A 42-year-old woman previously healthy came to the emergency department in 2012 with severe pain on her right toes, which started one week earlier. She denied hypertension, dyslipidemia, and smoking. She was taking oral contraceptives containing estrogen. Her physical examination revealed livedo reticularis on her lower limbs (Figure 1) and dry gangrene of her fourth right toe, and some ischemic lesion on the plantar face of her first right toe and the fifth right toe (Figure 2).

Laboratory tests revealed a C-reactive protein of 8 mg/dl, erythrocyte sedimentation rate of 46 mm/first hour, positive lupus anticoagulant, and IgG anticardiolipin of 57 GPL. Blood cell count, blood chemistry, total and fractions cholesterol, and triglycerides were normal. Antithrombin III, C, and S protein, and homocysteine levels were all within the normal range, and mutant prothrombin and Leiden factor screening were negative. Transesophageal echocardiography was also normal.

Arterial Doppler of lower limbs revealed anterior tibial and peroneal artery occlusions of the right leg suggestive of local thrombus formation. She received local treatment, warming, and analgesia. She denied previous fetal loss or pre-eclampsia.

A diagnosis of antiphospholipid syndrome (APS) was determined and systemic anticoagulation with enoxaparin 2 mg/kg/day followed by warfarin was prescribed. She showed clinical improvement and spontaneous amputation of a gangrened portion of her fourth toe and the other lesions’ healing. After 12 weeks, lupus anticoagulant and IgG anticardiolipin remained positive, and she was well without any other clini-
cal features, keeping an international normalized ratio (INR) target of 3–4.

ASP is an autoimmune disease characterized by recurrent thrombosis and/or fetal loss associated with persistent antiphospholipid antibodies. The primary arterial manifestation is stroke. Deep venous thrombosis is the major problem regarding venous territory. The second most common manifestation is limb ischemia, as presented by our patient [1]. Livedo reticularis is the most common dermatological manifestation of ASP, which is a coagulation disorder. It may also be a marker for APS severity [2-4], and may appear in up to 40% of APS patients as initial manifestation [2]. Anticoagulation therapy should be given over a long period, and probably for life.

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References

Capsule
Systems vaccinology of the BNT162b2 mRNA vaccine in humans
Arunachalam et al. used a systems vaccinology approach to comprehensively profile the innate and adaptive immune responses of 56 healthy volunteers who were vaccinated with the Pfizer–BioNTech mRNA vaccine (BNT162b2). Vaccination resulted in the robust production of neutralizing antibodies against the wild-type SARS-CoV-2 (derived from 2019-nCOV/USA_WA1/2020) and, to a lesser extent, the B.1.351 strain, as well as significant increases in antigen-specific polyfunctional CD4 and CD8 T cells after the second dose. Booster vaccination stimulated a notably enhanced innate immune response as compared to primary vaccination, evidenced by a greater frequency of CD14+CD16+ inflammatory monocytes, a higher concentration of plasma IFNγ, and a transcriptional signature of innate antiviral immunity. Consistent with these observations, single-cell transcriptomics analysis demonstrated an approximately 100-fold increase in the frequency of a myeloid cell cluster enriched in interferon-response transcription factors and reduced in AP-1 transcription factors, after secondary immunization. Finally, the authors identified distinct innate pathways associated with CD8 T cell and neutralizing antibody responses, and show that a monocyte-related signature correlates with the neutralizing antibody response against the B.1.351 variant.

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Capsule
Age-related immune response heterogeneity to SARS-CoV-2 vaccine BNT162b2
Although two-dose mRNA vaccination provides excellent protection against SARS-CoV-2, there is little information about vaccine efficacy against variants of concern (VOC) in individuals above eighty years of age. Collier et al. analyzed immune responses following vaccination with the BNT162b2 mRNA vaccine in elderly participants and younger healthcare workers. Serum neutralization and levels of binding IgG or IgA after the first vaccine dose were lower in older individuals, with a marked drop in participants over 80 years old. Sera from participants above eighty showed lower neutralization potency against the B.1.1.7 (Alpha), B.1.351 (Beta) and P.1. (Gamma) VOC than against the wild-type virus and were more likely to lack any neutralization against VOC following the first dose. However, following the second dose, neutralization against VOC was detectable regardless of age. The frequency of SARS-CoV-2 spike-specific memory B cells was higher in elderly responders (whose serum showed neutralization activity) than in non-responders after the first dose. Elderly participants showed a clear reduction in somatic hypermutation of class-switched cells. The production of interferon-γ and interleukin-2 by SARS-CoV-2 spike-specific T cells was lower in older participants, and both cytokines were secreted primarily by CD4 T cells.

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