

In the name of God

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CRRT in patients with covid19

introduction

- New data on the coronavirus disease has revealed that kidney involvement appears to be frequent in people who have tested positive and developed symptoms

- **Proteinuria or hematuria often occurs at the beginning or during the infection, with a few patients even developing acute kidney injury (AKI), thus indicating that COVID-19 also attacks the kidneys.**
- **Given the involvement of kidneys during coronavirus infection, patients should also be monitored after the disease.**

Is there a preferred HD modality or CRRT in patients with COVID19 in ICU

- **Based on a patient's clinical status and the facility's resources, clinicians can decide to provide either intermittent hemodialysis or CRRT to patients requiring hemodialysis.**
- **For infection control purposes, limit the healthcare personnel (HCP) exposed to patients with suspected or confirmed COVID-19 to those essential for their care.**

- **In the intensive care unit (ICU), CRRT is usually managed by an ICU nurse; due to this, use of CRRT may help limit the number of HCP exposed to the patient. For ICU patients with end-stage renal disease with a dialysis fistula or graft, clinicians can weigh the risks and benefits of placing a dialysis catheter for CRRT (in order to limit HCP exposure) or performing intermittent hemodialysis**

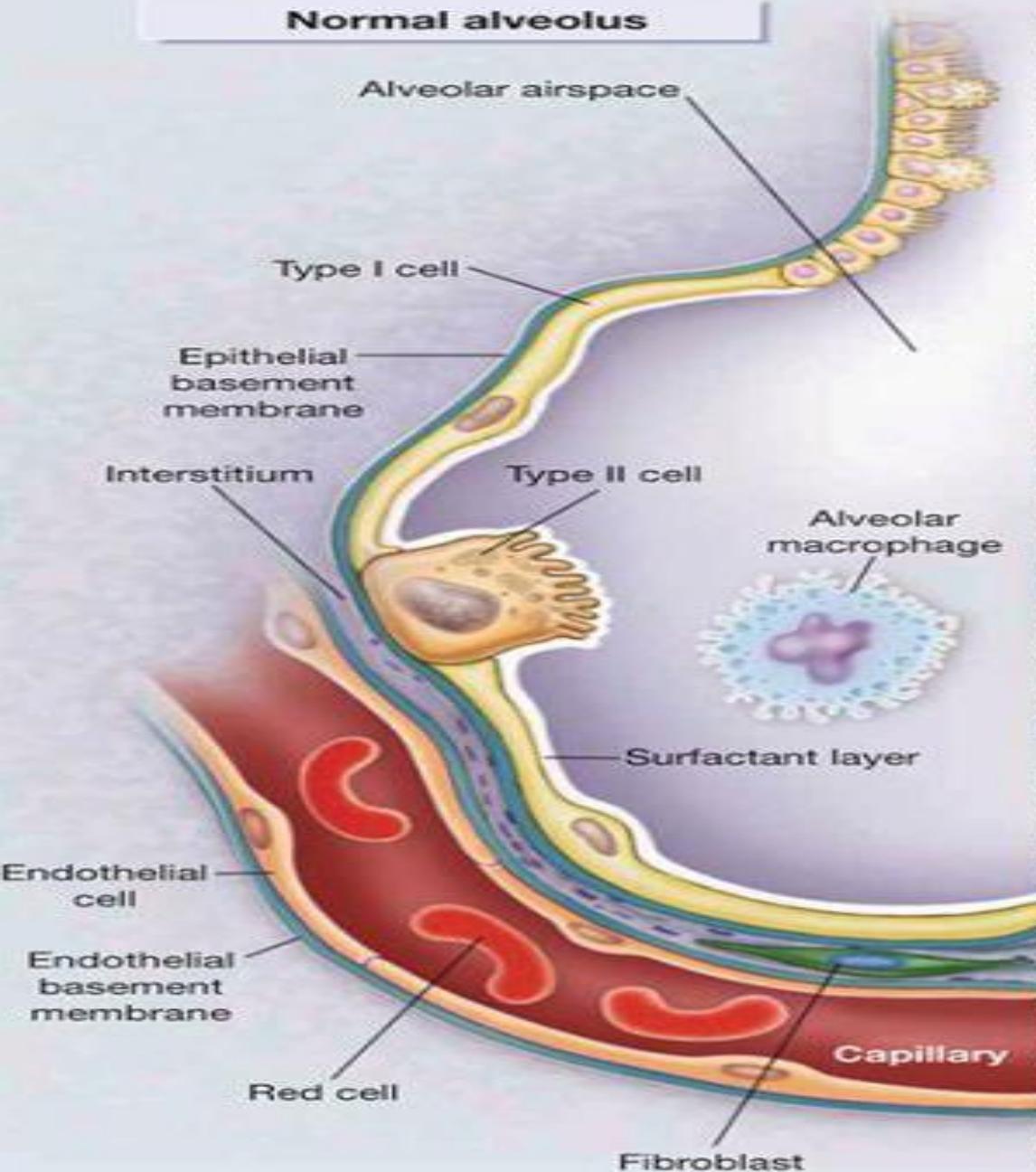
- **When any component of inpatient dialysis resources is low, urgent start peritoneal dialysis (PD) for AKI can be considered .**
- **Outcome data are limited, but acute PD appears to be as effective as other forms of RRT in the setting of AKI with no difference in mortality**

