

The value of blood D-dimer test in the diagnosis of walk-in patients with venous thromboembolism

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Abstract: Venous thromboembolism (VTE) and related pulmonary thromboembolism are life-threatening diseases that require efficient diagnosis and clinical management. While the diagnosis and treatment of VTE in hospitalized patients has been extensively studied, less has been reported on walk-in patients with VTE. Here we report on four outpatients with VTE that were efficiently diagnosed using the blood D-dimer test and successfully treated.

Keywords: venous thromboembolism, pulmonary thromboembolism, blood D-dimer test

Introduction

Venous thromboembolism (VTE) and related pulmonary thromboembolism (PTE) are life-threatening diseases that require efficient diagnosis and clinical management.¹ VTE frequently occurs in hospitalized patients, especially in those who have undergone orthopedic surgery, had limited mobility, suffered from trauma, or developed malignant tumor.^{2,3} While several reports have been published on the diagnosis and treatment of VTE in inpatients, much less has been published on walk-in patients with VTE.

D-dimer, a breakdown product of fibrin, can be measured in the blood relatively easily and noninvasively. It is considered a useful marker for the early detection of VTE or PTE. From 2007 to 2009, four patients presented to our outpatient clinic with VTE that were efficiently diagnosed with the D-dimer blood test and successfully managed.

Case presentations

Of the four patients, one was male and three were female. They were aged 55, 65, 84, and 91 years and lived age-appropriate daily lives, were not bedridden, nor had they recently undergone surgery. The chief complaints were swelling and/or mild ache in their legs. None complained of chest pain or dyspnea suggestive of PTE, but in all four cases blood D-dimer levels were elevated, ranging from 4.89 to 43.07 $\mu\text{g/mL}$ (43.07, 21.12, 9.27, and 4.89; normal: $<0.72 \mu\text{g/mL}$). All four patients were referred to a department of cardiology for ultrasonography of the lower limbs. Deep vein thrombosis (DVT) of the lower limbs was confirmed in all four cases. Asymptomatic pulmonary thromboembolism was detected by contrast-enhanced pulmonary multidetector computed tomography (CT) in three of the four patients, but was not performed in the 91-year-old patient. None of the patients had identifiable risk factors for VTE, such as obesity, recent surgery, immobility, or long airline travel. No patients had antiphospholipid syndrome, protein S deficiency, or protein C deficiency.

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Therefore, the combination of swelling and/or mild ache of legs and a positive D-dimer test was considered to be of great diagnostic value for VTE and reducing their risk of life-threatening PTE.

Case 1

An 83-year-old Japanese man with cervical degenerative disease, nephritic syndrome, hypertension, and hypercholesterolemia (255 mg/dL) visited our outpatient clinic in January 2008. Three weeks before the visit he noticed swelling of his right leg. Physical examination revealed marked swelling of the right leg, but no tenderness, no warmth, and a negative Homan's sign. A blood test showed an elevated D-dimer level of 21.12 $\mu\text{g/mL}$. The patient was sent to the cardiology department of a hospital. Lower extremity ultrasonography confirmed DVT, and contrast-enhanced pulmonary multidetector CT revealed thrombosis in the right pulmonary artery. An inferior vena cava filter was placed urgently. Heparin therapy was begun, and warfarin therapy was subsequently started. The patient was successfully treated.

Case 2

In July 2009, a 91-year-old Japanese woman visited our outpatient clinic because of swelling of her right leg. Physical examination revealed swelling, but no tenderness, no warmth, and a negative Homan's sign. A blood test showed an elevated D-dimer level of 9.27 $\mu\text{g/mL}$. The patient was sent to the cardiology department of a hospital and ultrasonography confirmed DVT. Because of her advanced age, contrast-enhanced pulmonary multidetector CT was not performed. She was successfully treated with warfarin.

Case 3

In May 2009, a 65-year-old Japanese woman visited our outpatient clinic because of swelling and mild pain in her right leg. Physical examination revealed swelling of the right leg and a positive Homan's sign. The D-dimer blood level was elevated at 43.07 $\mu\text{g/mL}$. The patient was sent to the cardiology department of a hospital. Ultrasonography confirmed DVT of the right leg, and contrast-enhanced pulmonary multidetector CT revealed a pulmonary artery embolism. She was successfully treated with heparin and warfarin.

