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Case Report

Poikilodermatous Mycosis Fungoides: A Rare Case Treated with Low-Dose Methotrexate

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ABSTRACT

Mycosis fungoides (MF) is a subtype of cutaneous T-cell lymphoma (CTCL) and a primary cutaneous lymphoma. Poikilodermatous MF (PMF) is a rare clinical variant of MF. Systemic chemotherapy, such as methotrexate (MTX), may be administered as monotherapy or in combination at low doses in MF. A 64-year-old man with PMF has been reported. History and physical examination revealed hyperpigmented and hypopigmented macules on the chest, abdomen, both arms, back, and upper legs, along with erythematous macules on the right medial thigh. The diagnosis of PMF is based on clinical manifestations and histopathological features of atypical lymphocyte cell infiltration in the epidermis. In addition, immunohistochemical examination also supports the MF diagnosis. The patient received chemotherapy consisting of monotherapy with MTX at low doses. During the third month of observation following MTX therapy, a few of the hyperpigmented and hypopigmented macules appeared to have diminished; some of the erythematous macules had transformed into hyperpigmented macules, and there were no new lesions. The purpose of therapy is to control the disease. Administration of low-dose MTX as a monotherapy may result in clinical improvement, but further observation is necessary. PMF may have a better prognosis than other clinical variants of MF.

Keywords: Cutaneous T-cell lymphoma, Mycosis fungoides, Poikilodermatous mycosis fungoides, Methotrexate.

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INTRODUCTION

Mycosis fungoides (MF) is a primary cutaneous lymphoma and the most common subtype of cutaneous T-cell lymphoma (CTCL). [1,2] The incidence of MF is reported to be only around 0.4–0.64 per 100,000 people per year.[2] The most common age for MF is over 55 years, and men are more likely than women.[3] Clinical symptoms classify MF into patches, plaques, tumors, and erythroderma. Each stage progresses gradually over time.[3,4] The World Health Organization-European Organization for Research and Treatment of Cancer (WHO-EORTC) has suggested a modified version of MF that takes into account the variations in clinical and histopathological characteristics. This modified version includes classic-type MF, folliculotropic MF (FMF), pagetoid reticulosis, and granulomatous slack skin.[2,5] Non-WHO-EORTC variations classify several subtypes of MF. These include granulomatous MF (GMF), poikilodermatosis MF (PMF), hypopigmented MF, and syringotropic MF.[6] PMF is a rare form of CTCL.[7] Clinical manifestations of PMF include erythematous patches or plaques, hypopigmented and hyperpigmented macular lesions, telangiectasis, and atrophy.[7] It. Although the goal of MF therapy is to impede the progression of the disease, it does not provide life extension.[2] The selection of MF therapy is modified in accordance with the patient's age, stage, and overall health.[2] Therapies for MF in its early stages include intralesional or topical corticosteroids, phototherapy, radiotherapy, and chemotherapy.[2] One form of chemotherapy used to treat early-stage MF is low-dose methotrexate (MTX) and can be given for PMF.

CASE

A 64-year-old male came with the chief complaint of hyperpigmentation macules and hypopigmentation macules on the chest, stomach, arms, back, or upper legs, and also erythematous macules on the inner side of the right thigh, which did not feel itchy, painful, or numb. The lesion started two years ago as hyperpigmentation macules on his right thigh, which did not include pruritus, pain, or numbness. Two months later, the skin lesions developed around the right arm, along with the appearance of hypopigmentation macules on the right rear thigh. One year ago, the patient had developed hyperpigmentation macules in the region of the left arm and thigh, devoid of pruritus, pain, or hypesthesia. New hypopigmentation lesions were observed in the upper legs, stomach, and arms without the presence of pruritus, pain, or hypesthesia. Six months later, the medial right thigh developed erythematous macules, while the stomach and back developed new hyperpigmented macules. The patient came to the dermatologist and was previously diagnosed with ptyriasis versicolor. Patients received medication topically and orally, but there had been no improvement. He had a tremendous amount of sun exposure in the past by working outdoors, yet he has never used any sunscreen or protective apparel. A history of smoking was acknowledged.

