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Case Report

A puzzling diagnosis: mycosis fungoides masquerading as pyoderma gangrenosum

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ABSTRACT

Mycosis fungoides (MF) is a form of cutaneous T cell lymphoma that initially affects the epidermis, and is characterized by the clonal proliferation of mature cluster of differentiation (CD4)+T cells. We report a 73-year old male presenting with chin and right axillary skin lesions that had ulceration and granulating areas. Initial biopsy revealed mixed inflammatory cell infiltrate, which suggested an initial diagnosis of pyoderma gangrenosum. Despite treatment, the progressive worsening of the skin lesions prompted multiple repeat biopsies, which eventually revealed a predominance of T cells within the infiltrate. A T cell receptor rearrangement resulted in elevated monoclonal T cell populations, confirming a diagnosis of MF. Subsequent positron emission tomography (PET) scans revealed metastatic involvement of the disease, which ultimately led to the patient's death. Clinical presentations of MF can mimic several different clinical entities, including pyoderma gangrenosum. This report highlights the importance of a multimodal approach to the diagnosis of unidentified skin lesions.

Keywords: Mycosis fungoides, Pyoderma gangrenosum, Cluster of differentiation, Cutaneous T cell lymphoma

INTRODUCTION

Mycosis fungoides (MF) is the most prevalent subtype of cutaneous T cell lymphoma (CTCL). It is generally characterized by a clonal proliferation of mature CD4+T cells and involves the epidermis.[1,2] The early stages of MF were first described by Jean Alibert and Ernest Bazin as persistent, progressive erythematous patches or thin plaques of variable size and shape located on sun-protected areas with a scaly surface.[1,2] Progression of the disease may lead to tumor formation.[3] Due to numerous subtypes with various presentations, the differential diagnosis of MF is broad and may include: inflammatory skin disorders, such as dermatitis, granulomatous diseases, infections, and psoriasis.[4-8] For this reason, it has been named "a great imitator" by many and poses significant challenges to dermatologists and dermato pathologists alike.

CASE REPORT

A 73-year old male with a history of diabetes mellitus, congestive heart failure, chronic kidney disease, and chronic obstructive pulmonary disease (COPD) presented in November 2014 with a pigmented lesion on his chin. This lesion was initially treated with desiccation and curettage by his primary care provider (PCP) in October 2014, but worsened initially and developed swelling, pruritus, and oozing. Cultures at that time revealed Staphylococcus; however, topical antibiotics were ineffective. He was referred to dermatology, at which time the lesion demonstrated a rim of indurated dermal

nodules around a central scar with ulceration and oozing (Figure 1).

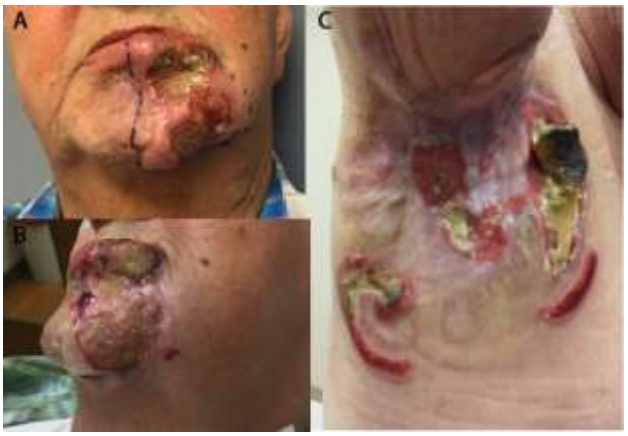

Figure 1: Clinical images of the patient's left chin and right axillary lesions upon initial presentation to the dermatology clinic, (A) represents a front-facing view of the patient, (B) represents a lateral view of the chin lesion, and (C) front-facing view of the patient's axillary lesion, resembling pyoderma gangrenosum.

Acid-fast bacilli smear and culture of the chin lesion were negative, and initial biopsy of the lesion revealed mixed inflammatory cell infiltrate (Figure 2). He was treated with clobetasol for contact dermatitis, later receiving intralesional injections of triamcinolone the next several months, all of which were ultimately ineffective.

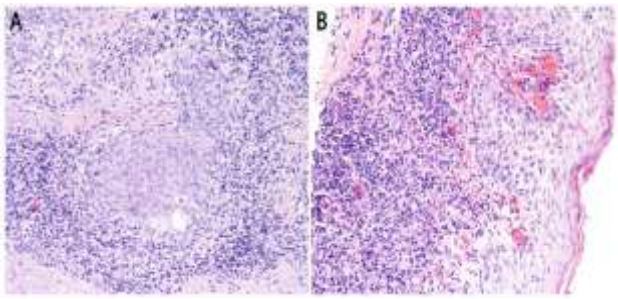

Figure 2: Demonstrates the initial biopsy of the patient's (A) Chin lesion on high-powered magnification, demonstrating a mixed inflammatory cell infiltrate (B) axillary lesion on high-powered magnification, demonstrating areas of tissue necrosis with mixed inflammatory cell infiltrate.

