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A CASE REPORT: TRANSFORMATION OF ERYTHRODERMIC PSORIASIS TO CUTANEOUS T-CELL LYMPHOMA

LAPORAN KASUS: TRANSFORMASI ERITRODERMA PSORIATIKA MENJADI LIMFOMA SEL T-KUTAN

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ABSTRACT

Background: *Erythrodermic psoriasis (EP) is a severe type of psoriasis, a chronic inflammatory disease characterized by general erythematous condition with thick scale all around the body. The treatment of EP consists systemic medications like cyclosporine or methotrexate and biologic agents, which lately suggested related to the development of cutaneous T-cell lymphoma (CTCL) in severe psoriasis patients.*

Case Report: *A 45-year old, Javanese male was diagnosed previously with EP that transformed to CTCL. His previous history, he was histologically confirmed as psoriasis vulgaris since 2014 and was treated regularly with methotrexate. After 5 years, he gradually suffered several episodes of erythrodermic condition and was diagnosed with erythrodermic psoriasis with unusual pruritic hyperkeratotic plaques and ulcers on his trunks without any general lymph nodes enlargement. Peripheral blood smear showed Sezary cell and histopathology result confirmed CTCL. He was treated with combination of radiotherapy, phototherapy and topical regiments with a good result and acceptable.*

Discussion: *Several studies suggested that severe psoriasis had increased the susceptibility of CTCL, especially with the use of cyclosporine, methotrexate or biologic agents as the treatment. In this case, methotrexate might play role in the development of CTCL or enhanced the transformation of EP to CTCL. Combination of localized radiation therapy, NBUVB and topical therapy gave a quiet good result for the skin condition and increased patient's quality of life.*

Conclusion: *Erythrodermic psoriasis might transform or develop to CTCL which in this case was probably related to the use of methotrexate.*

Keywords*: cutaneous T-cell lymphoma, erythrodermic psoriasis, methotrexate*

ABSTRAK

Latar Belakang. Eritroderma psoriatika (EP) merupakan bentuk psoriasis yang berat dan kronik, ditandai dengan kemerahan disertai sisik yang tebal di hampir seluruh tubuh. Tatalaksana EP terdiri dari pengobatan sistemik sepertik siklosporin atau metotreksat, seta agen biologis, yang akhir-akhir ini diperkirakan berhubungan dengan perubahan bentuk klinis dari psoriasis menjadi limfoma sel-T kutan (CTCL).

Laporan Kasus. Seorang laki-laki, suku Jawa berusia 45 tahun sebelumnya telah didiagnosis sebagai eritroderma psoriatika berdasarkan hasil pemeriksaan histopatologik yang mendukung psoriasis sejak tahun 2014. Pasien mendapatkan terapi berupa metotreksat secara regular. Setelah 5 tahun, pasien mengalami beberapa kali episode eritroderma dan gambaran klinis terakhir, terdapat lesi plak hiperkeratotik anuler disertai dengan ulserasi dan gatal yang hebat. Pada pemeriksaan darah tepi ditemukan Sel Sezary dan pada pemeriksaan histopatologik mendukung diagnosis CTCL.

Pasien diterapi dengan kombinasi radioterapi, fototerapi dan topikal dengan hasil yang memuaskan.

Diskusi. Beberapa penelitian menyatakan psoriasis berat meningkatkan risiko kerentanan menjadi CTCL, terutama pada penggunaan siklosporin, metotreksat dan agen biologi sebagai lini pertama tatalaksananya. Pada kasus ini, penggunaan metrotreksat diduga berperan pada transformasi eritroderma psoriatika menjadi CTCL. Kombinasi terapi dengan radioterapi lokal dengan NBUVB serta terapi topikal memberikan hasil yang cukup baik pada kulit dan meningkatkan kualitas hidup pasien

Kesimpulan. Eritroderma psoriatika dapat mengalami transformasi menjadi CTCL dalam kasus ini diduga akibat penggunaan metotreksat.