The physical examination showed multiple lesions of hypopigmented macules and hyperpigmented macules on the chest, abdomen, both arms, back,

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and both upper legs, with an irregular border, the smallest size being 0.5 x 0.8 cm and the largest size being the size of an adult's palm, clear boundaries, not raised, and dry (Figure 1A,1C, and 1D). On the right medial thigh, multiple lesions of erythematous macules appeared, irregular in shape; the smallest size was 0.2 x 0.3 cm, and the largest size was 5 x 6 cm. Some of the borders were firm, not raised, and dry (Figure 1B).

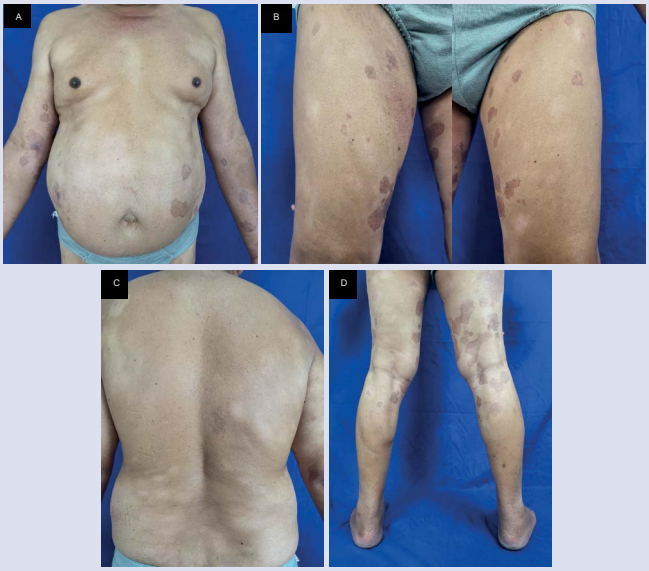

Figure 1. (A,C,D) Multiple hyperpigmentation and hypopigmentation macules over the trunk, arms, back and both posterior thigh (B) Erythematous, hyperpigmentation and hypopigmentation macules on both anterior thigh.

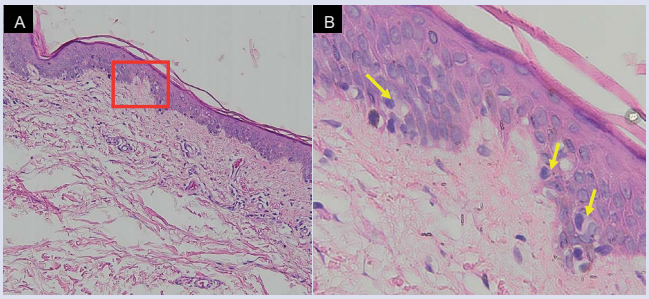

Figure 2. Histopathological examination (A and B) showed atrophy of the epidermis infiltration (red box) and atypical lymphocyte cells in the intraepidermis (yellow arrow).

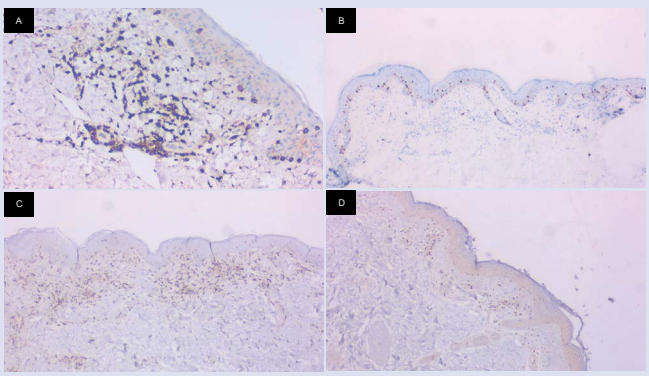

Figure 3. Immunohistochemistry showing CD3-positive (A), CD4-positive (C) with higher ratio than CD8-positive (D), and Ki67-positive (B).

