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LUNG ABSCESSES WITH FORMATION OF SEVERAL CAVITIES AND PNEUMOMEDIASTINUM AS RARE COMPLICATIONS IN COVID-19

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Abstract

Pneumonia caused by severe acute respiratory syndrome coronavirus 2 emerged in China at the end of 2019. SARS-CoV-2 is a highly pathogenic and transmissible coronavirus that primarily spreads through respiratory droplets and close contact. A growing body of clinical data suggests that a cytokine storm is associated with COVID-19 severity and is also a crucial cause of death from COVID-19. Because of the severe immunomodulation and lymphocyte depletion caused by this virus and the subsequent administration of drugs directed at the immune system, bacterial and fungal superinfection can occur. We are presenting a case of lung abscesses developed in CoVID-19 patient as complication. We hypothesized that corticosteroid therapy administration could have predisposed the patient with COVID-19 to develop superinfection of bacterial origin leading to formation of multiple lung abscesses due to a diminished innate immune response. A lung abscess is a cavity of the pulmonary parenchyma filled with fluid caused by infection or necrotic debris. High rates of morbidity and mortality are associated with lung abscess despite appropriate antibiotic therapy and better supportive care.

Clinicians have to highly consider the probability of the pulmonary abscess development in CoVID-19 patients administered the high therapeutic dosage of steroids despite the evidence of the absence of procalcitonin elevation in dynamics, intoxication signs and febrile fever. A chest computerized tomography scan has to be done even in case of a small suspicion of such complications.

Keywords: *COVID-19, COVID-19 complications, lung abscess, procalcitonin.*

Introduction

From the beginning of the COVID-19 outbreak in December 2019 in Wuhan City, China, the novel COVID-19 has emerged as a global healthcare crisis [*Wu Z, McGoogan JM, 2020*]. COVID-19 manifests as a multisystem disease, however, the lung represents the most common affected target organ [*Wu Z, 2020*].

The diagnosis of COVID-19 is based on the clinical manifestations, laboratory testing, and imaging. Reverse transcription polymerase chain reaction (RT-PCR) test from nasopharyngeal swab samples and typical chest computerized tomography (CT) characteristics confirms the diagnosis of COVID-19. Chest CT scan had a sensitivity of 97% for diagnosing COVID-19 based on physicians' experience, which is even superior to RT-PCR [*Ai T et al., 2019; Udugama B et al., 2020*].

Several complications of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-19) have been described: respiratory failure, cardiac and cardiovascular, thromboembolic, neurologic, inflammatory complications, secondary infections [*McIntosh K, 2021*]. According to the published reports, a portion (7.2%) of COVID-19 patients are sometimes co-infected by other microbial pathogens, adding to the severity of these cases and raising difficulty in the diagnosis, prognosis, and treatment [*Chen X et al., 2020; Garcia-Vidal C et al., 2021*].

While it is difficult to predict which patients will develop these complications, elevations in certain biomarkers have been associated with worse outcomes [*McIntosh K, 2021*]. Procalcitonin (PCT) is an effective biomarker to reliably distinguish viral

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from bacterial infections in the lower respiratory tract [*AL-Azeema AA; et al., 2013; Sager R et al., 2017*], and has been associated with bacterial co-infection and progression to severe disease in patients infected with COVID-19. Procalcitonin is more specific for bacterial infections than other inflammatory markers, such as white blood cell count, erythrocyte sedimentation rate, and C-reactive protein (CRP). It may not rise in contained localized infections such as tonsillitis, sinusitis, cystitis, uncomplicated skin/soft tissue infections, abscesses. Notably, Procalcitonin production is not impaired in immunocompromised states such as neutropenia, corticosteroids, bone marrow or solid organ transplantation, and human immunodeficiency virus (HIV). [*Rhee C, Mansour KM, 2021*]

There are scarce case reports available describing lung abscesses in patients with COVID-19 [*Kashin M et al., 2020; Renaud-Picard B et al., 2020; Selvaraj V 2020; Zamani N et al., 2021*]. We are presenting a case of lung abscesses developed in CoVID-19 patient as complication. We hypothesized that corticosteroid therapy administration could have predisposed our patient with COVID-19 to develop superinfection of bacterial origin leading to formation of multiple lung abscesses due to a diminished innate immune response.

Case presentation

A 43-year-old man was admitted to hospital on the 13th day of the disease with complaints of fever up to 40°C, severe weakness, shortness of breath, cough, myalgia, arthralgia. No chronic lung disease: chronic obstructive bronchitis, bronchial asthma, was recorded on admission. Underlining medical conditions included gout, dietary controlled hypertension.