Kata kunci: *CTCL, eritroderma psoriatika, metotreksat.*

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BACKGROUND

Erythrodermic psoriasis (EP) is a severe type of psoriasis, a chronic inflammatory disease characterized by general erythematous skin condition covered by thick scales over 80% body surface area.[1] The occurrence of EP is estimated 1 – 2,25% among all psoriatic patients.[2] The pathogenesis of EP is not well understood compared to classic psoriasis vulgaris, which it is caused by abnormal interaction between T-lymphocytes, dendritic cells, keratinocytes, neutrophils, and proinflammatory cytokines, leading to activation of the Th17 and Th1 immune axes. Clinical appearance of EP may consist of erythematous skin condition over 80% of body surface area caused by generalized vasodilatation, oedema, pruritus, thick scales with or without desquamation, nail changes and accompanied by systemic symptoms like fever, chill, tachycardia, malaise, and dehydration.[1,2]

Severe psoriasis, including EP, is usually treated with systemic medication like cyclosporine or methotrexate or even biologic agents to control the skin proliferation and inflammation

processes. in several studies and case reports showed that systemic medications for severe psoriasis may induce the occurrence of cutaneous T-cell lymphoma (CTCL).[3,4] Gelfand et.al. (2006) showed there were a positive relation between psoriasis and CTCL. In this study showed that patients with severe psoriasis had 10.75-fold increased risk to develop CTCL, while patients with mild psoriasis had 4.1 increased relative risk of developing CTCL.[5] It may be related with systemic medication of psoriasis or not.[3]

In this article, we reported a case of patient with previously diagnosed as EP and was treated with methotrexate who lately developed unusual pruritic hyperkeratotic plaques which finally confirmed as CTCL.

CASE REPORT

A 45 years old, Javanese man, with previously histologically diagnosed as psoriasis vulgaris since 2014 and treated with methotrexate 15mg per week. After 5 years he came to hospital with erythrodermic skin condition, with thick scales around his body, shivering and edema in early 2019. At the first, his erythrodermic condition was thought related to his psoriasis (erythrodermic psoriasis). He was hospitalized and treated with systemic corticosteroid (dexamethasone 5mg twice daily), methotrexate 15mg per week and topical potent corticosteroid ointment. The patient was discharged after 5 days of hospitalization with a better condition and was asked to continue medications and revisit to the dermatology clinic a week after discharge.

This patient suffered about 3 times episodes of erythrodermic psoriasis, but at the last episode, he came with unusual hyperkeratotic plaques on his trunk that very itchy and ulcerated (Figure 1 and 2).

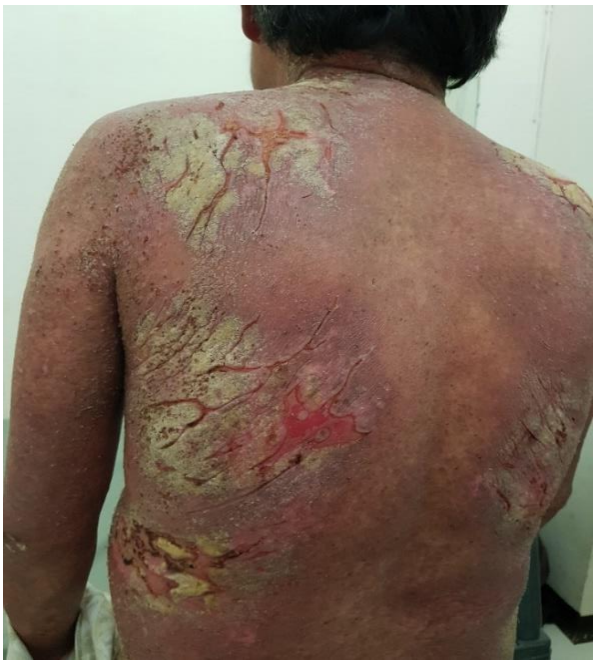

Figure 1. Unusual itchy and ulcerated skin plaques on the patient's trunk. Other skin was generalized erythematous.

