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Cutaneus T-Cell Lymphoma in 53 Years Old Woman: Histopathological Features

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Abstract

Cutaneous T-cell lymphomas (CTCLs) are clinically heterogeneous T-cell lymphomas that arise in the skin and are characterized by their clinical and pathological features. The pathogenesis of CTCL is not fully understood. The incidence of CTCL increases significantly with age, with a median age at diagnosis at about 55 years of age and a four-fold increase in incidence appreciated in patients over 70. A 53 year old woman presented with complaints of reddish spots and lumps on her left forearm and back which spread to her chest, stomach and legs. On examination, a lump the size of a golf ball was found on the left forearm and back as well as reddish spots that felt itchy and painful. Histopathological examination with HE staining showed proliferation of lymphoid follicles without a germinal center and monotonous cells of small to medium size partially surrounding the tubular glands in the dermis layer. Immunohistochemical examination revealed positive for CD 45 as well as CD 3 and negative for CD 20. A case of CTCL has been reported in a 53-year-old woman. Histopathological examination and immunohistochemistry are important to diagnose this disease.

Introduction

Cutaneus T-cell lymphoma (CTCL) is a heterogeneous T-cell lymphoma that clinically appears on the skin and is characterized by its clinical and pathological picture (Jawed et al., 2014). *Cutaneus T-cell lymphoma* (CTCL) can mostly be classified as mycosis fungoides (MF) or sezary syndrome (SS) (Bradford et al., 2009; Criscione & Weinstock, 2007). Mycosis fungoides (MF) as the most common CTCL represent 60% to 80% of the entire CTCL while sezary syndrome (SS), variants of erythroderma and leukemia affect less than 10% of patients with CTCL (Kaye et al., 1989).

The pathogenesis of CTCL is not yet fully understood (Willemze et al., 2019). Genetic evidence strongly implies ultraviolet (UV) radiation as a risk factor for CTCL (Elenitoba-Johnson & Wilcox, 2017; Park et al., 2021). Epidemiological studies have been conducted but have been less successful in identifying other environmental or viral-related risk factors for most CTCL subtypes with the exception of *Human T-Cell Lympotrophic Virus type-1* (HTLV-1) infection in adult T-type leukemia/lymphoma cells (Whittemore et al., 1989). Recent research suggests that drugs can induce antigen-triggered or discriminatory T cell lymphoproliferation (Jahan-Tigh et al., 2013; Magro et al., 2003).

The incidence of CTCL increases significantly with age with the median age at diagnosis being about 55 years and a four-fold increase in incidence occurs in patients over 70 years of age (Agar et al., 2010; Bradford et al., 2009). Although CTCL can occur in children and young

adults, it is very rare and is often associated with histopathological variants of MF (Jung et al., 2021). CTCL incidence is more common in men and blacks than in women (Bradford et al., 2009). Patients with CTCL have a higher incidence of secondary malignancies, including other non-Hodgkin lymphomas, lung cancer, bladder cancer and melanoma, so they require proper screening (Goyal et al., 2020).

In this case report, we reported a case of CTCL in a 53-year-old woman with clinical manifestations in the form of a lump that appeared on the left forearm and back then enlarged to the size of a golf ball and appeared reddish patches that felt itchy on the patient's chest, abdomen and legs without being accompanied by pain. The purpose of this case report is to know and understand CTCL cases from the perspective of histopathological images.

Methods

A 53-year-old woman was consulted by an international colleague to the Dermatology and Venereology department of the Regional General Hospital (RSUD) Dr. Moewardi Surakarta with complaints of lumps on the left forearm and back since 2 months ago. Two months earlier, a marble-sized lump appeared on the left arm that felt itchy, then the patient scratched the lump and became a wound. The patient did not treat the complaint. One week earlier, the patient complained of a new lump next to the breast. The lump that had been there since 2 months ago grew to the size of a golf ball and appeared reddish patches that felt itchy on the patient's chest and abdomen without being accompanied by pain. Patients also complained of reduced appetite and weight loss of 6 kg in the last 2 months. The patient complained of more and more lumps appearing on the back and side of the patient's breasts accompanied by pain. Redness spots begin to spread to the patient's legs. Then by international colleagues, the patient is consulted to the dermatology and venereology department for further treatment.

