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Thoracic Intervention of Post-Coronavirus Empyema: A Single Centre's Experience

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Abstract **Case Report**

Introduction*:** Since December 2019, several cases of unknown-origin pneumonia started to be diagnosed in Wuhan, China. One month later, The World Health Organization (WHO) recognized the responsible pathogen as the 2019 novel coronavirus and the global catastrophe has since been a major mortality cause up until today. We report the first surgical series of five patients with COVID-19 who had empyema thoracic after bilateral interstitial COVID-19 pneumonia, presenting a complex medical challenge in Malaysia. ***Method: Single centre, retrospective study and collection of data done via EHIS system on 5 patients in cardiothoracic surgery department in 2021. ***Conclusion*:** This report highlights the importance of rare complications such as empyema after COVID-19 pneumonia and the need for continued monitoring for this complication in patients who fail to improve during their hospital stay clinically. COVID-19 pneumonia appeared as typical viral pneumonia on thin-section CT. Accurate identification of CT imaging manifestations may help in the precise staging of the disease for clinical diagnosis and treatment. The outcome of these effusions is related to the interval between the onset of clinical symptoms and presentation to the physician, comorbidities, and time management. The primary treatment of pleural empyema is a course of a single or a combination of antibiotics. However, an early antibiotic treatment alone is usually not enough if it progresses to a complicated PPE and empyema. The majority of cases require surgical treatment with drainage of the pleural cavity.

Keywords: Empyema, Decortication, COVID-19, SARS-CoV-2.

1.0 BACKGROUND

Since December 2019, several cases of unknown-origin pneumonia started to be diagnosed in Wuhan, China. One month later, The World Health Organization [1] recognized the responsible pathogen as the 2019 novel coronavirus 2. The associated respiratory manifestation was later named the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the outbreak was named coronavirus disease 2019 (COVID-19). The disorder rapidly became a worldwide pandemic emergency and Globally, as of 12 March 2022, there have been 452,201,564 confirmed cases of COVID-19, including 6,029,852 deaths. In Malaysia, from 3 January 2020 to 12 March 2022, there have been 3,741,986 confirmed cases of COVID-19, with 33,567 deaths reported to WHO.

The most common clinical presentations include fever, dry cough, and tiredness. About 20% of patients became seriously ill, requiring hospitalization for difficulty breathing. Complications of COVID are ARDS and necrotizing pneumonia. Rarely positive pressure ventilation would result in a barotrauma-related air leak and pneumothorax, as reported by Aiolfi *et al*., in a case of persistent pneumothorax secondary bleb rupture in 2 intubated SARS-CoV-2 patients. Goursaud and colleagues described severe necrotizing pneumonia caused by SARS-CoV-2 and treated with ECMO and another case of hemorrhagic shock related to a spontaneous left hemothorax [2]. One of the most disastrous long-term complications of COVID would be empyema thoracis.

Pathogenesis & Pathophysiology of Viral Empyema/COVID empyema

Pleural empyema was divided into three stages according to the classification of the American Thoracic Society [3]. Stage 1 refers to the exudative stage, with thin liquid, a low cellular content, and an easily expansible lung; The second stage is termed fibrinopurulent, with accumulations of frank pus, large numbers of polymorphonuclear leukocytes, fibrin, and a

tendency to form loculations and a membrane limiting lung expansion; and an organization characterizes the third stage; fibroblasts grow into the exudate from the visceral and parietal pleural surfaces. An inelastic membrane called the pleural peel is formed and may encase the lung, with the potential to prevent lung expansion and restrict respiration

In the United States, a multi-center observational study included 11 adult COVID-19 survivors who had recovered; there was evidence of small airway disease, including basement membrane fibrosis in the airways, high rates of emphysema, and inflamed lung interstitium with predominantly lymphocytic inflammation and enema [4].