- Of these, **sustained, low-efficiency dialysis (SLED)** and **prolonged intermittent RRT** are the two most easily rolled out emergently using available equipment.
- SLED uses standard machines, and lower dialysate and blood-flow rates over a longer time period . Prolonged intermittent RRT uses CRRT machines running at higher prescribed clearances for 8–12 hours.

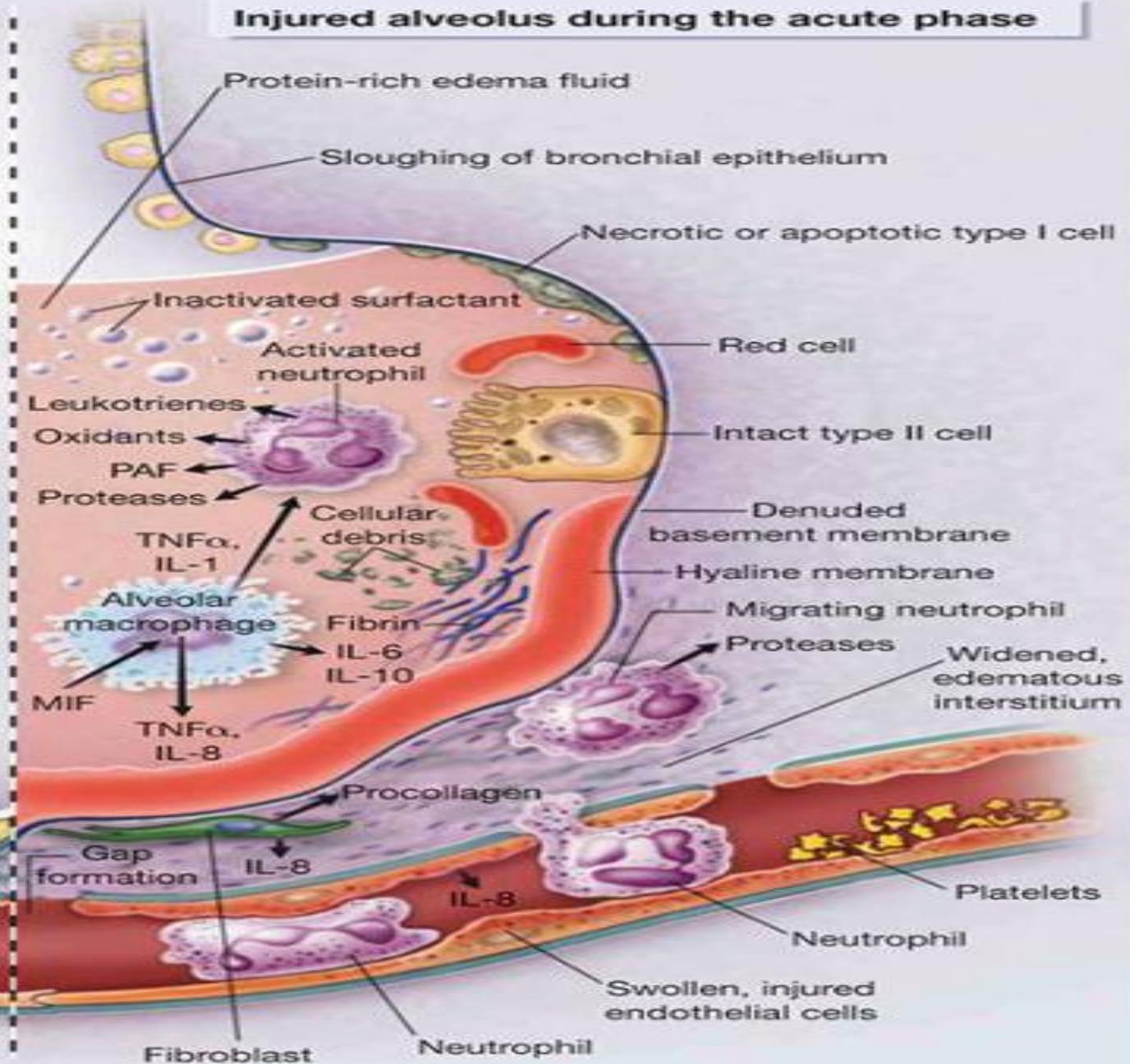
- **According to Berlin definition of ARDS 2020, acute respiratory distress syndrome is characterized by increased pulmonary blood vessel permeability and decreased air-containing lung tissue due to pulmonary inflammation.**

