Pulmonary embolism and acute psychosis, a case report of an outpatient with a mild course of COVID-19

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Abstract

Introduction The increased risk for thromboembolism in hospitalized COVID-19 patients has been communicated extensively. The fact that home quarantined patients can develop pulmonary embolism, however, has so far not been reported. Furthermore, attention should be brought to psychotic developments in COVID-19 patients.

Case Presentation We report a 46-year-old previously healthy patient with a mild course of COVID-19, who developed a massive pulmonary embolism with right heart strain while being home quarantined. He was hospitalized and anticoagulant therapy was started. Nine days after admission, the patient appeared increasingly psychotic and suffered from hallucinations as well as paranoid thoughts. After treatment with risperidone and valproate the patient's condition improved. At a follow-up one month after discharge, he was completely recovered regarding the respiratory, cardiac and psychic situation.

Conclusion SARS-CoV-2 infection cannot only increase the prevalence of thromboembolism in hospitalized patients, but also in outpatients. COVID-19 also increases the risk of developing psychiatric reactions.

Introduction

A high rate of venous thromboembolism has been reported in patients with COVID-19. Therefore prophylaxis for venous thromboembolism is recommended during and after hospital admission for these patients. [1] Acute psychosis in COVID-19 patients may develop as reaction to the psychic trauma of intensive care treatment, as manifestation of cerebral involvement of the infection, as secondary effect of immunological or metabolic imbalance, as known from other virus infections, or as side effect of medication. [2–6] Pulmonary embolism in an outpatient with a mild course of COVID-19, complicated by an acute psychosis, has so far not been described.

Case Presentation

On April 7th 2020 a 46-year-old, previously healthy, Caucasian male was admitted because of acute dyspnea and left-sided thoracic pain since several hours. Eighteen days before admission, he had started to suffer from a dry cough, hemoptysis, dizziness, headache, dysgeusia with a metallic taste, diarrhea and vomiting. Although the symptoms relieved after 10 days, he still felt extreme fatigue and spent most of the time in bed. Due to reduced appetite, he had lost 8 kg. He never smoked, reported no intake of drugs and had no family history of thromboembolism. On day 17 after symptom onset, he reported pain and swelling of the right calf.

Physical examination showed an obese (BMI 30,5 kg/m^2) patient with a respiratory rate of 25/min and a blood pressure of 140/90 mmHg. The ECG showed sinus-tachycardia (120/min) and descending ST-segment depressions with negative T-waves in the leads II, III, aVF and an incomplete right bundle branch

block. Arterial oxygen pressure was 65,6 mmHg (normal range 75-100 mmHg) at room air, therefore he received 4 l/minute oxygen via nasal cannula.

Blood tests showed a N-terminal prohormone of brain natriuretic peptide level of 3.890 ng/l (normal range < 84 ng/l), troponin T-hs (63 ng/l; normal < 14), D-dimer 17,0 mg/l (normal range < 0,5 mg/l) and lactate dehydrogenase of 267 U/l (normal range 135-225 U/l). The calculated Well's Score war 10 points, indicating a high probability of pulmonary embolism (40,6%). A therapy with weight-adjusted low molecular weight heparin (10.000 IE Enoxaparin sodium twice daily) was started. The suspected diagnosis of pulmonary embolism was confirmed by computed tomography (shown in Fig. 1). In computed tomography, the right ventricle/left ventricle ratio was 1,6, indicating a 2,5-fold increased risk for all-cause mortality and five-fold increased risk for pulmonary embolism mortality. [7] Due to organizational reasons, echocardiography was not carried out in the acute phase.

The patient did not show any clinical signs of right heart failure. According to the ESC Guidelines for acute pulmonary embolism the patient was categorized an intermediate – high risk patient. [8] The pulmonary severity index (PESI original version) was 96 points, indicating class III and therefore a moderate 30-day mortality risk of 3,2 – 7,1%. As the patient showed elevated troponin-levels, he was later categorized intermediate-high risk. [8] Since the patient was hemodynamically stable, we decided not to perform thrombolysis and monitored his heart rate and blood pressure closely.

Because of the symptoms preceding admission, a nasopharyngeal swab was taken, and reverse transcription polymerase chain reaction test was positive for SARS-CoV-2. The patient was transferred to a COVID-19 unit to another hospital. Anticoagulant therapy was switched to edoxaban 60 mg once daily after five days (shown in Fig. 2).

