

## CASE REPORT

# The importance of histopathology findings in lymphomatoid papulosis

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## Abstract

Lymphomatoid papulosis, part of the controversial group of cutaneous lymphoproliferative pseudolymphoma disorders, raises important clinical and histopathological problems. It is a chronic, recurrent, clinically characterized by papular necrotic lesions and papulo-pustular nodules, sometimes self-limiting and characterized by histopathological changes suggestive of cutaneous lymphoma (CD30-positive). Since its introduction, in 1968, the term "lymphomatoid papulosis" was subject to dispute in terms of classification in malignancies, premalignant or benign skin disease. We submit for consideration the case of a man with papulo-necrotic skin lesions evolving for about one year with post therapeutic remission and relapses, with histopathology of lymphomatoid papulosis. The evolution under systemic glucocorticoids has been favorable, with remission of skin lesions in about three months without relapses to date.

**Keywords:** lymphomatoid papulosis, cutaneous pseudolymphoma, skin biopsies.

## Introduction

Lymphomatoid papulosis (LyP) is a chronic cutaneous disorder, recurrent, self-limited, characterized by papular skin lesions and papulo-pustular necrotic nodules with histological features suggestive of malignant lymphoma (CD30+) [1]. Lymphomatoid papulosis is part of primitive CD30+ lymphoproliferative skin diseases, forming alongside lymphomas with anaplastic large primitive cell (C-ALCL) the second largest group of cutaneous T-cell lymphomas (25% of cases) [2]. This group includes cases previously diagnosed as regressive atypical histiocytosis, rare cases of primitive skin Hodgkin's lymphoma.

The first citation of this clinical entity dates from 1968 and is described by Macaulay [3], was presented continue contradictions on the benign/premalignant or malignant condition of the disease. LyP represents approximately 15% of cutaneous T-cell lymphoma (CTCL).

It is now considered a cutaneous T-cell lymphoma with reduced malignancy having the clinical and histological features in common with the primitive cutaneous anaplastic large cell lymphoma, including the presence of T-lymphocyte (LyT) with aberrant phenotype and cell clones with TCR aberrant gene in 60–70% of patients [1, 4].

## Aim

This paper aims at reporting the importance of histopathology findings in a case of lymphomatoid papulosis, at discussing the significance of early diagnosis and treatment planning and at presenting our option for the diagnosis algorithm in order to ensure a close cooperation between the dermatologist and the pathologist.

## Patient, Methods and Results

In the context of the above-mentioned theoretical data, we present the case of a male patient, aged 26, with insignificant pathological history who came in the Clinic of Dermatology, "St. Spiridon" Emergency Hospital, Iassy, Romania, for papulo-pustular necrotic lesions, asymptomatic, localized at the right temporal area, with a tendency to confluence, occurring about two months ago.

We have verbal and written informed consent from the patient for publication of the case, including photos.

From the patient's history emerges earlier diagnosis of deep folliculitis. The culture made of purulent secretion covering the lesion showed presence of *Pseudomonas aeruginosa*. Based on these results was established systemic treatment with antibiotics according to the antibiogram, topical treatment with antibiotics, ointments with favorable evolution, the skin lesions healing with alopecia scar. Four–five weeks after the onset, papular skin lesions reappeared in the periphery of necrotic scar area, which resulted in patient hospitalization into the Clinic of Dermatology, "St. Spiridon" Emergency Hospital, Iassy, to complete the investigation and establishment of therapeutic conduct.

On admission in the Clinic of Dermatology, physical examination revealed atrophic purplish scars with peripheral papular, papulo-necrotic and ulcerated lesions, localized on the temporal and zygomatic area, scar alopecia and discrete symptoms characterized by pain and stinging (Figure 1).

Laboratory investigations conducted at the admission into the Clinic of Dermatology were normal, except for the isolation of methicillin-resistant *Staphylococcus aureus*



sensitive to Linezolid, Vancomycin, Teicoplanin in the secretion from the wound. The imaging investigations were without pathological changes.