Pleural effusion is an uncommon complication of COVID-19 infection. Zhang et al. examined 34 consecutive COVID-19 patients and reported only 1 case with pleural effusion [5]. Another study reported the absence of pleural empyema at the beginning of the symptomatology but an increase in the cases during the clinical course of the disease [6]. In the case of lower respiratory tract infection, the virus generates a robust inflammatory response with pro-inflammatory cytokines release, oxidant stress, and damage to the alveolar epithelium. In addition, viral vasculitis, pulmonary microvascular thrombosis, and embolism have been described [7]. The combination of severe inflammatory syndrome with the onset of reactive pleural effusion and the exposure to severe risk factors might have facilitated the bacterial superinfection and the consequent development of pleural empyema.

Incidence & Mortality Rate

Parapneumonic effusions are an uncommon complication of Covid-19, which can be categorized as uncomplicated, complicated, or empyema thoracis, with rates of 2–3% of all cases of pneumonia, although the rates have been slowly rising over the years [8-10]. Hospitalized patients have the highest frequency of parapneumonic effusions. Uncomplicated effusions consist of free-flowing sterile interstitial fluid caused by the inflammation associated with pneumonia. Generally, it resolves with the administration of antibiotics [11]. Complicated parapneumonic effusions are due to bacteria or other microorganisms' invasion of the pleural space. Due to the prompt clearance of bacteria, the fluid is also typically sterile and cloudy in color. These effusions usually require drainage and antibiotics [11].

Some studies have investigated the frequency of parapneumonic effusions in COVID-19. For example, in a meta-analysis, Chong *et al*., reviewed 47 observational studies with 4981 COVID-19 patients at risk of developing pleural effusion. They found a low incidence of 7.3% for parapneumonic pleural effusions, which increased in critically ill patients or had multisystem inflammatory syndrome [12].

Empyema thoracis results from the accumulation of pus when microorganisms like fungi, mycobacteria, or pyogenic bacteria invade the pleural space and are associated with high morbidity and mortality worldwide [13]. Furthermore, a study done by Guan CS *et al*., showed that the incidence of empyema increases throughout a hospital stay [7]. Thus, it is essential to consider empyema in patients with long and complicated hospital stays.

2.0 CASE SUMMARIES

Our cases presented with 17-67 years old with a predominantly Malay population and male gender with only one active smoker. Most patients completed two-dose vaccination, with only one patient having an additional booster dose received. Their Body Mass Index (BMI) averaged 19.4 Kg/m2 (range 15.3 – 27.4 Kg/m2). Neither underlying medical comorbidities nor smoking status predisposes the patients to have an increased risk of developing this complication of COVID-19 infection (Table 1).

Table 1: Demographic Characteristics

	Case 1	**Case 2**	**Case 3**	**Case 4**	**Case 5**
Age (years)	24	23	67	17	61
Mean ± SD	38.4 ± 23.6				
Race	Malay	Malay	Chinese	Indian	Malay
Gender	Male	Female	Male	Male	Male
Comorbid	--	Iron Deficiency Anemia	Hypertension, Gout	Intellectual disability	Hypertension, Diabetes Mellitus, Dyslipidemia
Smoking	Active smoker	Non-smoker	Non-smoker	Non-smoker	Non-smoker
Pack years	4	--	--	--	--
Vaccination Status					
Completion	Yes	NA	Yes	No	Yes
Booster Dose	No	NA	No	--	1
Height (cm)	179	150	167	175	162
Mean ± SD	166.6 ± 11.4				
Weight (kg)	55	42.7	50	47	72

Mean ± SD)	53.3 ± 11.4				
BMI (Kg/m2)	17.2	19.0	17.9	15.3	27.4
Mean ± SD	19.4 ± 4.7				

Table 2 shows the clinical presentations of the surgical cohorts presented to our center. The common presenting symptoms include shortness of breath, fever, and cough. One out of five patients had atypical symptoms such as diarrhea. The range of duration from PCR COVID to developing symptoms of empyema was as acute onset as four days to late presentation up to 5 months. All five patients were hemodynamically stable prior to surgery.

