Diagnostic Challenges and Treatment Options for Cutaneous T Cell Pseudolymphoma: A Case Study with Rituximab Treatment

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Patient: Female, 46-year-old
Final Diagnosis: Cutaneous T cell pseudolymphoma
Symptoms: Enlarged cervical lymph nodes
Medication: —
Clinical Procedure: —
Specialty: Hematology

Objective: Rare disease
Background: Pseudolymphoma is a rare disorder that can mimic lymphoma both clinically and histologically. It usually affects middle-aged females. Since pseudolymphoma is a rare disorder not only is diagnosing the condition difficult, but there is also a lack of standardized treatment guidelines. In the literature, anti-CD20 monoclonal antibody rituximab is described as an effective treatment option.

Case Report: 46-year-old female fell ill suddenly with swelling and enlargement of her chin. Multiple skin biopsies were done, which were re-evaluated multiple times as well. Each ended with a new diagnosis for the patient. Finally, in the last revision of biopsy material, pseudolymphoma was confirmed. The patient received multiple courses of corticosteroid treatments – locally and systemically – without long lasting effect. After diagnosis of pseudolymphoma, the patient was started on intravenous rituximab and this treatment was effective.

Conclusions: Cutaneous pseudolymphoma is a diagnostic challenge. Rituximab is a treatment option for refractory pseudolymphoma. Since there are no treatment guidelines for pseudolymphoma, more clinical studies are needed to establish best treatment options for these patients. Therefore, each reported clinical case is important.

MeSH Keywords: Genes, T-Cell Receptor • Pathology • Pseudolymphoma

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Background

Cutaneous pseudolymphoma is a term used to describe skin lesions that have some clinical and/or histopathologic resemblance to lymphoma [1]. There are B cell pseudolymphomas, T cell pseudolymphomas and pseudolymphomas of mixed cellularity [2]. Historically multiple lymphoproliferative disorders affecting skin have been classified by different authors and textbooks under the term “pseudolymphoma” with different names, including Castleman disease, Kimura disease, pseudomycosis fungoides, actinic reticuloid, lymphocytoma, Jessner’s lymphocytic infiltration, and many others [1,3,4]. This creates a diagnostic problem and challenges pathologists in proper histological diagnosis. In case of suspected cutaneous pseudolymphoma, diagnosis is backed by negative T-cell receptor rearrangement [5]. Pseudolymphoma can present as solitary nodule or plaque or as disseminated lesions, with the localized type usually seen in middle-aged females [6,7]. Pseudolymphoma usually is a benign hyperplastic lymphocyte reaction to known or unknown antigen stimulus. These factors are associated with the development of pseudolymphoma: acupuncture, body piercing, Borrelia burgdorferi infection, insect bites, hirudotherapy and tattoos [4,6,8,9]. Since pseudolymphoma is a rare disorder not only is diagnosing the condition difficult, but there is also a lack of standardized treatment guidelines and various approaches are used, including topical, intralesional and systemic corticosteroids, psoralen and ultraviolet A therapy, and others [5]. In the setting of refractory cutaneous pseudolymphoma, we found at least 4 articles that described anti-CD20 monoclonal antibody rituximab as an effective treatment option [10–13]. There are known cases of pseudolymphoma progression to malignant lymphoma, especially if the antigen stimulus continues, so regular follow-up is mandatory [5,14].

Case Report

Our patient was a 46-year-old female who fell ill suddenly on April 1, 2016. In the evening our patient, while watching TV at her home, felt that her chin was suddenly growing in size. She then took pictures of her face with her cellphone at once. The chin area was tender to a touch, and slight cyanosis was visible (Figure 1). The patient did not have fever or any other complaints. The patient observed red maculopapular rash without pruritus in the affected area 3 years prior to this. From the patient’s history, we know that partial thyroidec- tomy was carried out in 2013. There are no other comorbidities in the patient’s history. The patient was a non-smoker and rarely used alcohol, there was no data on substance abuse in the patient’s history.

The patient first turned to a local dermatologist for help, and subsequently, she received antibacterial treatment with amoxicillin and antihistamines (chloropyramine) orally, and local treatment with acidum fusidicum ointment was started. The patient’s condition did not improve with this treatment, so at the beginning of May 2016, the patient was hospitalized in the Department of Dermatology and treatment with systemic intravenous glucocorticosteroids was started (intravenous dexamethasone for 4 days). While receiving this treatment the clinical picture improved and the patient was discharged. The patient’s symptoms returned when the treatment with glucocorticoids was discontinued.