The patient had no previous history of similar complaints or a history of malignancy, hypertension, diabetes mellitus, and a history of food and drug allergies. In the patient's family, there was also no history related to similar complaints, malignancy, hypertension, diabetes mellitus, and allergies to food and medicines.

Physical examination found that the general condition was good, compost consciousness, blood pressure 123/81 mmHg, pulse 82/min, respiration 20x/min, temperature 36.6◦C, body weight 60 kg, height 160 cm, body mass index 23.4 kg/m2 *(normoweight)* and pain scale 2. There was no enlargement of lymphonody, liver or lien. The dermatological status of the mammary region, back, arms and both legs appears to have multiple, solitary, various-sized plaques and nodules, with an ertical base that secretes a clear odorless fluid accompanied by pain and itching (Figure 1).

The differential diagnosis in this case is *primary cutaneous follicle center lymphoma* (PCFCL), *primary cutaneous marginal zone B-cell lymphoma*, and *cutaneous T cell lymphoma* (CTCL). The patient was then carried out a supporting examination in the form of a histopathological examination using *a* biopsy punch 4.0 to help establish the diagnosis on April 5, 2023. In the macroscopic preparation, there is 1 piece of skin tissue derived from the antebrachia sinistra region measuring 0.5 cm.

A microscopic examination using Hematoxylin and Eosin (HE) staining on April 5, 2023, showed that no abnormalities were found in the epidermal layer. In the dermis layer, a proliferation of lymphoid follicles without *a germinal center* was found. Monotonous cells of small to medium size partially surround the tubule glands (Figure 2).

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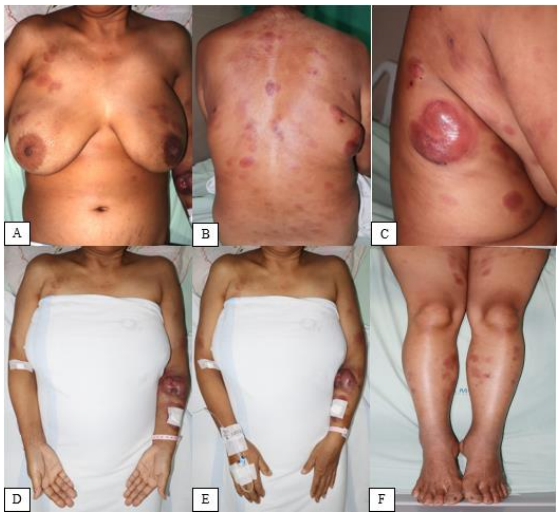

Figure 1. The mammary region (A), back (B-C), sinistra arm (D-E), and both legs (F) appear to have multiple, solitary, various-sized plaques and nodules, with an ertical base that secretes a clear, odorless fluid accompanied by pain and itching

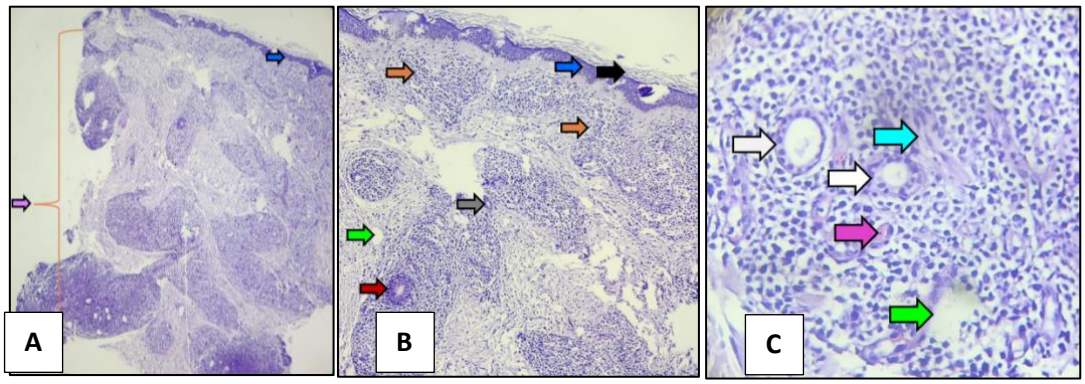

Figure 2. (A). There are no abnormalities in the epidermal layer of the skin. Tumor cells appear in the dermis layer (4x magnification); (B). Tumor cell granulomas (orange arrow) and hyperkeratosis (black arrow) (10x magnification) were seen; (C). Tumor cells appear to press the glandular tubules surrounded by monotonous cells (40x magnification).

