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Correlation of Neutrophil and Lymphocyte Status with Toxoplasmosis in Malignancy Patients Receiving Chemotherapy at Dr. M. Djamil Hospital

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A B S T R A C T

Toxoplasmosis is an infectious disease caused by the parasite *Toxoplasma gondii*. This infection is often an opportunistic infection in patients who have decreased immunity including malignancy patients undergoing chemotherapy. Malignancy and chemotherapy cause suppression of the spinal cord so that it can cause decreased production of blood cells. Profile and lymphocytes. The design of this study is a cross section with consecutive techniques. The study took place from November 2019 to January 2020 in the Chemotherapy Unit and the Clinical Pathology Laboratory of RSUP DR. M. Djamil Padang with a total sample of 54 people. This research was conducted by detecting anti-T. gondii IgG and IgM using the patient's medical record. The results showed that as many as 74% of malignant patients undergoing chemotherapy at RSUP Dr. M. Djamil Padang experienced toxoplasmosis with the detection of anti-T-gondii IgG in the patient's blood serum. There is no relationship between the decrease in the status of stem neutrophils, neutrophil segments, and lymphocytes with the incidence of toxoplasmosis in malignant patients undergoing chemotherapy at Dr. M. Djamil Hospital (p> 0.05).

Introduction

Toxoplasmosis is a type of zoonotic disease, which is a disease transmitted from infected animals to humans. This disease caused by *Toxoplasma gondii* and protozoa can be transmitted through consumption of raw or meat undercooked and ingested vegetables or raw fruits that contain the parasite *T. gondii*. [1] Animals that can transmit diseases toxoplasmosis includes cats, dogs, pigs, sheep, cows, and other types of pets. [2]

Toxoplasma gondii is estimated to infect 30 population in the world. This is associated with risk factors toxoplasmosis such as contact with animals pet, nutritional factors and environmental conditions. Humans can also be infected from eating meat containing raw or undercooked cyst, consume oocyst-contaminated water and from feces of infected cats. In individuals immunocompetent, commonly *T. gondii* infections can be controlled by the immune system so happen without symptoms. [3]

Infection by *T. gondii* can appear as one of the opportunistic infections that is considered as latent reactivation results. 4 Toxoplasmosis can occur in patients who have immune deficiency (immunocompromised), as in patients malignancies undergoing chemotherapy. Chemotherapy can cause a decrease in endurance. This is because chemotherapy drugs not only kill the malignancy cell, but also damage healthy cells. Drug chemotherapy affects the body's active cells and splitting, one of which is blood cells in the marrow bone. [5]

Emphasis in bone marrow (*myelosuppression*) due to chemotherapy causing blood cell production decreased. This decrease in blood cells causes a decrease in the number of leukocytes (leukopenia).[6] Research conducted by Choi *et al* shows that leukocytes are decreasing neutrophils and lymphocytes. [7]Decreased lymphocytes (lymphopenia) be a marker of patient sensitivity to agents chemotherapy and then it will spark neutropenia. [8] Neutropenia and lymphopenia causes decreased cytokine production, i.e. IFN γ, TNF α, and IL- 12 that play a role in helping the body fight *T. gondii* infection , so this condition can be trigger toxoplasmosis in patients malignancies undergoing chemotherapy. [8-10] Neutrophils play a role in the initial infection by *T. gondii* can be occur on days 7 to 14 days after chemotherapy. [6]

The prevalence of toxoplasmosis in patients malignancy in China was found to be 20.59% and in Turkey is 19%, whereas in Nepal the prevalence Toxoplasmosis was found to be higher in patients who ocular malignancy. 6 Prevalence based type of malignancy, toxoplasmosis found highest in lung malignancy (68%) followed by malignancy colon (61.9%), uterine malignancy (56.52%), malignancy liver (55%), kidney malignancy (52.24%), and breast malignancy (43.82%). [11]

Toxoplasmosis can be asymptomaticuntil it appears with a variety of signs andthe symptoms. Infection in immunocompetent individuals,generally can heal itself due to their presenceefficient immunity limits disseminationthe tachyzoite stage is developing rapidly. However, parasiteit still lives in the form of tissue cystsstroughout the life of the host. Cellular and immune systemhumoral, including T lymphocytes and macrophagescontrolling these tissue cysts. [12]

After being infected for several weeks, symptoms that look like flu or not symptomatic at all. However, in patients with immunocompromised, *T. gondii* parasite could cause neurological symptoms such as encephalitis and can attack the heart, liver and eyes (chorioretinitis) and can manifest into the brain as cerebral toxoplasmosis. [13]

Detection of toxoplasmosis is required at malignancy patients who are undergoing chemotherapy because toxoplasmosis can reduce quality of life patients and can also cause death.[3] Based on the background description above, researchers are interested in knowing the relationship of events toxoplasmosis with neutrophil counts in patients malignancies undergoing chemotherapy at Dr.M. Djamil Hospital.