On admission, the clinical examination found a conscious, tachypneic patient with a respiratory rate of 38-40 minute with oxygen saturation at 66% in ambient air (he wasn't transferred to intensive care unit (ICU) department due to the lack of ICU beds in Armenia at that time) and 84% under 15 *L/min* of oxygen by face mask, a heart rate of 103 beats per minute, and blood pressure at 120/80 *mmHg*. Moreover, the examination confirmed regular heart sounds, and there was no sign of right or left heart failure. Pulmonary auscultation found crepitation in both basal lungs.

The initial laboratory results showed a neutrophil-predominant leukocytosis (white blood cells (WBC) 12100 cells/μL, neutrophils 90%), lymphopenia (430 *cells/μL*) and elevated inflammatory markers (CRP 30 *mg/L*, ferritin 3000 *ng/ml*, fibrinogen 666 *mg/dL*, Interleukin-6 96.7 *pg/ml*, PCT 5.634 *ng/ml*) (**Tab.1**). SARS-CoV-2 polymerase chain reaction (PCR) nasopharyngeal swab was positive. A chest CT scan showed bilateral, peripheral, and subpleural ground-glass opacities with involvement of 50% of lung parenchyma, suggestive of an infection by SARS-CoV-2 (Fig.1). Because of elevated PCT, bacterial infection was suspected. Hence blood sterility, sputum, urine bacteriological tests were taken. Afterwards empiric antibiotic therapy with levofloxacin started and was eventually stopped after 10 days, when PCT was 0.6*ng/ml*, CRP 3.8 *mg/L* and the patient was afebrile for 4 days (Tab.1). All bacteriological cultures (blood, sputum, urine) that were performed, were negative. Steroid therapy with dexamethasone with a 12*mg/day* dosage has been conducted since the first day of hospitalization. On the 5th day of dexamethasone therapy, the patient's condition deteriorated (saturation of hemoglobin as measured by pulse oximetry (SpO_2) 58% in ambient air, 80-85% under 20 *L/min* of oxygen by reservoir mask) and dexamethasone was replaced with methylprednisolone 500 *mg/day* for 3 days, followed by gradual dose reduction as it mentioned in the table.

Since the 12th day of hospitalization (25 day of the disease) the patient's condition improved (SpO_2 70-72% in ambient air, SpO_2 90-93% on 15 *L/min*, respiratory rate 32 minute) on methylprednisolone treatment. Laboratory results also demonstrated positive changes (Interleukin-6 (IL-6) 18 *pg/ml*, ferritin 1216 *ng/ml*, CRP 3.8 *mg/L*, fibrinogen 419 *mg/dL*) (Tab.1). A chest CT scan showed bilateral, polysegmental, interstitial pneumonia with the involvement of 80-85% lung parenchyma.

As side effects of steroid ther-

To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world

Table 1.

Characteristics of the clinical course

Pneumomediastinum *Abscess* Day of discharge

Day of hospitalization	1	2	3	4	5	6	7	8	9	10	11	12	13	16	17	18	21	22	28	29	30	33	36	37	38	39
Lymphocytes 10^3µL		0.43				0.51					0.57				1.15					1.4			1.89			1.5
CRP		30				26					3.8				7					161		139	82			59
PCT		5.6		4.15		1.07					0.6				0.52			0.48		0.316				0.5		0.28
IL-6				97							18				16					86			67			56
Dexamethasone (*mg/day*)			12																							
Methylprednisolone (*mg/day*)							500			325	160		120		80			40				20				16
Levofloxacin (*mg/day*)						500																				
Meropenem (*g/day*)																						3				
Doxycycline (*mg/day*)																										200
Fever (°C)	<39.7			<38.1		<37.5				Normal					Normal				<37.8	<39.6		Subfebrile				

apy, he had steroid associated diabetes mellitus (controlled by insulin therapy), tachycardia, peripheral edema of feet (hypoalbuminemia minimum 30-31 *g/L* was identified too).

On the 17th day of hospitalization, a chest CT scan was repeated due to the lack of serious improvement expected at that stage of the disease (patient's respiratory signs were almost the same within the last few days: SpO_2 70-75% in ambient air, SpO_2 90-93% on 15 *L/min*, respiratory rate 30-34 minute). Chest CT scan showed minimum pneumomediastinum, subcutaneous emphysema in the neck and diffuse ground-glass opacities with moderately expressed liner and reticular thickening of interlobular septa. The patient was receiving methylprednisolone 80 *mg/day*, and no antibiotic therapy.

