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Case Report

CD30+ lymphoproliferative disorder in a patient with metastatic papillary thyroid carcinoma

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Abstract

Background
CD30+ lymphoproliferative disorders are rare and may feature a wide variety of presentations that mimic other conditions.

Purpose
A man with metastatic papillary thyroid carcinoma to skin who subsequently developed cutaneous anaplastic large cell lymphoma is described.

Methods
The PubMed medical database was used to search the following terms separately and in combination: ALCL, anaplastic large cell lymphoma ALCL, cutaneous anaplastic large cell lymphoma CALCL, cutaneous t-cell lymphoma CTCL, large t-cell lymphoma LTCL, lymphoproliferative, lymphomatoid papulosis LyP, mimic, papillary, thyroid cancer.

Results
CD30+ cutaneous anaplastic large cell lymphoma was diagnosed in a man with metastatic papillary thyroid carcinoma based on the temporal, histologic, and immunochemical features of an enlarging lesion. To the best of our knowledge, this is the initial description of a CD30+ lymphoproliferative disorder occurring in a patient with primary carcinoma of the thyroid.

Conclusion

Cutaneous lesions may present with various morphologies. Our patient had a previous history of metastatic papillary thyroid carcinoma to skin. His new chest lesion was originally suspected to be either an infection or a cutaneous metastasis. Multiple biopsies, not only for microscopic evaluation but also cultures for infectious organisms, were performed. Unexpectedly, a CD30+

lymphoproliferative disorder was diagnosed; subsequently the tumor spontaneously resolved. Therefore, when skin lesions appear that have more than one clinical presentation, it may be prudent for the clinician to collect representative samples of each distinct morphology to assure that an accurate diagnosis is established.

Keywords: ALCL, anaplastic large cell lymphoma, CALCL, carcinoma erysipelatoides, CTCL, cutaneous anaplastic large cell lymphoma, cutaneous T-cell lymphoma, large T-cell lymphoma, LTCL, lymphoproliferative, lymphomatoid papulosis, LyP, mimic, papillary, thyroid cancer

Introduction

The differential diagnosis for CD30+ lymphoproliferative disorders includes anaplastic large cell lymphoma, mycosis fungiodes, and lymphomatoid papulosis [1]. Cutaneous metastases secondary to papillary thyroid carcinoma are uncommon and typically present as nodules or plaques in the head and neck area [2]. We describe a man with a history of metastatic papillary thyroid carcinoma, including cutaneous metastases, who presented with a solitary lesion of cutaneous anaplastic large cell lymphoma.

Case synopsis

A 74-year-old man with metastatic papillary thyroid carcinoma presented to our office with a one month history of an asymptomatic, progressively enlarging chest lesion. He had previously been seen by his primary care provider who placed him on cephalexin, as a streptococcal skin infection was the most likely clinical diagnosis. However, the red confluent lesion not only persisted, but also increased in size and developed a central ulcer.

This patient's past medical history is significant for metastatic papillary thyroid carcinoma with metastasis not only to lung, but also to his nose. The details and features of his cutaneous metastasis have previously been described [3]. Initial treatments included not only a total thyroidectomy and several additional surgical excisions including that of an enlarged chest lymph node, but also radioactive iodine-131 and systemic antineoplastic therapy with capecitabine.

After the discovery of the metastasis to his nose, his metastatic tumor was evaluated for genomic aberrations: an abnormality in the RET receptor tyrosine kinase oncogene susceptible to the RET inhibitor vandetanib was discovered. Daily vandetanib was started, which stabilized the disease progression. Seven months after initiating vandetanib, he presented to our office with a dermatologic lesion on his chest.

A 3 x 9 cm erythematous, raised, scaling plaque with a 1.5 x 2 cm ulcerated center and a step off on the peripheral portion of lesion, reminiscent of carcinoma erysipelatoides, was present on his chest (Figure 1).

