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Case Report

Staphylococcus aureus costochondritis and chest wall abscess in a COVID-19 patient treated with tocilizumab

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is a worldwide pandemic, causing a global health threat. Up to 15% of the confirmed cases develop severe disease, requiring hospitalization or intensive care unit (ICU) admission. Tocilizumab, an IL-6 receptor antagonist, is a promising treatment of severe pneumonia with acute respiratory distress syndrome (ARDS) or cytokine release syndrome (CRS) in the course of COVID-19. We report a suppurative costochondritis and chest wall abscess in a severe COVID-19 patient treated with tocilizumab.

Keywords: Abscess, chest wall, costochondritis, COVID-19, tocilizumab.

Novel coronavirus-2019 (COVID-19) has led to a devastating pandemic, causing an emergent global health threat. Severe pneumonia, cytokine release syndrome (CRS), and acute respiratory distress syndrome (ARDS) are the leading causes of mortality and morbidity in the disease course. These patients mostly require intensive care and invasive procedures that facilitate secondary infections. Bacterial and fungal superinfections are reported in a significant rate of critically ill COVID-19 patients.[1] Several serious infections were also reported in patients treated with tocilizumab.[2,3] Herein, we report an atypical infectious complication in a severe COVID-19 patient treated with tocilizumab.

CASE REPORT

A 61-year-old, previously healthy man presented with dyspnea and fever for five days. He was diagnosed with COVID-19 by real-time polymerase chain reaction (RT-PCR) and hospitalized. Since thoracic computed tomography (CT) showed multiple infiltrates in both lungs and the patient had severe dyspnea, treatment with hydroxychloroquine, azithromycin, and favipiravir was initiated. On Day 6 of hospitalization, the patient's clinical status deteriorated while on this treatment and was admitted to the intensive care unit (ICU) due to tachypnea and a high level of oxygen demand. On ICU admission, he was in moderate respiratory distress with an oxyhemoglobin saturation of 91% on 15 L/min oxygen through a reservoir mask. He developed CRS, with severe lymphopenia (100/mm^3) and hyperferritinemia (1,271 ng/mL). He was placed in prone position with high-flow oxygen support, and he was treated with the first dose of 400 mg intravenous (IV) tocilizumab. On Day 2 of ICU stay (seven days after hospitalization), he rapidly progressed to acute hypoxemic respiratory failure, and a second dose of tocilizumab was administered. Later on, he was intubated due to worsening hypoxemia, accessory muscle use, and paradoxical abdominal respiration. A central venous

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catheter was placed in the right jugular vein. After eight days of mechanical ventilation support, the patient was successfully extubated.

One day after discharge from the ICU, the patient complained of the sudden onset of right shoulder and chest pain radiating to the right arm. His pain was exacerbated by sneezing, coughing, deep breathing and movements of the right shoulder and torso. On physical examination, he was afebrile, and his bilateral upper extremity muscle strength and glenohumeral joint range of motion were normal. However, both active and passive movements of the right shoulder were extremely painful. Redness, warmth, and swelling were observed around the right parasternal region. Palpation of the second and third costochondral joints caused pain in a referred distribution and reproduced the patient's symptoms. The chest radiograph was unremarkable. Laboratory findings revealed mildly elevated serum C-reactive protein (CRP) (15 mg/L; normal range: <5 mg/L), normal leukocyte count and moderate lymphopenia (1,000/mm^3), without any other significant abnormalities (Figure 2). Computed tomography scan revealed bilateral diffuse ground glass opacities, crazy-paving pattern, consolidation, minimal swelling of superficial subcutaneous tissues in the second and third right costal cartilage and degeneration in the right glenohumeral joint. The patient was diagnosed with Tietze syndrome and treated with paracetamol 1 g per day for three days. However, his pain progressively increased and spread into the neck. Both diclofenac 50 mg q.i.d. and tramadol 50 mg q.i.d. were administered three to four times a day to achieve effective analgesia. As he was oxygen-dependent, 40 mg IV methylprednisolone was administered for three days. Despite therapy with a non-steroidal anti-inflammatory drug and steroid, his shoulder and chest pain that referred to the neck increased. His sternoclavicular joint became remarkably swollen, red, and very tender (Figure 1a). Magnetic resonance imaging (MRI) was performed both on the chest and right shoulder to further evaluate the joints which revealed a fluid collection in the right sternoclavicular joint with extension into the chest cavity, suggesting a chest wall abscess (Figure 1b). Post-contrast T1-weighted images confirmed the inflammatory changes and showed a central avascular area within the abscess.

