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Molluscum contagiosum infection with features of primary cutaneous anaplastic large cell lymphoma

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Abstract

CD30+ T cell pseudolymphomas (CD30+ PSL) are a group of benign inflammatory cutaneous disorders that can develop in settings of viral infections or drug reactions. Owing to their histological similarities to malignant lymphomas, these benign infiltrates are occasionally misdiagnosed as malignant, causing significant concerns for patients and physicians. Herein, we report a patient with CD30+ PSL associated with molluscum contagiosum whose initial biopsy revealed atypical large CD30-expressing cells, leading to a misdiagnosis of primary cutaneous anaplastic large cell lymphoma and referral to our cutaneous lymphoma clinic. We report this case to demonstrate that reactive CD30+ infiltrate associated with molluscum contagiosum can be mistaken for T-cell lymphomas and patients should be reassured in these cases.

Keywords: molluscum contagiosum, primary cutaneous anaplastic large cell lymphoma, CD30+ T cell pseudolymphoma, CD30+ lymphomatoid infiltrate, reactive lymphoproliferative disorder

Introduction

Molluscum contagiosum (MC) is a cutaneous viral infection caused by a member of the *Molluscipox* genus of the poxviridae family [1]. It often presents as firm, flesh colored papules with central umbilication. In children and healthy adults, the infection usually presents as single or multiple discrete lesions, whereas in immunosuppressed patients, it often presents as hundreds of papular lesions [2]. Classically, lesions occur on the trunk, axillae, antecubital fossa, and popliteal fossa.

In most patients, MC is a clinical diagnosis that relies on detecting the classic clinical features. When biopsied, typical MC histopathology demonstrates a hyperplastic epidermal invagination with cells containing intracytoplasmic eosinophilic bodies, referred to as "molluscum bodies" [3]. In most cases, the surrounding dermis reveals little inflammatory infiltrate. Presumably, an exuberant anti-viral immune reaction is not formed owing to formation of membranous sacs surrounding the virion colonies within the infected epidermal cells. However, the molluscum bodies occasionally rupture and upon dermal exposure, a mononuclear or neutrophilic infiltrate develops [4]. A more exuberant inflammatory lymphomatoid reaction consisting of CD30+ cells can sometimes be seen in association with MC [5-9].

When a CD30+ lymphomatoid infiltrate develops in association with MC, there is a potential to misdiagnose the infiltrate as a malignant CD30+

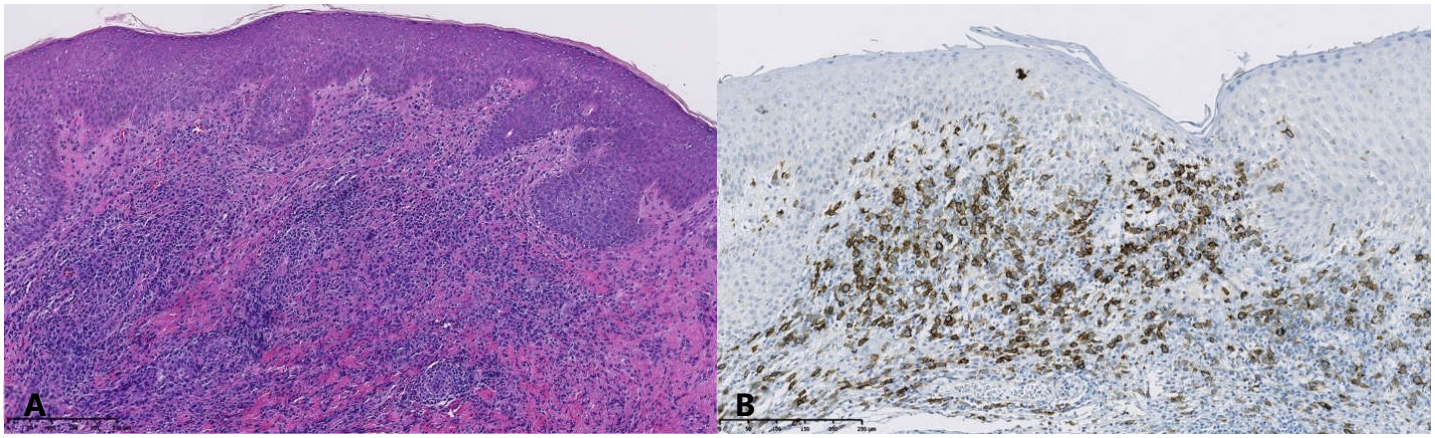

Figure 1. ***A)*** *Histopathology showing a dermal infiltrate consisting of atypical large cells with irregular nuclear contours and prominent nucleoli. H&E, 100×.* ***B)*** *Infiltrate consisting of atypical CD30+ large cells. CD30 immunohistochemistry, 130×.*

neoplasm resulting in unnecessary workups and unnecessary concerns for patients and physicians. Herein, we report a patient with MC who was initially misdiagnosed as having a primary cutaneous anaplastic large cell lymphoma (pcALCL).