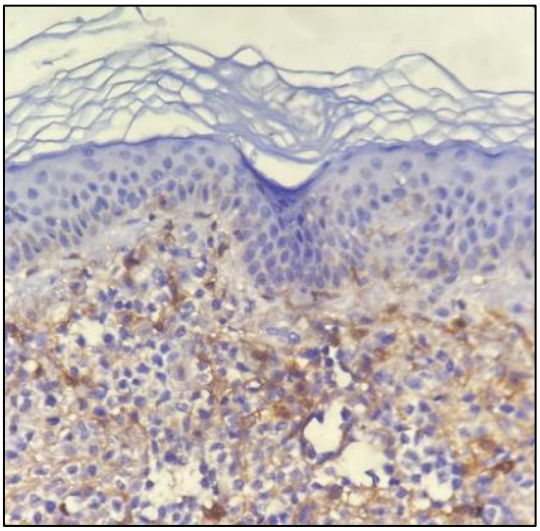

Figure 3. Positive CD45 immunohistochemical examination (40x magnification)

Other supporting examinations carried out are immunohistochemical examinations with CD45, CD20 and CD 3 which are carried out on April 14, 2023, positive results were obtained on CD

45 and CD 3 while negative results were obtained on CD 20 (Figure 3). The conclusion of histopathological examination results with staining HE, CD40, CD 20 and CD 3 supports the diagnosis of CTCL.

Based on the anamnesis, physical examination and histopathological examination in this patient leads to the diagnosis of CTCL. The patient was then consulted to the internal medicine department and received methamizole injection therapy 1 gram/8 hours, *glycyrrhizin* injection 2 amp in 100cc NS/24 hours, curcuma 1 tab/8 hours PO, albumin 1 caps/8 hours PO and wound treatment with mupyrosin 2% ointment and urea 10% on dry skin areas.

Result and Discussion

Cutaneus T-cell lymphoma (CTCL), characterized by malignant monoclonal T lymphocyte infiltration of the skin, is considered a heterogeneous group of extraneodal non-Hodgkin lymphomas. The skin is the most common place after the digestive system (Nahidi Y, Meibodi NT, Ghazvini K, 2015). The annual incidence of CTCL is about 0.5 per 100,000 and males are more affected than females (1.6:1 to 2.0:1). The mechanism of disease progression is unknown (Maj et al., 2015). Dysregulation of some genes and signaling pathways has been reported in CTCL, but its pathogenesis is unknown (Katona et al., 2013).

The International Society for Cutaneous Lymphomas/European Organization for Research and Treatment of Cancer classifies CTCL into MF and SS based on the clinical, pathological, biological and immunological picture (Devata & Wilcox, 2016). Diagnosis of CTCL is difficult in the early stages due to the presence of multiple clinical images and the lack of definitive diagnostic criteria. Therefore, in most cases, it takes an average of 6 years from the onset of the disease to the diagnosis (Kirsch et al., 2015). In the case, dermatological status and histopathology are examined with eosin hematocycline (HE) staining and immunohistochemistry.

Classic mycosis fungoides initially appear with erythematous patches and/or plaques with predilection on areas protected from the sun including the breast, buttocks, lower trunk and inguinal area and in MF patients can develop into skin tumors, erythroderma or systemic diseases with nodal, blood or visceral involvement (Hristov et al., 2023). In patients, there are nodules and reddish *patches* in the lower left arm region, breast, back, abdomen and both legs that feel itchy and painful.

Most patients with CTCL have a less clear and diverse histological picture, making it difficult to distinguish this disorder from other benign inflammatory diseases (Nahidi Y, Meibodi NT, Ghazvini K, 2015). Halo lymphocytes, exocytosis, epidermotropism, *pautrier* microabscesses, convoluted large hyperchromic lymphocytes in the epidermis and parallel lymphocytes in the basal layer are findings seen in the histological part of the MF (**Fig. 4**) (Pankratov et al., 2015). The results of the patient's histopathological examination showed that there were no abnormalities in the epidermal layer. In the dermis layer, a proliferation of lymphoid follicles without *a germinal center* was found. Monotonous cells of small to medium size partially surround the tubule glands.