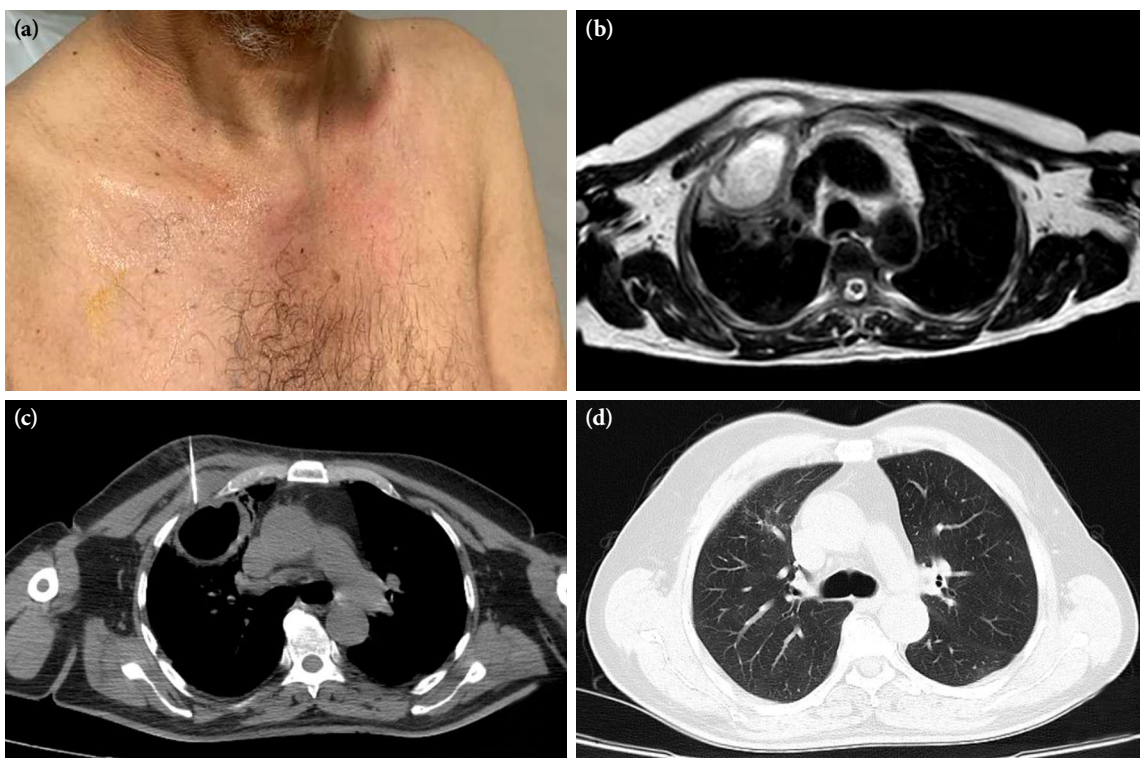
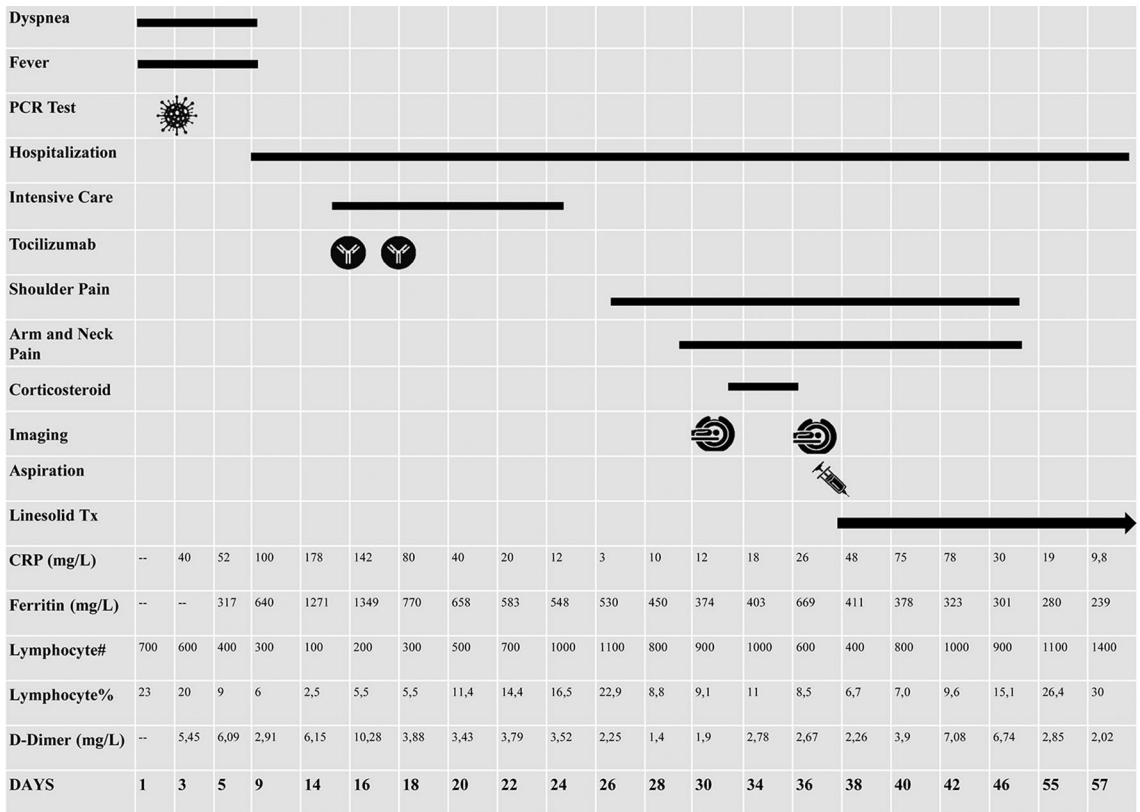