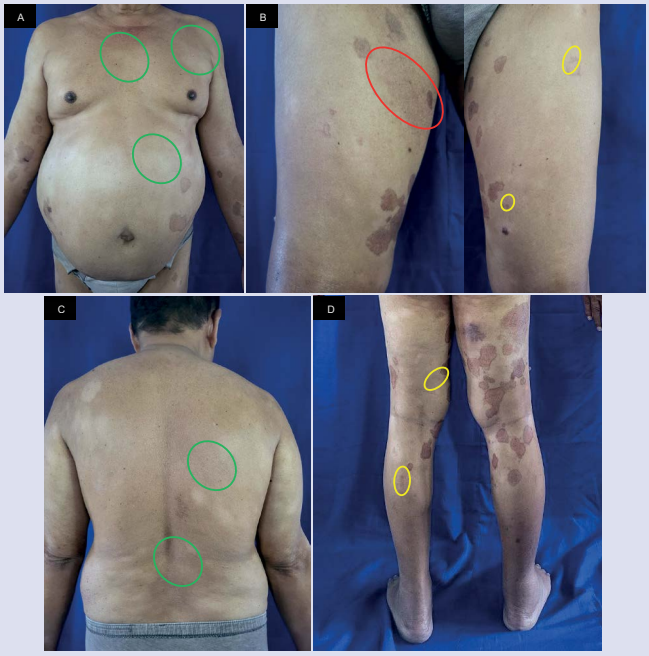

Figure 4. Some of the hyperpigmented (yellow circle) and hypopigmented macules (green circle) have diminished. Erythematous macules (red circle) transformed into hyperpigmented macules. There were no new lesions after the 3rd month of therapy.

All routine hematological and biochemical tests were normal. A peripheral blood smear was negative for Sezary cells. Histopatholgical examination of hyperpigmentation, hypopigmentation, and erythematous lesions revealed atrophy of the epidermis with seen infiltration of atypical lymphocyte cells in the intradermis. There was some dusting of inflammatory cells, lymphocytes, and histocytes, especially in the dermal papillae, including larger lymphocyte cells. Perivascular lymphocytes were also seen (Figures 2A and 2B). The immunohistochemistry showed positivity on CD3 T cells, especially on atypical lymphocyte cells in intraepidermis, and CD4 had a higher ratio than CD8 but was negative for CD20 (Figures 3A, 3C, and 3D). The results also showed positivity on Ki67 (Figure 3B).

Based on the clinical, laboratory, histopathological, and immunohistochemical findings, the patient was diagnosed with poikilodermatous MF, specifically a tumor at stage IB according to the tumor, node, and metastasis classification (T2N0M0). The patient was managed with low-dose methotrexate (15 mg/week). He appeared to have had a good response to the treatment. Some of the hyperpigmented and hypopigmented macules appeared to have diminished, while others that were erythematous underwent a transformation into hyperpigmented macules. No new lesions were observed after three months of treatment (Figures 4A - 4D).

DISCUSSION

Mycosis fungoides was first discovered by a French dermatologist named Alibert in 1806 and named pian fungoides (pian = yaw) because it is similar to yaws. [2] This disease was then called MF because, based on the clinical picture, it has a skin tumor shape that is similar to fungus. [2] MF is the most common CTCL disease.[7] MF disease mainly affects adults, with an age range of 55–60 years.[3] The incidence of MF is more often found in men than women, with a ratio of 1.6:1.[3] In this case, the patient is a 64-year-old man.

The pathogenesis and etiology of CTCL, including MF, are still not fully understood.[2] The etiology that is thought to cause CTCL is divided into endogenous factors and exogenous factors.[1,3] Lifestyle factors such as smoking and consuming alcohol are also considered risk factors for MF.[8] Other epidemiological studies have also found that exposure to ultraviolet radiation is associated with an increased incidence of MF.[8] Varela et al.,[8] in their research, found that workers exposed to sunlight had a higher incidence of MF. In this case, the patient is a 64-year-old man. In this case report, the patient has a history of smoking and a history of long-term sun exposure.

Poikilodermatosis mycosis fungoides is a clinical variant of MF, with clinical manifestations of macules or patches or plaques, hypopigmentation and hyperpigmentation, telangiectasia, and atrophy.[7] PMF is characterized clinically by "cigarette-paper" skin,[9] with a predilection for It involves the flexural areas and trunk,[10] especially the chest, gluteal, and abdomen,[11] but the lesions can also be generally distributed. Lesions may be asymptomatic, mildly itchy (rare), or have a stinging sensation.[11] Lesions develop slowly on pre-existing patches, especially areas that have been scratched or rubbed against clothing.[12] PMF may appear at the same time as classic MF lesions. In this patient, the clinical picture appeared in the form of erythematous macular lesions, hyperpigmented macules, and hypopigmentation macules which could support the diagnosis of PMF.

