Myelodysplastic Syndrome Presenting as Cutaneous Purpura

Howard Fein, MD, Cincinnati, Ohio
Brian B. Adams, MD, Cincinnati, Ohio

GOAL

To discuss cutaneous manifestions of myelodysplastic syndrome (MDS).

OBJECTIVES

1. To describe laboratory and chromosomal abnormalities associated with MDS.
2. To outline the diagnostic workup of MDS.
3. To identify important elements of the physical assessment of a patient with suspected MDS.

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Myelodysplastic syndrome is a preleukemic, clonal disorder of the hematopoetic stem cell. Cutaneous manifestations include infections, vasculitis, neutrophilic dermatoses, and leukemia cutis. Senile purpura is a common condition occurring in elderly individuals who lack other systemic or hematologic diseases. We present a case of myelodysplastic syndrome in which cutaneous lesions resembling senile purpura were the initial clinical manifestation.

Senile purpura (SP), originally described by Bateman[1,2] in 1836, is a common dermatosis affecting 14% of elderly individuals. Generally, this condition presents as nonpalpable purpura on the extensor surfaces of the forearms and hands.[3] SP is regarded as a benign disorder and was shown by Tattersall and Seville[4] to occur in patients who lacked other systemic or hematologic diseases. Although the exact cause of SP remains unknown, multiple etiologies including inadequately supported cutaneous blood vessels, abnormal macrophage phagocytosis, and zinc deficiency have been proposed.[5,6]

Myelodysplastic syndrome (MDS) is a preleukemic, clonal bone marrow disorder that primarily affects individuals above the age of 50.[7] Cutaneous lesions associated with MDS are classified as specific and nonspecific. Specific skin lesions are characterized by the presence of malignant hematopoetic cells within the dermis and show histologic features consistent with leukemia cutis.[8,9] Specific skin lesions in MDS occur rarely, are associated with rapid disease progression, and are indicative of a poor prognosis.[8,9]

Nonspecific lesions account for the majority of cutaneous manifestations in MDS[8]; these primarily include cutaneous infections, dermal vasculitis, and neutrophilic dermatoses.[8] Cases of MDS associated with erythema elevatum diutinum, atypical erythema nodosum, and granuloma annulare have also been documented.[10-12] In this report, we describe a case of MDS in which purpuric patches resembling SP were the initial clinical manifestation.

Case Report

A 74-year-old Caucasian male with a history of hypothyroidism and hypertension was referred to the dermatology clinic at the Veterans Administration Medical Center in Cincinnati for evaluation of asymptomatic purpura on his forearms for 6 months' duration.

Dr. Fein is a Resident Physician, University of Cincinnati, Department of Dermatology, Cincinnati, Ohio. Dr. Adams is an Assistant Professor, University of Cincinnati, Department of Dermatology, Chief of Dermatology, Veterans Administration Medical Center, Cincinnati, Ohio.
REPRINT REQUESTS to University of Cincinnati, College of Medicine, Department of Dermatology, PO Box 670523, Cincinnati, Ohio 45267 (Dr. Adams).

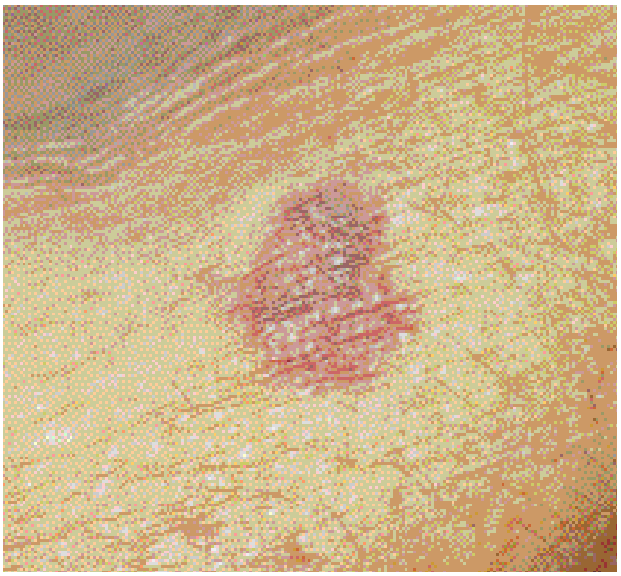

FIGURE 1. Involving the lateral aspect of the right forearm is a nonpalpable, purpuric patch.

Physical examination revealed a thin male who was 5 feet 9 inches tall and weighed 128 lbs. On the dorsal aspects of his arms and forearms were several nonpalpable, 1- to 4-cm purpuric patches (Figure 1). No mucosal hemorrhages were present. Further evaluation revealed no palpable adenopathy, abdominal masses, hepatomegaly, or splenomegaly. Histologic examination of one of the purpuric patches revealed dermal vascular ectasia and red blood cell extravasation consistent with a diagnosis of SP (Figure 2). The biopsy showed no evidence of vasculitis.

To completely evaluate his purpura, a focused review of systems was obtained.[13] Coinciding with the onset of purpura, the patient reported a 6-month history of fatigue, 25-pound weight loss, subjective fevers, and night sweats. Based on the above findings, several serologic tests were obtained. Complete blood cell count (CBC) with differential showed pancytopenia with hemoglobin of 10.3 g/dl, hematocrit 29.4%, white blood cell count 4,400/µl, and a platelet count of 63,000/µl. The mean corpuscular volume was markedly elevated at 115.7 fl (normal, 80 to 94 fl). The corrected reticulocyte count was 0.9%. A peripheral blood smear demonstrated 2+ anisocytosis and a few atypical lymphocytes. Prothrombin time was 12.7 seconds. Urinalysis revealed no hematuria. Thyroid stimulating hormone was 1.90 µIU/ml.

