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Review

The skin as a window to the blood: Cutaneous manifestations of myeloid malignancies

Alvin W. Li[a,1], Emily S. Yin[a,1], Maximilian Stahl[b], Tae Kon Kim[b], Gauri Panse[a], Amer M. Zeidan[b,2], Jonathan S. Leventhal[a,*,2]

[a] Department of Dermatology, Yale School of Medicine, New Haven, USA
[b] Department of Medicine (Hematology), Yale School of Medicine, New Haven, USA

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ABSTRACT

Cutaneous manifestations of myeloid malignancies are common and have a broad range of presentations. These skin findings are classified as specific, due to direct infiltration by malignant hematopoietic cells, or non-specific. Early recognition and diagnosis can have significant clinical implications, as skin manifestations may be the first indication of underlying hematologic malignancy, can reflect the immune status and stage of disease, and cutaneous reactions may occur from conventional and targeted agents used to treat myeloid disease. In addition, infections with cutaneous involvement are common in immunocompromised patients with myeloid disease. Given the varying presentations, dermatologic findings associated with myeloid malignancies can pose diagnostic challenges for hematologists and dermatologists. In this clinical review intended for the practicing hematologist/oncologist, we discuss the presentation, diagnosis, treatment, and prognostic value of the most common cutaneous manifestations associated with myeloid malignancies using illustrative macro- and microscopic figures and with a special emphasis on practical considerations.

1. Introduction

Patients with myeloid malignancies may present with a broad range of cutaneous manifestations at the time of diagnosis or later in the disease course. The skin findings are traditionally divided into two categories: (1) specific skin lesions characterized by direct infiltration of tissue by malignant hematopoietic cells and (2) non-specific lesions. In addition, patients may experience skin signs secondary to hematologic dysfunction including pallor, petechiae, and ecchymoses. These cutaneous findings may be mistaken for benign dermatologic disease, particularly in patients without a prior diagnosis of cancer. Cutaneous manifestations may be the first sign of underlying hematologic disease or an indicator of disease progression, affecting disease stage, prognosis and treatment. In addition, chemotherapeutic agents (e.g. cytarabine) and targeted drugs (e.g. sorafenib and other tyrosine kinase inhibitors) also commonly cause skin eruptions that could be difficult to differentiate visually from disease-related skin changes [1]. The differential diagnosis of skin lesions in the oncologic patient may also include infectious etiologies in addition to medication and transfusion-related reactions. Accurate diagnosis is vital to clarify the underlying pathogenic mechanisms and help direct the appropriate interventions. This clinical review will provide an overview of skin manifestations associated with each major subtype of myeloid malignancy to improve the diagnosis and management of patients using illustrative macro- and microscopic figures and with a special emphasis on practical considerations.

2. Direct invasion of neoplastic cells

2.1. Leukemia cutis (myeloid or granulocytic sarcoma) & leukemic vasculitis

Leukemia cutis (LC), also known as *myeloid or granulocytic sarcoma*, refers to the invasion of malignant myeloid blasts into the skin, resulting in identifiable cutaneous lesions (Table 1). LC can be subcategorized as leukemic vasculitis (LV) when leukemic cells infiltrate and destroy blood vessels within the dermis [2]. The mechanism underlying the migration of leukemic cells to the skin may be due to alteration of certain chemokine receptors and adhesion molecules on leukemic cells, but remains to be fully elucidated [3,4]. The incidence

* Corresponding author at: Department of Dermatology, Yale School of Medicine, 15 York Street, LMP 5040, New Haven 06511, USA.
E-mail address: jonathan.leventhal@yale.edu (J.S. Leventhal).
[1] AWL and ESY contributed to this manuscript equally and serve as co-first authors.
[2] AMZ and JSL contributed to this manuscript equally and serve as co-senior authors.

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Table 1
Cutaneous manifestations of myeloid malignancies.

Disorder	Associated myeloid malignancies	Dermatologic manifestations	Differential diagnosis and distinguishing features	Prognosis of underlying malignancy	Treatment
Direct invasion of neoplastic cells					
Leukemia cutis, leukemic vasculitis	AML, CML, MDS	**AML**: Violaceous, red to brown papules and nodules found on extremities, trunk, and face. May be hemorrhagic, ulcerative or purpuric. **CML**: Similar to LC in AML. Erythematous or violaceous papules, plaques and nodules involving the extremities, head and trunk. **MDS**: May present similarly to LC in AML and CML. Can present as a diffuse, pruritic, erythematous maculopapular rash. **Leukemic vasculitis:** may present similarly to LC or present as a vesiculobullous eruption or palpable purpura.	Cutaneous lymphoma • May appear similar to LC with violaceous papulonodules • Immunophenotype can help establish diagnosis Cutaneous lymphoid hyperplasia (lymphocytoma cutis) • Violaceus nodules or plaques that favor the face and upper trunk, typically asymptomatic • Associated with medications, arthropod bites, and infection • Histopathology will show lymphocytic infiltrate with plasma cells and eosinophils without leukemic cells Erythema nodosum • Tender erythematous plaques on pretibial shin • No leukemic infiltrate on histology Non-leukemic vasculitides • Palpable purpura typically on the extremities • No leukemic infiltrate on histology Morbilliform (exanthematous) drug eruption • Maculopapular, pruritic eruption, may be purpuric in areas of dependency • Typically, more widespread • Temporal association with drug exposure (eruption is typical 4–21 days after exposure or sooner on re-exposure) • No leukemic infiltrate on histology	Poor, often associated with progression of underlying malignancy	Treatment of underlying malignancy
Neutrophilic dermatoses					
Sweet's syndrome	AML, CML, MDS, polycythemia vera, myelofibrosis	Tender, erythematous nodules, papules and plaques on the upper extremities, face, and/or neck with concurrent fever and leukocytosis. Can also present as ulcerated plaques and	Cutaneous infection (bacterial, fungal, mycobacterial) • May mimic SS with pustules or larger abscesses • Obtain tissue cultures for	Poor, often foreshadows relapse of underlying malignancy	Systemic corticosteroids, potassium iodide, dapsone, colchicine

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