In general physical examination, we did not find any lymph nodes enlargement and to determine diagnosis, we performed a skin biopsy for histopathology examination and peripheral blood smear to find Sezary cell. Sezary cells were found in peripheral blood smear and from histopathology findings, the patient was confirmed as CTCL (mycosis fungoides) with epidermal hyperkeratotic with intraepidermal Pautrier microabscess, a bandlike upper dermal infiltrate of lymphocytes and other inflammatory cells (Figure 3). We suggested to do immunohistochemistry to determine CD3+ and CD4+, but unfortunately the patient refused due to economic reason.

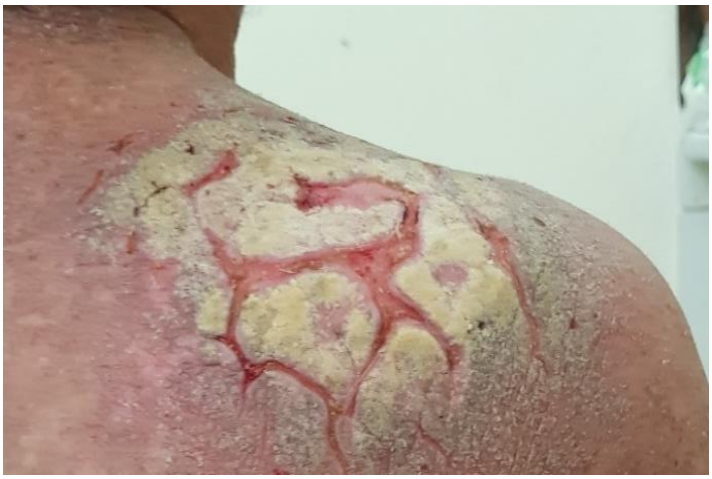

Figure 2. Close up documentation of the skin lesion. Hypertrophic skin plaque with deep fissures and ulceration.

Methotrexate medication for psoriasis was discontinued and then the patient was referred to radiotherapy department to have a sequence treatment of localized radiation therapy for total dose 40Gy. The skin lesions were significantly improved and the patient was returned to dermatology department to continue his medication. Following the radiotherapy, patient was been treated with combination between narrowband UVB (NBUVB) phototherapy (300mJ/cm2) once a week and topical regiment of super potent corticosteroid (clobetasol propionate 0,05%) cream and tretinoin 0,05% cream twice daily.

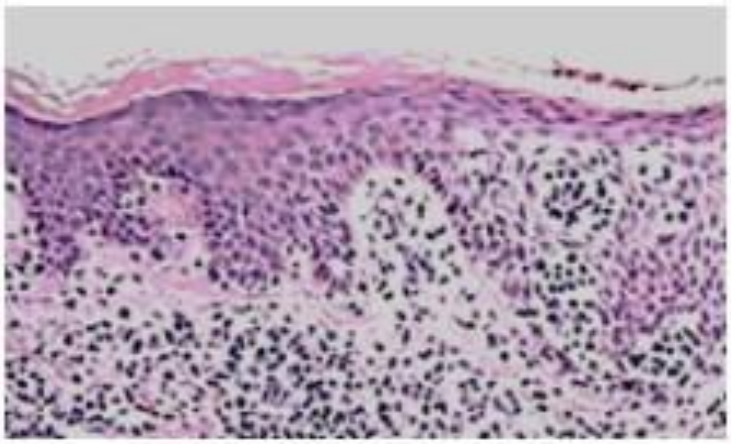

Figure 3. CTCL histopathology

The result of the combination therapy was good and acceptable. The itch complaint was reduced, and the lesions were flat with post inflammatory hypopigmentation (Picture 4 and 5). The patient is under control until now.

DISCUSSION

The diagnosis of CTCL was made based on clinical history, physical examination, laboratory and histopathologic findings. In this patient previous history, he had confirmed psoriasis vulgaris and was treated with methotrexate to control his disease, but later the psoriasis became progressive as erythrodermic psoriasis. The methotrexate was continued as systemic medication due to his psoriatic lesions. This patient suffered several episodes of erythrodermic condition, but at the latest occurred unusual hyperkeratotic plaques that very itchy with fissures and ulcers. This condition leaded us to another diagnosis such as CTCL (mycosis fungoides) that was finally confirmed pathologically and Sezary cells were found. We suspected there was a transformation from erythrodermic psoriasis to CTCL, might be related to methotrexate medication.

