will cause immunologic reaction that has role on auto antibodies production (autoAb). Autoantibody toward endothelia cell was found on dengue virus infection with different serotype, so it will cause apoptosis endothelia cell process (Zhou, 2002). On DHF/ DSS (Dengue Shock Syndrome) sufferer, the level of Abs anti trombosit and Abs endothelial is higher than dengue fever sufferer (Lien CF, 2003).

4.2 TNF-α

Macrophage is fagocitic cell which has important role in body defense system. Macrophage is Antigen Presenting Cell (APCs) that process antigen and provide to cell T for starting immune response. Dengue virus comes into macrophage cell through receptor Fc receptor (Fc $_{\gamma}$RI) immune complex mechanism (Reyes et al, 2005). Dengue virus simulation on macrophage cell will secrete some TNF α, IL -8, IL-6 and MMP 2. TNF α is proinflamasi cytokine which takes part on seriousness of DHF sufferer (Medin Lc, 2005). On this research, macrophage culture is explained with interleukin 17 recombinant (rh IL17) by using dosis (8 ng/ml) and time variation. There's increasing of TNF α level based time variation although statistically, there isn't significance difference (P > 0, 005). The highest increasing of TNF α level is 48 hours after explanation. In another research, TNF α will start to raise up on first day after infection and will reach the peak on the second day (Hober D, 1993). Research with dengue virus explanation on secretion macrophage TNF α reach the peak less than 2 – 4 days after infection (Zhou et al, 2002). Secretion proinflamasi cytokine on macrophage culture depend on dose and time explanation (Murphy PM, 1994).

IL-8

Cytokine IL-8 is pro inflammation cytokine which is its level do rise up on serious DBD sufferer. This cytokine has *pro inflammatory* effect, *chemotraktan*activation which is secreted by variety of cell type and takes part in inflammation process, wound healing, angiogenesis, metastasis and *lymphoid trafficking*. In this research, IL-8 increasing is different in meaning among time monitoring group (p < 0,000) with the highest level is on 48 hours. It's appropriate with the previous research that IL- 8 level reaches the peak on the two days after infection (Hober D et al, 1993). In another research, 61% of this cytokine was detected on DHF level IV and only 14% was detected on dengue fever sufferer (Chaturvedi et al , 2000).This shows the level of DHF shock is higher than non shock. Some researchers found that IL-8 started to be detected in some hours after infection, next it will disappear until the ninth days (Medin Lc, dkk.2005). Detection of IL-8 on DHF sufferer shows the situation into the serious situation Dengue Shock Syndrome (DSS). On infection caused by DEN 2 virus, ekspresin, IL-8 gene rises up maximally in six hours-after infection, next it will decrease after 24 hours (Ragano et al , 2001), IL-8 secretion will stimulate *platelet activating factor*, leukotriene so cause inflammation reaction, beside that it will activate activator protein -1 (AP-1), NF –kβ which will cause the increase of vascular permeability (Hober D, 1993). Inh general, thisa research appropriate with hypothesis of IL-8 cytokine profile.

On microstructure analysis, there are 375 genes which related with IL-8 cytokine that have connection with virus dengue infection on macrophage (Murphy PM, 1994). The increase of IL-8e also happens on infection causedby virus HSV1 and RSV in 6 hours after infection, next it will decrease step by step until 72 hours after infection. This interleukin 8 will stimulate endothelia cell to product prostaglandin E2 and *platelet activating factor (PAF)*, as strong vasodilator, this cause the presence of blood vessels dam, infiltration of inflamed cell and endothelia cell leakage (Chen Y, 2005).

4.3 MMP-2

Besides stimulate cytokine proinflammation, virus dengue infection also stimulate matrix metaloproteinase (MMPs) production especially MMP-2 which has gelatinolitic character and can increase cell endothelia permeability. In this research, MMP-2 level was measured based on time variation, there's significant increase between control and treatment group (p<0,000). In the research, it can be seen that the highest level is on time period 48 hours. In research by using cell dentdritic cell, MMP -2 started to be detected in three hours after virus infection and reach the top in 24 hours, next it will disappear after five days (Marrovich, 2001). This result is different with the above research. This is caused by different culture media. Dengue virus infection will stimulate cell macrophage and cell dendritic to secrete gelatinosa matrix such as MMP-2BD, MMP-9 and MMP-13 (Lei et al, 2001).

