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EDITORIAL

The immunopathology of COVID-19 VIRUS INFECTION

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The reported data for diagnosis of COVID19 are: high, increase of neutrophil / lymphocyte ratio more than 3.13, high LDH >250 , serum ferritin >300, D-dimer >0.5, CRP >100 . Also, patch opacities in chest x-ray and honey comb lesions in lung bases. To understand the immuno-pathology of COVID-19 , we should put in consideration that COVID-19 is RNA virus with a highly spread replication.

Initially during infection, the virus attacks the respiratory endothelial cells and produces adhesive molecules as *selectins* and cytokines including interferon. Interferon activates the systemic immunocytes (lymphocytes, monocytes and neutrophils) to form integrins. This integrins are captured by lung selectins at the infected site and form large colonies of leukocytes inside lung tissues. This colonies give the characteristic picture of batch opacities in chest x-ray and leukopenia (Conti et al., 2020).

Leukopenia is an uncommon picture of infection in bacterial infection usually due to bacterial endotoxin , but in viral infection this depends on virus pathway pathology.

LDH increases in some organ's pathology such as liver , heart and lung diseases. The rise of LDH is an indication of obstructive lung damage. This damage is secondary to wide spread of COVID-19 with increased inflammatory cytokines , IL-6 is one of them. The role of IL-6 is to activate liver cells to produce CRP and the hypothalamus to raise body temperature.

Now a question is raised , why COVID-19 is always complicated with multiple organ system failure ?

Our suggestion depends on the bases of our understanding of the immunopathology of the disease. The inflammatory processes activate the B-lymphocytes to produce specific antibodies against COVID-19. These antibodies attack and neutralize the activated virus. The reaction activate complement pathway as in Arthurs reaction and Serum sickness, the type III hypersensitivity reaction (Kumar, 2010).

The activation of complement is followed by activation of kallikrein system followed by activation of fibrinolytic, and clotting cascade. Those activations can explain the rise of serum D-dimer and vascular coagulation in lung tissues biopsy. We can confirm the value of thrombotic protocol in patients with COVID-19.

Therapeutic uses of hydroxy-chloroquine is of no value because this drug activates the an already active phagocytes . This could lead to Fenton type reaction (nitrous oxide attach to DNA inside the cell and destroy it) (Gautret et al., 2020). The use of IL-6 inhibitors is helpful to reduce body temperature but enhance virus spread (Buonaguro et al; 2020) . Both vitamin C and zinc, were claimed to have support of the immune system Neither vitamin C nor zinc has a clinical significance in the management in this condition .

Some patients used low doses of glucocorticoids to stop the complications of multiple organ viral spread and reduce the increase of inflammatory cytokines. However, there is no evidence to recommend the use of corticosteroid, but as anti-inflammatory agent, the use of corticosteroid should give precautions during its use.

The use of anti-coagulant drugs had proved to be lifesaving but we use the far end target to prevent the coagulation value to limit the spread of inflammation. Anti-coagulant should be immediately used in if D-dimer is positive (Ciceri et al., 2020 and Kollias et al., 2020).

The aim of therapy is to prevent the complications and improve the capacity of the immune system to get rid of the viral infection. This depends on preventing or alternating the activations of complement cascade . The use of C1-inhibitor should be used early as possible especially for old risky patients. This way, C1-inhibitor prevents the proteolytic cleavage of the later complement components, and inhibits proteases of the fibrinolytic, clotting, and kinin pathways. C1-inhibitor is the most important physiological inhibitor of plasma kallikrein, fXIa, and fXIIa. The expected mechanisms are to stop the lung Arthurs reaction and multiple organ affection.

The plasma therapy from convalescent patient is of no value because antibodies is of less value for killing the virus, due to virus mutations. Moreover, the antibody attack the virus in the serum but not when the virus is inside the cells. The cytotoxic CD8 attacks the cells that harbor the virus and let the virus released to serum and exposed to the specific antibodies . and prevent the virus from multiplying inside the cells (Li et al ; 2020) . C1-INH is one of acute-phase protein present in high concentration in acute inflammation and in recent convalescent plasma patients. This can explain the success responses in some infected patients with the use of convalescence plasma (Ivan, 2020).

The best way for preventing the spread of this micro-beast is by the use of vaccine therapy.

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