By August 2015, the chin lesion had coalesced into a large area of ulceration with surrounding erythema. The patient had also developed large, painful right axillary lesions with significant ulceration, a fibrinous base, and several granulating areas, raising concern for atypical pyoderma gangrenosum. Biopsy of the axillary lesions revealed tissue necrosis with mixed inflammatory cell infiltrate. Clindamycin and oral prednisone were prescribed by the patient's PCP without benefit. Surgical intervention was not recommended, but the patient elected to have axillary debridement with significant worsening of the lesions. The patient was treated conservatively with sterile dressings and was started on cyclosporine by dermatology. With no improvement, the patient was then referred to Indiana University Health for further evaluation. There, the patient underwent two right axillary biopsies and two biopsies of the left chin. Pathology was not definitively diagnostic and increased concern for pyoderma gangrenosum. He received adalimumab with significant improvement of axillary lesions, but worsening of the chin lesion. The patient then received mycophenolate mofetil and intravenous immunoglobulin (IVIg) treatment without benefit. The patient was hospitalized in 2016 due to growth of the lesion and severe pain. He was referred to another institution but was financially unable to make the trip. Repeat biopsy of the chin lesion was done in September 2016 which was reported as epidermal ulceration with atypical dermal histiocyte-predominant lympho-histiocytic inflammation with numerous eosinophils (Figure 3) concerning for a T cell neoplasm.

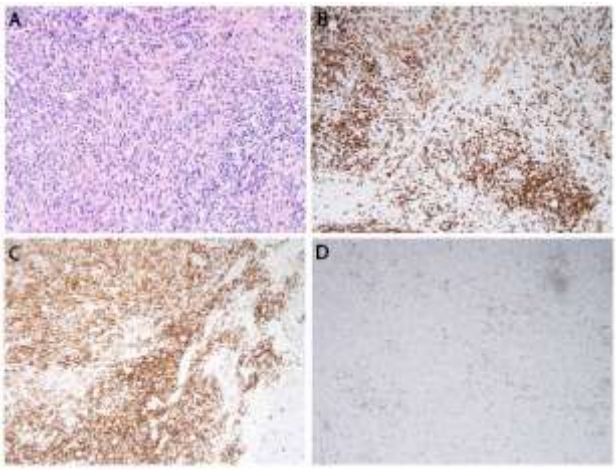

Figure 3: Final biopsy of the patient's chin lesion on high-powered magnification, which demonstrated (A) Epidermal ulceration with atypical dermal histiocyte-predominant lympho-histiocytic inflammation with numerous eosinophils (B) represents significant CD3 positivity of the pathologic specimen (C) represents significant CD4 positivity of the pathological specimen (D) represents loss of CD7 staining.

This biopsy was later sent to mayo clinic where pathology showed: "CD3 highlights the predominance of T cells within the infiltrate which demonstrates a slightly increased CD4:CD8 ratio. CD30 shows weak, focal staining in rare cells. The histopathologic and immunophenotypic features seen in the majority of the specimen favor a reactive process, however, given the hair follicle changes, follicular mucinosis in the setting of mycosis fungoides should be considered." A T cell receptor rearrangement study resulted in "isolated peaks are suspicious for a monoclonal T cell population, this finding is consistent with a T cell neoplasm, likely mycosis fungoides." In October 2016 a computed

tomography scan (Figure 4) revealed an enlarged soft tissue mass along the left half of the mandible consistent with malignancy, a 0.5 cm left neck lymph node, right lung nodule and moderately enlarged diffuse mediastinal lymph nodes. Biopsy of the right axilla revealed scar tissue. Palliative radiation to the face and neck was completed with good response. In March 2017, a new lesion on his neck adjacent to the radiation field was identified.

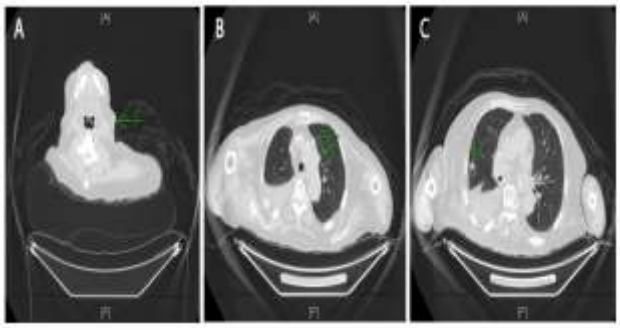

Figure 4: Computed tomography imaging of the head, neck and chest demonstrating initial spread of the patient's disease in 2016 (A) left cervical lymph node (B) mediastinal lymph nodes (C) right upper lobe of the lung. Arrows in the figure are pointing to the sites of disease spread.