A hematology/oncology consultation was requested for evaluation of pancytopenia and peripheral blood smear abnormalities. A bone marrow biopsy was subsequently performed and was significant for the presence of blast cells. The biopsy showed otherwise normal hematopoiesis. Chromosomal analysis of the bone marrow demonstrated a loss of the Y chromosome in 20% of the analyzed

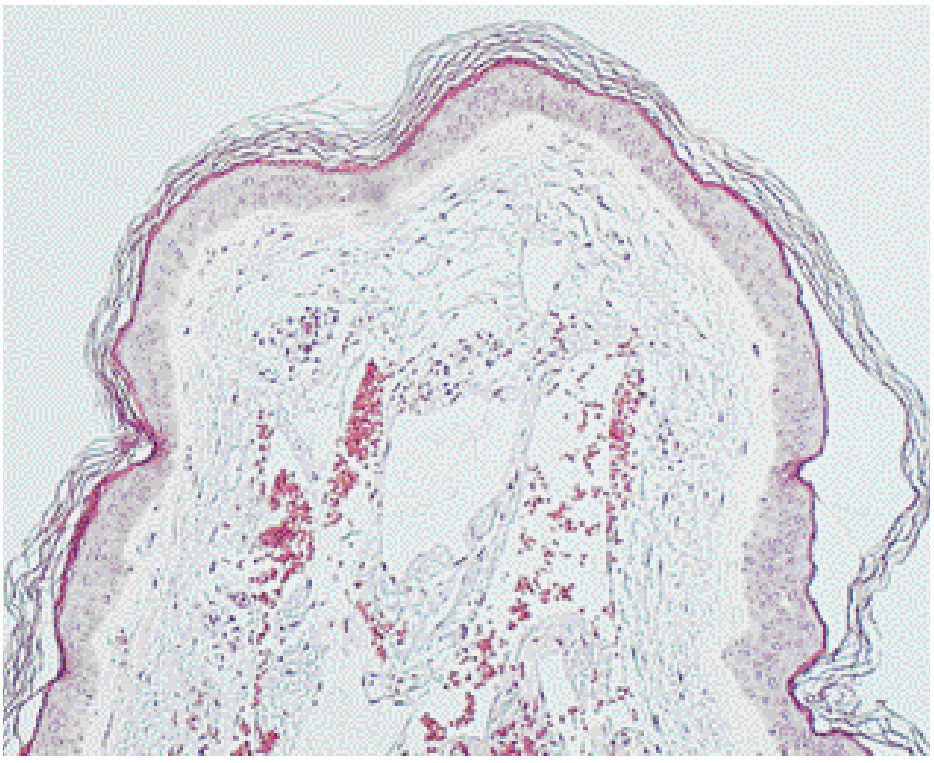

FIGURE 2. Dermal vascular ectasia and red blood cell extravasation. There is no vasculitis. (H&E stain; original magnification × 100).

cells. Peripheral blood was submitted for flow-cytometric analysis and showed no atypical immunophenotypes. Based on the above findings, a diagnosis of MDS was made.

Discussion

SP is a common dermatosis typically without clinical consequence. As such, the presence of purpura on the forearms of an elderly patient is given little attention during routine skin examination. Cutaneous purpura associated with hematologic disorders can occur as the result of thrombocytopenia. Cutaneous hemorrhages are, however, ordinarily not observed until the platelet count is reduced below 50,000/μl and are usually induced by trauma.[14] Spontaneous bleeding is unlikely unless the platelet count falls below 20,000/μl.[14] In our patient with MDS and in at least one other patient with acute myeloid leukemia, cutaneous purpuric patches were observed when the platelet count was greater than 60,000/μl.[15] In addition to the quantitative decrease in platelets, several qualitative platelet abnormalities involving morphology, membrane structure, and arachidonic acid metabolism have been reported in patients with myeloproliferative disorders including MDS.[16,17] Ultimately, however, the effect that these specific platelet abnormalities have on *in vivo* hemostasis is unknown.[16]

A diagnosis of MDS is suspected when a CBC demonstrates cytopenia of one or more cell lineages.[18] A bone marrow biopsy along with cytogenetic studies are used to confirm the diagnosis.[18] The cause of MDS remains unknown in the majority of cases, although an association with previous exposure to radiation, chemotherapeutic agents, benzene, and other organic compounds has been documented in some patients.[19] Chromosomal abnormalities are frequently found in bone marrow cells and have been reported in 40 to 60% of cases of MDS.[20] The most common cytogenetic abnormality involves either a complete or partial deletion of chromosome 5.[19,21] Loss of the Y chromosome has been reported in 5% of patients with MDS and was present in our patient[21]; however, Y chromosome loss is present in 1% of older men and is related to normal aging.[22]

Dermatologists frequently encounter older patients with purpuric patches localized to the forearms and hands and the most common diagnosis is SP. Cutaneous purpura resulting from other etiologies, however, may be clinically indistinguishable from SP. Since many of these patients may not have routine CBCs and because cutaneous purpura can be a clue to an underlying hematologic disorder, we suggest screening patients diagnosed with SP with a focused review of systems during their initial clinical presentation. Special attention should be given to the so-called "stage B" constitutional symptoms, which include weight loss, fever, and night sweats, which are associated with Hodgkin's disease and other malignancies.[23] This can easily be accomplished in less than 60 seconds. Ultimately this rapid, focused review of systems led to the diagnosis of MDS in our patient. The presence of systemic complaints in a patient with cutaneous purpura resembling SP should warrant further clinical evaluation.

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FACULTY DISCLOSURE
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Drs. Adams and Fein report no conflict of interest.