Radiotherapy in aggressive cutaneous pseudolymphoma: a case report and review of literature

Deepa Joseph, MD, Monica Malik Irukulla, MD, Syed Fayaz Ahmed, MD, Deepthi Valiyaveettil, MBBS, Syed Akram, MD

Department of Radiation Oncology, Nizam’s Institute of Medical Sciences, Hyderabad, India

Pseudolymphoma is a nonspecific disease characterized by lesions with lymphomatous-appearing but benign accumulation of inflammatory cells. They generally present as small ulcer-opaque nodular lesions confined to skin which often respond to local therapies. We describe an unusual presentation of an extensive and locally aggressive cutaneous pseudolymphoma in a 21-year-old male patient who presented with extensive cutaneous eruptions gradually progressing over 6 years to involve the entire circumference of his left arm. Magnetic resonance imaging scans of his left arm showed a lesion deeply infiltrating into the soft tissue reaching up to the humerus with intense periosteal reaction. He was successfully treated with radiotherapy after many failed attempts with surgery and chemotherapy.

Keywords: Pseudolymphoma, Radiotherapy

Introduction

Pseudolymphoma (PSL) is a nonspecific disease characterized by inflammatory response to known or unknown stimuli that result in a lymphomatous-appearing but benign accumulation of inflammatory cells [1]. It is a reactive process and usually has a benign course. Cutaneous pseudolymphoma (CPSL) has been described under various terminologies like sarcomatosis cutis, lymphocytoma cutis, lymphadenosis benigna cutis, pseudolymphoma of Spiegl and Fendt, cutaneous lymphoid hyperplasia and actinic reticuloid [1]. Most cases are idiopathic. Cases with known etiologies include reaction to tattoo dye or gold and other jewelry, arthropod bites, infection with Borrelia burgdorferi or molluscum contagiosum, leishmaniasis, vaccinations and acupuncture [2]. It has also been linked to certain drugs like anticonvulsants, antipsychotics, anti hypertensives, cytotoxics, anti rheumatics, antibiotics, antidepressants, anxiolytics, antihistamines, anti arrhythmics, sex steroids, and lipid lowering agents [1]. There are recent case reports implicating drugs like infliximab [3], zoledronic acid [4] etc. as the causative agents. CD8 positive CPSL has also been reported in human immunodeficiency virus (HIV) positive patients [5]. Pseudolymphomas have been described in various other sites and organs including eye, parotid gland, larynx, gastrointestinal tract, lung, tongue [6], orbit [7], kidney [8], breast [9] etc. We describe an unusual presentation of an extensive and locally aggressive CPSL in a young patient and his successful treatment with radiation therapy.

Case Report

A 21-year-old male presented with diffuse lesions over his left upper limb involving the full circumference of his arm extending till the elbow (Fig. 1A). The lesions initially started...
as a small nodule first noticed by him about 6 years ago and recurred despite repeated excisions, each recurrence being more extensive and aggressive than the previous. Histopathological evaluation suggested nonspecific inflammatory lesions. There was no history of any precipitating factors.

On evaluation, magnetic resonance imaging of the left upper limb revealed a fairly large, locally invasive cutaneous and subcutaneous lesion along the middle and lower third of left upper arm. Medially the lesion was insinuating between brachialis and triceps brachii muscle up to the shaft of the humerus with dense periosteal thickening. He also had associated atrophic changes in the muscles of the upper arm (Fig. 2).

Excision of the lesion with skin grafting was performed. Histopathological examination of the excised specimen revealed regular acanthosis of keratinized stratified squamous epithelium with elongation of rete pegs. Superficial dermis showed diffuse infiltrate with inflammatory cells. Deep dermis showed sheets of lymphoid aggregates along with tangible body macrophages. There was destruction of adnexal structures. Immuno-histochemical (IHC) studies showed CD3 positivity in most of the cells, CD20 was focally positive, CD30 was negative and a Ki-67 was 1% (Fig. 3). Hence he was diagnosed with CPSL with predominant T-cell infiltrate. His bone marrow biopsy revealed a reactive marrow. Chest and abdominal imaging were normal except for mild splenomegaly. Blood counts and chemistries were normal. Post-excision, the lesions recurred within 2–3 weeks and progressed rapidly to involve the entire circumference of the arm.

Subsequently, he was treated with chemotherapy with oral cyclophosphamide and prednisolone for 4 months followed by maintenance prednisolone for a total of 9 months. Response to chemotherapy was partial and lesions progressed on withdrawal of chemotherapy. There was no significant response to steroids alone. He was referred for radiation oncology opinion in view of rapid progression after stopping chemotherapy. Clinical examination at that time revealed extensive skin lesions involving the entire left upper arm, extending from the level of deltoid insertion superiorly to the elbow inferiorly. Lesions were diffuse, erythematosus, ulcero-nodular with foul smelling seropurulent discharge, bleeding and crust formation. Range of motion at the elbow joint was significantly reduced. Skin over the rest of his body was normal. He was in severe psychological distress due the nonhealing extensive skin lesions and the associated disability.

