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CASE REPORT
Coronary heart disease

Be aware of misdiagnosis tied to COVID-19 focusing: a case report of abciximab-induced alveolar haemorrhage thought to be SARS-CoV-2 in a patient with ST-segment elevation myocardial infarction

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Background Early diagnosis of diffuse alveolar haemorrhage (DAH) can be extremely difficult, as the common clinical picture is often attributed to more common clinical conditions. High degree of suspicion is key to diagnosis which can be much more difficult during the coronavirus disease 2019 (COVID-19) pandemic.

Case summary A 61-year-old man with inferolateral ST-segment elevation myocardial infarction treated by a stent to the left circumflex artery and intravenous abciximab treatment was started for the high thrombus burden. Two hours later, the patient developed dyspnoea and hypoxaemia. Chest examination revealed diffuse rales over both lung fields. Chest X-ray revealed bilateral diffuse alveolar infiltrates, while the echocardiography was normal. Chest computed tomography (CT) was performed and the 'crazy paving appearance', which is the typical radiological finding of COVID-19, was reported. The patient was considered to be suspected of COVID-19 and was transferred to a quarantine unit. Real-time reverse transcriptase–polymerase chain reaction (RT-PCR) test was obtained and azithromycin and hydroxychloroquine were initiated. 48 h later, 2.6 mmol/L reduction was observed in haemoglobin levels and haemoptysis was developed. After the second negative RT-PCR with an interval of 24 h, CT was repeated and the patient was diagnosed to have abciximab-induced DAH. The patient was later followed up conventionally and discharged after two weeks without additional complications.

Discussion DAH and COVID-19 might share common clinical and radiological findings during examination. The physicians must be aware of the high motivation of the COVID-19 pandemic which can lead to misdiagnosis by overlooking other important clinical conditions.

Keywords Alveolar haemorrhage • Coronavirus disease 2019 • Acute coronary syndrome • Case report

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Learning points

- Diffuse alveolar haemorrhage and coronavirus disease 2019 (COVID-19) might share the common clinic and radiological findings.
- The high motivation of the COVID-19 pandemic can lead to misdiagnosis or overlook of other rare and important clinical conditions.

Introduction

Early diagnosis of diffuse alveolar haemorrhage (DAH) can be extremely difficult, as the common clinical picture is often attributed to more common clinical scenarios such as viral pneumonia, pulmonary oedema, or pulmonary embolism. Herein, we present a case of abciximab-induced DAH, initially misdiagnosed as coronavirus disease 2019 (COVID-19) during the pandemic period.

Timeline

Admission to tde emergency room	Complaint of chest pain for 3 h and inferolateral ST-segment elevation on electrocardiography.
30 min after admission	Primary percutaneous revascularization performed and abciximab treatment was started for the high thrombus burden.
2 h after admission	Sudden onset of dyspnoea and hypoxaemia. In bedside ECHO, there were preserved ejection fraction (50%), estimated pulmonary artery pressure was calculated 30 mmHg by using continuous wave Doppler of the tricuspid regurgitation trace and no significant valve dysfunction or any mechanical complications of myocardial infarction.
8 h after admission	Despite the pulmonary oedema treatment, dyspnoea was not resolved and oxygen saturation remained <93% on supplemental oxygen, developed paroxysm of coughing without haemoptysis and the patient became febrile (37.9°C).
8.5 h after admission	A high-resolution chest computed tomography (CT) was performed and showed bilateral severe ground-glass opacity.
9 h after admission	The patient considered to be highly suspected of COVID-19 transmission and was transferred to a quarantine unit. Real-time reverse transcriptase–polymerase chain reaction (RT-PCR) test was obtained (test results were available within 24 h in our clinic) and antimicrobial therapy initiated with azithromycin and hydroxychloroquine.
48 h after admission	2.6 mmol/L decrease was observed in patient's haemoglobin levels and haemoptysis was developed. After the second negative RT-PCR, the diagnosis of abciximab-induced diffuse alveolar haemorrhage (DAH) was suspected.
50 h after admission	CT was repeated and the patient was diagnosed with DAH. Anti-antimicrobial and antiplatelet therapies were stopped (acetylsalicylic acid and clopidogrel), two units of erythrocyte transfusion was performed.
5th day	Acetylsalicylic acid and clopidogrel treatments were restarted.
14 days after admission	The patient's haemodynamic status and oxygenation stabilized over the next 12 days with only minor recurrences of haemoptysis and mild anaemia. He was discharged from the hospital without additional complications.

