CORRESPONDENCE

Venous Thrombosis during Spaceflight

TO THE EDITOR: Approximately 2 months into an International Space Station mission, obstructive left internal jugular venous thrombosis was suspected in an astronaut during an ultrasound examination that was performed as part of a vascular research study. The astronaut reported no headache or worsening of the facial plethora that is common in conditions of weightlessness. The astronaut had no personal or family history of venous thromboembolism. The physical examination revealed a prominent ipsilateral external jugular vein. Follow-up ultrasound examination performed by the astronaut, guided in real-time and interpreted by two radiologists on Earth, confirmed the presence of venous thrombosis with subacute characteristics (Fig. S1A in the Supplementary Appendix, available with the full text of this letter at NEJM.org); the contralateral internal jugular vein and the bilateral subclavian, axillary, popliteal, and femoral veins were unremarkable.

Multispecialty discussions ensued, weighing the unknown risks of thrombus embolism and retrograde extension into the sinus and cerebral veins against those of anticoagulation. Twenty vials containing 300 mg of enoxaparin each were available in the pharmacy of the space station, but no anticoagulation-reversal agent was available. Treatment with enoxaparin at a dose of 1.5 mg per kilogram of body weight once daily was started; the dose was reduced to 1 mg per kilogram once daily after 33 days to extend therapy until oral apixaban could be delivered to the space station with a supply spacecraft. Protamine and prothrombin complex concentrate were also sent to the space station. Transition to apixaban at a dose of 5 mg twice daily occurred 42 days after the diagnosis of venous thrombosis, and the dose was reduced to 2.5 mg twice daily 3 months after diagnosis.

Sonographic surveillance at 7-to-21-day intervals showed progressive organization and volume reduction of the thrombus (Fig. S1B and S1C). Flow through the affected internal jugular segment was first noted on treatment day 47, but only on augmentation by Müller maneuver (in which after a forced expiration, inspiration is attempted with a closed mouth and nose — i.e., the reverse of a Valsalva maneuver) (Fig. S1D and S1E); spontaneous flow was still absent after 90 days of anticoagulation. Apixaban treatment was stopped 4 days before the return to Earth. On landing, a point-of-care ultrasound examination revealed spontaneous flow in the supine position with residual thrombus flattened to the vessel walls (Fig. S1F), a finding consistent with images taken on the space station during the Müller maneuver; further anticoagulation was deemed unnecessary. Follow-up examinations revealed a small volume of residual thrombus 24

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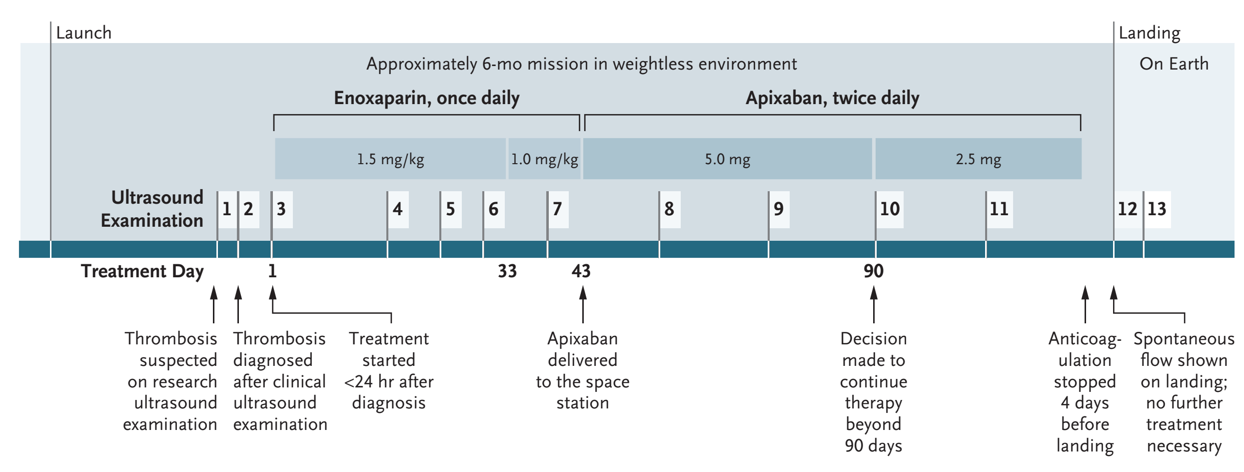

Figure 1. Timeline of Diagnosis and Treatment of Venous Thrombosis.

hours after landing and no thrombus 10 days after landing. A subsequent thrombophilia workup was unremarkable. On follow-up 6 months after the return to Earth, the astronaut continued to be asymptomatic. A summary timeline is shown in Figure 1.

Internal jugular venous thrombosis on Earth is typically associated with cancer, a central venous catheter, or ovarian hyperstimulation; unprovoked isolated venous thrombosis of the internal jugular vein is uncommon.[1-3] This case of venous thromboembolism in spaceflight highlights unique complexities of space medicine, such as the need for non–evidence-based clinical decision making; the need for patient-performed, radiologist-guided telemedicine ultrasonography; and a limited pharmacy in which long-term anticoagulation is not supported, syringes are a limited commodity, and drawing liquids from vials is a significant challenge because of surface-tension effects. Medical decisions in this case were implemented through concerted efforts across multiple space agencies to overcome the numerous logistic and operational challenges.

In addition, the observed blood-flow anomalies reveal gaps in our understanding of circulatory and hemostatic physiology.[4] Although cervicocranial venous overcapacity is a known effect of spaceflight, the resultant changes in flow organization, local whole-blood viscosity, and prothrombotic risk need exploration. Active astronaut surveillance and experimental models are critical to the development of prevention and management strategies for venous thromboembolism in weightlessness, especially with future plans for prolonged space travel to the Moon and Mars.

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Disclosure forms provided by the authors are available at NEJM.org.

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