

A Rare and Fatal Case of Cutaneous T-Cell Lymphoma (CTCL)

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ABSTRACT

Introduction: Cutaneous T-Cell Lymphoma (CTCL) is a form of Non-Hodgkin Lymphoma involving T-cell neoplasms mainly concentrated in the skin. Primary Cutaneous Peripheral T-Cell Lymphoma is Not Otherwise Specified (PTL-NOS) is the rarest case of CTCL disease.

Case Presentation: A female, 35 years old, complained of a lump on her face. In the last 3 months, the lump felt soft, contained a liquid that, when it ruptures, secretes Blood, and the crusty scar will blacken and easily bleed with pain. Physical examination of pale conjunctiva on the face, neck, chest, abdomen, back, and legs obtained nodules with a chewy consistency with erythema appearance in varying size. Some nodules that appear were covered in blackish crustae. The right lung has a decrease in the sound of breath, accompanied by swelling in both limbs. The conclusion of bilateral femur skin biopsy impresses cutaneous T lymphoma cells. Within three months, cancer developed into lesions spread almost throughout the body, and due to the rapid and progressive nature of cancer, its diagnosis developed into PTL-NOS.

Conclusions: Patients with PTL-NOS may come with solitary nodules such as red tumors in any area of the body. However, most often, patients come with symptoms of multifocal or diffuse scattered nodules. In enforcing the diagnosis, it takes a high level of suspicion, and multiple rebiopsies are necessary to enforce the diagnosis of CTCL.

INTRODUCTION

Cutaneous T-cell lymphoma (CTCL) is a heterogeneous group of lymphoproliferative disorders characterized by the clonal accumulation of neoplastic T lymphocytes in the skin. The incidence is higher in the African-American group and more in men than in women [1]. Cutaneous lymphoma is a proliferation of clonal T-cell lymphocytes or rarely from a natural killer (NK). Cutaneous lymphoma is classified based on variations in clinical manifestations, histopathology, immunophenotyping, and prognosis. One-fourth of cases of Non-Hodgkin's lymphoma are extra-nodal lymphoma. Cutaneous lymphoma is the second most abundant extra-nodal lymphoma after gastrointestinal lymphoma. The incidence is estimated at 1: 100,000 [1–3].

The etiology of cutaneous lymphoma is mostly unknown. However, there are several risk factors for the occurrence, namely immunodeficiency (the severe combination of immunodeficiency, hypogammaglobulinemia, common variable immunodeficiency, Wiskott Aldrich syndrome, and ataxia telangiectasis), infectious agents including Epstein-Barr virus (EBV), exposure to herbicides and organic solvents, foods high in animal fat, smoking, and exposure to ultraviolet light [3,4].

Clinical manifestations of spots, plaques, or tumors can be present simultaneously in the patient. At the stage of the tumor, lesions appear in various places with predilection such as on the face, body folds, and armpits; in women, there are areas under the breasts. This begins with a CTCL plaque or spot which develops into a malignant phase. At this point, the cells have behaved in a biologically malignant manner by spreading and expanding into nodules. This event is thought to be the development of a malignant T-cell clone. These nodules are red-brown or bluish-red, often present with ulcers, and can be a secondary infection. Ulcers in these tumors heal on their own. The development of these nodules is variable. Patients with tumors tend to develop aggressively. According to medical literature, cases have been reported in which individuals developed more than one form of CTCL at the same time [2].

For those with suspected lymphoma as suggested by their history and clinical examination, various diagnostic tests may be recommended. These may include biopsies, blood tests, specialized imaging tests, and/or additional tests [3,4].

Treatment for cutaneous lymphoma is given according to the symptoms and CTCL staging. Topical chemotherapy

(nitrogen mustard), electron beam therapy, psoralen with ultraviolet light (PUVA), and retinoids are given for skin involvement. The systemic therapy regimens provided include CVP (cyclophosphamide, vincristine, prednisone), CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), or FND (fludarabine, mitoxantrone, and dexamethasone). Purine analogs, interferon α , denileukin diftitox, or antibody therapy may also be given. The prognosis is based on the extent of skin exposure, its type and involvement of the lymph nodes, and metastases to other tissues [3,4].