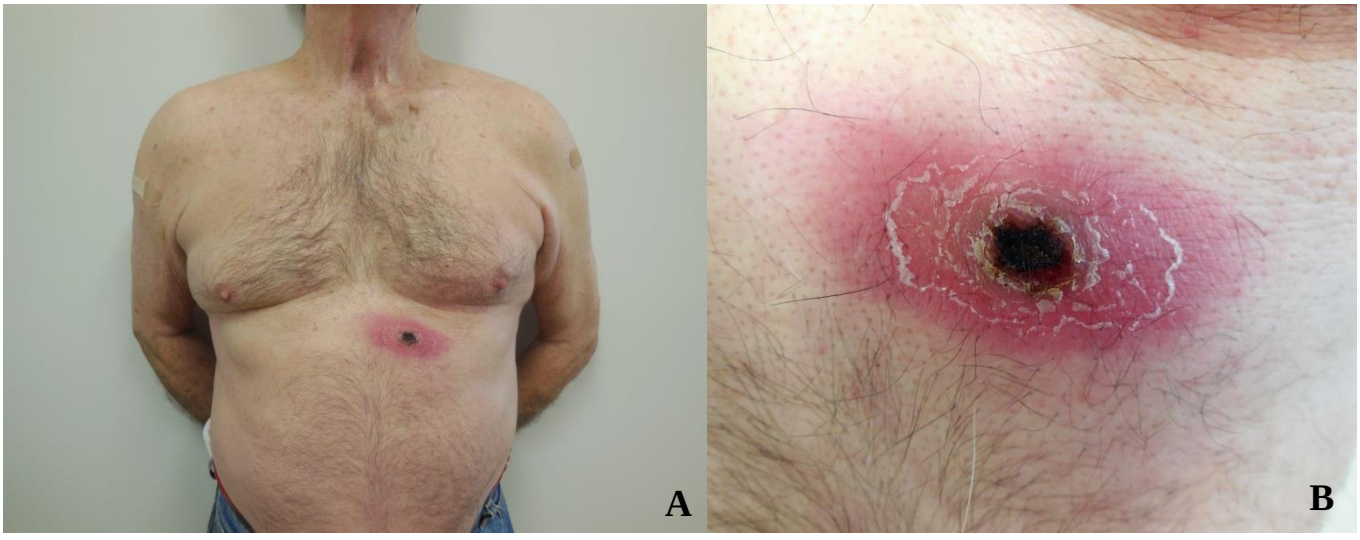

Figure 1. Distant (A) and closer (B) views of the 3 x 9 cm left chest lesion presenting as an erythematous and scaly plaque with a 1.5 x 2 cm area of central ulceration.

Three biopsies of the lesion were taken: two from the edge of the ulcerated, central region, one for histology, one for bacterial, fungal, mycobacterial, and viral cultures, and one from the erythematous peripheral surrounding region. Microscopic exam of the erythematous region showed acanthosis, hyperkeratosis, parakeratosis, and spongiosis with areas of neutrophilic infiltration in the epidermis (Figure 2).

