DOI: 10.3315/jdcr.2009.1030

Journal of Dermatological Case Reports

Mycosis fungoides and CD30+ cutaneous T-cell lymphoma simulating pyoderma gangrenosum in a patient with ulcerative colitis

Fares Salameh, Aviv Barzilai, Sharon Baum, Henri Trau

Department of Dermatology, Chaim Sheba Medical Center, Tel Hashomer, The Sackler School of Medicine, Tel Aviv University, Israel

Corresponding author:

Fares Salameh M.D.

Department of Dermatology

The Chaim Sheba Medical Center, Tel Hashomer 52621 Israel

E-mail: *faressalameh@hotmail.com*

Key words:

cutaneous T-cell lymphoma, inflammatory bowel disease, mycosis fungoides, ulcer, ulcerative colitis, pyoderma gangrenosum

Abstract

Background: Pyoderma gangrenosum is estimated to occur in 5% to 12% of ulcerative colitis patients. Primary CD30+ cutaneous large cell lymphoma is the second most common cutaneous lymphoma. It may coexists with mycosis fungoides.

Main observations: We report a 38-years-old female patient with 12 year history of ulcerative colitis, treated previously with 5-aminosalicylic acid and systemic corticosteroids. The disease has been in remission for the past 1.5 years, with no maintenance treatment. The patient then developed a rapidly progressing ulcerated lesion clinically simulating pyoderma gangrenosum. Physical examination revealed also a small number of hairless hypopigmented patches on the upper and lower limbs which she claimed to have appeared 4 years ago. Surprisingly a histological evaluation of the ulcer revealed a CD30+ primary cutaneous large cell lymphoma, while histology of hypopigmented lesions revealed mycosis fungoides, patch stage. T-cell receptor gene rearrangement from the two lesions didn't reveal the same T Cell clonalitiy and the patients lymphoma was stable.

Conclusion: Our case presents the rare coexistence of primary mycosis fungoides and primary CD30+ cutaneous large cell lymphoma, rather than the CD30+ cutaneous large cell lymphoma developing from mycosis fungoides. This case also presents the development of a pyoderma gangrenosum-like lesion of CD30+ cutaneous large cell lymphoma in a patient with ulcerative colitis. An observation that emphasizes the need for a high index of suspicion in cases diagnosed as pyoderma gangrenosum based solely on clinical appearance.

Introduction

Primary cutaneous T-cell lymphoma (CTCL) represents a heterogeneous group of neoplasms derived from skin-homing T cells. Apart from mycosis fungoides (MF), primary CD30+ CTCL is the most common group, accounting for approximately 25% of all CTCLs.[1] The spectrum of primary CD30+ CTCLs includes lymphomatoid papulosis (LyP), primary cutaneous large cell lymphoma (PCLCL), and borderline CD30+ lesions.[2] These three types may coexist in the same patient with overlapping clinical and histopathological features and may be associated with other types of lymphoproliferative disorders including Hodgkin's lymphoma and mycosis fungoides (MF).[3] CD30+ PCLCL was reported to coexist with MF as an independent lymphoproliferative disorder or develop secondarily from MF.[4,5,6,7,8]

We describe a patient with MF patch stage coexisting with CD30+ PCLCL presenting as a pyoderma gangrenosum (PG) like lesion.

Case report

A 38-years-old woman with a 12 years history of ulcerative colitis was admitted to our department for an investigation of a rapidly progressing ulcerated lesion on her right thigh which appeared 9 days previously. Ulcerative

colitis was diagnosed due to the clinical signs and was confirmed by biopsy. Consequently, she was treated with 5-aminosalicylic acid and systemic corticosteoids, with remission for the past 1.5 years, with no maintenance treatment given according to the patient's wish.

According to anamnesis, the lesion started as a superficial hemorrhagic pustule and progressed to a 4 cm ulcer with raised edges. Prior to her admission a treatment with potent topical steroids; topical antibiotics as well as 20 mg/day of oral prednisone for 4 days, did not control the progression of the lesion. She reported also the appearance of a similar smaller lesion at the left thigh 6 month before her current admission. This lesion spontaneously resolved with a residual hyperpigmented patch.

