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COURSE CODE: MLS 406

QUESTION: Discuss the etiology, origin, structure and pathophysiology of COVID-19

The world is suffering from pandemic, the corona viral disease 2019(COVID 19). The Corona virus disease(COVID 19) is a highly transmittable and pathogenic viral infection caused severe acute respiratory syndrome-like(SARS-like) bat viruses , therefore bats could be the possible primary reservoir. the intermediate source of origin and the transfer to humans is not known, however, the rapid human to human transfer has been confirmed widely.

ETIOLOGY: Corona viruses are positive stranded RNA viruses with a crown like appearance under the electron microscope(coronam is the Latin term for crown) due to the presence of spike glycoproteins on the envelope. the subfamily Orthocoronavirinae of the Coronaviridae family(order Nidovirales) classifies into four genera of CoVs: Alphacoronavirus (alphaCoV), Betacoronavirus (betaCoV), Deltacoronavirus (deltaCoV), and Gammacoronavirus (gammaCoV) . Furthermore, the betaCoV genus divides into five sub genera or lineages. Genomic characterization has shown that probably bats and rodents are that probably bats and rodents are the gene sources of alphaCoVs and betaCoVs. On the contrary, avian species seem to represent the gene sources of deltaCoVs and gammaCovs.

 SARS-CoV-2 belongs to betaCOVs category. it has a round or elliptic and often pleomorphic form, and a diameter of approximately 60-140nm. like other CoVs, it is sensitive to ultraviolent rays and heat. Furthermore, these viruses can be effectively inactivated by lipid solvents including ether (75%),ethanol, chlorine-containing disinfectant, peroxyacetic acid and chloroform except chlorhexidine.

 in genetic terms, Chan et al have proven that the genome of the new HCoV, isolated from a cluster-patient with atypical pneumonia after visiting Wuhan, had 89% nucleotide identity with bat SARS-CoV-2. Its single-stranded RNA genome contains 29891 nucleotides, encoding for 9860 amino acids. Although its origins are not entirely understood, these genomic analyses suggest that SARS-CoV-2 probably evolved from a strain found in bats. the potential amplifying mammalian host, intermediate between bats and humans, is, however , not known. Since the mutation in the original strain could have directly triggered virulence towards humans, it is not certain that this intermediary exists.

 Origin and transmission of SARS-CoV-2

The SARS-CoV-2 is a β-coronavirus, which is enveloped non-segmented positive-sense RNA virus (subgenus sarbecovirus, Orthocoronavirinaesubfamily) [6]. Coronaviruses (CoV) are divided into four genera, including α−/β−/γ−/δ-CoV. α- and β-CoV are able to infect mammals,while γ- and δ-CoV tend to infect birds. Previously,CoVs have been identified as human-susceptible virus,among which α-CoVs HCoV-229E and HCoV-NL63,and β-CoVs HCoV-HKU1 and HCoV-OC43 with low thogenicity, cause mild respiratory symptoms similar to a common cold, respectively. The other two known β-CoVs, SARS-CoV and MERS-CoV lead to severe and potentially fatal respiratory tract infections .

 The virus is transmitted via 2 route:

1. The faecal- oral route: It is believed that and infected person goes to the toilet wipes their bottom and do not wash their hands properly then touch other surfaces in the bathroom and someone comes and also touches those surfaces and potentially inoculating themselves with the virus
2. Respiratory droplet: they have the potential to spread between 3-6ft, they can stay on surfaces for approximately 24 hours. It can also be airborne for 3 hours.

There are asymptomatic carriers who do not show symptoms but have the ability to spread the virus. The virus then gets to the respiratory system and then attack the alveoli and attach to the type 2 pneumocyte. type 2 pneumocyte produce surfactant that decrease surface tension within the alveoli and reduces the collapsing pressure.

 The virus has different protein spike on it and one of the protein spikes that is significant is called the S-spike. The S-spike on the CPVID 19 binds unto specific receptors on the type 2 pneumocyte and the receptor is called Angiotensin Converting enzyme(ACE) type. once it binds to COVID 19, it allows the virus to be engulfed into the cell and then release the positive sense single stranded RNA into the cell and then release the positive sense single stranded RNA into the cytoplasm of the type 2 pneumocyte. Once it is released into the cell it can do a couple of things.