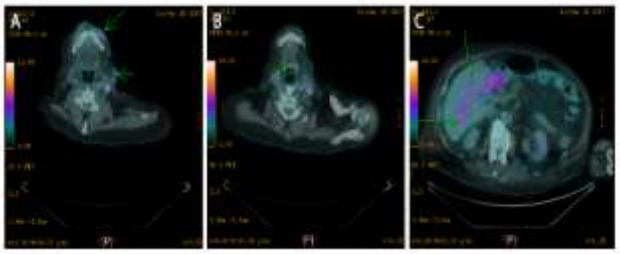

Figure 5: Positron emission tomography imaging of the whole body (not shown in its entirety) from 2017 (A) dDemonstrating hypermetabolic activity in the left mandible and left cervical lymph nodes (B) right cervical lymph nodes (C) multiple metastatic lesions in the liver. Arrows in the figure are pointing to hypermetabolic lesions indicating metastatic disease.

A positron emission tomography (PET) scan (Figure 5) revealed interval development of the moderately enlarged diffuse mediastinal lymph nodes with fairly intense uptake (SUV=10), interval development of small but metabolically active cervical lymph nodes (left>right), new severe thickening in the region of the gastric antrum with intense uptake, 4 new small liver lesions with increased uptake and a few small new parenchymal nodular densities in the lungs with metabolic uptake. Excisional biopsy of a hypermetabolic left neck node revealed atypical lymphohistiocytic infiltrate with numerous eosinophils suspicious for involvement by T cell lymphoma and polyclonal B cells with no loss of T cell antigens. The patient unfortunately passed away secondary to disease in May of 2017, nearly 3.5 years after initial presentation.

DISCUSSION

Given the varied presentations of MF, the diagnosis of this disease requires a combination of histologic and clinical findings.[1,2,9] One histopathologic hallmark of the disease is epidermotropism, or T cells in the epidermis, which can be atypical and involve only minimal spongiosis along with superficial dermal lymphoid infiltrate.[9,10] However, this diagnosis is rarely simple, and is one of the most debated issues in dermatology, as findings are commonly focal and not obvious. To facilitate ease of diagnosis, the international society for cutaneous lymphomas (ISCL), has proposed guidelines, whereby immunohistochemistry, clinical and histopatho logical characteristics, and T cell receptor rearrangement studies are combined in equivocal cases.[10]

To better distinguish MF from other inflammatory conditions and various cutaneous neoplasms, several histologic criteria have been proposed.[16] Based on these criteria, parameters that suggest a MF diagnosis include Pautrier's microabscesses, disproportionate epidermo tropism, atypical intraepidermal lymphocytes surrounded by halos, exocytosis, lymphocytes aligned with the basal layer, epidermal lymphocytes larger than dermal lymphocytes, and hyperconvoluted intraepidermal lymphocytes.[16] At times, and in this case, it is difficult to differentiate between CTCLs and benign reactive lymphoid hyperplasia. A loss of the T-lineage antigens CD2, CD3, CD5, and CD7 in CTCLs is helpful in making this distinction.[17]

Nashan et al. conducted a literature review on the varying clinical presentations of MF, and found that it can mimic more than fifty clinical entities.[5] Our patient had disease that mimicked pyoderma gangrenosum. To date, there are only two cases of CD8+MF simulating pyoderma gangrenosum in the English literature.[11,12] Additionally, there have been two reported cases of CD30+CTCLs simulating pyoderma gangrenosum.[13,14] Finally, there is one reported case of MF bullosa mimicking pyoderma gangrenosum.[15] To our knowledge, this is the first reported case of a CD4+MF masquerading as pyoderma gangrenosum.

Extracutaneous dissemination is sometimes observed in patients with MF, most notably in patients with tumors or generalized erythroderma (30-40% of patients).[18] Most commonly, the liver, lung, spleen, and gastrointestinal tract are involved. Patients with extracutaneous disease at presentation that involves any viscera or lymph nodes have a poor median overall survival, less than 1.5 years.[18] In our case, by the time the patient had reached dermatology, his disease already demonstrated clinical spread to axillary lymph nodes, and PET scan later demonstrated disseminated disease. Unfortunately, our

patient died of his disease nearly 3.5 years after diagnosis.