CASE PRESENTATION

A 35-year-old woman came to the emergency room of Mas Amsyar Kasongan General Hospital because she complained of a soft red lump on the face and neck for three months before going to the hospital. The lump initially was not realized by the patient and only appeared on the neck and behind the ear, but over time, it was felt to get bigger accompanied by complaints of fever. The lump felt soft and was filled with fluid that bled out when it burst, and the crusty scars

blackened and bled easily with pain. This lump multiplied over time and appeared all over the body with varying sizes. The patient also admitted that along with the appearance of the lump, there were complaints of a decrease in appetite and weight loss. She sometimes felt tired and congested with activities. The patient slept in a half-sitting position using a high pillow.

Physical examination showed compos mentis awareness that looked moderate sick, GCS 4-5-6, blood pressure 100/70 mmHg, HR 110x/minute, RR 26x/minute Tax: 37.20C, and Sp.O2 98%. Physical examination showed pale conjunctiva. On the face, neck, chest, stomach, back, and legs, there were nodules with spongy consistency erythema that appeared in varied sizes; some nodules appeared to be covered with blackish crustae. The right lung has decreased breath sounds accompanied by swelling in both legs. Laboratory examination in February 2020 showed anemia (8 gr/dl), MCV (98.8fl), MCH (32.4 pg), thrombocytopenia (147.000/ul), lymphopenia (15.4%), monocytosis (22.4%), LDH (3535 U/L), and hypoalbuminemia (2.4 g/dl).

The timeline of the disease progression can be seen in **Figure 1**. From physical examination and laboratory

