Development of pulmonary embolism in a nonhospitalized patient with COVID-19 who did not receive venous thromboembolism prophylaxis

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Purpose. Coronavirus disease 2019 (COVID-19) has been associated with thrombotic complications such as stroke and venous thromboembolism (VTE), and VTE prophylaxis for hospitalized patients with COVID-19 is recommended. However, extended postdischarge VTE prophylaxis and VTE prophylaxis for nonhospitalized patients with COVID-19 are not routinely recommended due to uncertain benefit in these populations.

Summary. Here we report development of a pulmonary embolism (PE) in a young patient without other VTE risk factors who was treated for COVID-19 in an emergency department (ED) and discharged home without VTE prophylaxis, which was consistent with current recommendations. The patient presented to the ED 12 days later with complaints of chest pain for 1 day and was found to have a PE within the segmental and subsegmental branches of the left lower lobe.

Conclusion. This case suggests that nonhospitalized patients with COVID-19 may be at higher risk for VTE than patients with other medical illnesses and warrants further research into the risk of VTE in outpatients with COVID-19.

Keywords: anticoagulation, COVID-19, prophylaxis, pulmonary embolism, venous thromboembolism

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Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel coronavirus first described in China in December 2019, leads to the development of coronavirus disease 2019 (COVID-19).[1] Thrombotic complications related to COVID-19, such as stroke and venous thromboembolism (VTE), have been reported.[2-4] Due to the observed risk of thrombosis, VTE prophylaxis for hospitalized patients with COVID-19 is recommended.[1,5-7] Extended postdischarge VTE prophylaxis and VTE prophylaxis for nonhospitalized patients with COVID-19 remain questionable practices and are generally not recommended.[2,5-7] In this article we report a case of pulmonary embolism (PE) in an ambulatory patient that developed 2 weeks after discharge from an emergency department (ED) following diagnosis of COVID-19 and treatment without DVT prophylaxis.

Case report

A 32-year-old, overweight (weight, 90 kg; body mass index, 28) African American male with a past medical history significant for asthma (not managed with any medications) presented to the ED of an academic medical center with cough, shortness of breath, diffuse chest pain (associated with cough), fevers, chills, myalgia, and diarrhea that had developed over 5 days. The patient's vital signs were stable aside from a temperature of 38.4°C. An electrocardiogram (ECG) revealed normal sinus rhythm, and a chest x-ray revealed minimal hazy opacities within the right midlung. Laboratory work included a basic metabolic panel (BMP) and complete blood count (CBC) with differential. Results were normal except for a slightly low serum sodium concentration (133 mEq/L), chloride

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concentration (96 mmol/L), and absolute lymphocyte count (12,000/μL). The patient was suspected to have a viral upper respiratory infection or possibly COVID-19. A test for the COVID-19 virus was performed and resulted positive the next day. The patient was informed, given isolation instructions, and discharged.

The patient returned to the ED 12 days later with complaints of left-sided pleuritic chest pain lasting 1 day. He reported resolution of shortness of breath, fevers, chills, myalgia, and diarrhea and improvement in cough. He denied any recent hospitalizations, prolonged periods of immobility, trauma, smoking, or a history of cancer or prior VTE. He also denied a family history of VTE but reported a history of stroke in his mother. In the ED, vital signs and results of the BMP, CBC with differential, troponin I, B-natriuretic peptide, and liver function tests were normal except for a slightly low absolute lymphocyte count (10,000/μL) and percentage of lymphocytes (12%) and an elevated percentage of neutrophils (77%). A repeat COVID-19 test and measurements of D-dimer, C-reactive protein, and fibrinogen levels were not ordered. An ECG revealed normal sinus rhythm. A computed tomography pulmonary angiogram was positive for PE within the segmental and subsegmental branches of the left lower lobe. No right heart strain was identified. A lower extremity venous ultrasound was not performed. The patient was started on therapeutic weight-based enoxaparin therapy (1 mg/kg twice a day), admitted for observation for a couple hours, and then, because he remained clinically stable, discharged home on enoxaparin within 24 hours of arrival to the ED. The next day, following prior authorization approval, the patient was called and given appropriate instructions on how to switch from enoxaparin to an apixaban regimen of 10 mg twice a day for 7 days, then 5 mg twice a day.

The patient received routine phone follow-up by a new primary care provider 5 days after discharge and by the medical center's direct oral anticoagulant (DOAC) screening service 6 days after discharge.[8] During these follow-up phone calls, he reported adherence to the prescribed apixaban regimen and continued to complain of chest pain but reported an improvement in pain severity. The patient also reported occasionally coughing up a small amount of blood-tinged sputum and denied any other signs or symptoms of bleeding. Another routine phone follow-up was performed 12 days after discharge by the DOAC screening service, and the patient continued to report improvement in chest pain and no significant bleeding. At the time of writing, the plan was for the patient to be treated with apixaban for at least 3 months.

KEY POINTS

- Despite the observed risk of thrombosis in patients with COVID-19, extended postdischarge venous thromboembolism (VTE) prophylaxis and VTE prophylaxis for nonhospitalized patients with COVID-19 remain questionable practices.
- This report describes a case of development of a pulmonary embolism in a young, ambulatory patient without other risk factors for VTE shortly after diagnosis of COVID-19.
- This case suggests that nonhospitalized patients with COVID-19 may be at a higher risk for VTE than patients with other medical illnesses and warrants further research into the risk of VTE in this population.

