ISSN: 2754-494X

Journal of Dermatology Research Reviews & Reports

SCIENTIFIC Research and Community

Case Report

Open Access

Psoriasis Vulgaris (PV) Exacerbation in Acute Myeloid Leukemia (AML) Patient Treated with Cytarabine/Daunorubicin (C/D)

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ABSTRACT

Adverse reactions associated with chemotherapeutic agents to treat acute leukemia such as cytarabine and daunorubicin (C/D) have been reported regularly, however, psoriasis vulgaris is a rare adverse event. We report a 46-year-old Indonesian man presented with multiple erythema scaly plaques on his trunk for one month. He was diagnosed with acute myeloid leukemia (AML) 4 months ago, and received remission-induction chemotherapy for AML with a high-dose combination of C/D.

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Received: October 09, 2024; **Accepted:** October 16, 2024; **Published:** October 22, 2024

Keywords: Acute Myeloid Leukemia, Cytarabine, Daunorubicin, Psoriasis Vulgaris

Introduction

Acute myeloid leukemia (AML) is an aggressive type of hematologic cancer characterized by the clonal proliferation of myeloid blasts in the bone marrow, peripheral blood, or other tissues. Globally, the incidence of AML has increased by 15% and consistently crowned the most common leukemia type in adults, it represents approximately 10% of all morbidities of blood cancer annually. Mortality due to AML is about 10.000 cases or 20% of all hematologic cancers. The management approach to AML remained static for decades, combination of C/D is indicated for the treatment of newly diagnosed therapy-related AML. Cytarabine (Ara-C) is a nucleoside metabolic inhibitor and Daunorubicin (DNR) is an anthracycline topoisomerase inhibitor. This combination has remained essentially effective internationally as conventional induction regimen for AML. The current standard regime is DNR for three days and Ara-C as the continuous seven days infusion, or more commonly known as "7+3". Daunorubicin is usually given intravenously, with standard dose of 60 mg/m2 for the first 3 days, along with 100-200 mg/m2 of cytarabine intravenously for consecutive seven days. Adverse effects associated with these agents have been reported regularly, however, psoriasis vulgaris is not often referenced [1-4].

Psoriasis is a chronic inflammatory autoimmune disease that is characterized by sharply demarcated erythematous scaly plaques that occurs in 3% of the world population, yet it is inconsistent among regions, dominated by Caucasian and Scandinavian populations that contributes around 11%. Several risk factors may exacerbate psoriasis and induce flare-ups, which divided by classic and emerging risk factors. Classic risk factors including mechanical stress, infections, common drugs like beta-blockers and lithium, air pollutants, psychological stress, hormonal disturbance, and metabolic imbalance have been scientifically proven to have responsibility to worsen flare-ups of psoriasis. Emerging risk factors or newly identified risk factors such as immunotherapy for oncologic disease, biological drugs, and vaccines have been reported in literatures, however its certainty still needs to be discussed [5,6].

The primary pathogenesis of psoriasis believed has the association with the involvement of T helper (Th) 17 and 22 that causes dysregulation of keratinocytes, inflammatory cells, and blood vessels. Stimulators that break self-tolerance, potentially through autoantibodies, stimulates the activation of dendritic cells (DCs), which results in the secretion of tumour necrosis factor-alpha (TNF-α) and interferon alpha (IFN- α). These inflammatory cytokines then stimulate the release of interleukin (IL) 23 and 12. IL-23 aids the dissemination of Th-17 and 22, which leads to the production of IL-17 and IL-22 simultaneously. On the other hand, IL-12 cultivates the proliferation of Th1 cells, which contributes to the production of IFN-γ and TNF-α, intensifying the inflammatory process [5,6].

Case Illustration

A 46-year-old man presented with multiple erythematous scaly

plaques all over his trunk for one month. The patient went to the outpatient department because his symptoms were getting worse. He had a history of psoriasis that has not recurred for decades. He was diagnosed with new course of AML 4 months ago and received remission-induction chemotherapy for AML with 100 units/m2 (daunorubicin 44 mg/m2 and 100 mg/ m2). He developed progressive erythematous plaques on his body a week post-chemotherapy. His condition worsened after the second course of C/D, with 3 weeks interval after the first chemotherapy); this situation made his stress got worst. The erythematous plaques got wider and more prominent, with silvery thick scales on his trunk. His Auspitz's sign was positive.