His condition was improving very slowly: SpO_2 80-85% in ambient air, SpO_2 91-93% on 5 *L/min*, respiratory rate 26 per minute, normal body temperature. On the 22nd day of hospitalization, subfebrile fever and on 24th day, a chest pain recorded in the patient, respectively. The results of laboratory examinations, chest X-ray, electrocardiogram, echocardiography, and the abdominal sonography reveled no remarkable findings.

On the 29th day, the patient became febrile (maximum fever 39.6) and the chest X-ray showed abscess in the left lung. CRP (161 *mg/L*), ferritin (more than 3000 *ng/ml*), IL-6 (86 *pg/ml*) were elevated (Tab.1**).** Oxygen saturation was improving in dynamics. The sputum bacteriological examination conducted and empiric antibacterial treatment with meropenem started [*Kuhajda I et al., 2015*]. Streptococcus pneumoniae and Staphylococcus aureus were isolated in the bacteriological culture of sputum and they were sensitive to meropenem. The serological examination for Aspergillus was not conducted. The treatment with methylprednisolone continued with 20 *mg/day* dosage and was not stopped because the patient was still on oxygen therapy. Antibiotic treatment with meropenem lasted for 10 days and was replaced with doxycycline because the laboratory analyses and the patient's condition had improved.

On the 34th day the chest CT scan was repeated and showed diffuse infiltration of both lungs with destructive cavities in the left lung (the size of biggest cavity is 4.5×1.5 *cm* in the upper lobe).

The patient was discharged on the 39th day of

hospitalization with SpO_2 90% in the ambient air, T 37.2°**C**.

Low-molecular-weight heparin was prescribed with therapeutic dose throughout the hospitalization period.

At hospital discharge the patient was prescribed oral doxycycline 100 *mg* every 12 *hours* (the duration depends on the follow up of pulmonologist), anticoagulation therapy, and two-week duration methylprednisolone.

Follow up within one month after the hospital discharge showed no deterioration, he continued to have subfebrile fever for 5 days after discharge and received doxycycline for two weeks. Oxygen saturation was between 92-95% on ambient air.

One month after the hospital discharge the chest CT scan showed total (100%) infiltration of lung parenchyma as ground-glass opacities and reticular pattern, and destructive cavities especially in the left lung (the size of biggest cavity is 4.1×2.0 *cm* in the upper lobe of the left lung). A cavity in the lower lobe of the right lung with almost 1.4 *cm* in size was shown. In most cavities the walls were thin and there was no fluid in them (Fig.1). The blood analysis showed that PCT 0.09 *ng/ml*, IL-6 29.6 *pg/ml*. Glucose level in the blood was back to its normal.