Physical examination revealed a deep ulceration, 4 cm in diameter, with a violaceous border on the medial aspect of the proximal right thigh, a hyperpigmented patch 2 cm in diameter on the distal anterior aspect of the left thigh. In addition few hairless hypopigmented patches 2 to 4 cm in diameter on the upper and lower limbs were noted. The patient reported that these lesions had appeared 4 years ago. Her other physical findings were unremarkable.

Routine blood tests including complete blood count (CBC), prothrombin time, partial thromboplastin time, liver and renal function tests, venereal disease research laboratory (VDRL) test, antineutrophil cytoplasmic antibody test, partial thromboplastin time test, antiphospholipid and serum protein revealed normal results. Chest radiograph was normal too.

Two skin biopsies were taken, the first from the border of the PG like lesion on the right thigh and the second from one of the hypopigmented lesions on the left arm. The first biopsy revealed lymphoid aggregates composed of large atypical cells throughout the whole dermis with epidermotropism, prominent acute inflammation with numerous neutrophils and abscesses formation, numerous eosinophils were also present (Fig. 1). On immunohistochemical stains the large lymphoid cells were positive for CD3 and CD30 (Fig. 1) and negative for CD20, EMA, CD15, ALK-1, CD4 and CD8. Most of the small reactive lymphocytes were CD8 positive. The K167 proliferation antigen was positive in at least 70% of the large lymphoid cells; features compatible with CD30+ cutaneous T-cell lymphoma. The second biopsy revealed an interface dermatitis involving the hair follicle with focal exocytosis of lymphocytes and post inflammatory changes with few medium sized irregular lymphocytes in the epidermis. Immunohistochemical stains revealed lymphocytes with CD8:CD4 ratio of 1:1; features compatible with early patch stage MF. According to these findings further investigation included total body CT scan and bone marrow biopsy without any significant findings.

T-cell receptor gene rearrangement from the two biopsies didn't reveal the same T Cell clonalitiy. The CD30+ PLCLC legion resolved in 2 month period after treatment with local radiotherapy. Later the patient was also referred to phototherapy treatment for the patch stage MF.

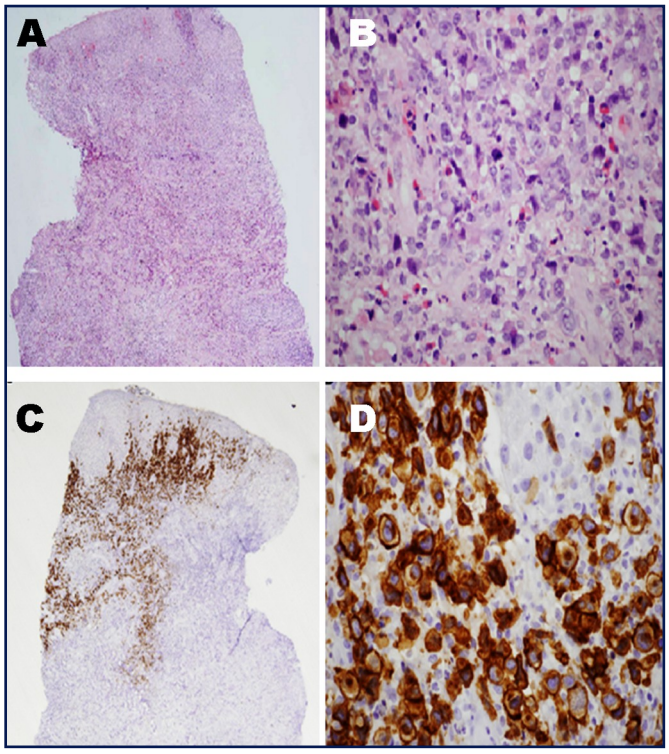

Figure 1

Histology from the border of the PG like lesion on the right thigh, revealing lymphoid aggregates composed of large atypical cells throughout the whole dermis with epidermotropism (A,B). Immunohistochemically the lymphoid cells were positive for CD30 stain (C,D).

