Insight into acute myocardial injury caused by COVID-19

Accepted 20th April, 2020

ABSTRACT

The outbreak of novel coronavirus pneumonia began in late 2019 in Wuhan, Hubei province, and rapidly spread to many provinces in China as well as other countries. Here the character of novel coronavirus and myocardial injury in COVID-19 was mini reviewed. Wish to provide reference for the prevention and treatment of COVID in future.

Key words: Novel coronavirus, pneumonia, myocardial injury.

INTRODUCTION

The outbreak of coronavirus disease 2019 (COVID-19) began in late 2019 in Wuhan, Hubei province (Chan et al., 2020). The rapid spread of COVID-19 is a challenging public health problem in China and all over the world (Wu et al., 2020). Current knowledge of COVID-19 indicates that, while most cases have a good prognosis, a substantial share require critical care. In particular, a higher percentage of elderly patients and those with hypertension and cardiovascular disease require critical care after infection and have higher than average mortality rates. According to clinical data analysis of 71,234 cases in China, the mortality rate of COVID-19 patients with cardiovascular disease is 10.5% (Wu and McGoogan, 2020).

COVID-19 is mainly characterized by respiratory symptoms. However, some patients have clinical manifestation of severe cardiovascular damage (Mohammad et al., 2020). Of death cases of COVID-19 reported in China, 35% of patients had a history of hypertension and 17% had a history of cardiovascular disease. Of patients without potential cardiovascular disease risk factors, 11.8% had increased cardiac troponin-I (cTnI) level or cardiac arrest during hospitalization (Wang et al., 2020). Understanding the damage caused by COVID-19 to the cardiovascular system and the underlying mechanisms is of great importance to treatment response.

Virology of SARS-CoV-2

Coronaviruses are a group of non-segmented, enveloped, positive-sense RNA viruses that cause respiratory tract infections in humans (Fehr and Perlman, 2015). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which causes COVID-19 is the third-known highly pathogenic coronavirus after SARS-associated coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), the two most well described coronaviruses. SARS-CoV and MERS-CoV were responsible for large-scale outbreaks in 2003 and 2012, respectively (Fehr and Perlman, 2015). Prior to the COVID-19 outbreak, six coronaviruses have been documented to have the ability to infect humans. The current classification of coronavirus has identified four genera (α, β, γ, δ) (Fehr and Perlman, 2015). SARS-CoV-2 is a new type of coronavirus, that belongs to Beta-coronavirus lineage B (Lu et al., 2020). Viruses of the genus Beta-coronavirus are enveloped, single-stranded RNA viruses that infect wild and domestic animals as well as humans. SARS-CoV-2 exhibits some structural differences when compared with the known coronaviruses that infect humans (Zhu et al., 2020). Gene detection shows that the genome of SARS-CoV-2 has 86.9% homology with the nucleotide sequence of SARS-CoV (Zhu et al., 2020).

Acute myocardial injury caused by COVID-19

Previous studies indicated that patients with SARS had elevation of myocardial enzymes and cardiac diastolic dysfunction (Pan et al., 2003), suggesting coronavirus
infection can initiate acute myocardial injury. An analysis of 138 cases of COVID-19 in Wuhan showed that the incidence of complications in intensive-care unit (ICU) patients was significantly higher than in general ward patients (Wang et al., 2020). Among the cases analyzed, 43 patients (31.2%) had hypertension, 20 patients (14.5%) had cardiovascular disease, 10 patients (7.2%) suffered from acute cardiac injury, and 23 patients (16.7%) had arrhythmia (Wang et al., 2020). The levels of biomarkers of myocardial injury in ICU patients (36 cases) were significantly higher than those in non-ICU patients (102 cases) (median creatine kinase (CK)-MB level 18 U/l versus 14 U/l, P*<0.001; hs-cTnl level 11.0*pg/ml versus 5.1*pg/ml, P*=0.004) (Wang et al., 2020). In another study of 41 COVID-19 cases in Wuhan, 5 patients (12%) showed clinical manifestation of acute myocardial injury. The plasma level of troponin-I (> 28 pg/ml) in critical patients was significantly higher than those in mild patients, and rapid atrial fibrillation occurred in some severe and critical patients (Huang et al., 2020). A retrospective study on 188 patients of COVID-19 showed that 1/3 of patients had a level of hs-cTnl ≥ 6.126 pg/ml on admission, and the mortality rate was as high as 50% (Wu et al., 2020). A study analyzing cardiac CT imaging of 41 patients of COVID-19 showed that the average CT value of epicardial adipose tissue in severe and critical patients was smaller than that of healthy individuals, and myocardial interstitial edema was obvious in severe and critical patients (Hui et al., 2020). Therefore, the current state of knowledge of COVID-19 suggests that patients with severe symptoms usually have acute myocardial injury.