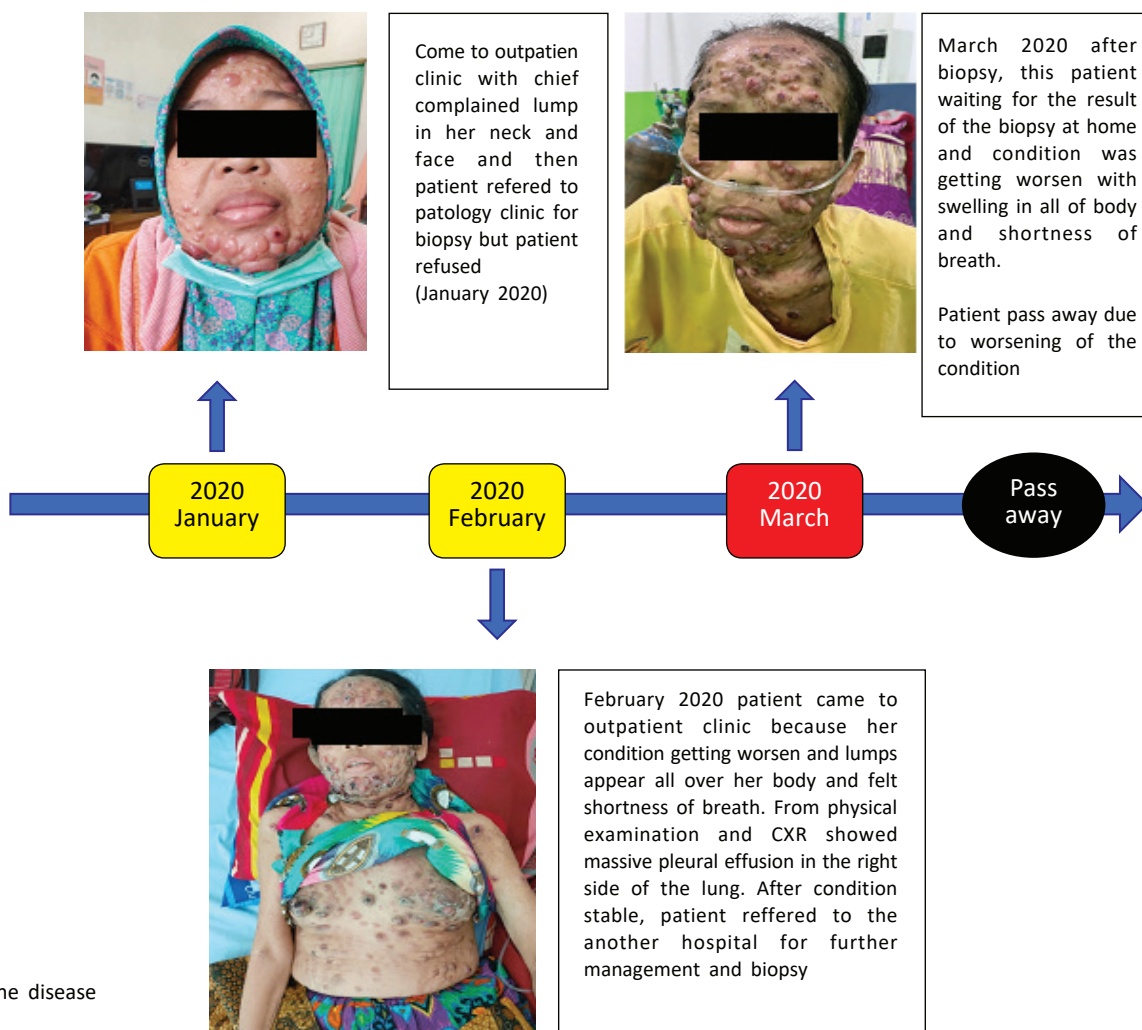


Figure 1.
The timeline of the disease progression

results, she was diagnosed with multiple nodules suspected of skin cancer with macrocytic anemia, hypoalbuminemia, and pleural effusion with suspected pulmonary metastases (Figure 2). The patient was then referred for an anatomical pathology examination.

The patient was then referred to the Anatomical Pathology section for the examination of a skin biopsy. Biopsy tissue was taken from a bilateral femoral region. The results showed a macroscopic image of a small tissue on the left and right thighs (Figure 3). The microscopic image also showed the same picture in the form of a piece of tissue with a partly atrophic epidermis, micro-abscesses in the epidermis, and dermis lymphoid cells with relatively uniform round nuclei, coarse chromatin. Conclusions suggest Cutaneous T-cell lymphoma. It is recommended to do an immunohistochemical examination, namely the CD3+ examination.

DISCUSSION

In the case of suspected cutaneous lymphoma, the essential part is the diagnosis to differentiate the lesions that are found to be benign or malignant. Furthermore, the diagnosis will affect the treatment and prognosis of the patient [5]. The diagnosis should always be made based on a combination of physical examination, immunohistochemical examination, and histopathology. Additional supporting investigations in the form of immunohistochemical techniques of molecular biology are often required [6,7]. Cutaneous lymphoma is a proliferation of neoplasia of T or B lymphocytes, NK cells, and plasmacytoid dendritic cells in the skin [8]. Cutaneous lymphoma is a part of Non-Hodgkin's lymphoma and the second most common extranodal non-Hodgkin's lymphoma after Non-Hodgkin's lymphoma

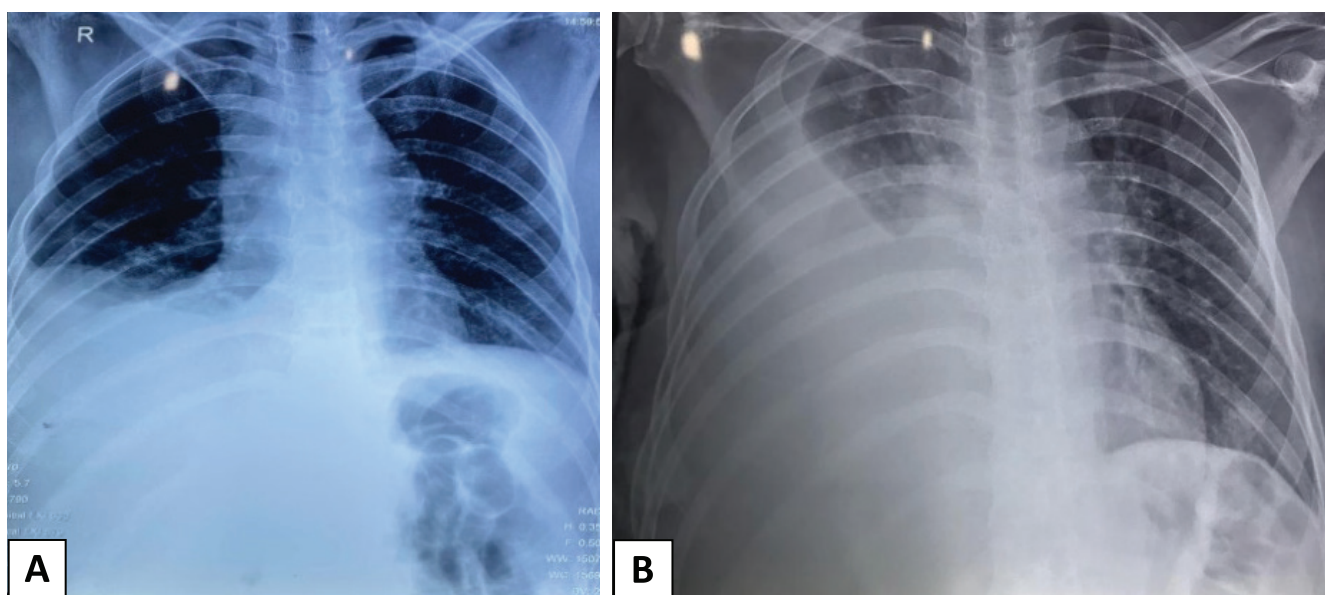


Figure 2. A. Chest X-ray posteroanterior position at one month after the appearance of the lump shows a minimal right pleural effusion; B. Posteroanterior position chest X-ray at three months since the first complaint showing right massive pleural effusion.