Table 2: Clinical Presentations

	Case 1	**Case 2**	**Case 3**	**Case 4**	**Case 5**
COVID Category	4	2	4A	3	2
Duration of COVID to respiratory symptoms (Days)	3	21	1	3	
Duration of COVID to Empyema Presentation (Days)	4	150	30	23	360
Presenting Symptoms					
Breathlessness	+	+	+	-	+
Fever	+	+	+	+	-
Cough	+	+	+	+	+
Pleuritc chest pain	-	-	-	+	+
Diarrhea	-	-	-	+	-

All patients had shown opacity, occupying half of left hemithorax with Meniscus sign on chest x-ray. Three patients (75%) had a multi-loculated effusion with air locules within and enhancing pleural thickening; empyema thoracis needs to be considered. The patient also noted a necrotic left lower lobe within the segmental collapse of the left lower lobe, sparing the superior segment. On top of the organizing pneumonia and effusion abnormality detected, it also incidentally picked up one subject (8%) with at least lobar and segmental PA (Table 3).

Table 3: Preoperative Assessments

	Case 1	**Case 2**	**Case 3**	**Case 4**	**Case 5**
Initial Intervention – Drainage					
Tapping	-	+	-	+	-
Pigtail	-	+	-	-	+
Chest tube	+	-	+	-	-
Cultures (from initial drainage)					
Causative micro-organism	*Pseudomonas aeruginosa*	No growth	No growth	No growth	
Biochemical					
White cell count (x 10^9/L)	26.4	7.3	14.0	5.8	
C-Reactive Protein (mg/L)	44.6	26.3	52.6	68.7	
Imaging					
Chest-X Ray	Opacity seen occupying half of left hemithorax	Meniscus sign seen over left hemithorax	White-out left lung	Meniscus sign seen over left hemithorax	80% white-out left lung
CT Thorax					
Organizing pneumonia	< 25%	-	Multi-focal, peripheral	Lingular segment of LUL	-
Effusion	Moderate	Moderate	Multi-loculated	Large, loculated	Large, multi-loculated
Pneumothorax	+	-	-	-	
Pleural thickening	+, Slight	+, Slight	+	+	+
Pleural split sign	-	-	-	-	+
Necrotizing appearance	-	+, small	-	-	-
Thrombus		+, lobar and segmental PA	-	-	-
Superimposed bacterial Pneumonia	+	-	-	-	-
Causative micro-organism	*Pseudomonas aeruginosa*	NA	NA	NA	NA

Table 4 shows the management and outcomes of COVID-19 empyema with surgery. All our patients were started on empirical antibiotics, including Penicillin, Cephalosporin, and Carbapenem group

antibiotics, prior to decortication. Thoracotomy was the preferred approach for complete decortication. One patient was initially planned for video-assisted thoracoscopic surgery (VATS). However, it was later converted to thoracotomy due to limited access for complete decortication. Post-operatively, most of our patients had good lung expansion, ranging from 80% to complete lung expansion. Figures 1-3 showed a series of pre-operative and post-operative chest X-rays and the CT images in the axial and coronal sections of three patients in our series.

Intraoperative specimens sent for histopathology mostly revealed features of inflammation (chronic, acute on chronic, and necrotizing granulomatous inflammation). All pleural fluids and biopsies sent for microbiology tests were negative for SARS-CoV-2 infection. No COVID test was repeated after the surgical intervention.

No significant complications were seen post-operatively. Two patients who underwent surgery had air leaks post-surgery. However, lungs were well expanded, and patients were clinically well. The longest ICU stay was eight days, most patients required at least two days of ICU care, and the shortest duration of ICU admission was only a day.

The mean length of ICU and hospital stay was four days. All patients were discharged home well with outpatient thoracic clinic appointments. Subsequent clinic follow-ups with chest x-rays showed well-expanded lung fields and resolution of symptoms. Patients were under our follow-up for three months before being discharged.