- During the onset of ARDS, a large number of inflammatory mediators (cytokines such as TNF- α , IL-1, IL-6, IL-8, and IL-10) are involved to cause **a cytokine storm**, resulting in excessive lung inflammation and lung damage
- In severe cases, the patients develop dyspnea after one week. Some may progress rapidly to **acute respiratory distress syndrome (ARDS), septic shock, liver failure** metabolic acidosis difficult to correct and coagulopathy

Normal alveolus



Injured alveolus during the acute phase



- **In a early study published on Jan 24, 2020, about one-third of patients developed acute respiratory distress syndrome (29%) or received intensive care (32%)of them died.**
- **Researchers say that cytokine storms occurs in critically ill patients**

- **Another updated study published on Jan 29, 2020 shows opinions that virus particles spread through the respiratory mucosa and infect other cells, induce a **cytokine storm** in the body, **generate a series of immune responses**, and cause changes in peripheral white blood cells and immune cells such as lymphocytes. Some patients progressed rapidly with ARDS and septic shock, which was eventually followed by multiple organ failure.**

- **Jan. 29th, 2020, Chen et al** published the first retrospective analysis of 99 patients infected by SARS-CoV-2 on **the Lancet** . It reported 52% infected patients were observed increase of IL-6, indicated the potential existence of cytokine storm in COVID-19 progress.