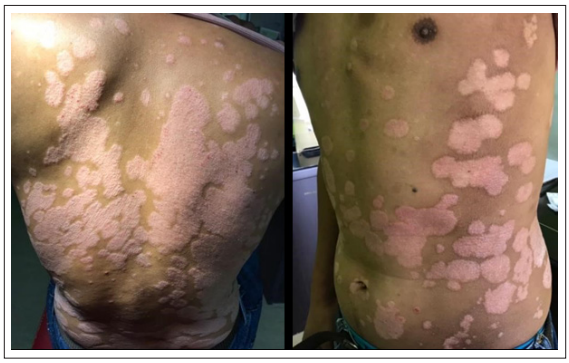

Figure 1: Skin Lesions found on the Patient

From dermatologic examination, we described the lesions as multiple, discrete, well-defined raised border, with thick white psoriasiform scales located at the patient's chest, belly, and back. (Figure 1). The patient was diagnosed with psoriasis vulgaris, and prescribed with a mixture of mometasone furoate 0.1% cream, salicylic acid 5%, and Vaseline Album, loratadine 10 mg, also narrow-band ultraviolet B (NBUVB) phototherapy. His skin lesions got better after 2 weeks, thus the therapies continued without stopping the chemotherapy.

Discussion

Psoriasis is a chronic autoimmune, multisystem inflammatory disease that associated with multiple comorbidities including malignancy. The pathogenesis of psoriasis is constant inflammation process, which leads to uncontrolled keratinocyte proliferation and dysfunctional differentiation. Uncontrolled proliferation of keratinocyte actively produces endothelial growth factor (VEGF) and vascular permeability factor (VPF), affecting blood vessels dilatation, angiogenesis, and hyperpermeability, which contributes to positive Auspitz's sign (pinpoint bleeding when the scales scraped away) [5-7].

Psoriasis flare refers to the worsening or exacerbation of psoriasis that triggered by several risk factors. In our patient, we have several hypotheses regarding his condition, however, we suspect that the chemotherapy agent is the primary culprit. Daunorubicin/Cytarabine is the combination that is accepted worldwide. There is only one case report published in the literature on patient with daunorubicin/cytarabine chemotherapy from Iran. A reported a 43-year-old with no history of psoriasis and known history of 6 month diagnosed AML receiving C/D twice and started developing psoriasis lesion on the face. Histological examination of the biopsy from the cheek lesion revealed acanthosis with rete ridge elongation, parakeratosis with focal hypogranulosis, a large pustule of Kogoj and perivascular lymphocytic infiltration into the upper dermis, aligned with the diagnosis of psoriasis [8].

Although still unclear and needs further investigation, however, C/D thought to contribute to the occurrence of psoriasis and its flare-ups due to the involvement of immune dysregulation, although C/D inhibits Th17 and Th22 along with the pro-inflammatory agents IL-17 and 22, however, if given in higher dose, for example, in our patient (100 units/m2), seems like giving a paradoxical effect, with increasing cellular immunity [8].

No permanent cure of psoriasis up until now, but a range of treatments can improve symptoms and minimize the appearance of skin lesions. The treatment choice is depending on Psoriasis Area and Severity Index (PASI) score. This score indicates the severity of psoriasis based on three parameters; erythema, induration, and desquamation. Our patient's PASI score is 10, which indicates mild disease. We give our patient high potency topical steroid (mometasone furoate 0.1%) combined with salicylic acid 5% (keratolytic agent), and Vaseline album in order to have better penetration and distribution of the medication, also reducing the scales and softens lesions. We also combined the topical mixture with phototherapy, NB-UVB at 311 nm as the first line treatment. NBUVB leads to decrease pro-inflammatory cytokines and suppressed cutaneous T-cell mediated immune system [9,10].

Conclusion

Diagnosis of psoriasis vulgaris was made based on history and clinical symptoms. Despite its rarity, physicians should be aware of potential of psoriasis to flare up in the setting of the combination of high dose C/D to treat acute myeloid leukemia. Treatment is centred around symptomatic management as needed and continues the chemotherapy treatment.

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