MMP-2 mechanism in vascular permeability change by disturbing remodeling matrix extracellular process needs metalloproteinase (MMPs) matrix. This permeability relates with the vanish of adhesion molecule endothelia 1 trombosit (PECAM -1) and adhesion molecule vascular endothelium cadherin (VE – cadherin) cell and redistribution from F-aktin fiber. This becomes molecular basic on plasma leakage process on DHF caused by virus infection and matrix metalloproteinase gelatinolitic (Asahi et al, 2001). In another research, it was got virus den 2 infection will increase MMPs level especially for MMP2 which its activity is in adhesion and cell inflamed migration. Onvirus HIV infection, the level of MMP-2 and MMP-9 rise up that will cause the change of blood vessel permeability.

The characteristic of DHF is the occurrence of plasma leakage, it happens from low until high level so it can cause shock. Complex interaction among virus, immune host response and cell endothelia will cause interference of barrier integrity and cell endothelia function so that it causes plasma leakage. The third step of research was aimed to prove the occurrence of plasma leakage and endothelia culture (HUVECS) with pored media and added with albumin 2%, next it's flatted by activated macrophage (supernatant) which has been flatted by IL-17 recombinant. There's significance difference (p<0.000) among treatment groups. Activated macrophage (secrete cytokine TNF – α, IL-8 and MMP 2) can cause interendothelia junction widen, so that plasma leakage happened. Blood vessel permeability is controlled by the connection among cell endothelia which is mediated by vascular endothelium cadherin (VE-cadherin) transmembran protein (Dejana E, 2008) TNF – α

can cause blood vessel permeability widen through fosporilasi tyrosin , disturb protein VE-cadherin transcription that cause down regulation of VE- cadherin expression and apoptosis (Hofmann S, 2002).

Cell endothelia produces adhesion molecule such as cadherin, PECAM -1 that is placed on antar cell relation, consisted by F- actin fiber. Metalloproteinase (MMP-2) matrix is protein gelatinase which its level is high on DBD with shock. Dengue virus infection on monosit imatur will induct cytokine proinflammation production of IL -8, TNF-α, MMP – 9, MMP-13, MMP-2. The increase of MMP-2 on DHF cases with shock compared by DHF non shock shows that there's connection between plasma leakage and pathogenesis on DHF shock (Rothman AL, 2004). MMP-2 secretion will activate MAPK track so that fosporilasi ERK happened on protein p38 cause destruction on endothelia cell (Holvoet et al, 2003).

Interleukin 8 on DHF sufferer has kemotraktan activity, neutrophil degranulation, activate receptor C5a and C3a through protein p38 and p44 so that inflammation reaction and infiltration cell happened (Irene B, et al, 2002).

5. Conclusion and Suggestion

From the research, it can be concluded that:

1. It occurs the increase of Th17 and IL-17 level on DHF shock sufferer.
2. Interleukin 17 increase the secretion of IL-8, MMP-2 and TNF-α by macrophage on DHF
3. TNF- α, Il-8 and MMP-2 cause plasma leakage on endothelia culture.
4. There's correlation between IL-17 and plasma leakage level on cell endothelia culture.
5. Plasma leakage on DHF shock happens as the result of IL-8 secretion, MMP-2 and TNF-α by macrophage which is inducted by IL-17.

5.1 Suggestion

The result of research shows there's IL-17 role on DHF pathogenesis through macrophage activation so that secrete cytokine TNF-α proinflamasi , IL-8 and MMP-2. This shows that not only Th1 and Th2 that have roles on DHF pathogenesis, but also Th17 which is as producer cell IL-17, it has been proved to have role on the occurrence of plasma leakage on DHF. On the next research, it's expected to do better as following:

1. The measurement of cytokine IL-17 plasma on DHF sufferer is done by serial based on fever day, to know variation and the highest level of IL-17 in the blood.
2. Shelf time variation needs to be reconsidered whether it needs longer duration (72 hours) or only 48 hours.
3. It needs to do measurement of other cytokines which is stimulated by IL-17, but not produced by macrophage to know how much its role on plasma leakage.
4. The research need to be done to make antiinterleukin 17 antibody to block IL-17 so it's expected to be able to avoid the more serious of plasma leakage

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