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Initiation of Cotrimoxazole in Patients with Suspected Pneumocystis Pneumonia in HIV Infection: Case Report

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Abstract: ***Pneumocystis Carinii Pneumonia (PCP) or also known as Pneumocystis Jirovecii Pneumonia is a disease that has a high morbidity and mortality rate in patients with decreased immunity, one of disease in HIV/AIDS patients. Human immunodeficiency virus (HIV) have dramatically increased the prevalence of PCP, and have become an alarming complication of the late stages of HIV infection. In this case described patient HIV with PCP suspicion, that have symptoms asphyxiation, cough, fever and weight loss of about 10 kg for two months, treated with oxygen NRB 8 lpm, OAT category I, levofloxacin, nystatin drop, methyl prednisolone and transfusion with PRC to Hb 13, but no improvement after two weeks. The result of LDH serum is 1224 U/L, the absence of BAL and CT-Scan. The treatment this patient is cotrimoxazole 3x960 mg. The cotrimoxazole continued for 21 days and patient recovered accordingly. Cotrimoxazole can be given as a prophylaxis and a therapy on PCP infected with HIV. The therapeutic dose depends on the enormousness of the disease.***

Keywords: PCP, HIV, cotrimoxazole, pneumocystis jirovecii pneumonia

1. Background

Pneumocystis Carinii Pneumonia (PCP) or also known as Pneumocystis Jirovecii Pneumonia is a disease that has a high morbidity and mortality rate in patients with decreased immunity, one of disease in HIV/AIDS patients. Human immunodeficiency virus (HIV) have dramatically increased the prevalence of PCP, and have become an alarming complication of the late stages of HIV infection.[1] The mortality rate of PCP is 10-20% in early infections, increases the demand for mechanical ventilation.[2]

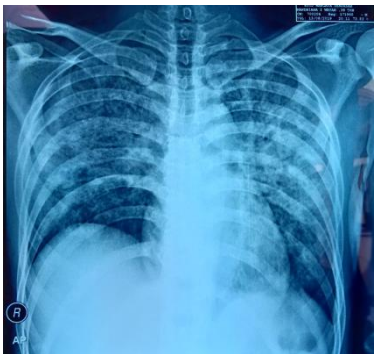
PCP is very difficult to diagnose because the symptoms and signs of the disease are not specific. Patients with PCP show symptoms of fever, cough, shortness and in some cases suffer from respiratory failure. [4]An examination that can be made to diagnose PCP is with checks of bronchoalveolar lavage (BAL) and CT-Scan. The facility's limited application screening is one of the constraints in PCP's diagnosis, so that our therapeutic treatment is often overdue. In PCP there is an increase in the LDH serum, an LDH examination containing a high sensitivity but low speciality. Because of a less specific examination that patients with PCP symptoms and were not cured by antibiotic broad spectrum therapy and CD4 <200 were given cotrimoxazole therapy. cotrimoxazole can reduce mortality rates in adult HIV patients that have ART, PCP and TB patients, but their use is still low-wide.[3]

2. Case Presentation

Male, 31 years old comes with complaints of asphyxiation since 1 week, which became even worse a day ago, patients have been complaining of coughing for 3 weeks, not phrasing, and fever and sweat. The patient also complained of the loss of appetite, weight loss of about 10 kg in the past two months. For the past six months, patient complain has diarrhea but not continuous.

During the physical examination, a patient has tachypnea saturated with oxygen discharge. In patients there are anemic conjunctivitis, oral candidiasis and an auscultation sound subtle rhonchi in both lungs.

Patient performed thorax X-rays with a infiltrate on both lungs with the appearance of pneumonia, dd/ pulmonary TB. The patient also had TCM examination with result : MTB undetected, and the PITC results on this patient are reactive with CD4 23. The result of blood count that is hemoglobin (Hb) 7,9 g/dl.



Picture 1: Appears to infiltrate on both lungs

At the beginning of the examination, patient were diagnosed with clinical HIV/AIDS with pulmonary TB in clinical confirmation, oral candidiasis and anemia. Treatment given with oxygen NRB 8 lpm, OAT category I, levofloxacin, nystatin drop, methyl prednisolone and transfusion with PRC to Hb 13.

But two weeks after treatment with OAT category 1, patient still complaining asphyxia and saturation is declining, so that the oxygen supply is increased to NRB 10 lpm. The patient for an LDH exam with results 1224 U/L, due to absence of BAL and CT-Scan, so the patient was treat by cotrimoxazole 3x960 mg. After six days of cotrimoxazole treatment the patient went through an accelerated recovery

with a good saturation without oxygen use. The cotrimoxazole continued for 21 days.