CONCLUSION

In conclusion, this case highlights the importance of considering MF in any differential of an inflammatory skin condition, especially when it fails to resolve with standard treatment regimens. Additionally, this case illustrates an extremely rare presentation of CD4+MF, the first reported in the literature to date. This case highlights the importance of multimodal approaches to the diagnosis of unexplained skin lesions, including skin biopsy, immunohistochemistry, and flow cytometric analysis, to arrive at the correct diagnosis most efficiently.

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REFERENCES

1. Willemze R, Cerroni L, Kempf W, Berti E, Facchetti F, Swerdlow SH, et al. The 2018 update of the WHO-EORTC classification for primary cutane ous lymphomas. Bloo. 2019;133(16):1703-14.
2. Olsen E, Vonderheid E, Pimpinelli N, Willemze R, Kim Y, Knobler R, et al. Revisions to the staging and classification of mycosis fungoides and Sezary syndrome: a proposal of the International Society for Cutaneous Lymphomas (ISCL) and the cutaneous lymphoma task force of the European Organization of Research and Treatment of Cancer (EORTC). Bloo. 2007;110(6):1713-22.
3. Agar NS, Wedgeworth E, Crichton S, Mitchell TJ, Cox M, Ferreira S, et al. Survival outcomes and prognostic factors in mycosis fungoides/Sézary syndrome: validation of the revised International Society for Cutaneous Lymphomas/European Organisation for Research and Treatment of Cancer staging proposal. J Clinic Oncol. 2010;28(31): 4730-9.
4. Willemze R. Mycosis fungoides variants-clinicopathologic features, differential diagnosis, and treatment. Semin Cutan Med Surg. 2018; 37(1):11-7.
5. Nashan D, Faulhaber D, Ständer S, Luger TA, Stadler R. Mycosis fungoides: a dermatological masquerader. Br J Dermatol. 2007;156(1):1-10.
6. Martínez-Escala ME, González BR, Guitart J. Mycosis Fungoides Variants. Surg Pathol Clin. 2014;7(2):169-89.
7. Zackheim HS, McCalmont TH. Mycosis fungoides: the great imitator. J Am Acad Dermatol. 2002;47(6):914-8.
8. Ahn CS, ALSayyah A, Sangüeza OP. Mycosis fungoides: an updated review of clinicopathologic variants. Am J Dermatopathol. 2014;36(12):933-48
9. Cerroni L. Mycosis fungoides-clinical and histopathologic features, differential diagnosis, and treatment. Semin Cutan Med Surg. 2018;37(1):2-10.
10. Pimpinelli N, Olsen EA, Santucci M, Vonderheid E, Haeffner AC, Stevens S, et al. Defining early mycosis fungoides. J Americ Academ Dermatol. 2005;53(6):1053-63.
11. Saha M, Jain BB, Chattopadhyay S, Podder I. CD8-positive Mycosis Fungoides Masquerading as Pyoderma Gangrenosum. Indian J Dermatol. 2016; 61(5):580.
12. Dueck D, Hermes B, Audring H, Kohl PK. [CD8-positive, CD30-negative cutaneous T-cell lymphoma simulating pyoderma gangrenosum]. Hautarzt. 2002;53(2):114-7.
13. Salameh F, Barzilai A, Baum S, Trau H. Mycosis fungoides and CD30+ cutaneous T-cell lymphoma simulating pyoderma gangrenosum in a patient with ulcerative colitis. J Dermatol Case Rep. 2009; 3(2):30-3.
14. Cozzani E, Scaparro M, Rongioletti F, Pierri I, Pimpinelli N, Parodi A. Pyoderma gangrenosum-like CD30+ cutaneous T-cell lymphoma in a patient with mycosis fungoides. J Eur Acad Dermatol Venereol. 2015;29(4):819-21.
15. Ho KK, Browne A, Fitzgibbons J, Carney D, Powell FC. Mycosis fungoides bullosa simulating pyoderma gangrenosum. Br J Dermatol. 2000;142(1):124-7.
16. Smoller BR, Bishop K, Glusac E, Kim YH, Hendrickson M. Reassessment of histologic parameters in the diagnosis of mycosis fungoides. Am J Surg Pathol. 1995;19(12):1423-30.
17. Nasu K, Said J, Vonderheid E, Olerud J, Sako D, Kadin M. Immunopathology of cutaneous T-cell lymphomas. Am J Pathol. 1985;119(3):436-47.
18. Zinzani PL, Ferreri AJ, Cerroni L. Mycosis fungoides. Crit Rev Oncol Hematol. 2008;65(2):172-82.

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