Discussion

The present case describes a patient with ulcerative colitis presenting to our department with pyoderma gangrenosum - like lesion and hypopigmented alopetic patches with histological features compatible with CD30+ PCLPC and early patch stage MF respectively. This patient is of interest in two different aspects. Firstly, to the best of our knowledge and after a thorough review of the literature, this is the first reported case of CD30+ PCLCL presenting as PG like lesion in a patient with ulcerative colitis. Yet, PG-like lesions have been previously reported to represent NK/T cell lymphoma,[23] B cell lymphoma[25] and mycosis fungoides.[24] Secondarily, the coexistence of CD30+ PCLCL and MF is remarkable too. The coexistence of CD30+ lymphoprolifirative disorders with MF has been reported previously,[4,5,6,7,8] sometimes with confirmed identical clone, presenting different clinical aspects of a unique T-cell monoclonal expansion. The prognosis has been shown to change greatly according to the type of CD30+ lymphoprolifirative disorder associated with MF. Transforming of MF to large cell lymphoma is usually associated with aggressive biological behavior and rapidly fatal outcome with a mean survival from transformation to death of 22 months,[12,13,14] whereas MF coexisting independently with CD30+ lymphoprolifirative disorder carries a favorable prognosis.[4,8,13,14,15,16] Verqier *et al*.[12]

showed that the conversion of MF to a large cell variant including CD30+ PCLPC usually occurs in the advanced cutaneous lesions. The mean duration between the first cutaneous lesions of MF (reported by patients) and transformation was 14 years.[12] Gallado *et al*. reported 12 patients with LyP coexisting with MF. A slow clinical course was observed in the majority of patients. He found 58% T-cell clonality in LyP biopsies and 50% of plaque stage MF. In each individual case, where T-cell clonality was detected, both mycosis fungoides and lymphomatoid papulosis specimens exhibited an identical peak pattern by automated high-resolution PCR fragment analysis, confirming a common clonal origin.[13]

A review of the literature revealed two cases MF appearing after successful treatment of CD30+ PCLPC[7,9] and only two cases of MF coexisting with CD30+ PCLPC at the same time (Table 1)[4,8] one of them revealed the same pattern of T-cell receptor gene rearrangement. The two lymphoproliferative disorders coexisted for 11 years before diagnosis in the first case[4] and 5 years in the second[8], confirming that MF coexisting independently with CD30+ lymphoprolifirative disorder carries a favorable prognosis.[13,14,15,16] In our patient the hypopigmented MF patches were noticed 4 years before the development of the CD30+ PCLCL lesions; furthermore the T cell clonality from the 2 legions didn't match. Therefore our case is thought to be consistent with the rare coexistence of MF and CD30+ PCLCL, rather than CD30+ PCLCL transformed from MF. The hypopigmented type of MF is one of the less common presentation of this disease, it is characterized by early onset (mean age at diagnosis is 34), occurrence in dark skinned individuals and good prognosis.[17] Our patient matched this description by having Fitzpatrick skin type III, age of onset of the hypopigmented lesions of 34 and benign course of the disease for the past 4 years.

PG is an idiopathic, painful, chronic neutrophilic inflammatory and ulcerative skin disease characterized by a wide variety in its clinical presentation and outcome. The pathogenesis is unknown, but autoimmune mechanisms including immune-complex-mediated neutrophilic vascular reactions have been suggested.[18] Approximately 50-70% of patients with PG have an associated systemic disease, most frequently inflammatory bowel disease. It is associated with ulcerative colitis more commonly than Crohn's disease, occurring in 5% to 12% and 1% to 2% of patients, respectively.[10,11] Other associated diseases include, arthritis, malignancy, and hematological diseases including myelodysplastic syndrome,[19] cutaneous T cell lymphoma[20] and even CD30+ anaplastic large cell lymphoma.[21] Histopathological findings in PG are nonspecific. Biopsies may demonstrate edema, mixed inflammatory infiltrate, predominantly neutrophilic infiltrate, lymphocytic vasculitis, follicular-based pustule, or necrosis and hemorrhage. In spite of the heterogeneous histological picture of PG, histopathological examination of the ulcer can help to differentiate PG from some of its mimickers, including Wegener granulomatosis, polyarteritis nodosa, sporotrichosis, antiphospholipid syndrome[22] and variable types of lymphoma including extranodal NK/T-Cell lymphoma nasal type,[23] mycosis fungoides[24] and primary cutaneous B cell lymphoma.[25] In our patient the diagnosis of PG was very tempting due to the history of UC, but the histological results revealed the right diagnosis. Therefore, a high index of suspicion is required in cases diagnosed as PG based solely on clinical appearance.