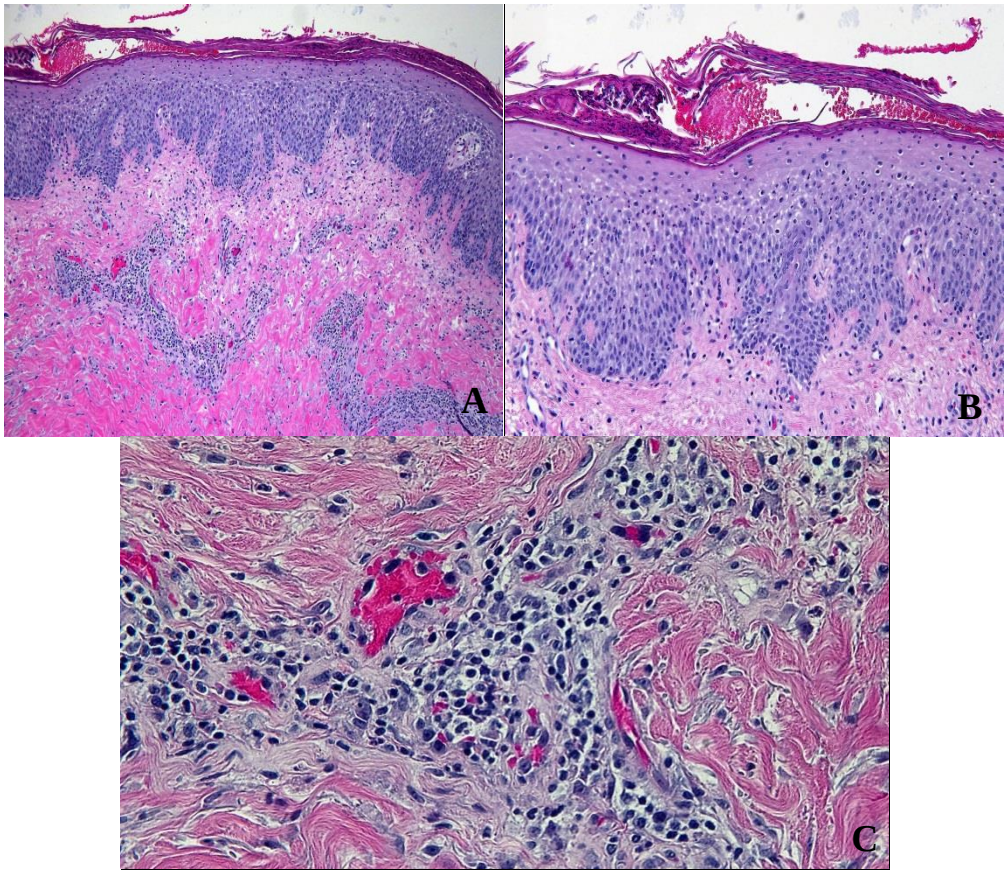

Figure 2. Low (A), medium (B), and high (C) magnification views of the biopsy specimen from the lateral, raised erythematous region with step off clinically reminiscent of erysipelas. There is crust, parakeratosis and hemorrhage within the stratum corneum. There is acanthosis, hyperkeratosis, and spongiosis with neutrophilic infiltration of the epidermis (neutrophilic spongiosis) (a and b). Perivascular lymphocytes present in the dermis (c). Hematoxylin and eosin; A = 10x, B = 20x, C = 40x.

The dermis displayed perivascular lymphocytes. These findings were not consistent with that of malignancy, but were considered to be reactive changes of neutrophilic spongiosis. The ulcerated edge in the central aspect of the lesion displayed epidermal hyperplasia with areas of neutrophilic spongiosis and a dense infiltrate of large cells (Figure 3).