Table 4: Managements and Outcomes

	Case 1	**Case 2**	**Case 3**	**Case 4**	**Case 5**
Antibiotics					
Cephalosporin (2nd generation)	-	-	-	+ Cefuroxime	-
Cephalosporin (3rd generation)	+ Ceftriaxone, Ceftazidime	+ Ceftazidime	-	-	-
Penicillin	+ Amoxicillin/ Clavulanate, Piperacillin/ Tazobactam	+ Amoxicillin/ Clavulanate, Piperacillin/ Tazobactam	+ Amoxicillin/ Clavulanate, Piperacillin/ Tazobactam	+ Amoxicillin/ Clavulanate, Piperacillin/ Tazobactam	+ Amoxicillin/ Clavulanate, Piperacillin/ Tazobactam
Macrolide	-	+ Azithromycin	-	-	-
Carbapenem	-	-	-	+ Meropenem	-
Surgical approach	VATS converted Thoracotomy	Thoracotomy	Thoracotomy	Thoracotomy	Thoracotomy
Operative findings					
Amount of drainage (mls)	800	-	550	50	-
Characteristics of fluid	Hemoserous	Purulent	Purulent	Purulent	Hemoserous
Cortex	Thick	Thick	Thick	Thick	Thick
Adhesion	-	-	-	Dense	
Trapped lung	+	-	-	-	
Post-Decortication					
Lung expansion	Full	60%	80%	Full	95%
Airleak	Minimal	Small	Small	No	Minimal
Intraoperative samples for culture	*Pseudomonas aeruginosa*	No growth	*Enterococcus faecium*	*Escherichia coli*	No growth
Histopathological examination	Acute on chronic inflammation	Necrotizing granulomatous inflammation Ziehl-Neelson positive	Acute on chronic inflammation	Chronic inflammation	NA
Outcomes					
Mortality	No	No	No	No	No
Airleak	Resolved	Resolved	Present	No	Resolved
Sepsis	No	No	No	No	No
Surgical site infection	No	No	No	No	No
Organ failure	No	No	No	No	No
Duration of postoperative					
ICU stay (days)	1	2	2	8	1
Hospital stay (days)	8	14	27	14	7

Image 1a: This image shows the initial chest x ray of a patient with left lung empyema. This PA film demostrates a unilateral opacification of the left lung, with contralateral deviation of the trachea

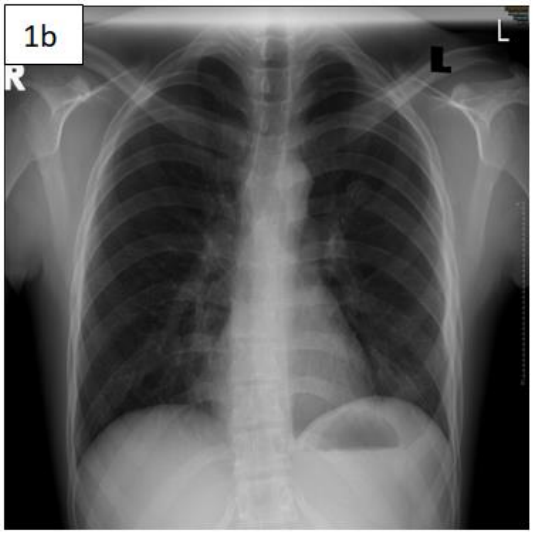

Image 1b: PA film of the chest x ray taken post operatively showing fully expanded lungs with no residual effusion