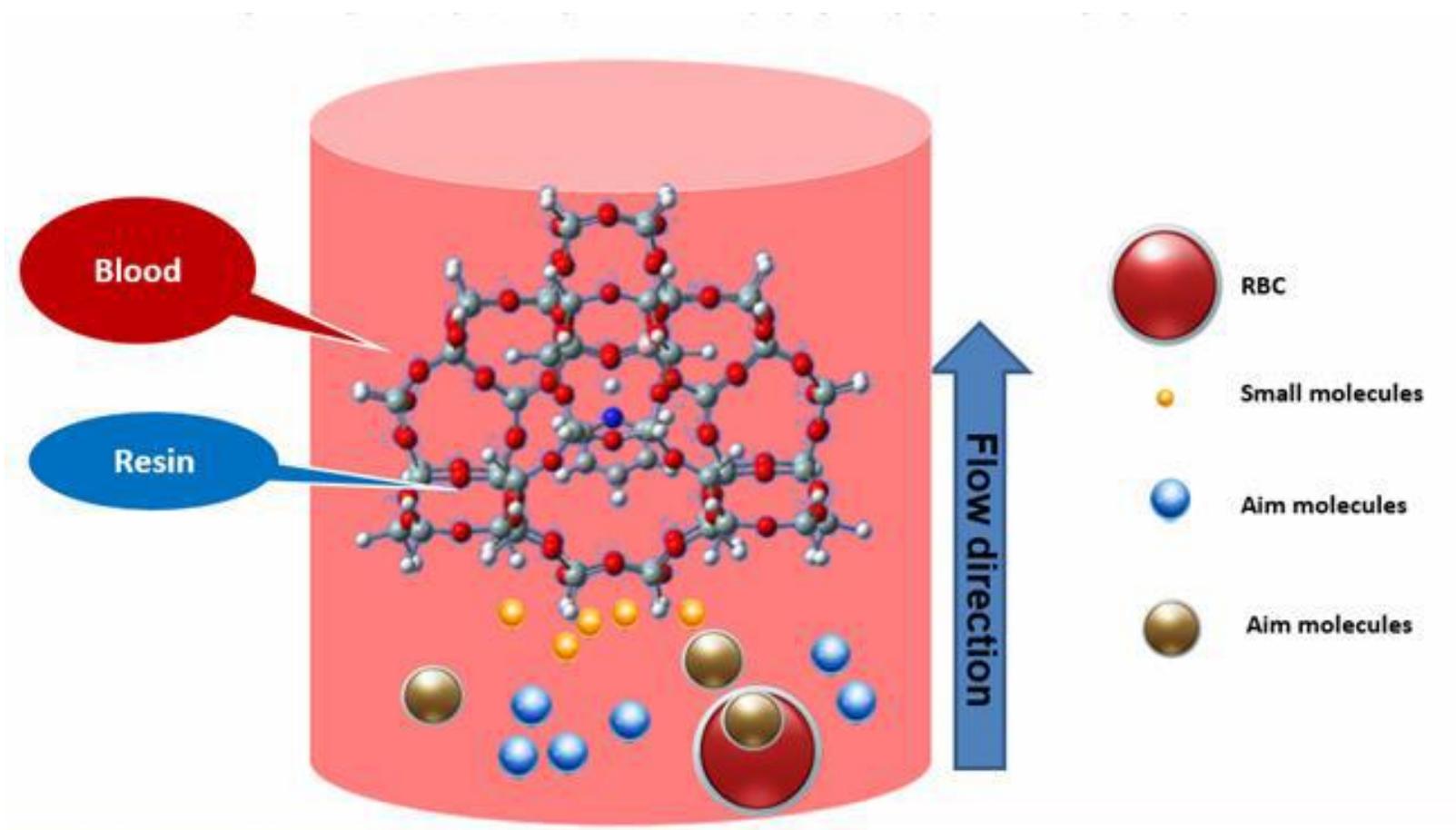
- **The Peak Concentration Hypothesis of Prof. Claudio Ronco**, the dean and founder of the International Renal Research Institute of **Vicenza, Italy**, indicates that quickly and massively removing inflammatory mediators and cytokines from the blood can reduce the damage to organs.
- (Artif Organs, Vol. 27, No. 9, 2003)

- **The threshold hypothesis of Prof. Patrick M. Honore**, a critical medicine expert from Belgian, indicates that there is a balance between the blood and tissue, by removing the inflammatory mediators and cytokines from the blood will also reduce the levels of the substances in the tissue.
- **(Critical Care Medicine 2004; 32:896-897)**

- **From January to December 2018, a retrospective observational study of 15 cases of sepsis caused by influenza and other diseases was performed in the ICU of the Aachen University Hospital in Germany. The patients were treated with HA hemoperfusion and observed changes in various cytokines and prognosis.**

- Hemoperfusion including new sorbent cartridges designed to remove cytokines and other circulating mediators should be considered facing **the sepsis like syndrome** induced by cytokines.

- **During the hemoperfusion therapy, the patient's blood is directly contacted with the adsorbent in the hemoperfutor, the metabolites and poisons in the body are adsorbed by the adsorbent so as to remove these substances.**
- **If possible, the blood purification technology can be considered for the critically ill patients with high inflammatory response.**



tocilizumab Actemra

- **8 mg/kg (body weight) Tocilizumab once in 100 ml 0.9% saline solution and administered intravenously within no less than 60 minutes.**
- **1. Tocilizumab is an experimental medicine in the context of the management of severe COVID-19 disease. It should only be considered in patients with a care plan that includes a full range of critical care support and severe COVID-19 with suspected hyperinflammation. It should only be prescribed following multidisciplinary input and a consultant decision**

- **2. Cytokine release syndrome (CRS), also termed hyperinflammation , is a complication of COVID-19 and is associated with high morbidity.**
- **3. Early identification of hyperinflammation in COVID-19 patients is essential. Serial monitoring of ferritin, C-Reactive Protein, fibrinogen, D-dimers and other inflammatory markers may identify hyperinflammation and allow early intervention.**
- **4. The evidence continues to emerge for the use of tocilizumab in this setting and therefore every effort should be made to collect relevant clinical outcomes. Each hospital should have a designated a member of staff to co-ordinate tocilizumab prescription and registry data.**

Case report

- **A 10-year-old boy developed fever, chills, myalgia, weakness, cough, tachycardia, tachypnea, retraction, and crackle in both lungs after contact with suspected family.**
- **He had no history of any underlying diseases. He was admitted to another Hospital. When he referred to our hospital, he had severe respiratory distress and oliguria**