Some studies showed that there were relation between psoriasis and CTCL.[3,5] Gelfand et al, (2006) using an unadjusted Cox proportional hazards model showed psoriasis had relative risk to develop lymphomas like Hodgkin's lymphoma, non-Hodgkin lymphoma and CTCL. Mild and severe psoriasis respectively had risk 4,1 and 10.7 times to develop CTCL. It might be related to its pathophysiology, treatments or the combination of those.[5]

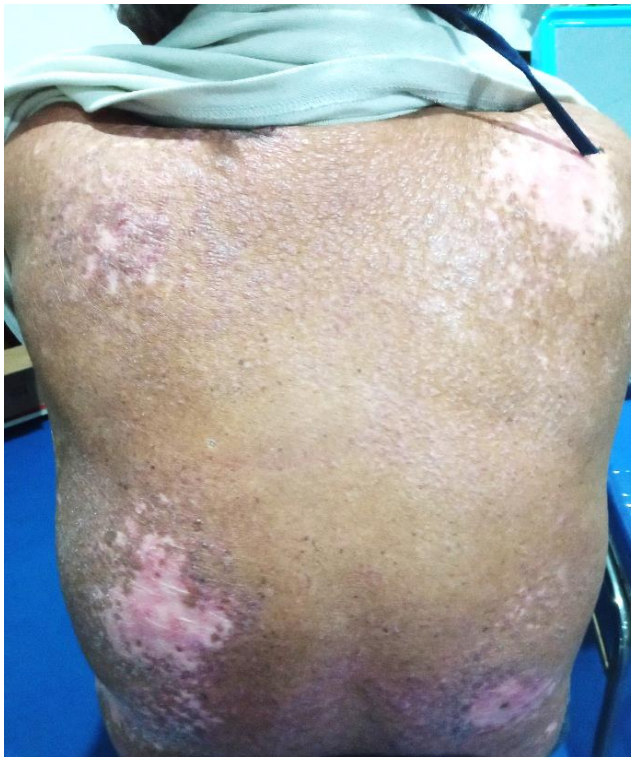

Figure 4. Patient's skin condition after combination treatment of radiotherapy, NBUVB phototherapy and topical regiment.