Receptor of SARS-CoV-2 and myocardial injury

The binding of the virus to host cell receptors is a significant determinant for the pathogenesis of infection. Li et al. (2003) first reported that SARS-CoV required the angiotensin-converting enzyme 2 (ACE2) as a receptor for viral entry (Li et al., 2003). Homology modeling showed that the binding domain of SARS-CoV-2 to the ACE2 receptor is similar to that of SARS-CoV (Zhou et al., 2020). A recent study showed that SARS-CoV-2 requires ACE2 as a receptor to enter cells (Hoffmann et al., 2020). When the virus was attached to the ACE2 receptor, the ACE2 receptor expression was down-regulated. ACE2 is a membrane-bound aminopeptidase that plays a vital role in the cardiovascular and immune systems. The down-regulation of ACE2 caused endothelial dysfunction, increased blood pressure, and decreased myocardial contractility, but it also increased the concentration of angiotensin II (Ang-II) and aggravated oxidative stress, inflammation and fibrosis (TeRiet et al., 2015). Liu et al. (2020) found that the plasma concentration of Ang-II in patients of COVID-19 was significantly higher than that of healthy individuals. The expression levels of Ang-II showed significantly positive correlation with viral load and degree of lung injury (Liu et al., 2020). It is suggested that SARS-CoV-2 infection is more likely to cause the imbalance of renin-angiotensin-aldosterone system (RAS-system), which may induce acute cardiovascular events such as hypertension, coronary plaque instability, arrhythmia and heart failure.

Oudit et al. (2009) found the distribution of ACE2 receptors had a positive correlation with virus replication, based on animal experiments and autopsy of SARS patients. The nucleic acid of SARS-CoV could be detected in the myocardium of 35% of patients infected with SARS-CoV (Oudit et al., 2009). ACE2 is widely expressed not only in the lung but also in the cardiovascular system. Electron microscopy has demonstrated that after SARS-CoV-2 infects the human body, the virus can directly attack ACE2 receptors on the surface of the lung and heart, resulting in lung and myocardial injury (Zhou et al., 2020). Further, the researchers suggested that COVID-19 is more likely than SARS to damage heart and lung.

Cytokine storm and myocardial injury

Patients with COVID-19 are reported to have higher expression levels of IL-2, IL-7, IL-10, G-CSF, IP-10, MCP-1, MIP-1A and TNF- alpha in the plasma (Huang et al., 2020). A study of 138 patients with COVID-19 showed that the expression level of interleukin-6 (IL-6) in plasma increased in 52% of patients and C-reactive protein (CRP) increased in 86% of patients (Wang et al., 2020). Another retrospective study on 188 patients with COVID-19 showed that the plasma level of IL-6 and CRP were higher in those patients with higher high-sensitivity cardiac troponin I (hs-cTnl) levels, while the level of lymphocytes and monocytes were lower (Wu et al., 2020). IL-6 and CRP are pro-inflammatory cytokines. Due to the elevation of IL-6, CRP and hs-cTnl concentrations in severe and critical patients, it is suggested that cytokine storm syndrome induced by COVID-19 accompanies acute cardiac injury (Chen et al., 2020).