1. It can use the host cell ribosome, it can then take mRNA and convert it to proteins and it is called TRANSLATION. It is translated to specific protein molecules.

The positive sense single stranded RNA has the potential to use

1. another enzyme called the RNA dependent polymerase which can take RNA and synthesize it. It takes the single stranded RNA and makes more RNA.

There is need for specific enzyme in order to be able to cleave the pollen proteins to the different viral components such as the enzyme, the nucleocapsid, the protein spikes and the single stranded RNA. The enzyme is proteinases and this process will bring about more viral particles thereby causing more damage to type 2 pneumocyte. The type 2 pneumocyte will become so damaged that it will release specific inflammatory media which will in turn tell the macrophage. Once the macrophage is stimulated it starts to secrete specific cytokines which are interleukin1(IL-1), interleukin6(IL-6) and tumour necrotic factor α(TNF- α) that cause tons of trouble. They go into the bloodstream and cause the endothelial cells to undergo vasodilation, it causes the smooth muscle to dilate but increase the capillary permeability by causing endothelial cell contraction and then fluid and plasma begin to flow out and leak into their interstitial spaces and also into the alveoli. Some of these fluids will try to enter into the alveoli when water accumulate around the alveoli, the surfactant concentrated will be reduced then the surface tension goes up and then the alveoli starts to collapse leading to decrease gas exchange which will lead to hypoxemia and increase in the work of breathing because one has to work extra hard to inhale as much air but not only to open the alevoli but to open it against the interstitial edema.

 All inflammatory mediators (IL-1,IL-6& TNF- α) also brings about tons of neutrophils. the inflammatory mediators begin to pull the neutrophils to the site where the virus is and they may try to destroy the virus by releasing the reactive oxygen species and proteases which maybe destroy the some virus and also start damaging both the type 1 pneumocyte and the type 2 pneumocyte thereby reducing the gas exchange and then reduction in the surfactant production and increase surface tension and collapse in the alveoli. The type 1and 2 pneumocyte getting destroyed slough into the middle of the alveoli, there will be collection of fluid, some protein deposition and cellular debris(type1 and type2 pneumocyte cellular debris, macrophages and neutrophils in the middle of the alveoli which leads to consolidation, which alters the gas exchange process and lead to hypoxemia. When the consolidation is taking place the contents in the alveoli begins to degrade, then the patient will coough it off which is a productive cough.

 The IL-1and IL-6, because they are produced in large amount travel to the central nervous system via the blood. In the CNS, there is the hypothalamus that regulates the body temperature, IL-1, IL-6, TNF- α in high concentration tell hypothalamus to release specific postglandins like PG20 that helps to release thermostat that increase the body temperature which leads to fever.

 When one is hypoxemic, it leads to low partial pressure of oxygen and stimulate chemoreceptors and they in turn trigger a reflex which causes sympathetic nervous system to become stimulated and try to increase the patient's heart rate band also have increased respiratory rate.

 If the inflammation of the lungs become more severe it starts leaking out to the blood stream and spreading, the systemic inflammatory response starts carrying it all over different parts of the body. This inflammation with the lungs lead to systemic inflammatory response syndrome which carries the inflammation to the heart where it causes septic shock. If the inflammation spreads throughout the circulatory system, it will cause increased capillary permeability within the system circulation and fluid starts leaking out and accumulating within the tissue spaces. The overall blood volume decreases and also causes vasodilation of the vessels which leads to the total peripheral resistance dropping thereby leading to hypotension and it leads to the decrease in profusion that can lead to multi system organ failure.

 If the kidney cannot be profused, when it did not get enough blood supply, it will not be able to get rid of creatinine, blood uric nitrogen(BUN) which leads to increase in both BUN and creatinine

 The liver is also not getting enough blood supply, the liver starts to release inflammatory enzyme such as AST, ALT, bilirubin which will be elevated or it will release Acute phase reactant protein which are CRP, fibrinogen and IL-6 which will be elevated.

References:

1. Riou J, Alathaus CL(2019). *pattern of early human to human transmission of Wuhan 2019novel coranavirus (2019-nCoV)*
2. Chun JF, Yaun S,et al. *a familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person to person transmission.*