Case presentation

On 24 March 2020, a 61-year-old man was presented to the emergency department with a history of chest pain that started 3 h prior to his admission. His electrocardiogram revealed inferolateral ST-segment elevation myocardial infarction (STEMI) (*Figure 1*). Treatment was started with clopidogrel, acetylsalicylic acid loading doses (600 mg, 300 mg, respectively), and bolus unfractioned heparin (5000 unit). Transthoracic echocardiography (ECHO) revealed left ventricular ejection fraction (EF) (45%) and inferior wall mild hypokinesia. On presentation, his physical examination was normal and past medical history was significant for only hypertension. The patient was taken emergently to the cardiac catheterization laboratory for primary percutaneous coronary intervention (PCI). Coronary angiography revealed thrombotic occlusion in the ostium of the first marginal branch of the proximal left circumflex artery (LCx) (*Figure 2*).

PCI of the culprit lesion in the LCx was performed using an everolimus-eluting stent and abciximab treatment was started (a 0.25 mg/kg bolus followed by a 0.125 μg/kg/min infusion for 12 h, intravenously) for the high thrombus burden. The patient was then transferred to the coronary intensive care unit without any complications. The initial laboratory tests results were unremarkable (*Table 1*).

Two hours following the procedure, the patient developed dyspnoea and hypoxaemia (SaO_2 of 89% while receiving oxygen through a nasal cannula at a rate of 2 L/min). Chest examination revealed diffuse rales over both lung fields and the bed side chest X-ray revealed bilateral diffuse alveolar infiltrates (*Figure 3*). In the bedside ECHO, there were preserved EF (50%), estimated pulmonary artery pressure of 30 mmHg and no significant valve dysfunction or any mechanical complications of STEMI. Intravenous diuretic therapy, morphine and supplemental oxygen via a face mask was initiated considering pulmonary oedema related to the myocardial infarction. Despite 6 h of treatment, the patient's dyspnoea was not resolved and his oxygen saturation remained <93% on supplemental oxygen, developed paroxysm of coughing without haemoptysis and became febrile (37.9°C). A high-resolution chest computed tomography (CT) was performed without contrast and showed bilateral severe ground-glass opacity with superimposed inter and intra-lobular septal