Immunohistochemistry is important for the diagnosis of skin lymphoproliferative disorders. These examinations can identify cell lineages from the neoplastic process. The antibodies used should include T cells (CD3, CD45 RO, CD4 and cytotoxic/suppressive CD8 subtypes), B cells (CD20 and CD79a), their subtypes (CD5, CD10 and bcl-6), *natural killer* cells (CD56), histiocytes (CD68) and antigen-presenting cells (S100 and factor 13A) (Slater, 2001). Immunohistochemical examination of patients carried out with CD45, CD20 and CD 3 obtained positive results on CD 45 and CD 3 while negative on CD 20.

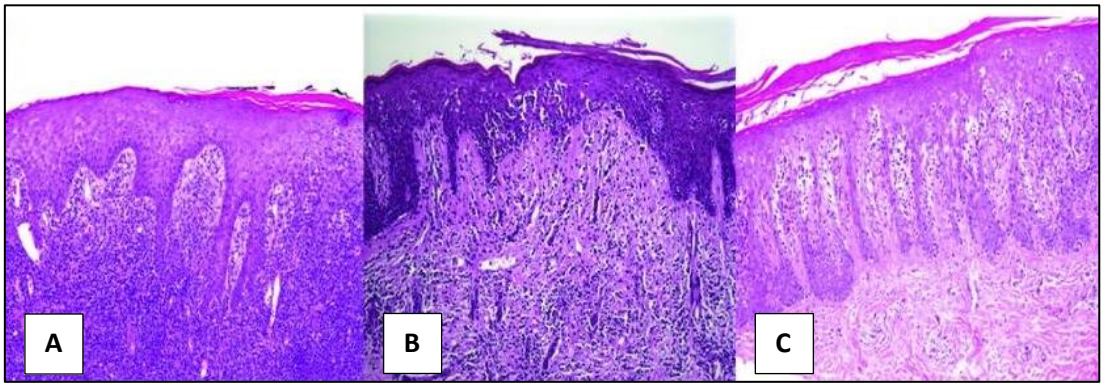

Figure 4. Histopathological picture of CTCL type MF (A) lymphocyte infiltration in the dermis and extending to the epidermis (B) lymphocytes with a circle around them on the epidermis as single cells and small groups with minimal spongiosis (C) psoriasiform epidermal hyperplasia with halo lymphocyte epidermotropism.(Kash et al., 2016)

There is no known cure for MF and SS therefore, the treatment options are mostly palliative (Ahmed et al., 2016). Treatment goals include relieving symptoms, promoting remission, and delaying disease progression while reducing significant side effects caused by therapy modalities(Choi et al., 2015). Corticosteroids in topical and systemic form are effective in treating CTCL (Nguyen & Bohjanen, 2015). Retinoids are effective in treating CTCL through anti-proliferation and apoptotic triggering effects. chemotherapy agents that have been used to treat CTCL include methotrexate, chlorambucil, gemcitabine, and pegylated doxorubicin (Olsen et al., 2016). Radiotherapy is an effective skin-directed therapy for the treatment of CTCL (Goddard et al., 2015). In this case, the patient was given therapy with 1 gram of matomizole injection/8 hours, *glycyrrhizin* injection 2 amps in 100cc NS/24 hours, curcuma 1 tab/8 hours PO, albumin 1 cap/8 hours PO and wound care with mupyrrosin ointment 2% and urea 10% on dry skin areas.

The prognosis of CTCL is influenced by several factors, including age, gender, stage, area of skin involved, disease progression and laboratory factors related to proliferation. Although there are several therapeutic options for CTCL, as the disease progresses and becomes refractory to treatment, malignant cells have a tendency to infiltrate the lymph nodes and peripheral blood vessels, resulting in a debilitating condition. Progression to the tumor stage in which neoplastic cells spread to lymph nodes and internal organs has been reported in less than 5% of CTCL cases (Rook et al., 2015).

Conclusion

A 53-year-old woman came in with complaints of lumps on her left forearm and back followed by patches on her breasts, abdomen and both legs that felt itchy and painful. Histopathological examination with HE staining showed a picture of the proliferation of lymphoid follicles without *germinal centers* in the dermis layer accompanied by small to medium monotonous cells partially surrounding the tubule glands. In immunohistochemistry examinations, positive review results were obtained on CD 45 and CD 3, but negative review results were obtained on CD 20. The histopathological conclusions in this case support the diagnosis of *cutaneous T-cell lymphoma* (CTCL).

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