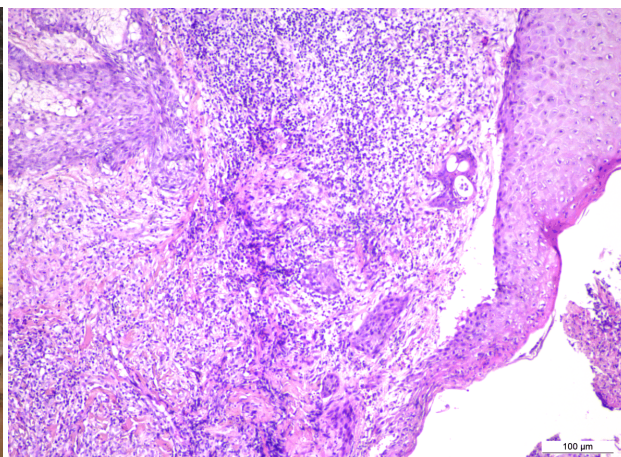
Skin biopsy was performed in the right temporal lesion localized with taking a nodular lesions with central necrosis area. Cutaneous histopathological result showed fragment showing a large area of ulceration covered by fibrin-leukocyte exudate. In the base of the ulceration, occupying almost all the derm, a polymorphous infiltrate is present that combines small lymphocytes, eosinophils

and large lymphocytes with vesicular nuclei with a central eosinophilic nucleolus. Cells show focal Sternbergoid allure. Mitotic activity is low (Figures 2 and 3).

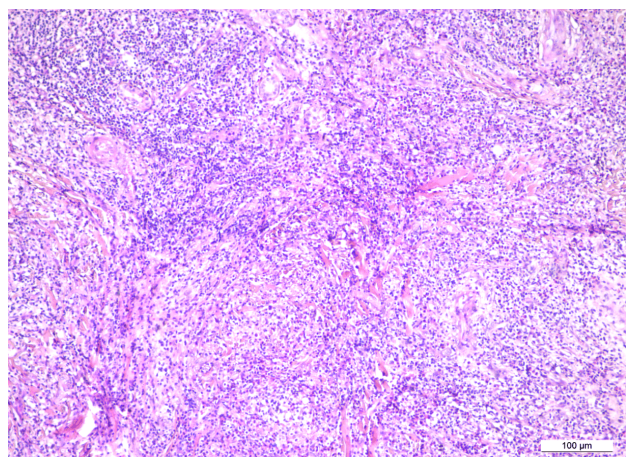
Immunohistochemistry (IHC) indicates CD30-positive large cells, nucleoli, CD3, CD5-positive in most cells in the dermal infiltrate, CD20-positive in rare lymphocytes, CD8-positive in rare small lymphocytes, CD15-negative in tumor cells and positive in granulocytes (Figures 4–8). IHC also indicates CD5-positive in most cells in the dermal infiltrate and negative in the perilesional tissue.



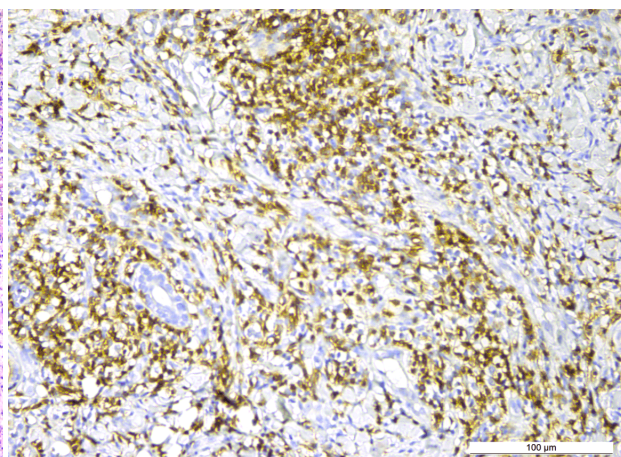
**Figure 1 – Clinical aspect.**



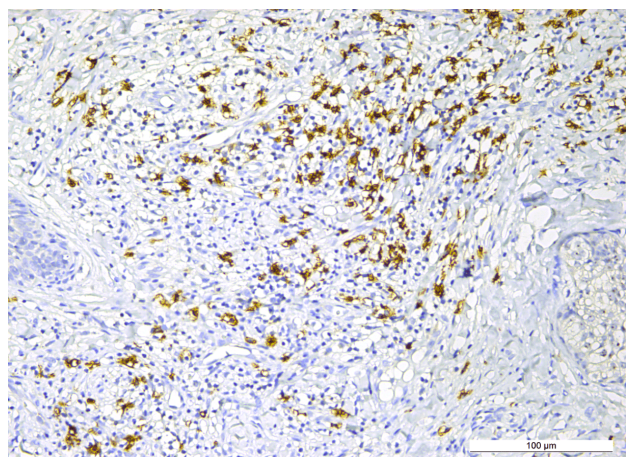
**Figure 2 – Epidermis with ulceration with polymorphous inflammatory infiltrate. HE staining, ×40.**