3. Discussion

Pneumocystis carinii pneumonia (PCP), or what's called pneumocystis jirovecii pneumonia (PJP) is a fungal infection that occurs in patients with immunocompromised and can be life-threatening. Those who carry PCP risk are cancer patients, HIV, transplant recipients, or patients who use immunosuppressive therapies. Pneumocystis carinii pneumonia are transmitted from person to person by air route. Pulmonary asymptomatic colonization can occur in people with normal immune systems, and become a reservoir for pneumocystis spread to individuals whose immune systems are weakened.[4] A meta-analysis of risk-factors associated with increased mortality from PCP include age, sex, delay in diagnosis, respiratory failure, solid tumours, high lactate dehydrogenase, low serum albumin, and bacterial, Aspergillus or Cytomegalovirus co-infection.[5] A clinical diagnosis of PCP was considered when at least two of the following variables were present: symptoms such as unproductive cough, fever and dyspnea; arterial partial pressure of oxygen (PaO2) lower than 65 mm Hg; and chest radiographs presenting fine bilateral, perihilar interstitial shadowing.[6]

Table 1: Classification of Pneumocystis Pneumonia[5]

Clinical factor	Disease Classification		
	Mild	Moderate	Severe
Dysnoea	On exertion	On minimal exertion/possibly at rest	At rest
Resting arterial tension	PaO_2 of > 11.0 kPa	PaO_2 8.1–11.0 kPa	PaO_2 < 8.0 kPa
Oxygen saturation	SaO_2 > 96%	SaO_2 of 91–96%	SaO_2 < 91%
Radiology	Normal/Minimal changes on CXR	Diffuse interstitial changes on CXR	Extensive interstitial changes with potential diffuse alveolar shadowing on CXR
Other		Possibly Fever	Tachypnoea at rest, fever, cough

Alternative serum testing for the diagnosis of PCP has not been established until now.[6] LDH is a cytoplasmic enzyme present in all major organ systems. The extracellular appearance of LDH indicates cell damage or cell death.[7]Elevated lactate dehydrogenase (LDH > 500 mg/dL) is associated with lung damage, and may be a useful adjunct test in the HIV-positive patient, where high concentrations may indicate severe disease.[5]Sensitivity LDH for PCP is reported to be up to 100%.[7] If levels are normal it can be used to exclude PCP, but limited specificity requires any elevated level to be confirmed with a mycological assay.[5] The gold standard for diagnoses PCP is *bronchoalveolar lavage* with *Gomori Methenamine silver* that appearance *ground glass appearance*.[8]

Trimethoprim-sulfamethoxazole is the standard for treatment and prophylaxis of Pneumocystis jiroveci pneumonia (PJP).[8] In settings in which co-trimoxazole prophylaxis for HIV/AIDS is initiated based on WHO clinical staging criteria only , co-trimoxazole prophylaxis is recommended for all symptomatic people with mild, advanced or severe HIV disease (WHO clinical stages 2, 3 or 4) [A-I]. Where CD4 cell testing is available, co-trimoxazole prophylaxis is recommended for everyone with a CD4 cell count <350 per mm3, particularly in resource-limited settings where bacterial infections and malaria are prevalent among people living with HIV. Some countries may choose to adopt a CD4 threshold of 200 cells per mm3 below which cotrimoxazole prophylaxis is recommended. This option is especially recommended if the main targets for co-trimoxazole prophylaxis are PCP and toxoplasmosis.[9]

Table 2: Initiation of co-trimoxazole prophylaxis among adults and adolescents living with HIV

Based on who clinical staging criteria alone (when CD4 count is not available)	Based on who clinical staging and CD4 cell count criteria[a]
WHO clinical stage 2, 3 or 4 **[A-I]**	Any WHO clinical stage and CD4< 350 cells per mm³[b] **[A-III]** OR WHO clinical stage 3 or 4 irrespective of CD4 level **[A-I]**
Universal option: Countries may choose to adopt universal co-trimoxazole for everyone living with HIV and any CD4 count or clinical stage. This strategy may be considered in settings with high prevalence of HIV and limited health infrastructure **[C-III]**.	