Since the CRP was elevated, he received ceftriaxone 2 g per day for five days. After the third day of receiving ceftriaxone the patient experienced hallucinations. After psychiatric consultation, the patient received risperidone 2 mg/d. The patient was discharged twelve days after the initial hospital admission to complete his quarantine at home. His medication at discharge was comprised of edoxaban 60 mg/day, which should be continued for at least three months. He was advised to see a psychiatrist after the end of home quarantine.

A few hours after discharge the patient was re-admitted to the same department because of a convulsing seizure, followed by focal seizures. The seizures imposed as intended movements and there was no loss of consciousness, tongue bite or incontinency. There was no prior history of seizures. The patient was given 1 mg lorazepam and 400 mg valproate, as he was very agitated and could not be contained otherwise.

Clinical neurologic investigation did not disclose any abnormalities. Cranial computed tomography and magnetic resonance imaging did not show any pathologic findings. Thus, the seizures were classified as psychogenic non-epileptic seizures. The patient imposed increasingly psychotic. He was found gurgling with disinfectant, smearing marmalade around his eyes and suffering from ever increasing generalized

fear and therefore he received repeated doses of lorazepam 2,5 mg (7,5 mg in total), as well as risperidone 3 mg in total and 25mg quetiapine. An adaption disorder with anxiety was diagnosed and on the second day, he was transferred to a psychiatric department, where he was found having optical and auditive hallucinations and was talking to non-existing people. He suffered from paranoiac thoughts and was convinced that metallic parts were implanted in his body. Accordingly, a dissociative disorder was diagnosed in addition to his adaption disorder.

A therapy with risperidone (1 mg twice daily) and valproate (500 mg twice daily) was started in order to treat a potential epilepsy, as well as the patient's psychogenic disorder. An improvement of the psychotic symptoms was observed. After two negative SARS-CoV-2 naso-oropharyngeal swabs. The patient was discharged three days later with valproate 500 mg twice daily and risperidone 1 mg twice daily, as well as edoxaban 60mg once daily.

At follow-up 32 days after discharge, the patient described himself as fully mentally recovered. There were no more hallucinations or panic attacks. The treatment with valproate was terminated by a psychiatrist one month after discharge because the seizures were described as voluntary movements. Physically, the patient feels fit and does not suffer from dyspnea anymore. Follow-up investigations including ECG and echocardiography showed no residual right heart strain. Thrombophilia screening did not show any abnormalities.

Discussion

Most of the published cases of COVID-19 associated venous thromboembolism occurred in hospitalized patients. [9,10] Venous thromboembolism can also occur in non-hospitalized patients with mild cases of COVID-19, may even lead to sudden cardiac death and may only be detected during autopsy. [11,12] In a prospective autopsy study among 12 COVID-19, one third has died from pulmonary embolism and deep venous thrombosis was found in 58%. [12] Obesity may increase the risk for developing venous thromboembolism in COVID-19 associated cases. [10] Reasons for the risk of venous thromboembolism in COVID-19 comprise endothelial dysfunction, excess thrombin generation and down-regulation of fibrinolysis, resulting in a hypercoagulable situation. [13]

An increased incidence of neuro-psychiatric diseases in patients and health-care workers following pandemics and various viral infections has been reported. [14] Potential reasons are reduced social contact, change in diet, decrease in physical activity and reduced exposure to sunlight. [15] Another possible explanation for psychotic episodes and putative manifestation of a mental illness after an infection such as COVID-19, is affection of the central nervous system. Peripheral and central nervous system involvements were found in connection with COVID-19, manifesting as headache, dysgeusia, hyposmia and necrotizing encephalitis. [16,17] These manifestations are thought to be a result of either hypoxia or inflammatory response. [18] In our patient, however, the seizure was interpreted as psychogenic and clinical as well as imaging studies did not show any neurologic abnormalities.

A further possibility is that the psychosis might be induced by the venous thromboembolism. More than 50 years ago, an association between venous thromboembolism and psychoses had been described. [19] An association between antipsychotic medication and venous thromboembolism is discussed since many years. [20] In our patient, however, the venous thromboembolism has started before initiation of antipsychotic therapy. Of note, in a case series of patients who developed a psychosis after COVID-19, three out of ten reported patients also suffered from venous thromboembolism. In the present, it is unknown whether patients who develop venous thromboembolism in COVID-19 are more prone to psychosis than patients without.

It is very unlikely that the psychosis in our patient was drug-induced. Psychotic reactions as adverse effects are well known in benzodiazepine use, as well as in acute benzodiazepine withdrawal, but also in some antibiotics and glucocorticoids. [2,5] Our patient, however, did not receive any drug for which psychosis has been described as a side effect.

A limitation of the presented case is that no diagnostic measure for search of a deep vein thrombosis was carried out and thus, venous thromboembolism was only a clinical diagnosis.