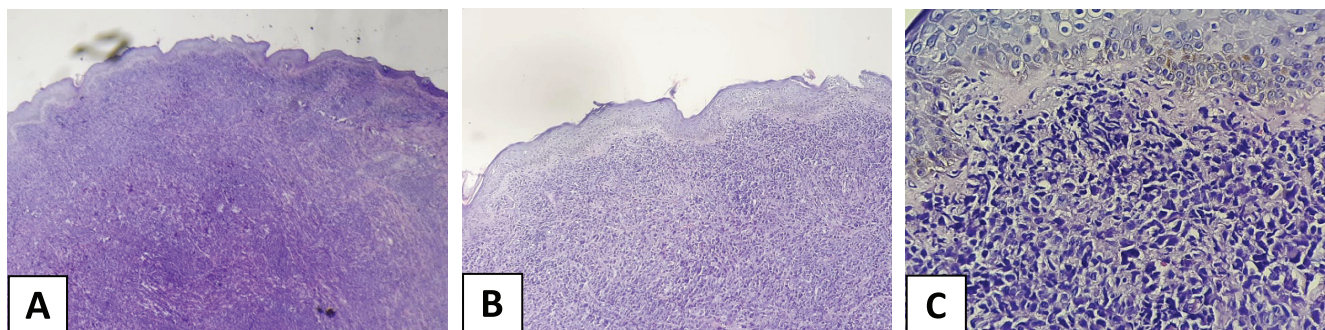


Figure 3. A and B show the macroscopic image of the lump biopsy small tissue on the left and right thigh; C shows the microscopic image atrophic epidermis, micro-abscesses in the epidermis and the dermis lymphoid cells with relatively uniform round nuclei, coarse chromatin

in the digestive tract. Cutaneous T-cell lymphoma was found in 75–80% of all cases of cutaneous lymphoma while 20–25% of cases are cutaneous B cell lymphoma [9].

The signs and symptoms associated with Cutaneous T-cell lymphoma vary greatly according to the case, the specific type of lymphoma present, and the disease progression. Cutaneous T-cell Lymphoma (CTCL) is a form of Non-Hodgkin's Lymphoma that involves T-cell neoplasms mainly concentrated in the skin. CTCL can vary widely in clinical presentation, prognosis, and histological and immunophenotypic descriptions [10]. The most common forms of CTCL are Mycosis Fungoides and Sezary's Syndrome, which account for approximately 65% of all CTCL cases. However, Primary Cutaneous Peripheral T-Cell Lymphoma is Not Otherwise Specified (PTL-NOS) is the rarest case of CTCL disease. According to the medical literature, cases have been reported in which individuals developed more than one form of CTCL at the same time [11].

The diagnosis of CTCL is based upon a thorough clinical evaluation, detection of certain symptoms and physical findings, a detailed patient's history, and a variety of specialized tests. Such testing is necessary to confirm the specific type (and subtype) of CTCL to assess the nature and extent of the disease and determine the most appropriate treatments [12]. In this case, because the patient's disease progresses rapidly and progressively and the problem of diagnosis, the patient does not have time to get therapy according to the type and staging of the disease.

PTL-NOS is a subtype of peripheral T-cell lymphoma. Peripheral T-cell lymphoma (PTCL) is defined as a diverse group of aggressive lymphomas that develop from mature white blood cells called T-cells and NK cells. PTCL occurs when T-cells develop and grow abnormally. About 30% of PTCL-NOS shows malignant T-cells infected by EBV. However, the relationship between EBV and the development and progression of PTCL-NOS related to EBV remains unclear [12].