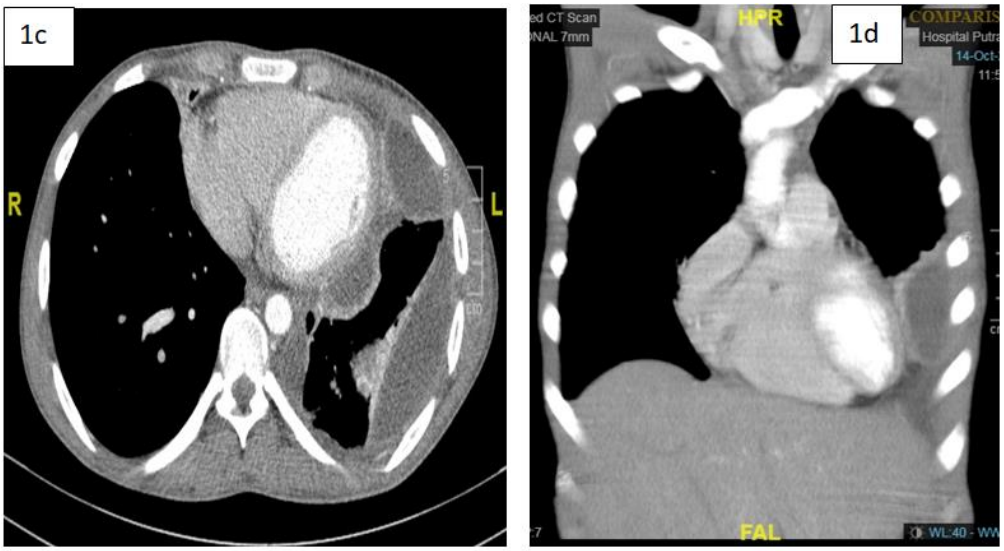

Image 1c and 1d: Pre operative CT thorax(axial and coronal views), showing left sided multiloculated pleural effusion with "split pleura" sign

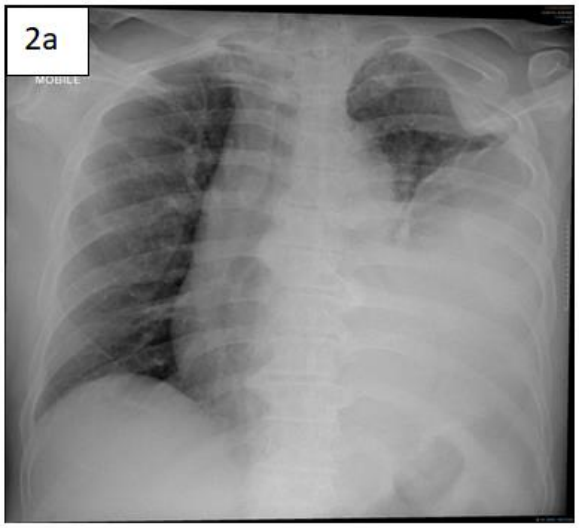

Image 2a: Pre operative chest x-ray showing a massive left sided effusion pleural effusion

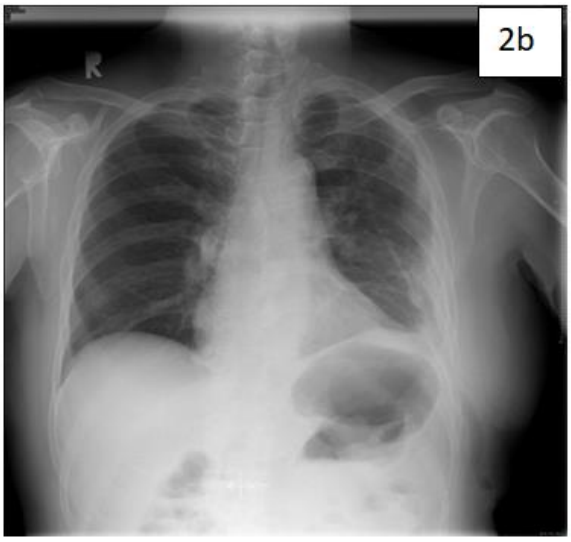

Image 2b: Post operative chest x-ray, showing good lung expansion with residual opacification on the chest x-ray