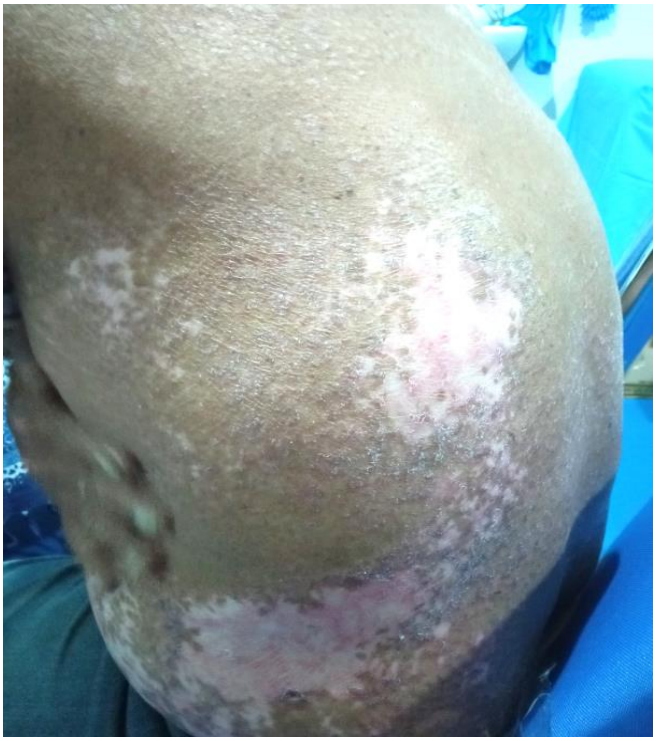

Figure 5. Post inflammatory hypopigmentation after combination therapy

In this case, the patient was confirmed histologically and diagnosed as psoriasis. He was treated with methotrexate and regularly controlled. After 5 years of methotrexate medication, he developed 3 episodes of erythrodermic skin condition and unfortunately we did not perform any skin biopsy and continued managing this patient as erythrodermic psoriasis. It might be one of the pitfalls in diagnosing CTCL. We noticed unusual plaques that very itchy and ulcerated on his trunk and thought out of the box to find another differential diagnosis by performing skin biopsy and peripheral blood smear to find Sezary cells.

According to several studies, psoriasis and CTCL might relate from their pathophysiology which Th1 and Th17 were commonly found in those two diseases. Transformation psoriasis to CTCL might be a result of chronic immune stimulation and lymphoproliferation stimulated by Th1 and Th17 excess activities.[4,6] Severe psoriasis like erythrodermic psoriasis likely had more relatively risk of developing CTCL than the mild form.[5,7]

Several studies postulated systemic medications of psoriasis like cyclosporine, methotrexate, anti-TNF-alfa and other biologic agents, might accelerate the onset and progression of the CTCL on psoriatic patients,[7-9] but other authors still speculated a transformation of psoriasis to CTCL might be caused by immunosuppressive therapies.[9,10] In a literature review conducted by Biondo et.al (2020), showed some studies about relation between psoriasis and CTCL had some bias and limitations such as diagnosis misclassification, the selection of the populations and assessment of psoriasis severity.[7, 11-15]

After being diagnosed as CTCL, this patient was treated with a sequence of localized radiation therapy and then continued with NBUVB and topical regiment with combination of clobetasol propionate and tretinoin. The outcome of the patient was good and acceptable. Management of CTCL is based on the stage. In early stage of CTCL (mycosis fungoides) (I1-IIA), the treatment is using skin directed therapies (SDTs), including topical corticosteroids (TCS), phototherapy, topical chemotherapy or retinoids, and radiotherapy.[16] In this case, there was no lymph nodes enlargement, but Sezary cells was found on the peripheral blood smear. We determined this as CTCL stage IB.

Radiotherapy is one of the best modality to treat CTCL, because CTCL is highly radiosensitive. The cure rate is almost 95%. Radiotherapy may be used as single therapy on single lesion of CTCL but sometimes need to be combined with other treatments. Electron beam therapy is most radiation therapy that frequently used. It delivers radiation primarily to involved skin layers and spares the radiation effect of the deeper tissues and organs.[17,18] Ultraviolet B is known as one of CTCL treatment modality that had been used for over 50 years. It was exclusively used as monotherapy but lately it is used as adjuvant therapy. Narrowband UVB is also used to treat CTCL. It is highly effective with durable response.[19] The USCLC recommended the use of NBUVB for maintenance therapy to decrease relapse rate of CTCL.[20,21]

Retinoids (in this case was tretinoin), is classified as "biological response modifiers" which have many different mechanisms on action for the cancer treatment. Retinoids are non-immunosuppressive and may boost immune function by inducing an antitumor response and may induce apoptosis of the malignant T-cells.[22,23]

Topical corticosteroids (TCS) play role in inhibition of lymphocyte binding to endothelium and intercellular adhesion. They also induce cell death of neoplastic lymphoid cells in CTCL by means of apoptosis.[24] Topical corticosteroid class I, such as clobetasol propionate, is the first choice of TCS used in CTCL[21,24]

Narrowband UVB, tretinoin and clobetasol propionate we used in this case, were classified as adjuvant therapy to maintain and reduce the relapse of the disease.

CONCLUSION

We reported a case of transformation of erythrodermic psoriasis to CTCL that might be related to the pathophysiology itself or even accelerated by methotrexate medication for the psoriasis. We treated the patient with localized radiation therapy followed by NBUVB and topical tretinoin and TCS with a good outcome and acceptable.

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DISCLOSURE

All writers disclosed there is no conflict of interest on this article. We had patient's permission to publish his pictures.

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