Cytokines play an important role in virus infection. Cytokines are divided into pro-inflammatory and anti-inflammatory. The elevation of pro-inflammatory cytokines induced by virus infection can promote the clearance of virus from host cells. After the virus is successfully cleared, the secretion of pro-inflammatory cytokines returns to normal. In some cases, virus infection may lead to imbalance of the immune regulatory network. The secretion of a large number of pro-inflammatory factors may lead to the outbreak of cytokine storm (Oakley et al., 2008).

Cytokine storm is an over activation of the immune system caused by infection, drugs or certain diseases (Ferrara et al., 1993). Coronavirus infection can induce a cytokine storm (Us, 2008). In SARS-CoV infection, cytokine
storm is generally considered a deadly, uncontrolled systemic inflammatory response resulting from the release of large amounts of pro-inflammatory cytokines and chemokines by immune effector cells (Us, 2008). Similar to those with SARS, individuals with severe MERS infection show elevated levels of IL-6, IFN-α, CCL5, CXCL8, CXCL10 in serum as compared with those with mild to moderate MERS. H1N1 influenza virus can also trigger a cytokine storm (Bautista et al., 2010).

Just as occurs in SARS and MERS, the cytokine storm will trigger a violent attack by the immune system on the body, causing acute respiratory distress syndrome (ARDS) and multiple organ failure, finally leading to death in severe cases of COVID-19. During the process of cytokine storm, both neutrophils and macrophages promote the abnormal secretion of a variety of cytokines in tissues and organs through a specific positive feedback mechanism, eventually leading to single or multiple organ damage and functional failure, even death (Osterholm, 2005). A large number of immune cells, combined with tissue fluid, gather in the lungs and block gas exchange between alveoli and capillaries in COVID-19. Meanwhile, immune cells kill a large number of normal cells while killing virus, which seriously damages lung ventilation, leading to ARDS and death because of hypoxia (Xu et al., 2020). Furthermore, a cytokine storm may affect atherosclerotic plaque stability, increase the risk of potential cardiovascular events, and cause angina pectoris or even acute myocardial infarction.

Monitoring and treatment for myocardial injury

The clinical manifestations of myocardial injury in COVID-19 are diverse. It is important to strengthen both the recognition and vigilance for myocardial injury caused by novel coronavirus infection and the monitoring of cardiac function and biomarkers of myocardial injury. Early detection of cardiac injury biomarkers is helpful in finding complications and evaluating disease condition and prognosis. For patients with cardiovascular diseases, dynamic monitoring of biomarkers (cTnl, Myo, CK-MB and NT-proBNP) and ECG is suggested.

Similar to SARS and MERS, there is currently no clinically proven specific antiviral agent available for COVID-19. The most important management strategy is supportive treatment, including oxygen therapy, conservatve fluid management, and use of broad-spectrum antibiotics to cover secondary bacterial infection. First, the novel coronavirus infection should be actively treated to control the progression of pneumonia. Second, medication should be given to improve myocardial energy metabolism. Third, if myocardial injury leads to arrhythmia, courses of action should be taken according to the type of arrhythmia and patient’s hemodynamics. Once there are signs of heart pump failure, life support therapy such as ECMO should be given as soon as possible. Individualized treatment according to the severity of myocardial injury is recommended.

CONCLUSION

In COVID-19, novel coronavirus infects host cells through ACE2 receptors, causing acute myocardial injury in severe patients, although the specific mechanisms are uncertain. Patients with cardiovascular disease have an adverse prognosis. Therefore, particular attention should be given to cardiovascular protection during treatment for COVID-19.

REFERENCES


Cite this article as:

Submit your manuscript at
http://www.academiapublishing.org/journals/mms