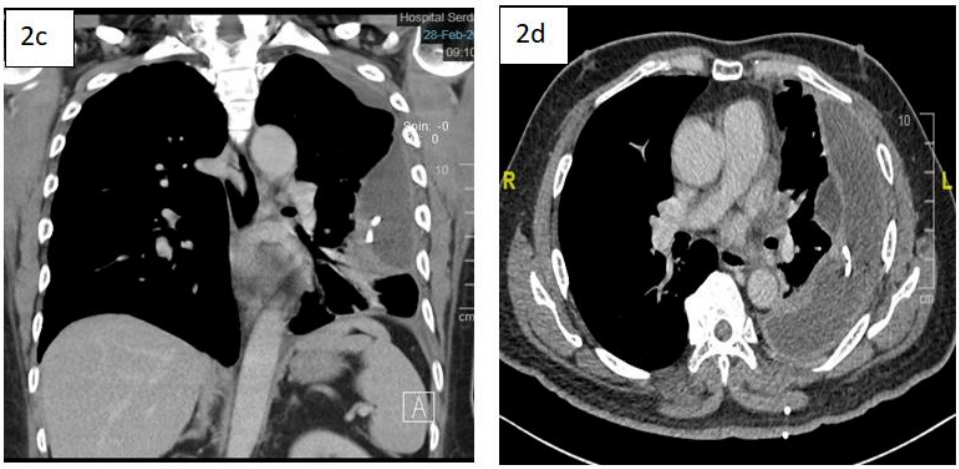

Image 2c and 2d: Represents the coronal and axial view of the pre operative CT Thorax. Multiloculated left pleural collection is seen with "split pleura" sign. The effusion is lenticular-shaped and creates an obtuse angles with the chest wall suggestive of empyema thoracis

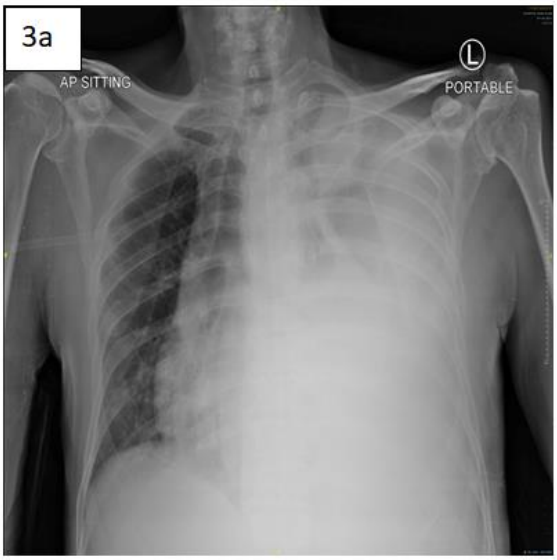

Image 3a: AP chest x-ray showing left sided white out opacification

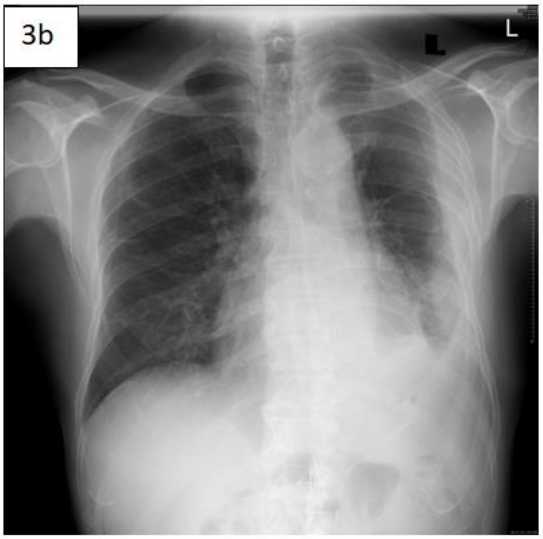

Image 3b: Post operative chest x-ray demonstrating well expanded lung with residual opacification over the left lower lobe

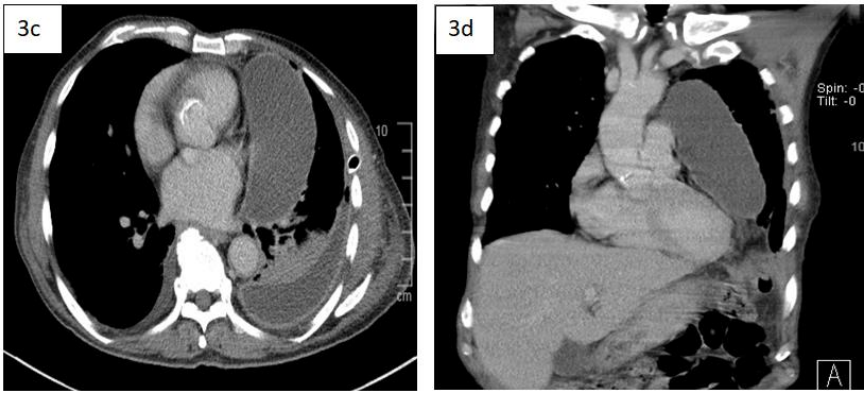

Image 3c and 3d: Pre operative CT thorax of the patient with left sided empyema thoracis, shows multiloculated left pleural effusion with "split pleura" sign