Figure 1. Image of the patient and imaging studies of chest wall. **(a)** Swelling and erythema on right costochondral joint. **(b)** Chest wall abscess including right sternoclavicular joint on magnetic resonance imaging (axial T2-weighted). **(c)** Computed tomography-guided needle aspiration of abscess. **(d)** Total recovery after antibiotic treatment).



CRP (mg/L)	--	40	52	100	178	142	80	40	20	12	3	10	12	18	26	48	75	78	30	19	9,8
Ferritin (mg/L)	--	--	317	640	1271	1349	770	658	583	548	530	450	374	403	669	411	378	323	301	280	239
Lymphocyte#	700	600	400	300	100	200	300	500	700	1000	1100	800	900	1000	600	400	800	1000	900	1100	1400
Lymphocyte%	23	20	9	6	2,5	5,5	5,5	11,4	14,4	16,5	22,9	8,8	9,1	11	8,5	6,7	7,0	9,6	15,1	26,4	30
D-Dimer (mg/L)	--	5,45	6,09	2,91	6,15	10,28	3,88	3,43	3,79	3,52	2,25	1,4	1,9	2,78	2,67	2,26	3,9	7,08	6,74	2,85	2,02
DAYS	**1**	**3**	**5**	**9**	**14**	**16**	**18**	**20**	**22**	**24**	**26**	**28**	**30**	**34**	**36**	**38**	**40**	**42**	**46**	**55**	**57**

Figure 2. Timeline of patient symptoms, medications, and laboratory findings.
PCR: Polymerase chain reaction; CRP: C-reactive protein.