- **Elevated C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) and leukopenia, lymphopenia were detected. Liver enzymes were elevated (SGOT=800IU/L, SGPT=1025IU/L) and RT-PCR was negative, and procalcitonin(42ng/l) and ferritin(780ng/ml) were high. LDH(800) Other laboratory data such as C3, C4, CH50, ANA, ANCA, HBS Ag HBCV Ab, HIV, CPK and troponin were normal. Echocardiography were done several times and they were normal. In urine analysis he had 4+ proteinuria, hematuria and pyuria. 24-hour urine protein was 80000mg/dL.**

- **At referral time, the blood oxygen was 65%, as measured. Imaging studies showed white lung in plain chest X ray (CXR) and typical CT scan findings of COVID- 19. He was intubated and received mechanical ventilation. In the first 48 hour we started CRRT with adsorbent filters. Our patient was treated with antiviral drug oseltamivir, chloroquine, FFP and IVIG (duo to severe sepsis and multiorgan failure) and albumin. He received several time platelet and packed cell as he needed.**

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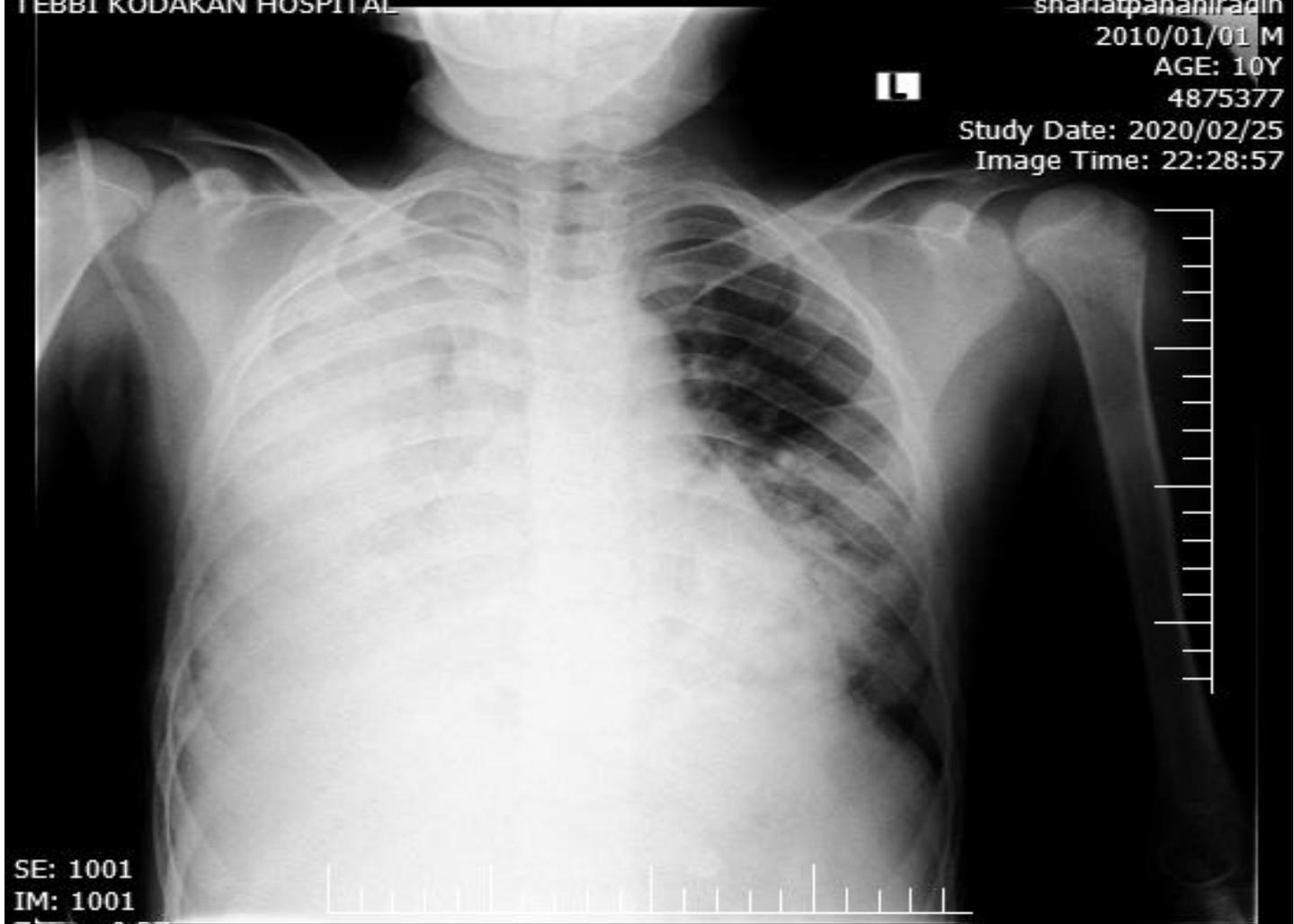
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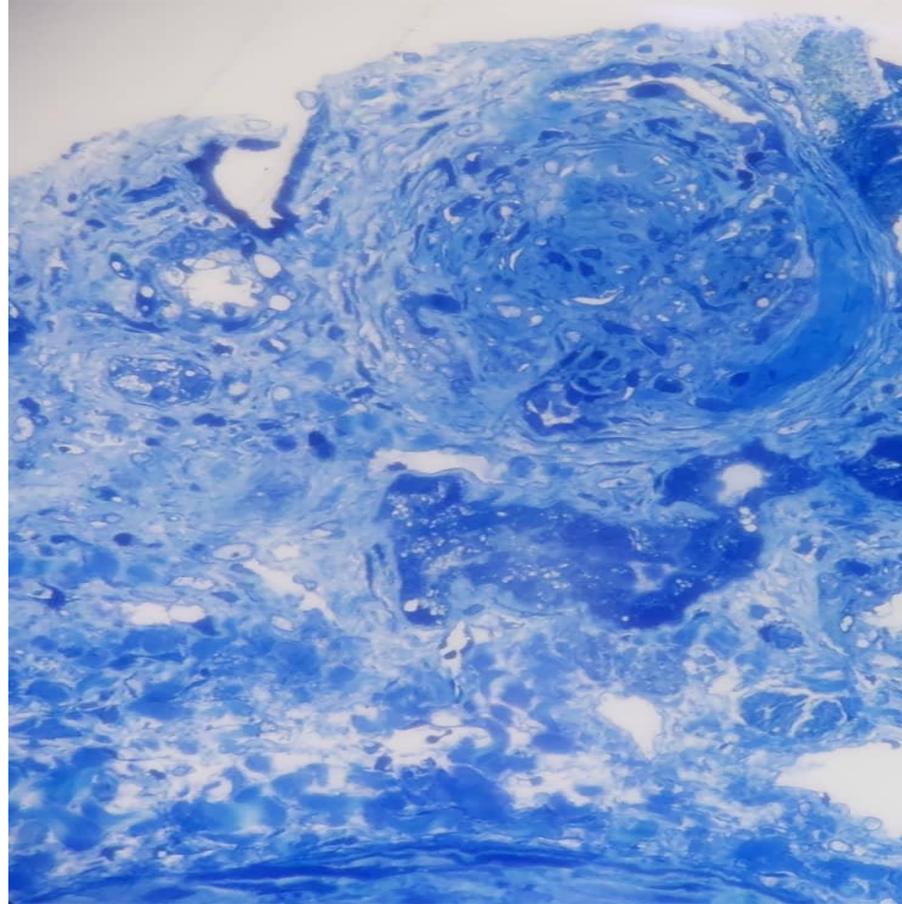
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- During hospitalization he had leukocytosis (41000per microlite), rising of blood urea, creatinine and also electrolyte disturbances. His course was complicated with unilateral pneumothorax.
- Finally, after 35 days he could breathe without respiratory machine assistance. Then he underwent renal biopsy that **showed glomerulosclerosis and acute tubulointerstitial nephritis**, tubular atrophy and interstitial fibrosis, suggestive of acute on chronic tubulointerstitial nephritis. Immunofluorescence study was negative. He received renal replacement therapy. After all oliguria gradually got better, and he discharged with order of hemodialysis twice weekly and continued corticosteroid and renal replacement therapy.



In our patient continues renal replacement therapy by hemofiltration and specific adsorbent filters to eliminate inflammatory mediators including leukotrienes can contribute to resolution of multi organ failure including liver and respiratory failure

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CONCLUSION

- In the extremely ill patients, the use of the HA cartridge reduced IL-6, IL-10 and TNF-alpha to a higher extend in surviving patients, indicating that these cytokines might be the potential biomarkers for HA hemoperfusion therapy.