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CASE REPORT

Paraneoplastic pemphigus as a presentation of acute myeloid leukemia: Early diagnosis and remission

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Abstract
Skin lesions are frequently encountered in clinical practice which can be a presentation of systemic diseases not excluding an occult malignancy. Commonly reported paraneoplastic dermatologic manifestations include acanthosis nigricans, dermatomyositis, erythroderma, hypertrophic osteoarthropathy, Sweet syndrome, and paraneoplastic pemphigus (PNP).
PNP is a rare autoimmune mucocutaneous disease characterized by severe stomatitis, polymorphic skin eruptions, and associated underlying neoplasms most commonly non-Hodgkin's lymphoma, chronic lymphocytic leukemia, and Castleman disease. PNP is characterized on histopathology as dyskeratotic epithelial cells with acantholysis with a typical immunofluorescence staining pattern of direct and/or indirect staining of intercellular, basement membrane, and dermoepidermal junction with immunoglobulin-G and C3. PNP has been described to have poor prognosis with a mortality range of 75–90% and a mean survival of less than 1 year.
We describe a previously unreported case of PNP associated with acute myeloid leukemia (AML) where the patient presented with a nonhealing ulcer and hemorrhagic crusting on the face that did not respond to antimicrobials and steroids. Investigations revealed leukocytosis with peripherally circulating blasts. Skin biopsy revealed an evolving PNP and bone marrow biopsy confirmed evidence of AML. The patient underwent induction, consolidation, and then successful allogenic bone marrow transplantation with complete remission. The skin lesion, which was initially refractory to treatments, surprisingly resolved within 7 days of starting induction chemotherapy.

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In this case, the skin lesion was a key factor in early diagnosis and instituting treatment for the underlying AML. Early intervention gave our patient a better outcome with an ongoing survival of 18 months since diagnosis, maintaining complete remission.

Introduction

Skin lesions are most commonly seen secondary to an infectious, autoimmune or allergic etiology. In some instances, skin lesions can be a manifestation of the myriad of systemic diseases including malignancies. The dermatologic involvement of the neoplasia can either be a primary tumor of the integumentary system, metastasis to the skin as in chloroma, or a paraneoplastic phenomenon. Commonly reported paraneoplastic skin manifestations include acanthosis nigricans, dermatomyositis, erythroderma, hypertrophic osteoarthropathy, Sweet syndrome, and paraneoplastic pemphigus (PNP) [1].

PNP presents as polymorphic cutaneous eruptions in the form of either bullous, erythematous, or verrucous papules or plaques, with or without intraoral mucosal involvement in the form of stomatitis, erosions, or ulcerations. It can also involve other mucosal regions, often the conjunctiva.

The incidence of PNP does not follow any geographic distribution or gender preponderance with a mean age at diagnosis of 51 years [2]. It has been associated with non-Hodgkin lymphoma, chronic lymphocytic leukemia, Castleman disease, thymoma, and rarely with Waldenstrom macroglobulinemia, Hodgkins lymphoma, and monoclonal gammopathy [3,4]. It has also been reported with solid tumor malignancies like adenocarcinoma of the pancreas, colon, breast, and prostate, as well as mesenchymal sarcomas [5]. Occasionally, medications like fludrabine and interferon-α have been shown to cause a flare up of PNP lesions in known patients [6].

We report a case of PNP associated with acute myeloid leukemia (AML) previously unreported in medical literature. This atypical presentation of AML as PNP led to the early diagnosis, treatment, and complete remission of the patient.

Case report

A 59-year-old man, with no significant past medical history, presented to his primary care physician with a lesion on his face. He had a recent molar tooth extraction 1 month previous with no associated complications. He was a current smoker with a 20-pack-year smoking history. He had a family history of lung cancer, colon cancer, and uterine cancer, and no personal or family history of any autoimmune disease.

The lesion was just limited to his lower face around the perioral area. The patient denied any recent infection, rashes, swollen lymph nodes, fever, night sweats, bleeding, or any pain. He had no recent history of travel, trauma, insect, tick or animal bite, or any exposure to sick contacts. He did complain of stomatitis but without any oral ulcers.

On physical examination, the lesions were black, indurated, and ulcerated, with hemorrhagic crusting involving the entire lower lip along the vermilion border and infranasal area (Fig. 1). No other skin lesions were identified. There was no palpable cervical or peripheral lymphadenopathy, petechial rash, buccal lesions, or oral ulceration.

Considering the lesion to be a bacterial infection, he was initially treated with oral antimicrobials as an outpatient. With no clinical improvement, routine investigations were done that revealed leukocytosis with peripherally circulating blasts (Fig. 2) raising concern for a hematological malignancy, for which he was referred to our inpatient hematology service.

Complete blood count revealed a white cell count of 24,300/uL with 29% blasts and no bandemia, platelet count of 33,000/uL, hemoglobin of 9.1 g/dL, and hematocrit of 27. Other investigations revealed elevated lactate dehydrogenase of 664 mg/dL (normal: 140–280 mg/dL) and normal uric acid of 6.4 mg/dL (normal: 3.4–7.0 mg/dL). There was no evidence of disseminated intravascular coagulation and other laboratory tests including serum sodium, potassium, blood urea nitrogen, creatinine, and liver function tests were normal. Serum protein electrophoresis also did not reveal any monoclonal bands.

The patient was initially started on empiric antimicrobial coverage with valacyclovir, vancomycin, cefepime, and micafungin, along with dexamethasone, due to concerns of being in an immunocompromised state. A bone marrow biopsy along with a biopsy of the skin lesion was then pursued.

Microbiological analysis of the skin biopsy showed no evidence of herpes simplex virus in tissue culture, absence of viral cytopathic changes, or any fungal elements. Epstein-Barr virus DNA polymerase chain reaction was also negative. Wound cultures grew mixed oropharyngeal bacterial flora with few *Candida albicans*. Skin lesions remained

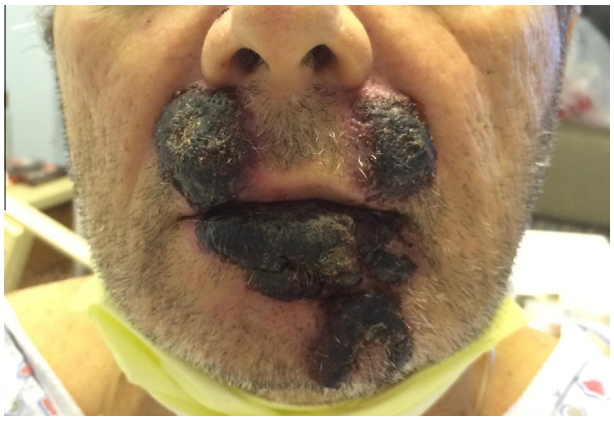

Fig. 1 Gross appearance of the skin lesion.

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