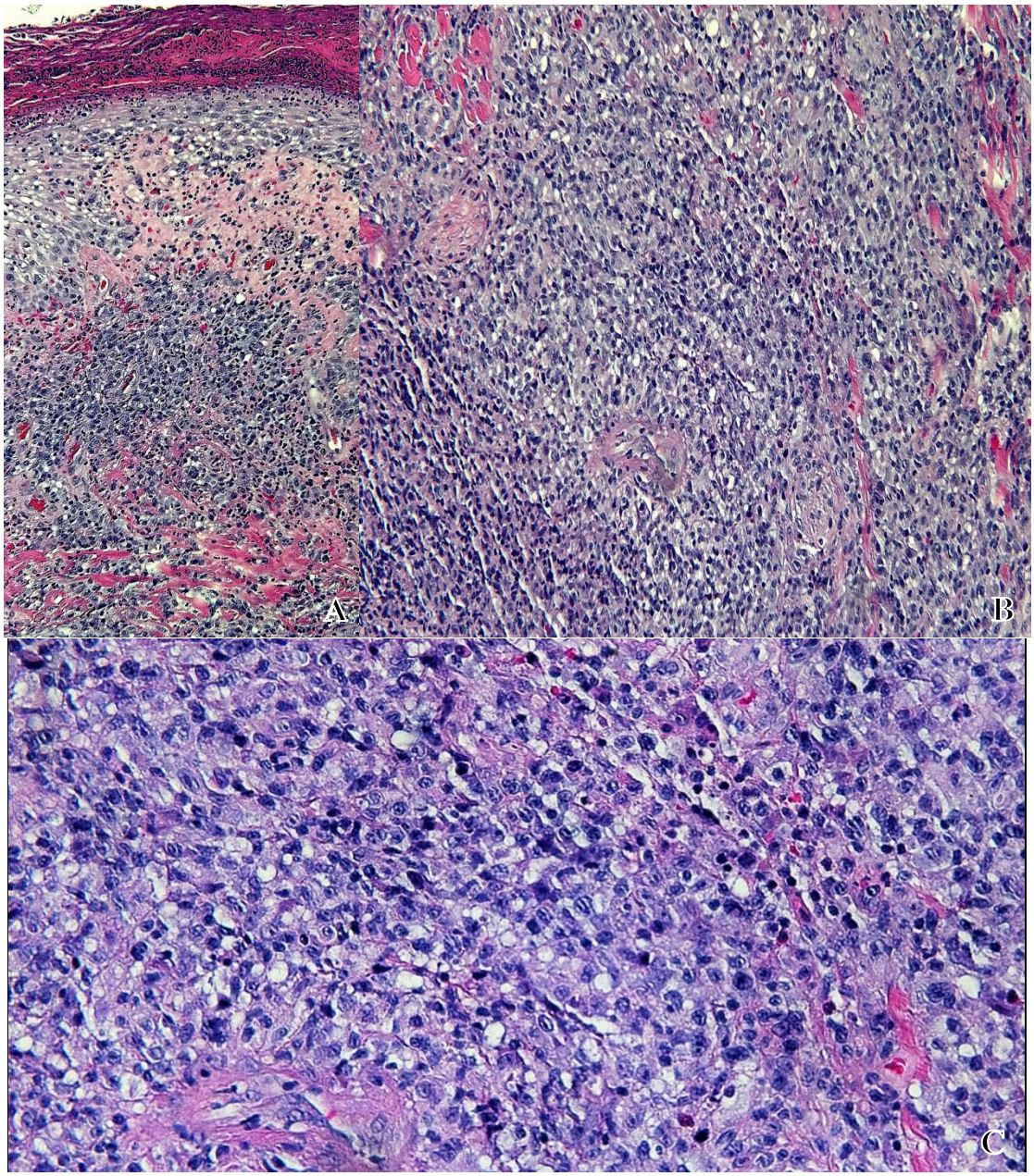

Figure 3. Low (A), medium (B), and high (C) magnification views of the central ulcerated aspect of the lesion. An ulcer with adjacent parakeratosis and neutrophilic crust is present. A dense inflammatory infiltrate consisting of large lymphocytes is present in the dermis. Hematoxylin and eosin; A = 10x, B = 20x, C = 40x.

Immunohistochemical staining revealed sheets of CD3+, CD4+, CD30+ lymphocytes; the tumor cells were negative for anaplastic lymphoma kinase (ALK1) and Epstein–Barr virus-encoded small RNA (EBER) on in situ hybridization (Figure 4). All of the cultures were negative for infectious organisms.

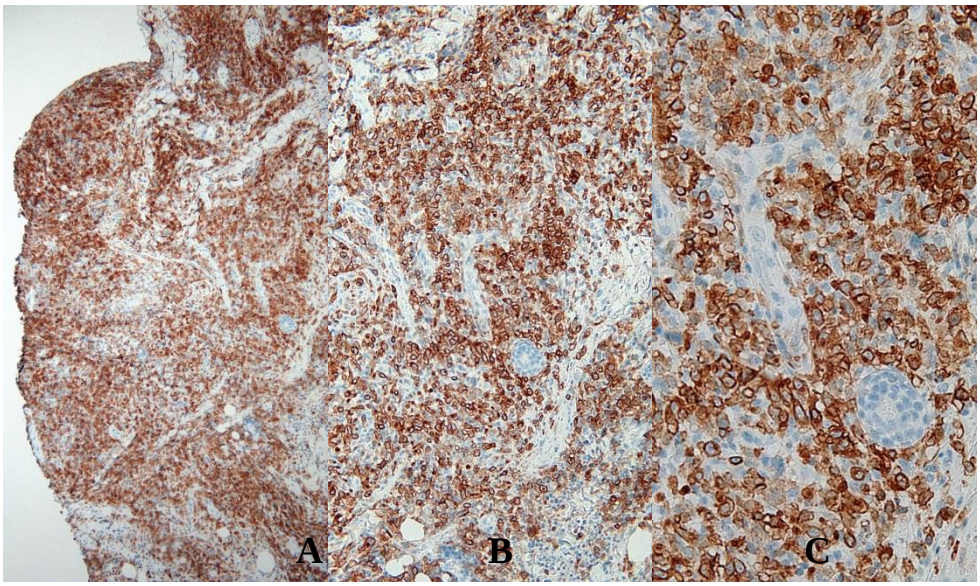

Figure 4. Immunohistochemical staining of the biopsy from the central ulcerated aspect of the lesion displayed non-epidermotrophic, dense inflammatory infiltrate consisting of large, anaplastic T-cells. Low (A), medium (B), and high (C) magnification views after immune staining for CD30 show diffuse positive staining of the large atypical lymphocytes in the dermis. Hematoxylin and eosin; A = 10x, B = 20x, C = 40x.

CD30+ lymphoproliferative disorder was diagnosed; correlation of the clinical and morphologic presentations was most consistent with a solitary lesion of CD30+ cutaneous anaplastic large cell lymphoma. Systemic workup was negative for any additional evidence of lymphoma. Treatment options for the single lesion were being considered; however, the entire lesion resolved spontaneously within the next month. There have not been any new lesions at follow-up after one year.