Materials and Methods

In this study, 54 blood sample from malignancy patients from Dr. M. Djamil Hospital. Subject inclusion criterias were allmalignant patients undergoing chemotherapy at the RSUP DR. M. Djamil Padang and willing to be the subjectresearch by signing the consent formparticipate as provided. Subject exclusion criteria was malignant patients who have just had onechemotherapy. Samples were examined by ELISA test using VIDAS kit.

Results and Discussion

In this study, from 54respondents, there were 19 male patients35 female and patients.Based on age, the average number of respondentswere aged 56-65 years as many as 16 respondents,low stem neutrophil status were found in 24respondents, low segmented neutrophil status were foundin 18 respondents, low lymphocyte status were foundin 19 respondents, and the incidence of toxoplasmosisfound in 40 respondents with IgG titersincreased in 40 respondents (74.1%).

The results of this study are in accordance with the studythe other was carried out by Narges *et al* in Iranstated that 29 out of 29 (100%) blood samplespositive breast malignancy patients have an infectiontoxoplasmosis. Other research results by Bajnok *etal* in 2018 in England found 72 out of 72(100%) positive patient samples of malignancy experienced toxoplasmosis.[14] Research conducted byBaiomy in 2010 stated that the ratio of the incidence of parasitic infection in immunocompromised and immunocompetent patients was 30% and 10%.[15] And there is no correlation between stem neutrophils status with toxoplasmosis. From 54 respondents, 44.4% respondents have decreased stem neutrophils status (p >0.05), 51.9% of respondents have normal stem neutrophils status and 3.7% of respondents have increased in stem neutrophil status.

In this study find no correlation between segmented neutrophil status with toxoplasmosis. From 54 respondents, 33.3% of patients have decreased segmented neutrophils status (p> 0.05), 35.2% of patients have normal segmented neutrophil status, and 31.5% of patients have increased segmented neutrophil status.

Neutrophils include neutrophils that differentiate in maturity or are known as segment neutrophils and immature or stem neutrophils. Stem neutrophils are young forms of segment neutrophils that play a role in the initial phase of infection consisting of a small percentage of peripheral neutrophils, while segment neutrophils are mature neutrophils that are present in large numbers in the blood circulation. Both stem neutrophils and segment neutrophils contribute to the initial infection of T. gondii by invading damaged tissue and releasing IL-12 cytokines.[20]

Decreased neutrophils that occur in patientschemotherapy is associated with a decrease in IFN-kadar levels,TNF-α, and IL-12, cytokines are known to be important inparasitic control of *T. gondii* . When an infection occurs by the parasite*T. gondii* , neutrophils will play a role in the initial stages forstimulates IFN-γ as the main mediator of resistancethe host has *T. gondii* . Research conducted bySusan et al showed that hostsmore susceptible toinfections of *T. gondii*when having multiorgan disease that can cause uncontrolled replication of tachyzoit in the blood.[16]

There is no correlation between lymphocyte status withtoxoplasmosis. From 54 respondents, 35.2% of respondents have decreased lymphocyte status (p > 0.05), 37.0% of respondentshave normal lymphocyte status, and 27.8% of respondentshave increased lymphocyte status.

Decreased lymphocytes (lymphopenia)can be a marker of patient sensitivity tohaematological toxicity due to chemotherapy agentschemotherapy will induce lymphopeniabefore neutrophil decline (neutropenia).[8] When there is an infection by *T. gondii*, antigenwill be presented by Antigen Presenting Cell (APC) and then

willgives a signal to the lymphocytes to be activated. This activation leads to proliferation, differentiation, and specific functions of lymphocytes. Lymphocytes will secrete cytokines such as IFN-γ and TNF-αwhich acts as a mediator in the fight against infection *T. gondii*. IFN-γ is the main mediator of resistanceagainst *T. gondii* and so forthintracellular mechanism to kill parasites andinhibits its replication.[17] In addition, cytokinesothers who can also respond to *T. gondii* infection in including IL-2, IL-7, and IL-5 which are also secreted by lymphocytes.[18]

CD4 and CD8 T cells have a regulatory functionas a mediator against *T. gondii* infection.During the initial period of infection, T cells will contributeoptimally to control infections that occurby increasing cytokine production.[17] However,in other malignancieslike Hodgkin's lymphoma, the decreasing of lymphocytes can occur as a mediator in *T. gondii*.[19] (Fig. 1–3 and Table 1).