Case 4

In May 2007, a 58-year-old Japanese woman visited our outpatient clinic because of swelling and mild pain in her right leg. The D-dimer blood level was elevated at 4.89 $\mu\text{g/mL}$. The patient was sent to the cardiology

department of a hospital. Ultrasonography confirmed DVT, and contrast-enhanced pulmonary multidetector CT revealed a small thrombus in both pulmonary arteries. She was successfully treated with heparin and warfarin.

Discussion

We describe here four cases of walk-in patients with VTE who visited our outpatient clinic between 2007 and 2009 with lower extremity pain and swelling and elevated D-dimer blood levels. They were all found to have VTE, which was successfully diagnosed and treated, in part, due to the D-dimer test.

In patients with hemodynamic stability, the diagnostic workup for unilateral lower extremity swelling and pain consists of clinical assessment, the D-dimer test, lower extremity ultrasonography, and multidetector CT.⁴ The negative predictive value of the D-dimer test is 99%, indicating that it is reliable for ruling out DVT. The specificity of a positive D-dimer test is reduced in patients with cancer, pregnant women, and hospitalized and elderly patients. However, the combination of any one of the clinical findings of Homan's sign, swelling, tenderness, discoloration, and warmth with a positive D-dimer test is of great diagnostic value (higher specificity and positive predictive value).⁵ The specificity of a positive D-dimer test should be higher in outpatients with the findings either of Homan's sign, swelling, tenderness, discoloration, and warmth of lower limb than those without these findings.

Hypercoagulability can be caused by elevated levels of coagulation factors such as fibrinogen or factors VIII, IV, or XI. However, elevated levels of these factors are found in only around 20% of patients with VTE.⁶ Indeed, only one of our four patients (case 3) had elevated levels of serum fibrinogen (431 mg/dL). In contrast, the D-dimer levels were elevated in all four cases, indicating that the D-dimer test is of greater diagnostic value than fibrinogen and other coagulation factors. The potential disadvantage of the D-dimer test is that it may not be specific, as levels may be elevated in patients with cancer, pneumonia, and with a recent history of surgery.

In a histopathological study of 51 autopsy cases of outpatients with massive PTE, fresh and organized thrombi were detected in both pulmonary arteries and deep lower-extremity veins in 82.4% of cases, suggesting a recurrent, subclinical history of thrombosis.⁷ Furthermore, 28 cases had preexisting symptoms, only 10 of whom had consulted a doctor.⁷ However, none of these 10 patients had PTE definitively diagnosed or treated. The findings from these 51 autopsy cases suggest that proper diagnosis and early treatment could prevent death due to PTE in outpatients.

Prevention of VTE has been widely discussed mainly in relation to inpatients and post-surgical patients. However, the accumulation and analysis of more data on outpatients with suspected and confirmed VTE may help to improve detection and treatment in this population and prevent deaths.

DVT occurs under conditions of venostasis, vessel wall damage, hypercoagulability, or some combination of these three (Virchow's triad). Long flight syndrome is known to occur with airline flights longer than 3 hours.⁸ VTE associated with prolonged immobility while sitting at a computer has been reported as "eThrombosis".⁹ The incidence of DVT in elderly people who sit for a long time may be lower in Japanese than in other populations because sitting Japanese style on *tatami* mats for many hours is difficult and requires frequent changes of position or standing breaks. However, in Japan, this type of sitting has become less common in recent years, and prolonged sitting in a chair is now more common, along with exposure to the risks of venostasis. In addition to greater longevity, this type of change in lifestyle among elderly Japanese could lead to an increase in VTE among outpatient cases, and two of the patients presented in this report were elderly (84 and 91 years old).

In summary, we report here four walk-in patients with VTE that were diagnosed with the aid of a D-dimer blood

test and successfully treated. The D-dimer blood test in the presence of swelling or pain in the lower extremity is of great value in diagnosing VTE among outpatients and reducing their risk of life-threatening PTE.

Disclosure

No conflicts of interest were declared in relation to this paper.

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