A histopathological examination can help confirm the diagnosis of MF.[1,2] A typical histopathological picture of MF is Pautrier's microabscess,[1] namely an accumulation of cells with clear boundaries in the epidermis layer, which consists of atypical lymphocytes with polymorphic nuclei.[13] Other histopathological features of MF can be found in the form of atrophy in the epidermis layer,[12] hyperkeratosis or parakeratosis, there is vacuolar alteration in the basal layer,[14] and sometimes Sézary cells can be found.[9] In the dermis layer, there are atypical T cell infiltrates, band-like or perivascular lymphohistiocytic infiltrates, enlarged blood vessels, pigment incontinence, and loss of rete ridges.[9,11] The histopathological evaluation of the hyperpigmentation, hypopigmentation, and erythematous lesions showed epidermal atrophy with the presence of infiltrating atypical lymphocytes in the epidermis. There were scattered inflammatory cells, specifically lymphocytes and histocytes, present in the dermal papillae, including larger lymphocyte cells. Additionally, lymphocytes were observed around blood vessels. The results of the histopathological examination supported the diagnosis of MFP by being correlated with the clinical picture of erythematous macule lesions, hyperpigmented macules, and hypopigmented macules in the patient.

Immunohistochemistry examination in MF is characterized by peripheral T lymphocyte epidermotropism whose phenotype is CD3+, CD4+, and CD8-.[2] Ki-67 is a marker that shows the proliferation of tumor cells.[15] CD4 > CD8 ratio also has high sensitivity and specificity for establishing a diagnosis of MF.[16] The results of the immunohistochemistry examination in this case patient were positive for CD3, CD4, and CD8, with brown color on atypical lymphocytes intraepidermis, however the ratio of were found higher for CD4 than CD8. This results supporting the diagnosis of MF.

Management of MF depends on the stage of the disease, general condition of the patient, age of the patient, choice and experience of the doctor, and availability of treatment.[2] The main goal of therapy is to control progression, achieve remission, and improve quality of life. [2] MF therapy is divided into skin-directed therapy (SDT), systemic therapy, and combination.[17] However, systemic therapy can also be given at an early stage, such as MTX.

Based on the World Health Organization-European Organization for Research and Treatment of Cancer (WHO-EORTC), MTX is second-line therapy in stages IA–IIB (early stage).[18] MTX can be given as monotherapy or as part of combination therapy.[19] Methotrexate is a folic acid antagonist and is also used as a chemotherapy agent in malignant cases.[20,21] The mechanism of action of MTX is by inhibiting folic acid metabolism and inhibiting the action of dihydrofolatase reductase (DHFR).[22] Folic acid is an essential substance for cell growth and replication, while MTX is effective in preventing the growth of malignant cells because MTX can inhibit the synthesis of deoxyribonucleic acid (DNA) in cell mitosis.[22] MTX can be given at a low dose of 10–25 mg/week and an average dose of 15 mg/week for MF.[19] The patient in this case report had an MFP lesion with a generalized distribution, and the patient's condition was limited due to the patient not being able to have routine control, so the patient was given MTX therapy. The patient was given MTX therapy at a dose of 15 mg/week for three months and showed clinical improvement in the form of some lesions fading and no new lesions appearing. The patient plans to continue therapy with monthly therapy evaluations.

CONCLUSION

PMF is a rare clinical entity that presents differently than typical MF. It offers a favorable prognosis and a good response to systemic treatments. MTX can be given for PMF therapy as monotherapy to control disease progression.

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None.

CONFLICTS OF INTEREST

The authors have no conflict of interest to declare.

CONSENT STATEMENTS

The authors acquired explicit written consent from patients to publish their photographs and medical information in both print and online formats, with the acknowledgment that this information may be accessible to the public. The authors have retained the patients' consent forms, although they were not submitted to the journal.

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