A CT-guided fine needle aspiration of the lesion withdrew 10 mL of purulent liquid (Figure 1c). Gram stain showed numerous polymorphonuclear leucocytes without any bacteria, and acid-fast stain was negative. Culture of the liquid revealed methicillin-sensitive *Staphylococcus aureus* (MSSA). As he had a known beta-lactam allergy, he received a two-week course of IV linezolid. He responded well to therapy and was discharged home with oral clindamycin 300 mg t.i.d. A CT and MRI performed at one month of follow-up which showed a decrease in the diameter and content of the abscess (Figure 1d). Written informed consent was obtained from the patient for publication of this case report and accompanying images.

DISCUSSION

In this report, we present a life-threatening secondary infectious complication in the course of severe COVID-19. Early reports from China showed that up to two-thirds of COVID-19 patients in the ICU setting died from secondary infections.[1,4] The risk increases with prolonged duration of illness, requirement of intubation or catheterization, and utilization of immunosuppressant drugs, such as corticosteroids or tocilizumab.

In our case, the most likely scenario is asymptomatic transient bacteremia related to the central catheter or other invasive procedures and hematogenous progression of infection to the costochondral joints and sternoclavicular joints. On the other hand, two doses of tocilizumab could have facilitated bacteremia and progression of the infection. Tocilizumab is a humanized monoclonal antibody, targeting circulating interleukin-6 (IL-6) receptors. It has been under compassionate use in COVID-19 patients with safety concerns.[8] Tocilizumab has a warning for risk of serious infections including tuberculosis, bacterial, invasive fungal, viral, and other opportunistic infections. Currently, there is limited published evidence on the safety of tocilizumab in the treatment of severe COVID-19. It seems to be safe according to rheumatoid arthritis experiences. Even so, severe *S. aureus* infections have been reported in rheumatoid arthritis patients treated with tocilizumab.[5,6] Also, limited data from chimeric antigen receptor T-cell (CAR-T)-mediated

CRS support the safety of short-term tocilizumab use.[7] However, the use of tocilizumab for COVID-19 poses a much more higher risk of infection, as its distinguishing features of severe lung injury arise from viral replication, concurrent viral sepsis, and immune exhaustion.[8] Although secondary infections are considered to be increased in COVID-19 patients, there are still limited data reporting atypical bacterial co-infections in these patients.

The IL-6 plays a central role in fever response to infections. Suppression of IL-6 may mask inflammatory responses, such as fever and CRP production, developed by secondary infections.[6] Therefore, a delay in diagnosis and treatment of serious infections may occur. The early diagnosis of secondary infections necessitates extra-attention and clinical sense, as in our case. At the beginning, we suspected of Tietze syndrome rather than infectious costochondritis and abscess formation.

Infection of both the costochondral and sternoclavicular joints is an uncommon condition. While hematogenous spread and contiguous spread from adjacent structures are considered to be common causes of infectious costochondritis, uncontrolled infection of costochondral joints may also spread to adjacent structures by lymphatics or capsular rupture.[9]

Tietze syndrome is a benign, sterile, painful arthropathy involving the upper costochondral joints. Unlike costochondritis, Tietze syndrome presents with visible swelling and skin erythema, and it is distinguished from suppurative costochondritis by the absence of fever and leukocytosis.[10] In our case, the initial diagnosis was Tietze syndrome, since there was no fever or no increase in CRP with normal CT imaging findings.

In conclusion, during follow-up of COVID-19 patients treated with tocilizumab, physicians should be aware of secondary infections.

Declaration of conflicting interests

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