Conclusions

Our case is consistent with the rare coexistence of MF and CD30+ PCLCL, rather than CD30+ PCLCL transformed from MF. Moreover, this case outlines the association of CD30+ PCLCL pyoderma gangrenosum-like lesion with ulcerative colitis, which to the best of our knowledge have not been reported before. This association emphasizes the need for a skin biopsy in any case of PG, even where there is a high index of suspicion based on clinical setup.

References

1. Bekkenk MW, Geelen FA, van Voorst Vader PC, Heule F, Geerts ML, van Vloten WA, Meijer CJ, Willemze R. Primary and secondary cutaneous CD30 (+) lymphoproliferative disorders: a report from the Dutch Cutaneous Lymphoma Group on the long-term follow-up data of 219 patients and guidelines for diagnosis and treatment. *Blood*. 2000; 95: 3653-3661.

Table 1. Clinical features of patients with mycosis fungoides coexisting with primary CD30+ cutaneous large cell lymphoma.

Patient No.	Authors	Duration of coexistent MF & PCLCL lesions	Age at diagnosis	Sex	Pattern of TCR gene rearrangement in MF & PCLCL lesions
1	Woodrow *et al.*[8]	5 years	33	M	Identical
2	Kang *et al.*[4]	11 years	59	M	Not Identical
3	Our case	4 years	34	F	Not Identical

MF (mycosis fungoides); PCLCL (primary cutaneous large cell lymphoma); TCR (T- cell rearangment); M (male); F (female).

