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Non-Genomic Pathway Corticosteroid in HIV Patient with Pneumocystis Pneumonia - A Case Report

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Abstract: ***Steroid hormones are known to mediate physiological cell functions. Corticosteroid are known to have genomic and non-genomic mechanism. Non-genomic mechanism occurs faster than genomic pathway and referred to as extranuclear mechanism. This non-genomic mechanism exerts rapid inhibitory effects on human neutrophil degranulation at the cellular level. We present a 23-year-old patient with HIV and Pneumocystis pneumonia admitted at Wangaya Regional Hospital Denpasar who treated by high dose methylprednisolone to control the inflammation. High dose corticosteroid showed a non-genomic effect in this patient. Non-genomic effect has fast action to control inflammation. We have to control the inflammatory agent properly to achieve an optimal healing of patient. However, the use of high doses corticosteroids should carefully determine to avoid its side effects.***

Keywords: Non-genomic corticosteroid, High-dose corticosteroid, HIV, *Pneumocystis* pneumonia

1. Introduction

Steroid hormones are known to mediate physiological cell functions. Classic steroid nuclear hormone receptor activity activated by binding of a steroid hormone ligand to its receptor. Then the receptor undergoes a conformational change that results in the dissociation of HSPs, translocation to the nucleus, dimerization, association with various coregulators, and binding to specific sequences of DNA termed hormone response elements (HREs). This mechanism pathway occurred in cytoplasmand called steroid genomic mechanism.[1] The genomic mechanism produces changes in the levels of specific mRNA.[2]

Nuclear receptors may already be located in the nucleolus prior to hormone binding. This situation allows signal transduction pathways and physiological changes independent of their actions in the nucleus, via a mechanism designated non-genomic mechanism.[3] Non-genomic mechanism occurs faster than genomic pathway and referred to as extranuclear mechanism. These non-genomic mechanismexert rapid inhibitory effects on human neutrophil degranulation at the cellular level.[4]It also activate the endothelial nitric oxide synthetase (e-NOS). Nitric oxide act in many of the inflammatory manifestation, including vasodilatation and inflammatory cell recruitment.To achieve non-genomic effect, we have to give high-dose corticosteroid.[5,6]

Pneumocystis pneumonia is a lung infection caused by fungus *Pneumocystis jirovecii*. Most patient who get PCP have an immunodeficiency condition like HIV/AIDS.[7,8,9] Severity of pneumonia is related to elevated uncontrolled inflammatory cell.[10] Marik et al. and Monton et al. was demonstrating that high-dose glococorticosteroid decrease systemic and lung inflammatory response such as IL-6, BAL neutrophilic count, and CRP) in mechanically ventilated patient. Glucocorticosteroids show benefit in HIV with *Pneumocystis* pneumonia with prednisone 80mg / day then tapered over 3 weeks.[11]

We present a case of HIV with *Pneumocystis* pneumonia admitted at Wangaya Regional Hospital Denpasar. This case report is substantial as a reminder that high-dose corticosteroid have a non-genomic mechanism which important to eliminate inflammatory mediator in pneumonia. The proper use of corticosteroid would make the patient relieve their symptom and reduce the ICU need.

2. Case Report

A 23-year-old male was admitted due to complain about breathless 2 weeks prior to hospitalization. The patient first complained of shortness of breath on 14 March (3 weeks prior to hospitalization) and get worse. The breathless got better when he took a rest for a moment. He also was diagnosed with HIV/AIDS since 7 months ago, but he took the ARV only once. Then he did not take the ARV until was hospitalized. He also had symptom of cough, chest pain, and fatigue. He had no symptom of fever, chills, and cold.

On vital sign assessment, the patient was fully conscious. Blood pressure was 120/80 mmHg and heart rate was 100 beat per minute. He had tachypnea (respiration rate = 25per minute) and 82% of oxygen saturation. On physical examination we did not get any abnormal finding in his lungs and others.

Laboratory examination revealed leukocytosis (15.17 x 10^3 /µL) with neutrophil predominance (84.4%) and low lymphocyte (15.1%) and thrombocytosis (616 x 10^3 /µL). Neutrophil Lymphocyte Ratio was found to be high (NLR ratio = 9.85). Liver enzyme test showed a slightly increase SGPT (56). Electrolyte examination showed mild hyponatremia (Natrium = 133 mmol/L). Blood gas analysis showed that the patient undergo acidosis metabolic fully

compensated. (pH = 7.39, pCO_2 = 34 mmHg, pO_2 = 51 mmHg, HCO3 = 21 mmHg). Chest x-ray of the patient revealed that he had pneumonia. To eliminate suspicion against covid-19, we did a swab antigen SARS-CoV-2 examination. The SARS-CoV-2 examination showed a negative result.

