A 78-year-old Caucasian female with a medical history significant for hypertension, diabetes and coronary artery disease was brought to the hospital for hemoptysis, cough and shortness of breath. Her symptoms had been going on for some time, but what prompted her to seek medical attention was the development of diffuse skin changes over large areas of her body.

Upon admission, the patient was placed on oxygen for hypoxia. Physical examination revealed bilateral crackles on chest auscultation and widespread ecchymoses affecting the upper and lower extremities, abdomen, chest and back. A petechial rash was also noted on the lower extremities (Figures A-F). CT scan of the chest demonstrated diffuse alveolar and interstitial pulmonary infiltrates with bilateral pleural effusions. Diffuse alveolar hemorrhage was confirmed at bronchoscopy. No endobronchial lesions were identified and bronchial washings were negative for fungal elements, acid-fast bacilli and *Pneumocystis carinii*. She had no family or personal history of bleeding disorders. Nevertheless, a review of her medications showed she had been started on aspirin and clopidogrel more than a year earlier after undergoing percutaneous coronary intervention (PCI) with drug-eluting stent (DES) placement. Aspirin and clopidogrel were withheld, and a workup was initiated to rule out a bleeding disorder, given the extensive and diffuse character of the bleeding.

CBC showed a mildly decreased platelet count at 99,000/mL. Fibrinogen and fibrinogen degradation products were normal and the peripheral smear was nondiagnostic. The coagulation parameters were within an acceptable range. ANA, ANCA, anti-glomerular basement membrane antibodies and cryoglobulins were all negative. Complement proteins C3 and C4 levels were mildly low at 71 mg/dL (normal: 79 to 152 mg/dL) and 13 mg/dL (normal: 16 to 38 mg/dL), respectively; the significance of this finding was not completely understood. Levels of factor VIII, factor IX and von Willebrand factor (vWF) were within normal range. Factor XIII assay was normal. Infectious workup did not reveal any pathogen to be responsible for the etiology.

Because the workup came back unrevealing, it was suspected that the combination of aspirin and clopidogrel was the probable cause of severe cutaneous bleeding. The patient was managed conservatively with antibiotics and supportive care while the platelet levels recovered. The bleeding resolved over the next few days, and she was discharged home in stable condition.

**Figures A-F.**

(A-B) Large subcutaneous ecchymoses covering the entire left (A) and right (B) upper extremities.

(C) Petechiae on bilateral lower extremities, scattered and in crops, with no purpuric manifestations.

(D) Large ecchymoses of the lower legs with few scattered petechiae noted on the upper legs.

(E) Smaller ecchymoses of various ages on the back.

(F) Multiple ecchymotic patches of variable size on the abdomen.
cause of the patient’s symptoms. Within a few days of stopping both drugs, the hemoptysis and dyspnea improved. The lung infiltrates also began to clear and the ecchymoses started to fade. Cardiology was consulted and recommended discontinuing clopidogrel and resuming low-dose aspirin once the symptoms resolved.

Discussion
This case illustrates a very rare clinical presentation of serious blood dyscrasia with extensive bleeding involving the skin as a consequence of dual antiplatelet therapy (DAPT). Antiplatelet therapy has become the mainstay of treatment for acute coronary syndrome. Although some patients with established coronary artery disease are maintained on a single antiplatelet agent with aspirin, DAPT is now considered standard of care for prevention of stent thrombosis in those undergoing PCI with stent implantation. However, bleeding remains a major concern with dual therapy as the risk is greater than with monotherapy.

Severe bleeding events with DAPT are uncommon, yet potentially life-threatening. Intracranial hemorrhage and gastrointestinal bleeds are consistently reported as major bleeding events; however, extensive bleeding into the skin has not been described before. Previous studies suggested the use of DAPT for at least a year after PCI to prevent stent thrombosis. There is recent evidence that such therapy beyond the one-year mark is beneficial in terms of reduction of the rates of stent thrombosis. Thus, with the increasing use of DAPT for longer periods, severe bleeding events may not be uncommon.

Both aspirin and clopidogrel inhibit platelet activation and aggregation but exert their antiplatelet effect using different mechanisms. Although aspirin acetylates platelet cyclooxygenase, leading to its inhibition and reduction of thromboxane formation, clopidogrel acts by modifying the platelet ADP receptor so that ADP does not bind to it. Thus, the two drugs act synergistically to inhibit platelet aggregation, which may explain the increased risk of bleeding when they are combined.

The severity and diffuse character of the subcutaneous hemorrhages along with the petechial lesions led us to believe our patient had a platelet defect; hence, aspirin and clopidogrel were withheld from the beginning. Moreover, the presence of petechial lesions is not characteristic of clotting factor deficiencies, and this possibility was excluded with the negative workup. Finally, a vasculitic process should always be considered in the differential diagnosis of an elderly person presenting with diffuse alveolar hemorrhage and a petechial skin rash, although our patient’s large ecchymotic areas were not a characteristic feature.

This case highlights the fact that severe bleeding events, although rare, need to be recognized in patients on DAPT. It is noteworthy that a thorough review of the patient’s medications is necessary to look for association with the presenting symptoms. Given the potential life-threatening nature of these complications, patients on DAPT should be educated about these side effects and advised to report any symptom of blood dyscrasia. Physicians should also weigh the benefits and risks of continuing such therapy beyond one year in high-risk patients.

REFERENCES