CASE REPORT

Sequential D-Dimer Measurements Can Reveal Asymptomatic Pulmonary Embolism in Patients With Burn Injuries

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ABSTRACT

Venous thromboembolism is diagnosed by clinical and imaging findings. Another possible test is measurement of D-dimers in the blood; high levels can signal endogenous fibrinolysis. The D-dimer test is a highly sensitive test for excluding venous thromboembolism but has low specificity. Consequently, its utility in patients with burn injuries has been questioned. Here, we describe the case of a patient with bilateral lower leg burns and skin grafting surgery who developed a pulmonary embolism despite prophylactic heparin administration. We discuss the diagnosis of this case and how the embolism could have been prevented.

KEY WORDS: ***D-dimer test, Deep vein thrombosis, Heparin, Venous thromboembolism***

INTRODUCTION

Patients with burn injuries are at increased risk of venous thromboembolism (VTE)[1] because of the emergence of a combination of thrombogenic factors known as Virchow's triad.[2] Although the true frequency of VTE in patients with burn injuries remains to be determined, the literature suggests its incidence is 0.9% to 60%[3,4] and 0.25% to 23%[1,5] in the absence and presence of thromboprophylaxis, respectively. Venous thromboembolism is a significant cause of mortality in burn patients: those who develop deep vein thrombosis (DVT) are twice as likely to die during admission than those who do not. Given the relatively low risks associated with heparin administration and this mortality risk of VTE, many units now routinely provide thromboprophylaxis.[6]

In general, VTE is diagnosed by clinical and imaging findings. Another possible test is measurement of D-dimers in the blood; high levels can signal endogenous fibrinolysis. It is a highly sensitive test for excluding VTE but has low specificity. Consequently, its utility in patients with burn injuries has been questioned.[7]

Here, we describe the case of a patient with bilateral lower leg burns who developed a pulmonary embolism (PE) despite prophylactic heparin administration. We discuss the diagnosis of this case and how the PE could have been prevented.

CASE REPORT

The patient was a 70-year-old woman without a history of notable illness. She was transferred to our hospital for skin grafting surgery 21 days after sustaining a third-degree scalding burn on both lower legs. Consequently, 25 days after injury, both legs were subjected to debridement and split-thickness skin grafting under general anesthesia. The skin grafts were from the lateral thigh. The grafts were 14/1000-inch thick, mesh grafted, and then implanted on the lower legs. The grafts were fully grown (Figure 1). The clinical events in the perioperative period are shown in Figure 2. At admission in our hospital for surgery, the Caprini score, which scores the patient according to about 40 thrombosis-promoting variables,[8] was determined. In our patient, the score was 4 because of the patient's age and the fact she would undergo surgery for more than 45 minutes. Consequently, she was deemed to be at high risk of VTE and was started on subcutaneous injections of 5000 unfractionated heparin units every 12 hours 4 days before surgery. The injections were paused on the day of surgery and continued after surgery for another 5 days. Blood coagulation tests, including tests for D-dimer, were conducted 3 days before surgery and repeated 7 days after surgery. The latter showed elevated D-dimer levels relative

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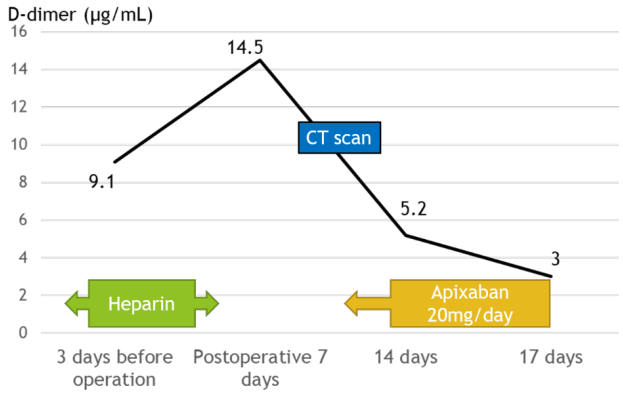
to preoperative levels (14.5 vs 9.1 μg/mL), which aroused suspicion of VTE.

Although the patient did not complain of any subjective symptoms, a contrast-enhanced computed tomography scan was performed 11 days after surgery. This led to the diagnosis of PE (Figure 3). The Pulmonary Embolism Severity Index of the patient was 70, which meant the patient had a low risk of 30-day death.[9] On the day of diagnosis, the patient was started on apixaban at 20 mg/day. Blood tests 14 and 17 days after surgery showed that the D-dimer levels dropped first to 5.2 μg/mL and then to 3.0 μg/mL. Consequently, on day 17, the apixaban dose was reduced to 10 mg/day. The patient's general condition was stable during the course of treatment, and she was transferred to the hospital for rehabilitation 23 days after surgery.

FIGURE 1. Clinical Photograph After Surgery on Day 25

A 14/1000-inch skin graft was taken from the lateral thigh, mesh grafted, and implanted on both lower legs. The grafts were fully grown.

FIGURE 2. Schematic Depiction of the Clinical Course and Changes in D-Dimer Levels



The patient was treated with heparin from the fourth day before surgery to the fifth day after surgery, with a hiatus on the day of surgery. D-dimer levels were measured on days -3, +7, +14, and +17 relative to the day of surgery. Contrast-enhanced computed tomography (CT) was performed on day +11, which led to the diagnosis of venous thromboembolism . On the same day, the patient was started on apixaban 20 mg/day, with level reduced to 10 mg/day 1 week later.