3.0 DISCUSSION

With growing global concerns about the COVID-19 outbreak, much disease-related information and guidelines for clinical management are missing. We reported 5 cases of thoracic empyema post-COVID-19 infection, which were successfully treated surgically

Stephanie *et al*., published a case series on 13 patients treated surgically post covid-19 infection From March 13, 2020, to July 18, 2020, from Manhattan Tisch Hospital. Among 13 patients, 17 operations were performed. Two patients (15%) had multiple operations due to ongoing bleeding. Of the 17 operations, 10 (61%) were performed in a minimally invasive fashion. The case series concluded that the majority (69%) of the patients operated on had been discharged, with a current survival of 77%. Patients who died were at high risk, with progressive respiratory distress leading to acute surgical intervention or age more than 70 years with multiple comorbidities [14]. In contrast to our series, our mortality was minimized to zero due to successful surgery and perioperative management.

The chest CT was essential as it revealed empyema, as it is a rare complication that should be considered in a COVID-19 patient who is not clinically improving [15]. The hallmark findings of COVID 19 include bilateral patchy ground-glass opacities with a predominantly peripheral distribution (organizing pneumonia). In addition, the most common pleural change in COVID 19 patients is pleural thickening, while pleural effusion is uncommon. These findings were present in most of our patients on top of other features such as necrotizing pneumonic patches and small pulmonary arterial thrombus.

Guidelines for the management of empyema in COVID-19 have not yet been established. Tessitore et al. discussed three cases of pleural empyema after bilateral interstitial COVID-19 pneumonia, which required combined medical and surgical treatment with open decortication [16]. The main treatment of pleural empyema is a course of a single or a combination of antibiotics. However, antibiotics alone are usually unsuccessful for pleural empyema, and most cases require surgical treatment with drainage of the pleural cavity [13]. All patients in our series received at least Penicillin group antibiotics, including Amoxicillin/ Clavulanate and Piperacillin/ Tazobactam. Some patients required escalation of antibiotic choices owing to superimposed bacteremia or sepsis. Thoracic empyema has been considered a surgical disease, with open decortication as the most definitive method of treatment [12] and non-operative management being associated with higher risk of mortality compared with surgical decortication [17].

Currently, surgical treatment of pleural empyema in COVID-19 patients is not yet described in literature due to the reduced number of cases and possibly due to the risk grade of the procedure. Moreover, the acute Middle East Respiratory Syndrome, similar to SARS-CoV-2, represents a poor prognostic indicator [18]. Therefore, thoracic empyema has been considered a surgical disease, with open decortication as the most definitive method of treatment [17] and non-operative management being associated with a higher risk of mortality than surgical decortication [19].

4.0 CONCLUSION

This report is the first case series of COVID-19 patients with surgically treated post-COVID pleural empyema published in Malaysia.

This report highlights the importance of rare complications such as empyema after COVID - 19 pneumonia and the need for continued monitoring for this complication in patients who fail to improve during their hospital stay clinically. COVID-19 pneumonia appeared as typical viral pneumonia on thin-section CT. Accurate identification of CT imaging manifestations may help in the precise staging of the disease for clinical diagnosis and treatment. The outcome of these effusions is related to the interval between the onset of clinical symptoms and presentation to the physician, comorbidities, and time management. The primary treatment of pleural empyema is a course of a single or a combination of antibiotics. However, an early antibiotic treatment alone is usually not enough if it progresses to a complicated PPE and empyema. The majority of cases require surgical treatment with drainage of the pleural cavity.

Considering that this is a rare but possible complication, we want to underline the importance of clinical and radiological surveillance and laboratory testing in individuals with a recent diagnosis of SARS-CoV-2. Moreover, these results suggest that it is worth investing in a surgical approach considering pleural effusion, together with SARS-CoV-2 manifestation, is a life-threatening condition.

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