Discussion

The spectrum of CD30+ lymphoproliferative diseases includes anaplastic large cell lymphoma, lymphomatoid papulosis types A, B, and C, and large cell transformation of cutaneous T-cell lymphoma. Primary CD30+ cutaneous anaplastic large cell lymphoma and lymphomatoid papulosis have many similarities. Often, clinical features are used to distinguish anaplastic large cell lymphoma from lymphomatoid papulosis [4].

Cutaneous anaplastic large cell lymphoma most commonly presents as a solitary lesion or regional nodules that often show ulceration, similar to what was exhibited by our patient. In contrast, lymphomatoid papulosis usually presents as multiple, spontaneously regressing lesions [1, 5]. The lesions of anaplastic large cell lymphoma typically persist. However, in the absence of therapy, spontaneous regression without relapse has been observed in 15% (12 of 79) of individuals with anaplastic large cell lymphoma [6]. Therefore, since the cutaneous anaplastic large cell lymphoma lesions may undergo spontaneous regression, similar to lymphomatoid papulosis, the temporal tendencies of the lesions may not be helpful when attempting to establish a definitive diagnosis. The first line treatment for localized anaplastic large cell lymphoma is radiotherapy [5]. However, our patient's lymphoproliferative tumor spontaneously resolved.

Histologically, cutaneous anaplastic large cell lymphoma typically displays a diffuse, non-epidermotropic infiltrate with cohesive, sheet-like proliferations of large anaplastic CD30+ lymphocytes [1]. The overlying epidermis may show a variable degree of pseudoepitheliomatous hyperplasia as observed in our patient [7]. Phenotypically, the tumor cells in lymphomatoid papulosis and anaplastic large cell lymphoma represent a proliferation of activated T-helper cells that are usually CD3+, CD4+ and CD30+ [8,9]. Lymphomatoid papulosis type C is the most histologically and immunophenotypically similar lesion to anaplastic large cell lymphoma; it is characterized by large atypical lymphoid cells in either formed sheets or large nodules [4]. Lymphomatoid papulosis type C has also been referred to as borderline lymphomatoid papulosis-anaplastic large cell lymphoma and may be differentiated through clinical examination [10].

To the best of our knowledge, the presence of a CD30+ lymphoproliferative disorder coincident with metastatic thyroid carcinoma has not been described. Thus, in an oncology patient with established metastatic papillary thyroid carcinoma to lung, skin, and

chest lymph nodes, the onset of a new, antibiotic-resistant erythematous lesion (with subsequent central necrosis) was suspected to represent another focus of cutaneous metastases [11]. Furthermore, the clinical presentation of this patient's lesion initially mimicked a streptococcal skin infection. However, despite antibiotic therapy, it developed into an erythematous, raised plaque with a step off and an area of central necrosis that was reminiscent of carcinoma erysipelatoides [12,13]. However, the solitary ulcerated plaque also raised the possibility of other infectious etiologies including deep fungal, mycobacterial, and viral (such as cytomegalovirus) infections. Therefore, the biopsies were not only performed for histologic examination, but also for bacterial, fungal, mycobacterial, and viral cultures. In addition, because the lesion displayed more than one clinical morphology, representative biopsies from each area of clinical presentation were performed. In contrast to the suspected presence of metastatic papillary thyroid cancer filling the dermal lymphatics (carcinoma erysipeloides), the erythematous portion of the plaque showed a dermal reactive pattern of neutrophilic spongiosis [12]. Indeed, the central ulcerated area, favored to represent necrosis secondary to tumor outgrowing its blood supply, showed epidermal hyperplasia and atypical, large CD30+ lymphocytes in the dermis, establishing the diagnosis of a CD30+ lymphoproliferative disorder most consistent with a solitary lesion of anaplastic large cell lymphoma.

Conclusion

A new cutaneous lesion in an oncology patient with metastatic papillary thyroid carcinoma to skin raises the possibility of new cutaneous metastases. Although the patient was on systemic anti-neoplastic therapy, the possibility of new resistance may have allowed for the development of new metastatic disease. However, other malignancies and etiologies, including infectious, need to be considered. Therefore, comprehensive evaluation of a new cutaneous lesion might include not only biopsy for histopathology, but also tissue procurement for cultures. In addition, when lesions display more than one morphology, it may be reasonable to obtain separate biopsies from each distinct area in order to establish the diagnosis.

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