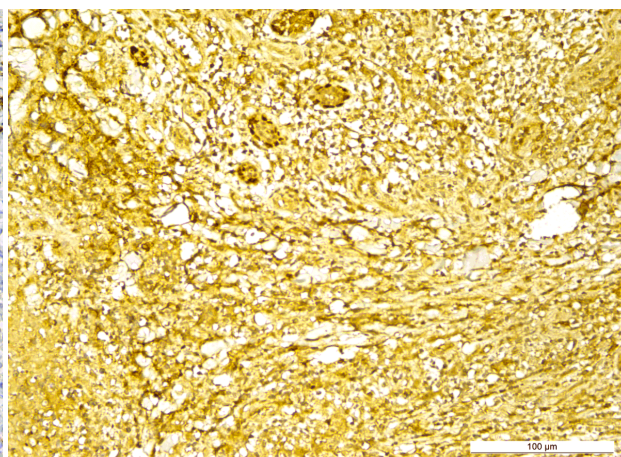
**Figure 3 – Epidermis with ulceration with polymorphous inflammatory infiltrate. HE staining, ×100.**



**Figure 4 – Immunohistochemistry CD3-positive in most cells in the dermal infiltrate. CD3 immunohistochemistry, ×200.**

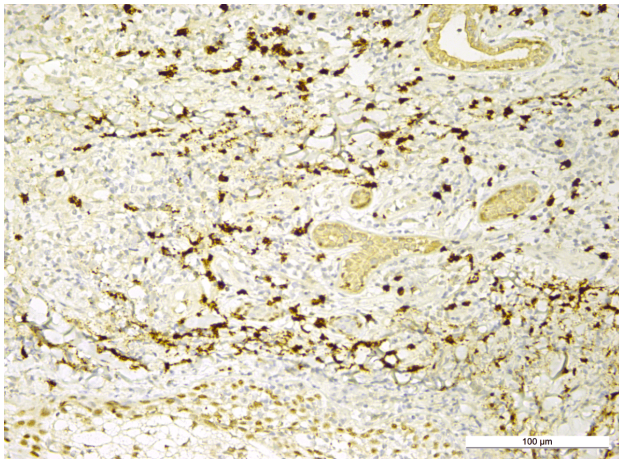


**Figure 5 – Immunohistochemistry CD20-positive in rare lymphocytes. CD20 immunohistochemistry, ×200.**

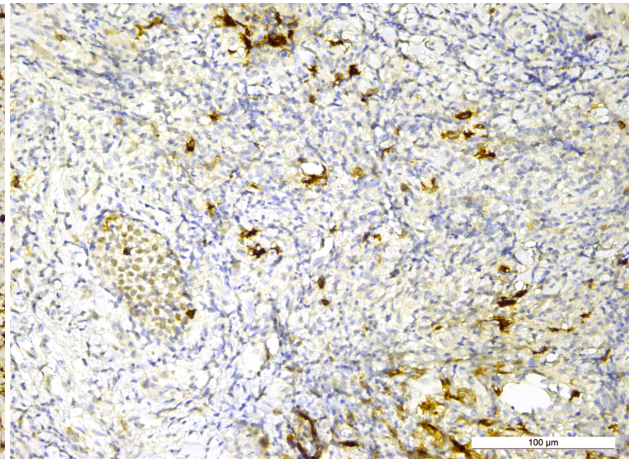


**Figure 6 – Immunohistochemistry CD5-positive in most cells in the dermal infiltrate. CD5 immunohistochemistry, ×200.**





**Figure 7 – Immunohistochemistry CD30-positive large cells, nucleoli. CD30 immunohistochemistry, ×200.**



**Figure 8 – Immunohistochemistry CD15-negative in tumor cells and positive in granulocytes. CD15 immunohistochemistry, ×200.**

Morphological and IHC associated clinical and evolutionary aspects led to the diagnosis of lymphomatoid papulosis type A.

In view of the therapeutic regimen, a consult in hematology-oncology service was made and they advise us to initiate therapy with Prednisone 60 mg/day, 10 days, with lowering of doses every 10 days, followed by control in the hematology-oncology outpatient facility.

Evolution was favorable, with the remission of skin lesions, remission maintained at the control at one, three and six months.

## Discussion

The peak incidence of cases of lymphomatoid papulosis is in the fifth decade of life, being a rare disease among children and youth. The youngest patient reported in the literature is 8-month-old and the oldest 84 years large studies indicating an average age of 35–45 years, gender ratio males/females – 15.5/1 [1].

Despite the appearance of a severe pathological examination, vital prognosis is good in most cases, 20% of patients having the risk of developing malignant lymphoma and non-lymphoma cancer [5].

Lymphomatoid papulosis etiology, as well as all cutaneous lymphomas is obscure, but among trigger factors we can include viral infections, also studies for HTLV-1, EBV, HSV 1, 2, 6 were inconclusive [6].