Case Synopsis

A 50-year-old healthy woman was referred to our specialty lymphoma clinic for evaluation of histologically diagnosed primary cutaneous anaplastic large cell lymphoma (pcALCL), a malignant CD30 expressing cutaneous lymphoma, of the groin. She reported the development of persistent asymptomatic "pink bumps" on her genital area for the past few months. The patient denied pain, pruritus, fever, fatigue, or changes in weight or appetite. She visited her gynecologist and underwent biopsy of one of these lesions revealing histological features suggestive of pcALCL.

Histopathological evaluation demonstrated a dermal infiltrate consisting of atypical CD30+ large cells with irregular nuclear contours and prominent nucleoli (**Figure 1**). Atypical cells exhibited positive staining for CD4, CD5, and Ki67 as well as loss of CD7. She underwent additional workup including a normal positron emission tomography-computed tomography scan and peripheral blood flow cytometry. Polymerase chain reaction did not detect a monoclonal T-cell population within the skin. Human T-cell leukemia virus type I titers were negative. She was then referred to our lymphoma clinic for further management. Upon examination, we discovered several firm, small pink or skin colored papules on the left groin (**Figure 2A)** and right suprapubic area in addition to one umbilicated papule on the left inguinal crease.

A second biopsy in our clinic revealed the presence of cup-shaped epidermal invaginations containing molluscum bodies in keratinocytes (**Figure 2B)**. Dermal atypical CD30+ large cells were appreciated, leading to a diagnosis of CD30+ pseudolymphoma associated with MC. Her lesions were treated with 5% topical imiquimod five times weekly for 6 weeks and subsequently resolved.

Case Discussion

CD30, a transmembrane receptor of the tumor necrosis factor family, is highly expressed in a spectrum of reactive and malignant lymphoproliferative disorders of the B and T cell lineages [10]. CD30 expression on atypical large lymphocytes is a hallmark of several T cell

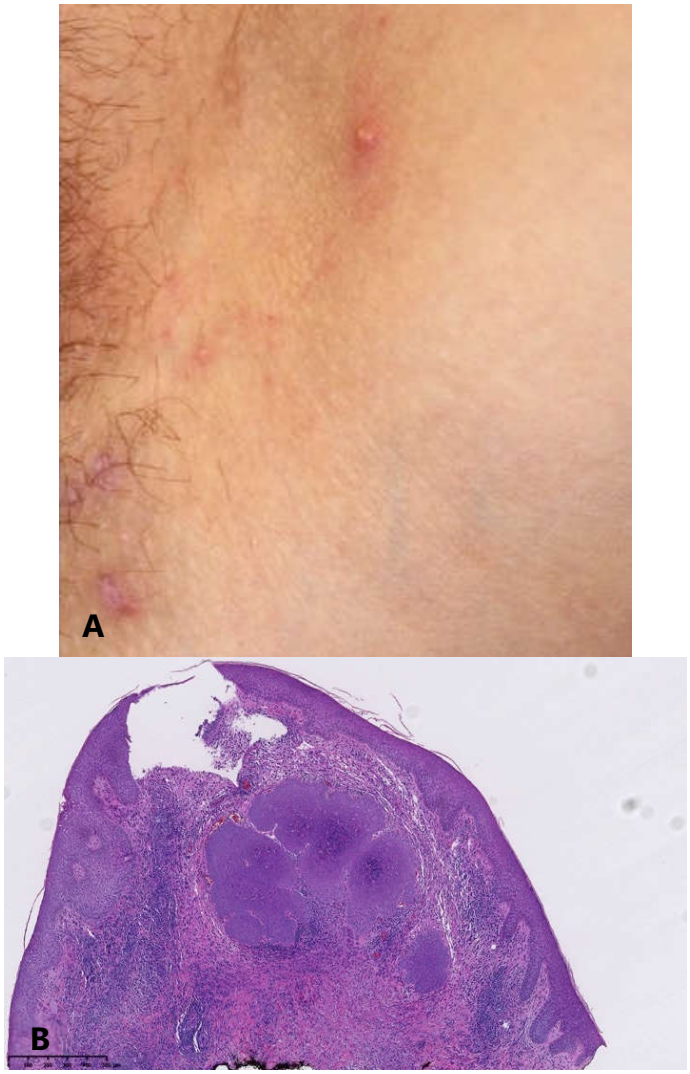

Figure 2. ***A)*** *Firm, small pink papules on the left groin of 50-year-old female.* ***B)*** *Histopathology showing epidermal invaginations containing molluscum bodies surrounded by an atypical large cell infiltrate. H&E, 40×.*