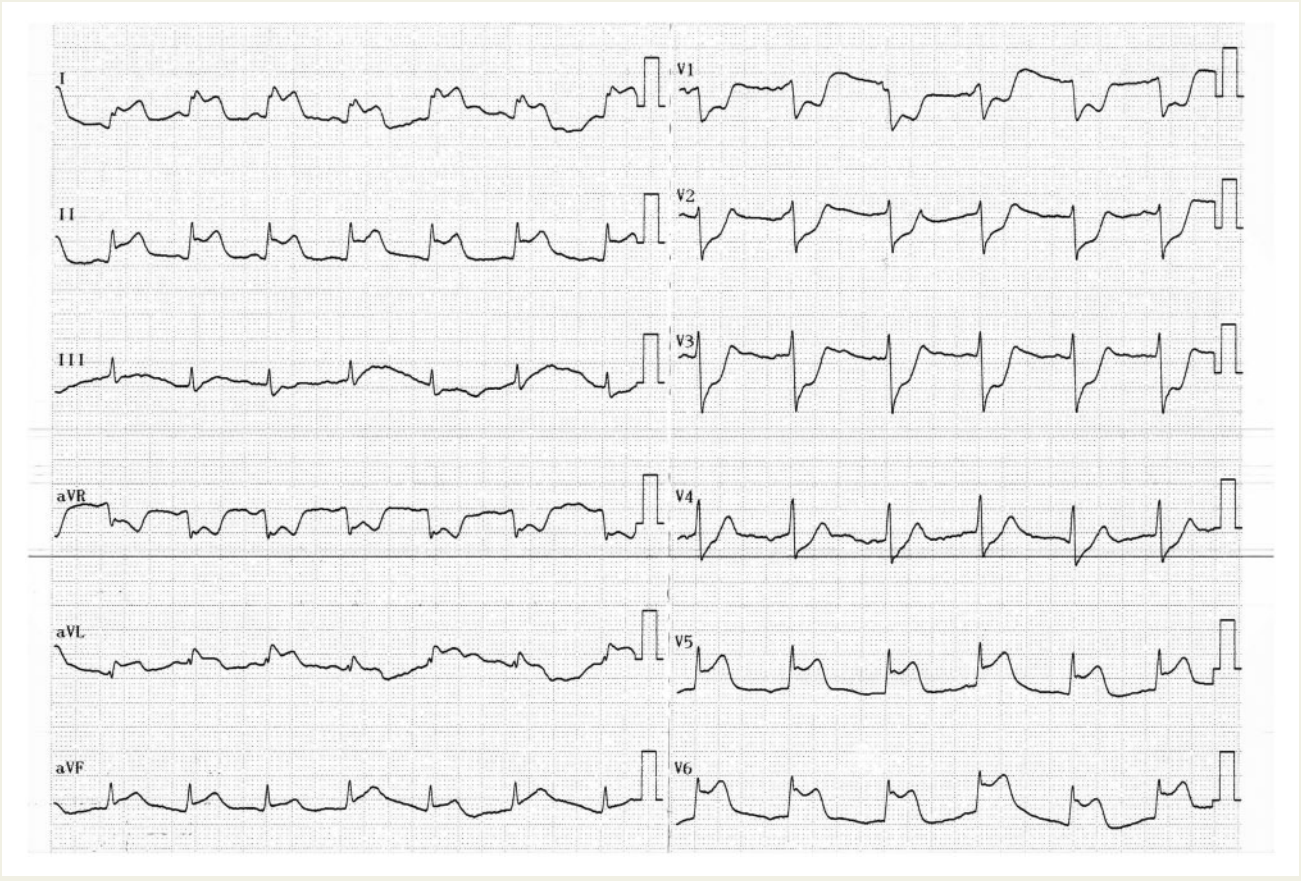


Figure 1 Initial electrocardiogram showing ST-segment elevation in inferolateral derivations.

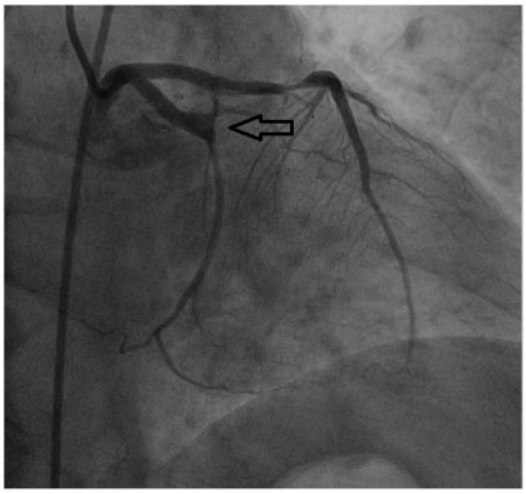


Figure 2 The total occlusion in the ostium of the first marginal branch of the proximal left circumflex artery in coronary angiography (arrow).

thickening (crazy paving appearance) and interstitial infiltrates (*Figure 4A*). Laboratory tests again revealed no remarkable changes with the exception of elevated d-dimer, lactate dehydrogenase (LDH), neutrophil count, and lymphopenia (*Table 1*). According to the CT and clinical picture, the patient was considered to be highly suspected of COVID-19 and was transferred to a quarantine unit. After nasopharyngeal and oropharyngeal swab for the real-time reverse transcriptase–polymerase chain reaction (RT-PCR) test and obtaining blood cultures, azithromycin and hydroxychloroquine treatments were initiated. During the subsequent 36 h, the symptoms persisted and first RT-PCR test was reported negative (test results are available within 24 h in our clinic). At the 48 h of admission, suddenly, a 2.6 mmol/L decrease in haemoglobin levels and haemoptysis were observed and the second RT-PCR result was also negative. The diagnosis of abciximab-induced DAH was suspected but not confirmed by bronchoscopy, since it was relatively contraindicated in recent myocardial infarction (MI).[1] Immediately, CT was repeated and evaluated together with the first CT and reported to be compatible with DAH by the council consisting of three separate radiologists (*Figure 4*). Azithromycin and hydroxychloroquine treatments were stopped, two units of erythrocyte transfusion was performed and ceftriaxone was started to avoid possible bacterial superinfection. Acetylsalicylic acid and clopidogrel treatments were interrupted and restarted again when the patient regained stable haemoglobin levels during the next 3 days. The patient's haemodynamic status and oxygenation stabilized over the next several days, with only minor