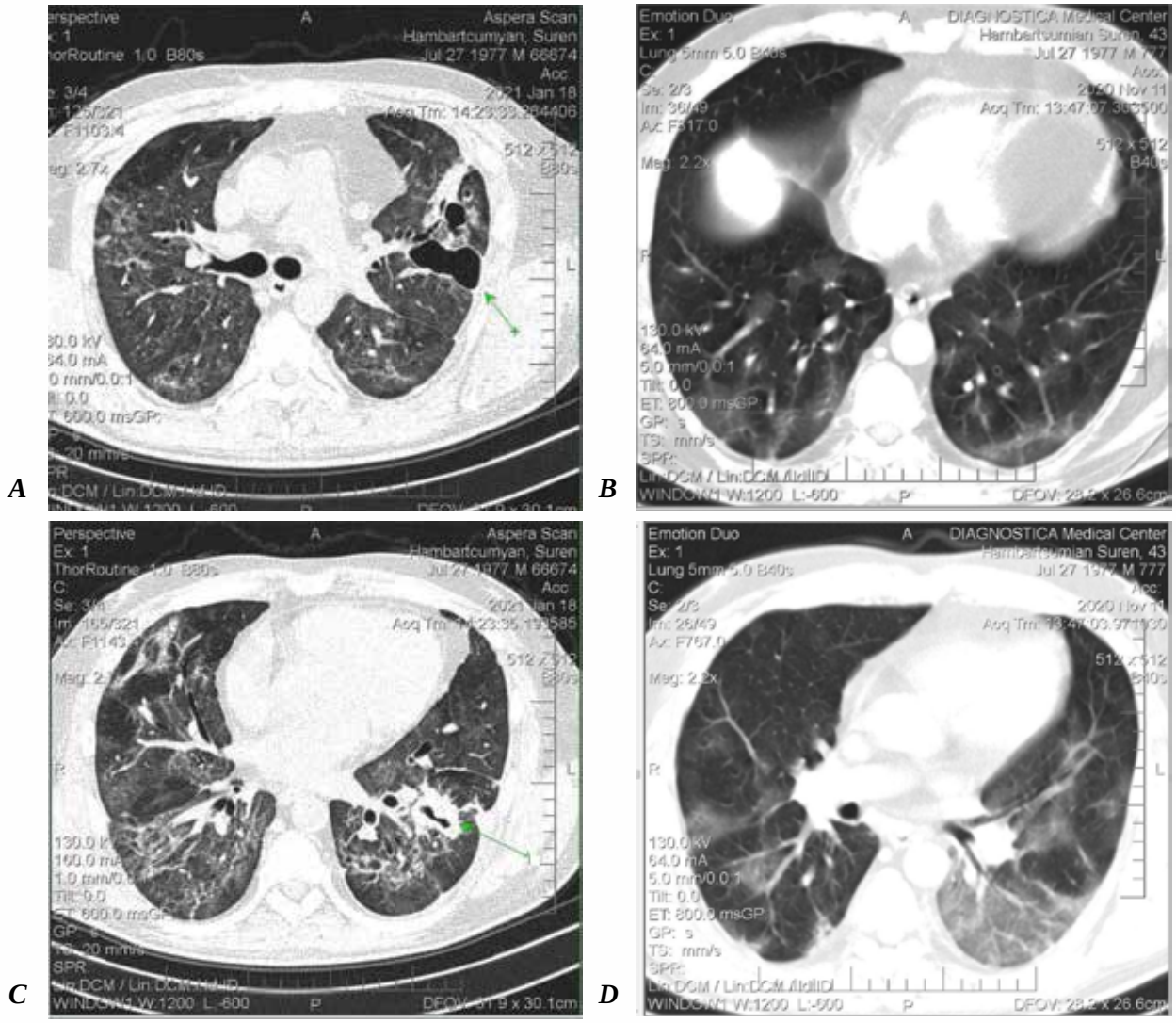

Figure.1. *Dynamic changes in CT examination*
(A,C)*. Axial chest CT, one month after being discharged, revealing total (100%) infiltration of lung parenchyma as ground-glass opacities and reticular pattern, except of that, there are destructive cavities especially in the left lung (the size of biggest cavity is 4.5×1.5 cm in the upper lobe of the left lung).*
(B, D) Axial chest CT showsbilateral peripheral, and subpleural ground-glass opacities with involvement of 50% of lung parenchyma, which are consistent with a COVID-19 infection, 13 days after symptom onset.

DISCUSSION

Because of the critical condition of the patient, pulse methylprednisolone treatment started and was titrated down as appropriate. As the patient was on oxygen therapy throughout the hospitalization period and the improvement was very slow, we had to continue steroid therapy throughout the period, knowing that prolonged steroid therapy is associated with high immunosuppressive status. When the patient had subfebrile fever and pain in the chest, complete blood count (CBC), IL-6, PCT, CRP, the chest radiography were repeated without any evidence of bacterial co infection and elevation of inflammatory markers. Even PCT decreased in dynamics. The patient did not have any signs of intoxication. Antibiotic treatment did not start in that period and it was clear that the important period for antimicrobial treatment was gone. After 7 days of subfebrile fever the patient started to have febrile fever and the chest radiography revealed multiple abscesses in the left lung. CRP was elevated, but PCT was still decreasing. This case again showed that PCT levels may not rise with localized infections such as parapneumonic effusion, empyema, osteomyelitis, localized abscess, etc.

Retrospectively, CT imaging may have been warranted earlier in his hospital stay, based on his slow response to treatment and ongoing oxygen requirements with subtle subfebrile fever. And in that case antibiotic treatment could be started earlier. As our patient responded to a broad-spectrum antibacterial treatment, fungal origin superinfection probability was not considered. According to available resources, if ICU CoVID-19 patient does not respond to broad-spectrum antibacterial treatment, antifungal, liposomal amphotericin B [*Heard K et al., 2020; Garcia JS et al., 2021*] suggested to administer.

CONCLUSION

Lung abscess is a very rare complication of CoVID-19 and can develop even if the patient doesn't have any chronic lung disease. It mostly develops when the patient is getting better after being critically ill with CoVID-19. Clinicians have to highly consider the probability of the pulmonary abscess development in CoVID-19 patients administered the high therapeutic dosage of steroids despite the evidence of the absence of PCT elevation in dynamics, intoxication signs, febrile fever. A chest CT scan should be done even in case of a small suspicion of such complications.

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