Discussion

The incidence of VTE in patients with COVID-19 is not well defined, as data are rapidly evolving and thromboprophylaxis varies among countries and institutions. Some reports have described VTE rates as high as 20% to 31% in patients hospitalized with COVID-19, with the majority of these patients admitted to an intensive care unit (ICU).[9-12] An article by Middeldorp et al[11] reported that 38% of 198 patients hospitalized for COVID-19 were admitted to an ICU, and those patients were found to have a higher rate of symptomatic VTE than patients admitted to a medical floor (28% vs 3.3%) despite thromboprophylaxis. Although the rate of symptomatic VTE was lower in patients admitted to the medical floor, it was higher than the estimated rate of VTE in acutely ill patients hospitalized with non–COVID-19 medical illness who do not receive appropriate thromboprophylaxis (2%).[13] Poissey et al[12] reported that 20.6% of the first 107 patients with COVID-19 admitted to their ICU experienced a PE; this was significantly higher than the frequency of PE in their ICU over a similar time interval in 2019 (6.1%) despite all patients in the former group receiving therapeutic or prophylactic anticoagulation. Due to this reported risk of thrombosis, VTE prophylaxis is recommended for all hospitalized patients with COVID-19.[1,5-7]

VTE rates in outpatients with COVID-19 or immediately after hospital discharge following treatment for COVID-19 have not been described.[7] Akel et al[14] reported a case series of 6 patients with COVID-19 (5 were 40 years of age or older and 1 was 28 years old) who were not critically ill or affected by major risk factors for VTE and mostly presented with a PE at the time of diagnosis of COVID-19 (1 patient presented with PE 10 days following an admission for COVID-19). That case series highlights the possibility of VTE in noncritically ill patients with COVID-19. However, it does not provide insight into the risk of VTE after discharge from a COVID-19–related hospital stay or in outpatients diagnosed as having COVID-19.

To our knowledge, there are currently no published data regarding extended postdischarge VTE prophylaxis and VTE prophylaxis for nonhospitalized patients with

COVID-19, and recommendations for VTE prophylaxis in these populations are extrapolated from data on hospitalized patients with acute medical illness. Patients hospitalized for certain medical illnesses have been shown to be at an increased risk for VTE even after hospital discharge, which has led to research investigating extended thromboprophylaxis after hospitalization.[15] This research has mainly been conducted in patients 40 years of age or older with an acute medical illness requiring hospitalization and an increased risk of thrombosis due to reduced mobility, increased age, elevated D-dimer levels, or elevated scores on a risk scoring instrument such as the modified International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) VTE risk score.[15-17] Results from these studies have not shown a consistent benefit of extended VTE prophylaxis, which did not routinely lead to a reduction in VTE or death; moreover, any reductions in VTE or death were frequently associated with an increase in major or clinically relevant nonmajor bleeding.[15-17]

The results from these studies do not support the routine use of extended postdischarge thromboprophylaxis, and current guidelines do not recommend extended-duration outpatient VTE prophylaxis in acutely ill hospitalized medical patients, critically ill medical patients, or medical outpatients with minor risk factors for VTE, such as infection.[18,19] There may be a benefit in certain high-risk cohorts; however, this needs to be balanced with the risk of bleeding.[16] Based on data from studies reviewed here, extended postdischarge VTE prophylaxis and VTE prophylaxis for nonhospitalized patients is generally not recommended in patients with COVID-19.[2,5-7] Postdischarge VTE prophylaxis, provided using Food and Drug Administration–approved regimens, may be considered in patients with COVID-19 who are at low risk for bleeding and high risk for VTE (eg, those with reduce mobility, active cancer, or a D-dimer level of >2 times the upper normal limit, as well as those receiving intubation and sedation for several days or with morbid obesity and a Caprini score of >8).[2,5-6,20] The patient described in this report would not have been considered at high risk for VTE because he did not have reduced mobility, active malignancy, or a history of prior VTE.[2] He also would not have met the inclusion criteria of studies investigating extended thromboprophylaxis because he was not hospitalized, was less than 40 years old, and did not experience reduced mobility.[15-17] Therefore, based on currently available data, thromboprophylaxis would not have been appropriate for him after diagnosis of COVID-19. However, this case of development of a PE in an ambulatory patient 12 days after COVID-19 diagnosis suggests that nonhospitalized patients with COVID-19 may be at a higher risk for VTE than patients with other medical illness and warrants further research into the risk of VTE in outpatients with COVID-19. There are several ongoing trials exploring anticoagulation strategies in patients with COVID-19; however, none are currently evaluating VTE prophylaxis in nonhospitalized patients.[21]

Conclusion

Current data do not support the routine use of VTE prophylaxis in nonhospitalized or postdischarge patients with COVID-19. The reported case of a young, nonhospitalized patient with COVID-19 developing a PE illustrates a need for further investigation into the risk of VTE in ambulatory patients with COVID-19.

Disclosures

The authors have declared no potential conflicts of interest.

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