The common clinical manifestations of lymphomatoid papulosis are the reddish brown papules or nodules that develop central hemorrhage/necrosis and spontaneous resolution in 3–8 weeks. Usually, the clinical examination revealed skin lesions in various stages of development, with a variable number of between a few injuries to a few hundred. The location can be on defined areas, which are arranged in groups, but can be found disseminated lesions, the areas of choice beings represented by the trunk and limbs. Evolution is toward spontaneous regression, with hypo/hyperpigmentation or atrophic varioliform scars. Also described was the healing without scars. Skin lesions are commonly asymptomatic [1, 6].

The evolution of the cutaneous lesions may vary from several months to decades, at 20% of patients lympho-

matoid papulosis rash may be preceded or followed by other cutaneous or systemic lymphoma such as mycosis fungoides (MF), primary cutaneous anaplastic large cell lymphoma (C-ALCL), or Hodgkin's lymphoma [6].

It is well known the possible spontaneous regression of cutaneous lesions of lymphomatoid papulosis. The mechanism of this regression is unknown; the suggested interaction of CD30 and its ligand (CD30L) may contribute to neoplastic T-cell apoptosis and regression of neoplastic lesions. The absence of TGF- $\beta$  inhibitor response due to a mutation encoding the type I TGF- $\beta$  receptor in CD30+ tumor cells is one of the factors incriminated in the progression of the tumor [4, 7].

The cases of lymphomatoid papulosis must be differentiated from skin involvement in systemic ALCL, MF CD30+, other well-defined cutaneous T-cells lymphoma expressing CD30+, and some pseudolymphoma, insect stings, viral infections, scabies, atopic dermatitis and other [1, 6].

Diagnostic algorithm of CTCL cases, including those of lymphomatoid papulosis, requires corroborating clinical criteria with histopathology and phenotyping [1, 8].

The first stage includes differentiation on clinical criteria between MF, MF variant, Sezary syndrome, and other CTCL, the dermatologist knows best their clinical manifestations. This step allows the identification of approximately 65% of cases of CTCL, represented by the MF and its variants. Also, in this step can be included clear cases with clinical characteristic of lymphomatoid papulosis [1].

The second step requires examination of skin biopsies, assessing the presence of CD30. The group of conditions being identified includes lymphomatoid papulosis, anaplastic large cell lymphoma and skin is about 25% of the cases CTCL [1]. Most cases present a very good prognosis and can be controlled and monitored by the dermatologist.

Knowledge of clinical criteria for diagnosis of characteristic cutaneous manifestations for CTCL allows identifying approximately 90% of cases of CTCL by these first two steps. The remaining 10% is the rare cases of T-cell lymphoma (cutaneous peripheral lymphoma,

subcutaneous paniculitis-like, epidermotropic aggressive cytotoxic CD8+ T-cells, and other) [9].

Lymphomatoid papulosis treatment is in most cases unsatisfactory recorded relapse after discontinuation of therapy. In determining the therapeutic management must be weighed the advantages and disadvantages of short-term therapy and the adverse effects [10]. In line with this, patients with fewer lesions do not require treatment, and small lesions, the cosmetic impact can benefit from low-dose MTX (5–20 mg/week), PUVA, Mechlorethamine (nitrogen mustard) or topical Carmustine (BCNU), low-dose Etoposide. Extensive skin lesions may remit spontaneously in 4–12 weeks, but can benefit from surgical treatment/radiotherapy [1].

Our case deserves to be discussed because of its features: onset age – 26 years, as being under the average age identified in clinical trials, the particular location of the lesions on the scalp and beard, with the location of the lesions, the association with *P. aeruginosa* and methicillin-resistant *S. aureus*, which led to a delay in positive diagnosis.

Evolution of skin lesions included spontaneous resolution [11–13]. The resolution of the lesions, unrelated with the antibiotic therapy instituted, resulted in misleading the medical practitioner, considering this development as a therapeutic effects of the substances administered. Relapse occurred shortly and put a question mark on the positive diagnosis. The pathological examination decided the diagnostic and led to the establishment of an appropriate treatment.

Lymphomatoid papulosis cases requiring long-term medical surveillance, due to numerous relapses recorded [11, 14, 15].

## ✉ Conclusions

Lymphomatoid papulosis is a chronic cutaneous disorder, recurrent, rarely seen in dermatological practice. The diagnostic must be established by a team: dermatologist and pathologist, but the dermatologist have the essential role in diagnostic, the dermatologist who based on clinical criteria demands histopathological examination, raising the suspicion of a possible lymphoma. Also, the histopathological examination in only step two in the diagnosis algorithm in our case it was the most important fact that establish the correct diagnosis.

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