The primary prophylactic agent for PCP is one single-strength TMP/SMX (80 mg TMP/400 mg SMX) daily or one double strength tablet (160 mgTMP/800 mg SMX)/daily. Alternative prophylaxis includes one double strength TMP/SMX tablet three times per week, dapsone alone or in combination with pyrimethamine and leucovorin, pentamidine aerosols or atovaquone.[5] It is recommended that prophylaxis in adults and adolescents be continued until CD4 T-cell counts are sustained at > 200 cells/mm3 for more than 3 months, but CD4+ cell percentage of >14%, and a sustained undetectable HIV plasma RNA levels can also be considered. If PCP was diagnosed when thepatient's CD4 count was >200 cells/mm3 life-time prophylaxis could be considered. Doses of cotrimoxazole treatment for PCP is TMP/SMX (15–20 mg/kg TMP; 75–100 mg/kg SMX), for the mild-severe diseases (example hypoxemia) corticosteroid adjuvant can be use.[5]

Table 3: Prophylactic and therapeutic options for the management of Pneumocystis pneumonia in HIV, haematology, and solid organ transplant recipients

Strategy	Population [Ref]		
	HIV-Positive [39]	Haematology [20,43]	Solid Organ Transplantation [44]
Prophylaxis	Front line: Trimethoprim/sulfamethoxazole one single-strength (80 mg TMP/400 mg SMX) daily or one double strength tablet (160 mg TMP/800 mg SMX)/daily. Second line: Trimethoprim/sulfamethoxazole one double strength tablet (160 mg TMP/800 mg SMX) three times per week Dapsone (50 mg twice daily) Dapsone (200 mg) + pyrimethamine (75 mg) + leucovorin (25 mg) weekly Dapsone (50 mg daily) + pyrimethamine (50 mg weekly) + leucovorin (25 mg weekly) Pentamidine aerosols (300 mg per month) Atovaquone 1500 mg daily	Front line: Trimethoprim/sulfamethoxazole one single-strength (80 mg TMP/400 mg SMX)/day or double strength tablet (160 mg TMP/800 mg SMX)/day or three per week. Second line: Dapsone (50 mg twice daily) Pentamidine aerosols (300 mg per month) Atovaquone (1500 mg daily)	Front line: Trimethoprim/sulfamethoxazole one single-strength (80 mg TMP/400 mg SMX)/day or double strength tablet (160 mg TMP/800 mg SMX)/day or three per week. Second line: Dapsone (50–100 mg once a day) Atovaquone (>1000 mg daily) Third Line: Pentamidine aerosols (300 mg every 3–4 weeks)
Treatment	Frontline: Trimethoprim/sulfamethoxazole (15–20 mg/kg TMP; 75–100 mg/kg SMX per day) For moderate to severe disease (i.e., hypoxemia) adjunctive corticosteroids should be used Second line for severe disease: Primaquine and clindamycin (30 mg/(600 mg × 3)) per day Pentamidine IV (4 mg/kg/day) Second line for mild/moderate disease: Dapsone (100 mg daily) + trimethoprim (15 mg daily) Atovaquone (750 mg BID)	Frontline: Trimethoprim/sulfamethoxazole (15–20 mg/kg TMP; 75–100 mg/kg SMX per day) Second line: Primaquine and clindamycin (30 mg/(600 mg × 3)) per day Pentamidine IV (4 mg/kg/day) Atovaquone (750 mg/ 2–3 per day)	Frontline: Trimethoprim/sulfamethoxazole (15–20 mg/kg TMP; 75–100 mg/kg SMX per day) with TMP administered by IV every 6–8 h. For hypoxemic patients potentially in combination with 40–60 mg of prednisolone (twice daily) Second line: IV Pentamidine (Initially 4 mg/kg/day over 1–2 h) Recipients of pancreas/islet transplants should receive an alternative second line therapy.

IV: Intravenous

In this case, PCP's suspicion referred to an X-ray image of bilateral predation with broad spectrum antibiotic therapy like levofloxacin and OAT category I, and patient still complaints asphyxia after that treatment. Furthermore, LDH serum in this patient is 1224 U/L that means there is a damage organ, in this case is pulmonary. The other thing that supports PCP's suspicions is HIV positive. The increase of LDH serum in HIV patient cannot be eliminated PCP disease.[5] The consensus of WHO about HIV explained that cotrimoxazole can be given as prophylactic and therapy to PCP with cd4 <200. For decrease mortality and morbidity on PCP infected HIV in this patient given cotrimoxazole.

4. Conclusion

Cotrimoxazole can be given asa prophylaxis and a therapy on PCP infected with HIV. The therapeutic dose depends on the enormousness of the disease. Cotrimoxazole can be given as a therapy if a clinical symptom leading to PCP, a rise of LDH and occur desaturation after the antibiotic broad spectrum. Early exposure to cotrimoxazole therapy can improve life expectancy in PCP patients.

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