Based on clinical and laboratory findings, his breathless was caused by pneumonia. The patient also diagnosed with HIV/AIDS before and did not take any ARV. So we believe that pneumonia was caused by *Pneumocystis jirovecii.* The patient was started on O_2 NRM 15 lpm, normal saline infusion, levofloxacin, ceftazidime, cotrimoxazole, esomeprazole, NAC, and methylprednisolone. We start with 2 x 62, 5 mg methylprednisolone then increase the dose to 2 x 125 mg to control the inflammation for 3 days. We tapered off the methylprednisolone dose to 2 x 62, 5 mg, and switched to oral 2 x 4 mg. All features of Pneumonia *Pneumocystis* completely resolved and he was discharged on the 10th day of hospitalization.

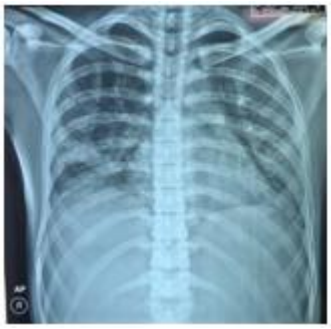

Figure 1: Chest x-ray

3. Discussion

This case report illustrate the use of corticosteroid in HIV/AIDS patient with PCP. The patient was diagnosed with HIV/AIDS 7 months ago prior to hospitalization. He did not take any ARV since was diagnosed. The reported patient showed symptoms of shortness of breath, cough, chest pain, and fatigue. Chest x-ray showed pneumonia. These symptoms, history of HIV/AIDS, and chest x-ray lead to a diagnosis of PCP. Another study showed that people with HIV/AIDS are more likely to get PCP when he did not get any ARV.[7, 8, 9]According to WHO, the patient was in 4th clinical stage of HIV/AIDS with PCP as the category.[12]

The patient was treated O_2 NRM 15 lpm, normal saline infusion, levofloxacin, ceftazidime, cotrimoxazole, esomeprazole, NAC, and methylprednisolone. We start with 2 x 62, 5 mg methylprednisolone to control the inflammation. Patient's oxygen saturation was 80% on room air and respiration rate was 25 per minute. Then he was oxygenize with O_2 NRM 15 lpm and reached 98% oxygen saturation and respiration rate was 22 per minute. This oxygenation was followed by methylprednisolone injection 2 x 62,5 mg. The patient still complain about his shortness of breath while he was doing some activity. On the third day we tried to tapered off the oxygenation using NRM 10 lpm and his saturation was 97%. Then on the forth day we tried to change the NRM with nasal cannula 10 lpm, but the saturation was 93%. We were back to use NRM 10 lpm because of the bad oxygen saturation.

On the fifth day, we increased the dose of the methylprednisolone to 2 x 125 mg for 3 days. The next day, patient felt an improvement in his shortness of breath and we tried to use nasal cannula 10 lpm. The saturation was 97% and respiration rate was 20 per minute. On the sixth day patient's respiration got better, we tapered the oxygenation to nasal cannula 5 lpm (Oxygen saturation = 96%). The next day (the last day we gave methylprednisolone 2 x125 mg) the oxygenation was tapered to nasal cannula 3 lpm, the oxygen saturation was 97% and respiration rate was 18 per minute. We tapered the methylprednisolone dose to 2 x 62,5 mg on the 8th day and patient felt huge improvement of his shortness of breath. On the 9th day we switched to oral methylprednisolone 2 x 4 mg and removed the nasal cannula. Patient had nothing to complain and discharged on the 10th day.

From this case, we can see the role of methylprednisolone in improving the patient's shortness of breath. At the first two days we gave 2 x 62,5 mg, but the symptom did not get better. Then we tried to overcome the symptom by using non-genomic pathway of methylprednisolone (2 x 125 mg). We treated the patient with high dose methylprednisolone to get its non-genomic effect.[13]Non-genomic mechanism occurs faster than genomic pathway and referred to as extranuclear mechanism. These non-genomic mechanismexert rapid inhibitory effects on human neutrophil degranulation at the cellular level.[14]It also activate the endothelial nitric oxide synthetase (e-NOS). Nitric oxide act in many of the inflammatory manifestation, including vasodilatation and inflammatory cell recruitment.[5,6]Non-genomic pathway effect is proven in this case. The respiration of the patient run into a huge improvement after he was given high dose methylprednisolone.High dose methylprednisolone was given for 3 days to minimize the occurrence of its side effect, such as glaucoma, depression, hypertension, infections, Cushing syndrome, etc. (Corticosteroid Adverse Effects , Yasir). Then we tapered off the dose to 2 x 62,5 mg methylprednisolone, and switched orally 2 x 4 mg.

4. Conclusion

High dose corticosteroid showed a non-genomic effect in this patient. Non-genomic effect has fast action to control inflammation. We have to control the inflammatory agent properly to achieve an optimal healing of patient. However, the use of high doses corticosteroids should carefully determine to avoid its adverse effects and secondary infection.

5. Declarations

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