Table 1 Baseline and follow-up laboratory parameters of the patient

Laboratory test result	Reference range	Admission to the emergency room	2 h after admission (at the time of dyspnoea and hypoxaemia beginning)	8 h after admission (despite of pulmonary oedema treatment, not resolved dyspnoea and hypoxaemia)
WBC (10^3/μL)	4.5–10.8	11	*12*	*14.5*
Hb (mmol/L)	8.0–11.0	9.12	8.5	8.4
Htc (%)	37–51	42	39	*32*
Platelet (10^3/μL)	150–400	171	168	178
Lymphocyte (10^3/μL)	0.8–4	1.5	1.2	*0.78*
Neutrophil (10^3/μL)	2–7	7	7	*10*
D-dimer (ng/mL)	0–200	116	—	*256*
CRP (mg/L)	0–5	4.5	—	*15.8*
LDH (IU/L)	<248	230	—	*561*
hs-cTn (ng/L)	<19.8	*500*	—	*11456*
Arterial blood gases				
pH	7.35–7.45	—	*7.49*	*7.51*
SO_2 (%)	95–99	—	*89*	*92*
PCO_2 (mmHg)	32–40	—	*30*	*29.7*
PO_2 (mmHg)	83–108	—	*55*	*63.6*
HCO_3 (mmHg)	21.8–26.9	—	24.7	*25.6*
Lactate (mmol/L)	0.5–1.6		*2.1*	0.9

CRP, C-reactive protein; Hb, haemoglobin; HCO_3, bicarbonate; hs-cTn, high-sensitivity cardiac troponin; Htc, haematocrit; LDH, lactate dehydrogenase; PCO_2, partial pressure of carbon dioxide; pH; blood acidity/alkalinity; PO_2, partial pressure of oxygen; SO_2, oxygen saturation. Italics represent values outside the normal reference range.

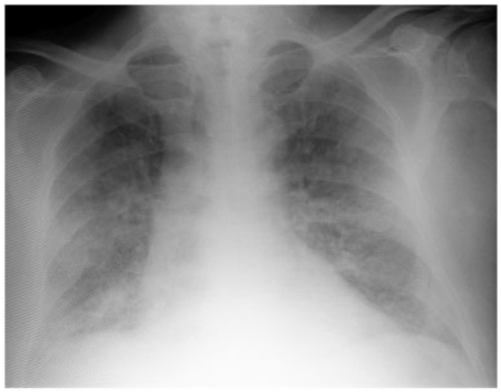


Figure 3 Bilateral diffuse alveolar infiltrates in chest X-ray.

recurrences of haemoptysis and mild anaemia that did not lead to haemodynamic disorder. He was discharged from the hospital 2 weeks later without additional complications.

Discussion

Severe acute respiratory syndrome coronavirus-2 causing COVID-19, first reported in Wuhan, China at the end of November 2019 and has spread worldwide.[2] The World Health Organization on March 11 declared COVID-19 a global pandemic. COVID-19 has a broad spectrum of symptoms, ranging from asymptomatic carriage to interstitial pneumonia and acute respiratory distress syndrome. In a study of 1099 patients in China with confirmed COVID-19, the most commonly reported symptom was fever (43.8–88.7%), followed by cough (67.8%), and shortness of breath (18.7%). On admission, ground-glass opacity was the most common radiologic finding on chest CT (56.4%). Lymphocytopenia was present in 83.2% of the patients on admission, elevated d-dimer and LDH being less common.[3] Although our patient was asymptomatic at the time of admission and was evaluated as low risk in terms of COVID-19 according to the past medical history and clinical picture; changing clinical (sub-febrile fever, dyspnoea, and hypoxaemia) and laboratory (elevated d-dimer, LDH, and lymphopenia) findings as well an abnormal CT result (bilateral severe ground-glass opacity) were compatible with COVID-19 during follow-up.

Early diagnosis of DAH can be extremely difficult, as the common clinical picture, such as haemoptysis, hypoxaemia, and chest radiological infiltrates, is often attributed to more common clinical scenarios such as viral pneumonia, pulmonary oedema, or pulmonary embolism. Misdiagnosis may result in inappropriate drug use, prolonged exposure to anticoagulation or even death. High degree of suspicion is key to diagnosis and this can be much more difficult during the COVID-19 pandemic. Especially in the early stages, CT findings in viral pneumonias and DAH consistently overlap and are therefore difficult to distinguish.[4–6] Recently, Kloth *et al.*[7] compared CT finds of viral pneumonias and DAH, reporting no statistically significant differences for ground-glass opacity, crazy-paving, centrilobular nodules, and parenchymal consolidations between the different subgroups. Kalra *et al.*[8] reported in a large records series of 5412