Classification of CTCL types of T-cells or NK cells are based on their manifestations (cutaneous, extranodal, nodal, and leukemic). The cutaneous type includes mycosis fungoides (MF), transformed MF, Sezary syndrome, primary cutaneous CD30+ T-cell disorder, primary cutaneous gamma/delta TCL. The extranodal type includes NK/TCL nasal type, enteropathy-associated TCL, and subcutaneous panniculitis-like TCL. Nodal type includes peripheral TCL-NOS, anaplastic large cell lymphoma (ALK +/-), and angioimmunoblastic TCL. Leukemic type includes adult T-cell leukemia/lymphoma, aggressive NK-cell leukemia, T-cell prolymphocytic leukemia, and T-cell large granular lymphocytic leukemia [10,12].

PTCL-NOS is a subtype of PTCL that is aggressive and predominantly nodal. Patients with PTL-NOS may present with a nodule that is solitary like a red tumor

on any area of the body. However, most often, patients present with diffuse or multifocal scattered nodule symptoms [10]. Many of these tumors become ulcerated and infected. Rapid (progressive) spread of skin tumors and systemic involvement are the main features to watch out for PTL-NOS as this type has a contributing five-year survival rate of less than 20% [10,11].

PTL-NOS may be challenging to diagnose because of the variability of immunophenotypes, most of which are CD4 positive. The CD 30 phenotype is usually rare or absent, and CD56 can be found positive but very rarely. Histopathologically, PTL-NOS shows nodular or diffuse infiltrates, moderate to the large size of pleomorphic and immunoblastic T-cells [9].

On the histopathological examination, atypical lymphocytes, or lymphoid cells, which vary in size from small to large, infiltrate the dermis and sometimes subcutaneously. Epidermotropism may occur. Angiocentric and angiodestruction are evident with extensive necrosis [8,9,13].

Immunohistochemical examination can use staining CD2 +, CD3 +, CD4 +, CD5 +, CD7 +, CD8 +, CD56 +, CD2 +, CD7 +, CD8 + staining showed the presence of atypical proliferation of T-cells and NK cells while CD3 +, CD4 +, CD5 + showed the presence of atypical T-cell proliferation. To state that the cancer cells were the atypical proliferation of NK cells, CD56 + staining was used [10,14]. In the case of PTL-NOS, age of more than 60 years, ECOG score (Eastern Cooperative Oncology Group) of more than or equal to 2, and LDH (lactate dehydrogenase) indicate increased bone marrow involvement and are independent predictors to assess a decrease in the survival rate [15]. The patient did not have time to undergo immunohistochemical examination and chemotherapy. The disease was progressing very rapidly and progressively, and the patient's condition did not meet the criteria for chemotherapy based on the Karnofsky score.

Due to the fast-growing nature of PTL-NOS, the therapies that can be done are systemic chemotherapy and/or stem hematopoietic cell transplantation. Because PTL-NOS is aggressive, most other treatments for CTCL such as interferon-alfa, retinoids, PUVA light therapy, and local radiotherapy can be given [16]. Systemic therapy regimens that can be administered include CVP (cyclophosphamide, vincristine, and prednisone), CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), or FND (fludarabine, mitoxantrone, and dexamethasone). Purine analogs, denileukin diftitox, or antibody therapy may also be given. The prognosis is based on the extent of skin exposure and its type and involvement of the lymph nodes and metastases to other tissues [3,4]. Previous studies have shown that cytokine therapy such as interferon-alpha is useful for mycosis type CTCL fungoides and Sezary syndrome but

ineffective for PTL-NOS therapy and can lead to worsening conditions [17]. Even with systemic chemotherapy and stem cell transplantation, the prognosis is still inferior in PTL-NOS cases [18].

Patients are given palliative or symptomatic therapy to reduce complaints such as morphine for cancer pain, WSD for pleural effusion, albumin transfusion for hypoalbumin, and PRC transfusion for anemia. The diagnosis was made based on anamnesis and physical examination where nodules or lumps (tumors) of varying sizes were found in various places such as on the face, chest, abdomen, back, and upper and lower extremities. These nodules are red-brown or bluish-red, often present with ulcers, and can be a secondary infection. Ulcers in these tumors heal on their own. The development of these nodules is variable. Tumors tend to develop aggressively.

CONCLUSIONS

Patients with PTL-NOS may come with solitary nodules such as red tumors in any area of the body. However, most often, patients come with symptoms of multifocal or diffuse scattered nodules. In enforcing the diagnosis, it takes a high level of suspicion, and multiple rebiopsies are necessary to enforce the diagnosis of CTCL. This case report was made for clinicians to be more careful in establishing the diagnosis so that patients get the right therapy and disease progression can be prevented.

DECLARATIONS

Competing of Interest

The authors declare no competing interest in this study.

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