Conclusion

We publish this case in order to raise the awareness of thromboembolic complications in connection with COVID-19, not only in hospitalized patients, but also in patients who stay immobile at home due to quarantine restrictions. Further research is needed to enhance the awareness of the psychiatric impact of pandemics such as COVID-19.

Patient Perspective

In a phone call follow-up, 32 days after discharge, the patient described himself as fully mentally recovered. The situation in the special COVID-19 isolation ward was a critical experience for him at that time. No previous mental illness had been known in the patient's history, and nevertheless, the situation was too much for him to bare. After the first discharge he felt unwell and was readmitted on the same day and transferred to a psychiatric hospital followingly. The whole experience made him do more sports and lose weight.

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- Data curation: Lead
- Supervision: Lead
- Visualization: Lead
- Writing – original draft: Lead
- Writing – review and editing: Lead

Claudia Stöllberger:

- Conceptualization: Equal
- Data curation: Supporting
- Supervision: Equal
- Visualization: Supporting
- Writing – review and editing: Equal

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Figures

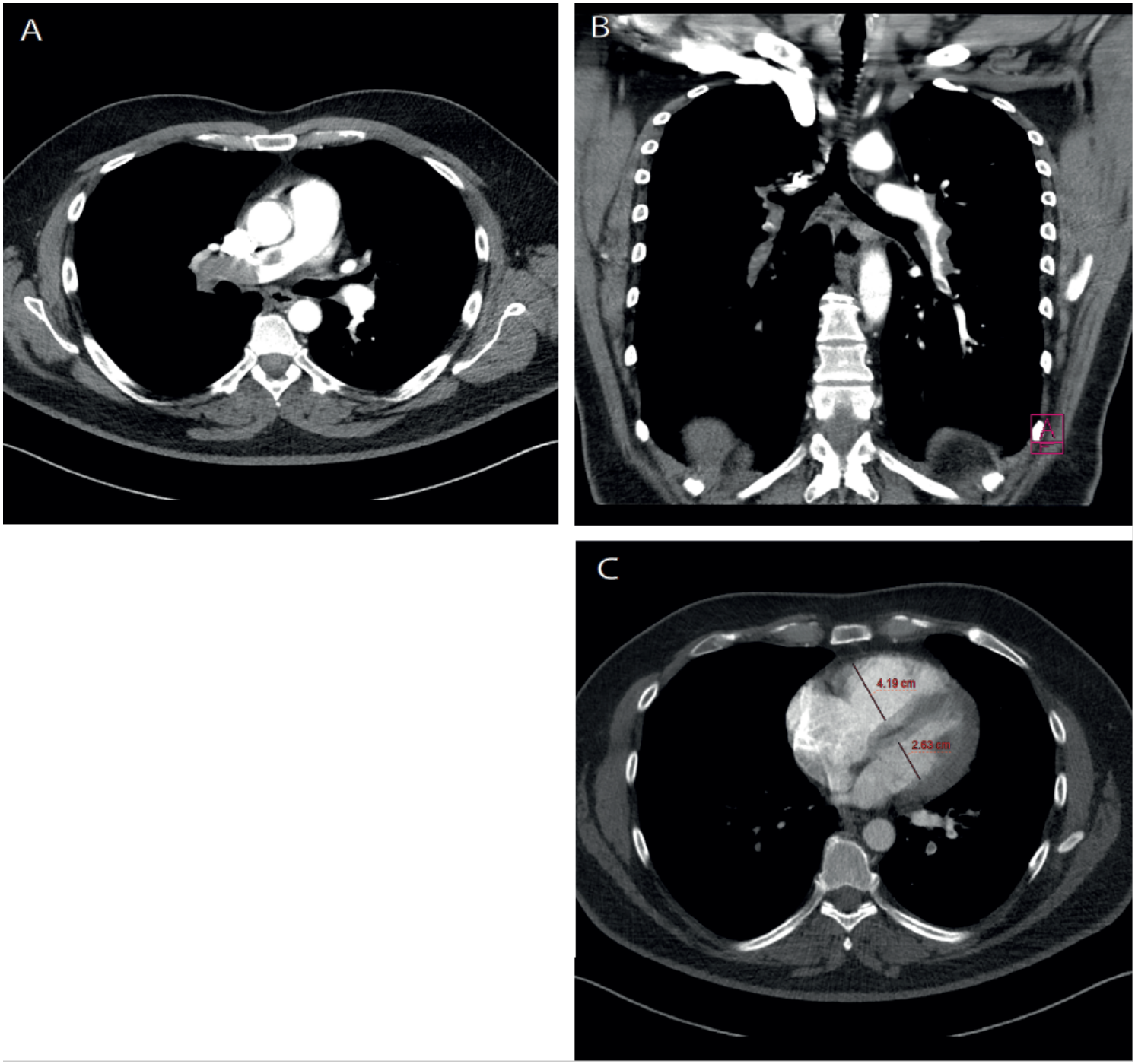

Figure 1

Computed tomographic (CT) pulmonary angiography A (axial) and B (coronal) image of CT scan revealing acute pulmonary emboli within the right main and left interlobar pulmonary artery causing contrast filling defects. Thromboembolism is further extending to multiple segmental and subsegmental branches of both pulmonary artery branches. C: Axial CT image showing morphologic signs of right ventricular strain including right ventricular dilatation and deviation of the interventricular septum towards the left ventricle. The right ventricle is dilated to 4,19 cm, while the left ventricle is 2,63 cm wide.

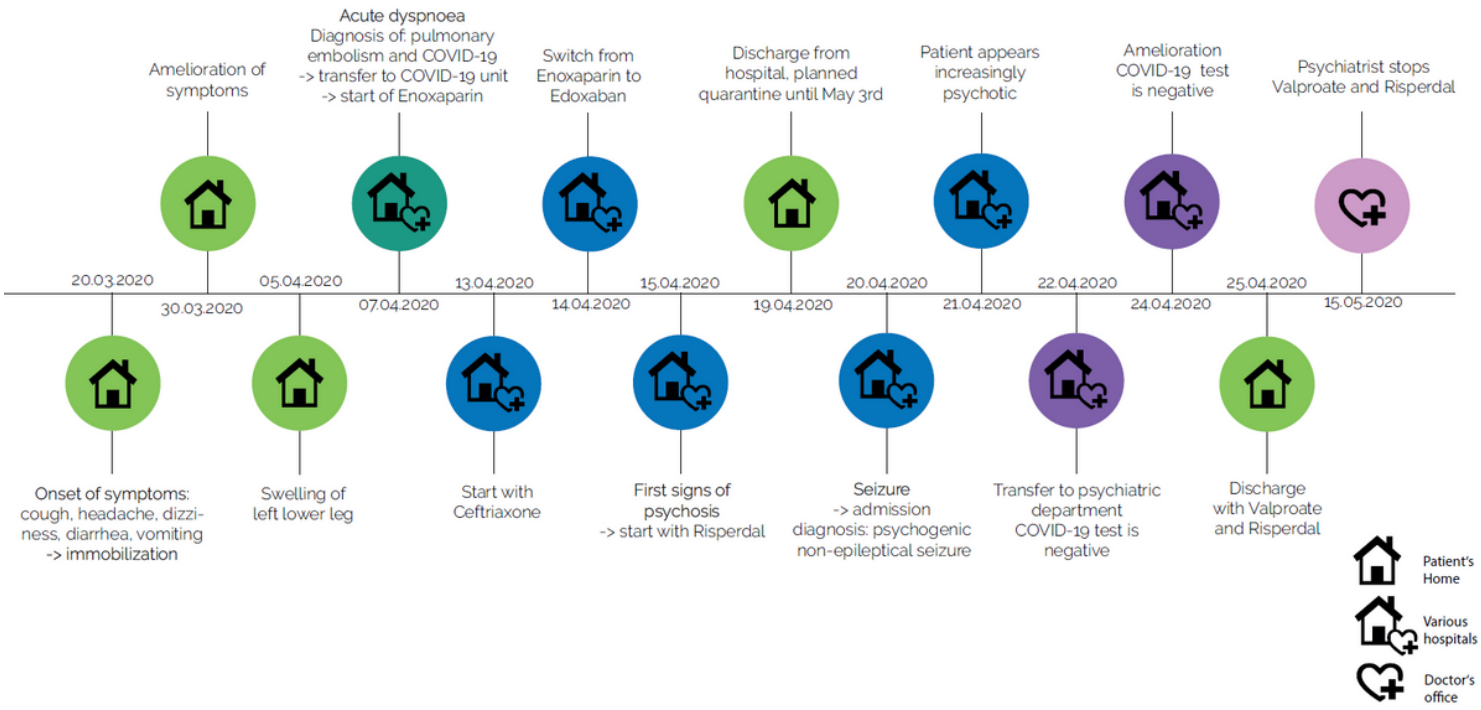

Figure 2

Timeline This figure is a timeline, showing the chronological order of events. Graphic was created using Adobe Illustrator 2020 ®