinous membrane, foamy macrophages, in some foci between lymphocytes, 'crescent' microorganisms on the foamy-fibril floor were observed. TMP-SMZ was given treatment (3 x 7.5 mg / kg) dose. Hypoxemia improved on the 7th day of treatment and the patient was discharged. Treatment was continued with oral TMP-SMZ for 21 days. At patient clinic control the regression observed on the X-ray (Figure 3).

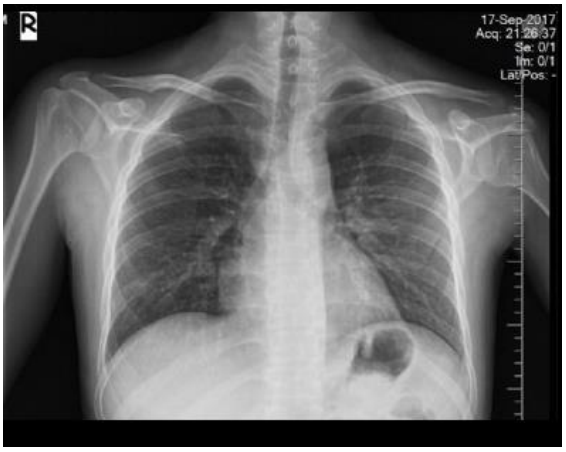

Figure 3. The regression observed on the control X-ray

DISCUSSION

Pneumocystis jirovecii formerly known as Pneumocystis carinii is a single-cell, eukaryotic microorganism. It was considered as a protozoan in the past but recent studies have shown that it was a fungus (1,2). Pneumocystis jirovecii can cause opportunistic infections in infected with human immunodeficiency virus (HIV) (+) and immunosuppressed patients (2). Pneumocystis jirovecii can cause life-threatening pneumonia in patients with impaired immunity such as those receiving moderate doses of oral steroids for greater than 4 weeks (3,4).

Immunosuppressed patients such as those with HIV and a CD4 cell count less than 200 per microliter, solid organ and hematopoietic stem cell transplant recipients, active hematologic malignancies and those who receive chronic glucocorticoid therapy among others are known to be at increased risk of developing Pneumocystis jirovecii pneumonia (2). Yale et al. reported that 50 of 116 patients with HIV (-) P.jirovecii pneumonia had respiratory failure and 33 of these patients had mortality in the hospital (5).

In a retrospective study, 18 patients infected with Pneumocystis jirovecii have been examined. Six of 18 patients were HIV (+) and the other 12 patients were HIV(-) and underlying disaese. Patients renal-transplant recipients (3) , haematological malignancies (3) , autoimmune diseases (2) , renal diseases (2) , advanced hepatocellular carcinoma and one was an infant with congenital cytomegalovirus disease, together with necrotizing enterocolitis(1), (6). Our patient has nephrotic syndrome and had been taking immunosuppressive (cyclosporin) treatment.

Clinical findings are usually nonspecific (3). Pneumocystis Jirovecii pneumonitis typical clinical manifestations include fever, nonproducing cough, and effort dyspnea. (7), Malaise and progressive shortness of breath can be seen (3). HIV(-) immunocompromised patients usually present more acutely (4). Our patient also had a fever, effort dyspnea and unproductive cough.

Dyspnea and hypoxemia, lower alveolar-arterial oxygen gradient can be profound (3,4). In our patient's arterial blood gas partial, oxygen pressure was 53 mmHg and the alveolar-arterial gradient was 52,75. Extrapulmonary manifestations including retinitis, thyroiditis, bone lesions and pneumocystosis of brain, liver, spleen and kidney are rare (4). Our patient had no extrapulmonary findings. Early X-rays may have no pathological findings (8). Typical computed tomography (CT) finding is ground glass opacity (8,3), but cystic lung disease, pneumothoraces, and nodules can be observed rarely (3).

Since Pneumocystis cannot be a cultured microscopic visualization of induced sputum or bronchoalveolar lavage fluid specimens remains the gold standard for diagnosis (3,4). PCR which may be less specific for active infection can be used for diagnosis (4). We obtained the lavage fluid from our patient with flexible bronchoscopy. And this suitable with literature.

Trimethoprim-sulfamethoxazole is the first choice in treatment and prophylaxis. Treatment was trimethoprim given daily 20 mg / kg; sulfamethoxazole in 100 mg / kg. The duration of treatment is 14-21 days. IV treatment can be switched to oral. Prophylaxis is recommended for high-risk patients (4). In first examination we started prophylaxis to our patient because the patient has not been diagnosed yet.And after diagnosis, we changed the prophylaxis to treatment.

Adjunctive corticosteroids are recommended for patients with moderate or severe PCP, defined by room air PaO2 <70 mmHg or alveolar-arterial oxygen gradient ≥35 mmHg, and should be given within 72 hours after starting PCP treatment (4).

Alternative treatments include primaquine plus clindamycin or atovaquone. or IV pentamidine (9). Cyclosporine related Pneumocystis jirovecii pneumonia can be seen (10).

CONCLUSION

The most important point for Pneumocystis jirovecii infection is a high clinical suspicion. Cases of cyclosporine-associated Pneumocystis jirovecii pneumonia have limited number. It should be come to mind that cyclosporine also causes Pneumocystis jirovecii pneumonia.

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