neoplasms such as lymphomatoid papulosis (LYP), anaplastic large cell lymphoma (ALCL), and large cell variants of cutaneous T-cell lymphoma [11]. CD30 expression is also observed in benign reactive T cell lymphocytic skin infiltrates in settings of viral infections and drug reactions. Benign and malignant CD30+ neoplasms share overlapping histological features that present diagnostic challenges. The accurate diagnosis of these entities requires a robust integration of histopathological features with the clinical presentation.

The benign CD30+ lymphomatoid reactions in the skin are termed "CD30+ T cell pseudolymphomas" (CD30+ PSL) and are observed in settings of viral, bacterial, and parasitic infections, drug reactions, and inflammatory conditions [12-14]. The most commonly encountered clinical settings for CD30+ PSL in a review of 28 cases of by Werner et al. included viral infections by parapox (8 cases), herpes (8 cases), and molluscipox (3 cases) viruses and drug reaction [3, 5]. Furthermore, CD30+ PSL in association with parapox virus mediated MC is reported in several pediatric and adult patients (**Table 1**), [6-9]. In the case of our patient, the presence of medium to large atypical CD30+ CD4 T cells adjacent to molluscum bodies was consistent with diagnosis of MC associated CD30+ PSL. As discussed above, owing to overlapping histological features, CD30+ PSL was misdiagnosed as pcALCL in our patient.

Histologically, pcALCL presents with predominantly large atypical CD4 T cell infiltrate with strong CD30 expression in more than 75% of cells. The atypical T cells exhibit irregular nuclear contours and although they are predominantly dermal based, may have an epidermal component. Clinically pcALCL presents as progressively enlarging tumors or nodules that may ulcerate [15]. It predominantly affects an older population and tends to present in the head and neck area. A diagnosis of pcALCL often relies on identifying the characteristic clinical and pathologic features in skin lesions but a computed tomography or positron emission tomography/computed tomography is essential to exclude possible systemic involvement. In our patient, the histological findings of large atypical CD4 T cell infiltrate with strong CD30 positivity were suggestive of pcALCL. However, the presence of molluscum bodies within the dermis and the lack of typical pcALCL clinical features ruled out the diagnosis of pcALCL.

Table 1. *Molluscum contagiosum pseudolymphomatous infiltrates with CD30 positivity.*

	Age and Gender	Clinical Presentation	Histological Features
de Diego et al., 1998 [6]	2-year-old male	1 pedunculated, erythematous, and crusted lesion on anterior chest	Epidermal invagination with molluscum bodies and ruptured cystic structure surrounded by dense infiltrate of large atypical T lymphocytes† Few CD30+ cells
Guitart et al., 1999 [7]	Patient 1: 7-month-old infant Patient 2: 8-year-old female	Patient 1: 2 yellow umbilicated and crusted papules on scalp since 2 months old Patient 2: 1 inflamed and tender nodule on abdomen present for 1 year	Patient 1: molluscum bodies surrounded by dense lymphoid infiltrate of large CD8 T lymphocytes 30% CD30+ cells Patient 2: central epithelium invagination with molluscum bodies and dermis with dense infiltrate of large CD8 T lymphocytes 20% CD30+ cells
Moreno-Ramírez et al., 2003 [8]	72-year-old female	1 painless, inflammatory and crusted nodule on external canthus present for 6 months	Epidermal invagination with molluscum bodies and dermis with infiltrate of large atypical CD4 T lymphocytes CD30+ on cells with large nucleus‡
Del Boz González et al., 2008 [9]	25-year-old female	1 rapidly enlarging umbilicated and crusted nodule behind right ear present for 2 weeks	Endophytic hyperplasia with molluscum bodies surrounded by infiltrate of small and large CD4 T lymphocytes Few CD30+ cells

† CD4 or CD8 expression not specified.
‡ CD30+ level of expression not specified.

Conclusion

In summary, our case demonstrated the difficulty in differentiating between CD30+ PSL in the setting of MC and CD30+ malignant processes. Oftentimes, it is difficult to distinguish these entities based on histopathology examination and immunohistochemical analysis alone. Patients with CD30+ PSL may experience unnecessary stress when faced with malignant pathological diagnoses. The unwarranted anxiety can be prevented by correlating clinical and histopathological features in these cases.

Potential conflicts of interest

The authors declare no conflicts of interests.

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