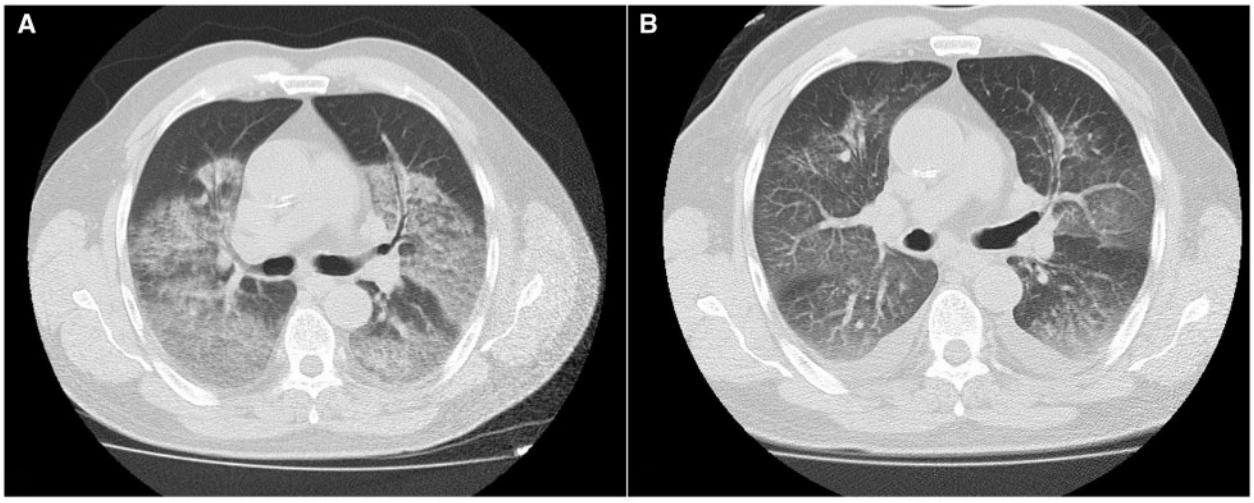
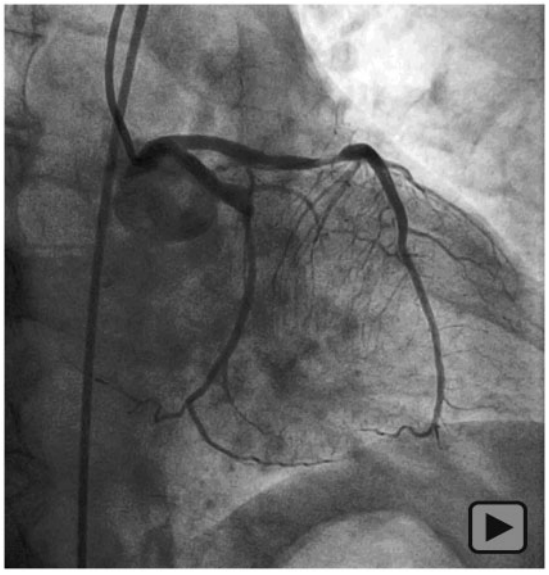


Figure 4 (*A*) First computed tomography shows severe ground-glass opacity with superimposed interlobular septal thickening and intralobular septal thickening (crazy paving appearance) and interstitial infiltrates involving the upper and middle lobes. (*B*) Control computed tomography shows ground-glass opacity without crazy paving appearance.



Video 1 Coronary angiographic image of the patient during primary percutaneous intervention

patients at Mayo Clinic that severe pulmonary haemorrhage was identified in seven patients out of the 2553 patients (0.27%) who received abciximab. Four diagnoses of seven patients in this study were based on major haemoptysis accompanied by a significant (≥1.24 mmol/L) decrease in haemoglobin concentration, abnormal chest radiographic findings, and hypoxaemia within the 2 h–2.6 days without the bronchoscopy. In this study, although the appearance of more than 20% hemosiderin-laden alveolar macrophages in bronchoalveolar lavage is the gold standard of alveolar haemorrhage diagnosis, we did not perform bronchoscopy since it was relatively contraindicated in recent MI.[1] Based on the clinical picture and radiological findings, we diagnosed our patient with abciximab-induced DAH collectively by a council consisting of cardiologists, chest disease experts, and radiologists.

Conclusion

DAH and COVID-19 might share common clinical and radiological findings during examination. Although we encounter more and more infected patient every day during the COVID-19 pandemic, our focus on COVID-19 should not cause us to overlook other rare and important diagnoses.

Lead author biography

Dr Turhan Turan is the associate professor of cardiology at University of Health Sciences Trabzon Ahi Evren Thoracic and Cardiovascular Surgery Training and Research Hospital (Turkey). He acquired his medical degree at the same university and currently working this university hospital. His research interests include percutaneous coronary interventions and peripheral arterial diseases.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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