Figure 1. Patient in April 2016 – initial changes.
In August 2016, the first skin biopsy from the chin was performed, where lymphocytoma was described: rich skin infiltration with T lymphocytes (CD3+) and focal CD20 positivity. This material was later reviewed twice by other pathologists. The first of these reviews concluded that histologically there was no evidence of lymphoproliferative disorder and suggested a possible diagnosis of connective tissue disorder. The second pathologist suggested a diagnosis of pseudolymphomatous folliculitis and noted the same infiltration with CD3+ T lymphocytes. Because definite diagnosis was not found, the skin biopsy was repeated in November 2016. This biopsy material was revived by 2 pathologists as well. The first one described inflammatory changes in the dermis with inflammation spreading in the hypodermis and muscle tissue, again noted no signs of lymphoproliferative disorder. The second pathologist reviewed this material on February 2017 and diagnosed the patient with small T lymphocyte lymphoma with monoclonal CD4+ T lymphocyte infiltration.

Approximately at the same time, the patient developed submandibular lymphadenopathy with diameter up to 1.8 cm. At the beginning of March, a lymph node biopsy was performed, and the skin biopsy was repeated for a third time. The histopathology answer from the lymph node biopsy was chronic nonspecific lymphadenitis. In skin biopsy, low grade T cell lymphoma was described again: morphological and immunohistochemical picture more consistent with primary skin small to medium sized CD4 positive T cell lymphoma. Later this material was reviewed by pathologists in Germany at Cologne Institute of Pathology; they find nonspecific changes in the lymph node biopsy. The skin biopsy was described as follows: the skin is covered with regularly matured squamous epithelium. In addition to larger necrotic areas, a mixed inflammatory infiltrate of lymphocytes, plasma cells, and eosinophilic granulocytes is observed mainly in the subcutis. The lymphocytes consist predominantly of CD3+ T cells, mainly CD4+ T helper cells but also some CD8+ cytotoxic T cells but are regularly mixed with CD79a positive B cells that show focal agglomeration (Figure 2). The cells show no signs of malignancy, no activated CD15 and CD30 positive B cells are found. Neither T-cell receptor loss is detected by

Figure 2. Immunohistochemistry of patient’s skin biopsy shows predominantly CD3+ T cells (A), most of them are CD4+ T helper cells (B), but some are CD8+ cytotoxic T cells (C), these cells are mixed with CD79a positive B cells that show focal agglomeration (D). (Magnification 200×).
immunohistochemistry nor is monoclonal rearrangement observed in molecular analyzes of the infiltrate. In summary it is classified as pseudolymphoma of the skin.

During different stages of investigation, the patient received prednisolone orally with short breaks (30 mg and lower doses), oral methotrexate for 10 weeks (dose unknown), but the resulting effect had been incomplete and non-persistent (Figure 3). During this period, the patient also received several cosmetic procedures, including laser therapy, without effect (Figure 4).

After confirming a diagnosis of pseudolymphoma, the patient was started on intravenous rituximab monotherapy 375 mg/m² once a week for 4 weeks. The patient’s condition on this treatment improved significantly – skin infiltration decreases: reduced swelling, redness and cyanosis (Figure 5). Treatment was finished in May 2018 and the patient has been symptom-free for 16 months.

**Discussion**

Pseudolymphoma is a rare disorder that can mimic lymphoma both clinically and histologically. It usually affects middle-aged females – as was the case with our patient. Due to diagnostic difficulties, our patient’s quality of life suffered because of late diagnosis and the need for multiple repeated biopsies. The final diagnosis of cutaneous pseudolymphoma was confirmed only when excluding T cell receptor rearrangements, thus excluding malignancy. This assay was important in differentiating between different lymphoproliferative disorders. It must be said that not only T cell receptor rearrangement...
assessment is important, but histopathology examination as a whole. As seen in our patient’s case, the experience of the pathologist or team of pathologists involved is also extremely important in diagnosing such a rare condition. If the lesions of cutaneous pseudolymphoma are on the face, as in our patient’s case, it can severely affect the patient’s quality of life due to the cosmetics defect. This is one of the reasons why in such cases, treatment should be started. Secondly, treatment is needed because pseudolymphoma can progress further into malignant disorder, like lymphoma. Since there are no guidelines for cutaneous pseudolymphoma management and treatment, after reviewing the available sources, it was decided to start treatment with rituximab, which was successful, and more than a year after the treatment was completed, there were no relapses. Several cases of successful treatment of cutaneous pseudolymphoma using rituximab have also been described in the reviewed literature.

Conclusions

Cutaneous pseudolymphoma is a diagnostic challenge. Rituximab can be used as a treatment option for corticosteroid-refractory cutaneous pseudolymphoma. Since there are no treatment guidelines for pseudolymphoma, more clinical studies are needed to establish best treatment options for these patients.

Conflicts of interest

None.

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