2. Ralfkiaer E, Delsol G, Willemze R, Jaffe E. Primary cutaneous CD30-positive T-cell lymphoproliferative disorders. World Health Organization classification of tumors. Pathology and genetics of tumors of hematopoetic and lymphoid tissues. IARC Press, Lyon (France) 2001. p. 221-224.
3. Kadin ME. Pathobiology of CD30+ cutaneous T-cell lymphomas. *J Cutan Pathol*. 2006; 33: 10-17.
4. Kang SK, Chang SE, Choi JH, Sung KJ, Moon KC, Koh JK. Coexistence of CD30-positive anaplastic large cell lymphoma and mycosis fungoides. *Clin Exp Dermatol*. 2002; 27: 212-215.
5. Leboit PE. Lymphomatoid papulosis and cutaneous CD30+ lymphoma. *Am J Dermatopathol*. 1996; 18: 221-235.
6. Louvet S, Dompmartin A, Troussard X, Galateau F, Moreau A, Reman O, Leporrier M, Leroy D. Spectrum of CD30 lymphoproliferative diseases from lymphomatoid papulosis to anaplastic large cell lymphoma. *Int J Dermatol*. 1996; 35: 842-848.
7. Lee MW, Chi DH, Choi JH, Sung KJ, Moon KC, Koh JK. A case of mycosis fungoides after CD30 positive anaplastic large cell lymphoma. *J Dermatol*. 1999; 27: 458-461.
8. Woodrow SL, Basarab T, Russell Jones R. Mycosis fungoides with spontaneously regressing CD30-positive tumorous lesions. *Clin Exp Dermatol*. 1996; 21: 370-373.
9. Samlowski WE, Conrath FC, Piepkorn MW, Kjeldsberg CR. Immunologic studies documenting the development of mycosis fungoides following successful therapy of a large-cell lymphoma. *Arch Pathol Lab Med*. 1985; 109:864-866.
10. Greenstein AJ, Janowitz HD, Sachar DB. The extra-intestinal complications of Crohn's disease and ulcerative colitis: a study of 700 patients. *Medicine (Baltimore)*. 1976; 55: 401-412.
11. Gregory B, Ho VC. Cutaneous manifestations of gastrointestinal disorders. Part II. *J Am Acad Dermatol*. 1992; 26: 371-383.
12. Vergier B, de Muret A, Beylot-Barry M, Vaillant L, Ekouevi D, Chene G, Carlotti A, Franck N, Dechelotte P, Souteyrand P, Courville P, Joly P, Delaunay M, Bagot M, Grange F, Fraitag S, Bosq J, Petrella T, Durlach A, De Mascarel A, Merlio JP, Wechsler J. Transformation of mycosis fungoides: clinicopathological and prognostic features of 45 cases. French Study Group of Cutaneious Lymphomas. *Blood*. 2000; 95: 2212-2218.
13. Gallardo F, Costa C, Bellosillo B, Sole F, Estrach T, Servitje O, Garcia-Muret MP, Barranco C, Serrano S, Pujol RM. Lymphomatoid papulosis associated with mycosis fungoides: clinicopathological and molecular studies of 12 cases. *Acta Derm Venereol*. 2004; 84: 463-468.
14. Cerroni L, Rieger E, Hodl S, Kerl H. Clinicopathologic and immunologic features associated with transformation of mycosis fungoides to large-cell lymphoma. *Am J Surg Pathol*. 1992; 16: 543-552.
15. Bekkenk MW, Geelen FA, van Voorst Vader PC, Heule F, Geerts ML, van Vloten WA, Meijer CJ, Willemze R. Primary and secondary cutaneous CD30(+) lymphoproliferative disorders: a report from the Dutch Cutaneous Lymphoma Group on the long-term follow-up data of 219 patients and guidelines for diagnosis and treatment. *Blood*. 2000; 95: 3653-3661.
16. Beljaards RC, Willemze R. The prognosis of patients with lymphomatoid papulosis associated with malignant lymphomas. *Br J Dermatol*. 1992; 126: 596-602.
17. Akaraphanth R, Douglass MC, Lim HW. Hypopigmented mycosis fungoides: treatment and a 6(1/2)-year follow-up of 9 patients. *J Am Acad Dermatol*. 2000; 42: 33-39.
18. Jorizzo JL, Solomon AR, Zanolli MD, Leshin B. Neutrophilic vascular reactions. *J Am Acad Dermatol*. 1988; 19: 983-1005.
19. Goto A, Yamamoto S, Notoya A, Takada A, Mukai M. Pyoderma gangrenosum complicated with myelodysplastic syndrome followed by rapidly progressing pyothorax-associated lymphoma: a case report. Hokkaido Igaku Zasshi. 2006; 81: 261-264.
20. Hussain W, Layton A, Baxter K, Scott D. Pyoderma gangrenosum preceding the onset of cutaneous T-cell lymphoma. *Clin Exp Dermatol*. 2006; 31: 284-286.
21. Saito S, Yasui K, Hosoda W, Ogawa M, Kobayashi N, Sakashita K, Koike K. CD30+ anaplastic large cell lymphoma complicated by pyoderma gangrenosum with increased levels of serum cytokines. *Eur J Haematol*. 2006; 77: 251-254.
22. Nguyen KH, Miller JJ, Helm KF. Case reports and a review of the literature on ulcers mimicking pyoderma gangrenosum. *Int J Dermatol*. 2003; 42: 84-94.
23. Delgado-Jimenez Y, Pérez-Gala S, Nam-Cha S, Jones-Caballero M, Fraga J, García-Díez A, Fernandez-Herrera J. Extranodal NK/T-cell lymphoma nasal type mimicking pyoderma gangrenosum. *Acta Derm Venereol*. 2007; 87: 176-177.
24. Carbia SG, Hochman A, Chaín M, Dei-Cas I, Lagodín C, Devés A, Woscoff A. Mycosis fungoides presenting with extensive pyoderma gangrenosum-like ulcers. *J Eur Acad Dermatol Venereol*. 2002; 16: 401-404.
25. Lami MC, Vabres P, Dreyfus B, Germain T, Guillet G. Primary cutaneous B-cell lymphoma mimicking pyoderma gangrenosum: first-line treatment with rituximab. *Br J Dermatol*. 2004; 151: 250-252.