Table.1 Characteristics of the toxoplasmosismalignancy patients receiviing chemotherapy

Characteristics	f	%
Gender		
Male	19	35.2
Female	35	64.8
Age		
17-25	4	7.4
26-35	9	16.716.724.1
36-45	9	29.6
46-55	13	5.5
56-65	16	
>65	3	
SStatus of Infection		
Positive	40	74.1
Negative	14	25.9
IgG dan IgM Titer		
IgG	40	74.1
IgM	0	0
Stem NetrophilsStatus		
Low	24	44.4
Normal	28	51.9
High	2	3.7
Segmented Netrofil Status		
Low	18	33.3
Normal	19	35.2
High	17	31.5
LymphocytesStatus		
Low	19	35.2
Normal	20	37.0
High	15	27.8

Fig.1 Correlation between stem neutrophils with toxoplasmosis

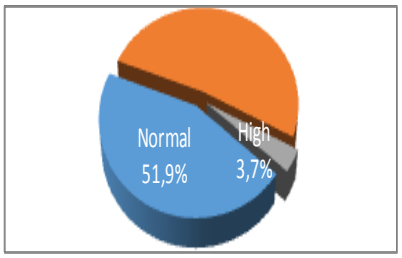


Fig.2 Correlation between segmented neutrophils with toxoplasmosis

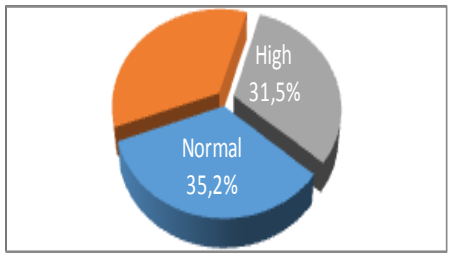
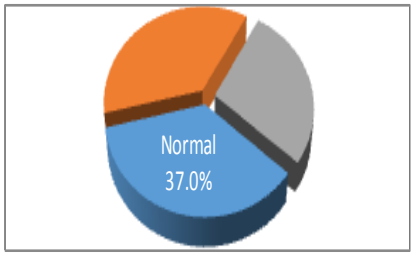


Fig.3 Correlation between lymphocyte with toxoplasmosis



In this study there is no relationshipbetween the neutrophil status of the stem, the neutrophil segment, andlymphocytes with the incidence of toxoplasmosis cancaused by a titer detected onrespondents who experienced toxoplasmosis were titersIgG anti- *T. gondii* , whereas IgM titers of anti *T.gondii*negative, meaning that the infection is an infectionchronic and can happen for more than a year,so the neutrophil value does not decrease. Thingthis can be caused by hygiene and immunity factorsrespondent. When receiving chemotherapy, decrease lymphocytes occur on the fifth day after chemotherapythen followed by a decrease in neutrophil status, thenlymphocyte status will gradually return to normal and neutrophil statusthe increase can be detected during the initial phase of toxoplasmosis infection, whereas the study did notcalculation is done on what day is doneblood draw after the patient underwent previous chemotherapy and blood test resultsseen from the patient's medical record so as to valuelymphocytes that are right after chemotherapy cannot be seen surely.[8]

If the research find IgG titerand IgM anti-*T.gondii is* positive, so it can shownew infections that occur less than 12 months orIgM positive reaction is false, so to enforce the diagnosis requires a re-examination after threeweek from the previous inspection withusing new blood specimens.

Based on the results of this study, the incidence of toxoplasmosis inmalignancy patients receiving chemotherapy Dr. M. Djamil Hospital as much as 74.1%. There isa decreasing of stem neutrophil status in malignant patients receiving chemotherapy at the chemotherapy installation Dr.M. Djamil Hospital.

The segmented neutrophil status and lymphocytes status did not have a significant decrease, and there are no a correlation between the status of stem neutrophils, neutrophilssegments, and lymphocytes with toxoplasmosisin malignant patients receiving chemotherapy atDr. M. Djamil Hospital.

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