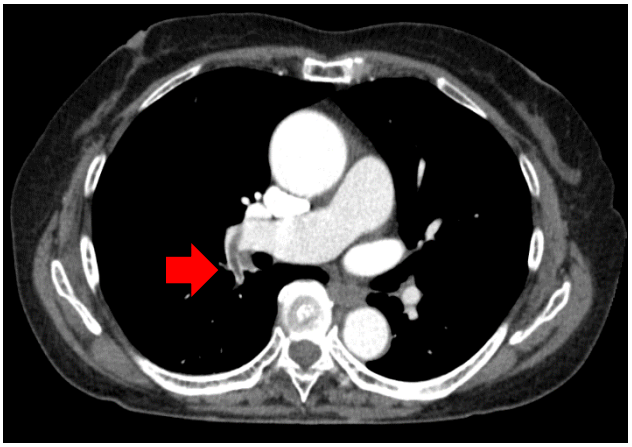
DISCUSSION

In the present case, although the patient with burn injury was prophylactically treated with heparin and lacked clinical signs of VTE, we became suspicious when the D-dimer levels rose from a preoperative level of 9.1 μg/mL to 14.5 μg/mL at about 1 week after surgery. Indeed, computed tomography revealed the presence of PE. This suggests that monitoring D-dimer levels over time can be a useful strategy for raising suspicion of the possibility of VTE in patients with burn injuries.

Previous studies have shown that the D-dimer test on its own has limited clinical utility because, although it is highly sensitive (80% to 100%), it has low specificity (20% to 63%).[7] However, previous studies have focused on D-dimer levels that were measured at a single timepoint. Here, we showed that following D-dimer levels over time after a clinical event such as surgery can be useful for alerting physicians to the possibility of VTE.

Our patient was started on heparin 4 days before surgery; after pausing the day of surgery, she continued on thromboprophylaxis for another 5 days after surgery. The elevated D-dimer levels were noted 2 days after heparin injections were stopped. It is possible that the PE arose in the 2 days after heparin was stopped, which suggests that the treatment should have been prolonged. However, given

FIGURE 3. Contrast-Enhanced Computed Tomography on Postoperative Day 11



Scan shows a contrast-depleted area in the main trunk of the right pulmonary artery (red arrow).

that the patient did not receive thromboprophylaxis during her 21-day stay in another hospital, it is more possible that the venous thrombus formed asymptomatically before the patient was transferred to our hospital. Thus, prophylactic administration of heparin should perhaps have been started earlier. Notably, specific guidelines are not available to suggest when after a burn this treatment should commence or how long to continue it. Further studies clarifying these issues are needed.

Our patient's risk of VTE, as defined by the Caprini score, was high. In contrast, with the consideration that her total body surface area burned was about 5%, the patient's burn-specific risk of VTE according to the weighted score defined by Pannucci and colleagues was 4, which corresponds to a 1% risk of VTE.[10] The International Society for Burn Injury guidelines for burn care[6] suggest that this score should be included in the Caprini score, in which case the patient's risk of VTE would have been expected to be higher. This is consistent with our findings.

CONCLUSIONS

We described a case of asymptomatic VTE after burn injury that was diagnosed by the increase of D-dimer over time. This suggests that sequential measurements of D-dimer could be useful for diagnosing VTE after burn injury. Our case also suggests that thromboprophylactic treatment should be instituted soon after burn injury, particularly when the burns affect both lower legs and are likely to curtail activities of daily living. Moreover, further research is needed to determine when to initiate thromboprophylactic administration and how long to sustain it.

REFERENCES

1. Fecher AM, O'Mara MS, Goldfarb IW, et al. Analysis of deep vein thrombosis in burn patients. *Burns.* 2004;30(6):591-593. doi:10.1016/j.burns.2003.12.019
2. Peng H, Yue L, Gao H, Zheng R, Liang P, Wang A, He A. Risk assessment of deep venous thrombosis and its influencing factors in burn patients. *J Burn Care Res.* 2020;41(1):113-120. doi:10.1093/jbcr/irz121
3. Rue LW 3rd, Cioffi WG Jr, Rush R, McManus WF, Pruitt BA Jr. Thromboembolic complications in thermally injured patients. *World J Surg.* 1992;16(6):1151-1154. doi:10.1007/BF02067085
4. Mayou BJ, Wee J, Girling M. Deep vein thrombosis in burns. *Burns.* 1981;7(6)438-440,
5. Wahl WL, Brandt MM, Ahrns KS, et al. Venous thrombosis incidence in burn patients: preliminary results of a prospective study. *J Burn Care Rehabil.* 2002;23(2):97-102. doi:10.1097/00004630-200203000-00005
6. ISBI Practice Guidelines Committee; Advisory Subcommittee; Steering Subcommittee. ISBI Practice Guidelines for Burn Care, Part 2. *Burns*. 2018;44(7):1617-1706. doi:10.1016/j.burns.2018.09.012
7. Ahuja RB, Bansal P, Pradhan GS, Subberwal M. An analysis of deep vein thrombosis in burn patients (Part 1): comparison of D-dimer and Doppler ultrasound as screening tools. *Burns.* 2016;42(8):1686-1692. doi:10.1016/j.burns.2016.08.005
8. Caprini JA. Thrombosis risk assessment as a guide to quality patient care. *Dis Mon.* 2005;51(2-3):70-78. doi:10.1016/j.disamonth.2005.02.003
9. Jiménez D, Aujesky D, Moores L, et al; RIETE Investigators. Simplification of the pulmonary embolism severity index for prognostication in patients with acute symptomatic pulmonary embolism. *Arch Intern Med.* 2010;170(15):1383-1389. doi:10.1001/archinternmed.2010.199
10. Pannucci CJ, Osborne NH, Wahl WL. Creation and validation of a simple venous thromboembolism risk scoring tool for thermally injured patients: analysis of the National Burn Repository. *J Burn Care Res.* 2012;33(1):20-25. doi:10.1097/BCR.0b013e318234d8b5