He was treated with radiation therapy to a total dose of 30 Gy in 15 fractions to the left arm. Radiation portals covered...
the entire involved area with 2-cm superoinferior margins. Treatment was delivered with 6 MV photons using parallel opposed fields of size 34 cm × 11 cm. During radiation, the lesions initially showed increased erythema and edema with spontaneous bleeding which subsided over 3 weeks. The seropurulent discharge gradually subsided and the treated area was replaced with healthy granulation tissue. There was near complete healing of the affected part, with few areas of scarring, over a period of 6 months (Fig. 1B). The range of motion at the elbow improved considerably. At 26 months following radiation, he had no signs of recurrence and was able to do active work.

Discussion

CPSL most often presents as a solitary nodule that can range from red brown to violaceous in color with a doughy to firm consistency. Other presentations include localized arrays of nodules, plaques or papules and rarely generalized forms [10]. These lesions are generally confined to skin and do not invade into the deeper planes [11].

Pathologically, CPSL is classified into ordinary PSL (O-PSL), PSL with predominant B-cell infiltrates (B-PSL), PSL with predominant T-cell infiltrates (T-PSL) and PSL with mixed and unclassified infiltrates [12]. Our patient had a predominant T-cell infiltrate in his lesions. CPSL is differentiated from cutaneous lymphoma based on the pathological appearance, IHC studies and/or molecular analysis and absence of systemic B symptoms. There have been suggestions to rename this entity as lymphoproliferations of undetermined significance as the terminology is ambiguous in some parts of the world [13].

CPSL lesions are known to regress spontaneously on removal of the known triggering factors. Many cases have been reported to resolve with a short course of topical/systemic steroids. Due to the heterogeneous presentations and clinical behaviors, optimal therapy remains unclear. Persistent disease has been managed with various modalities including local therapies like surgical excision, laser removal, cryosurgery or intralesional corticosteroids [14]. CPSL has also been treated with immunomodulatory agents such as

![Fig. 3. (A) Section shows skin with focal ulceration and acanthosis. Dermis shows diffuse inflammatory infiltrate (H&E, 100x). (B) Section shows dense infiltrate composed of lymphocytes, histiocytes, eosinophils, mast cells and neutrophils, along with foreign-body type giant cells (H&E, 100x).](image-url)
Aggressive cutaneous pseudolymphoma

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

References

1. Ploysangam T, Breneman DL, Mutasim DF. Cutaneous pseudolymphomas. J Am Acad Dermatol 1998;38(6 Pt 1):877-95.
2. Taylor RB, Fortney JA, Pollack RB, Metcalf JS, Jenrette JM. Radiation therapy for B-cell cutaneous lymphoid hyperplasia. Jpn J Radiol 2010;28:385-7.
3. Safa G, Luce K, Darrieux L, Tisseau L, Ortonne N. Erythrodermic CD8+ pseudolymphoma during infliximab treatment in a patient with psoriasis: use of cyclosporine as a rescue therapy. J Am Acad Dermatol 2014;71:e149-50.
4. Kitagawa KH, Grassi M. Zoledronic acid-induced cutaneous B-cell pseudolymphoma. J Am Acad Dermatol 2011;65:1238-40.
5. Ingen-Housz-Oro S, Sbidian E, Ortonne N, et al. HIV-related CD8+ cutaneous pseudolymphoma: efficacy of methotrexate. Dermatology 2013;226:15-8.
6. Robbins R, Peale AR, al-Saleem T. Pseudolymphomas. Am J Roentgenol Radium Ther Nucl Med 1970;108:149-53.
7. Gordon PS, Juillard GJ, Selch MT, Parker RG, Fu YS. Orbital lymphomas and pseudolymphomas: treatment with radiation therapy. Radiology 1986;159:797-9.
8. Fukuda H, Inoue Y, Nishimura Y, Takanashi R. Pseudolymphoma of the kidney: a case report. J Urol 1995;153:387-8.
9. Lin JJ, Farha GJ, Taylor RJ. Pseudolymphoma of the breast. I: in a study of 8,654 consecutive tylectomies and mastectomies. Cancer 1980;45:973-8.
10. Wood GS. Inflammatory diseases that simulate lymphomas: cutaneous pseudolymphomas. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K, editors. Fitzpatrick’s dermatology in general medicine. 8th ed. New York, NY: McGraw-Hill Companies, Inc; 2012.
11. Keri H, Fink-Puches R, Cerroni L. Diagnostic criteria of primary cutaneous B-cell lymphomas and pseudolymphomas. Keio J Med 2001;50:269-73.
12. Terada T. Cutaneous pseudolymphoma: a case report with an immunohistochemical study. Int J Clin Exp Pathol 2013;6:966-72.
13. Levy E, Godet J, Cribier B, Lipsker D. Pseudolymphoma of the skin: ambiguous terminology: a survey among dermatologists and pathologists. Ann Dermatol Venereol 2013;140:105-11.
14. Kluger N, Vermeulen C, Moguelet P, et al. Cutaneous lymphoid hyperplasia (pseudolymphoma) in tattoos: a case series of seven patients. J Eur Acad Dermatol Venereol 2010;24:208-13.
15. Tomar S, Stoll HL, Grassi MA, Cheney R. Treatment of cutaneous pseudolymphoma with interferon alfa-2b. J Am Acad Dermatol 2009;60:172-4.
16. Benchikhi H, Bodemer C, Fraitag S, et al. Treatment of cutaneous lymphoid hyperplasia with thalidomide: report of two cases. J Am Acad Dermatol 1999;40(6 Pt 1):1005-7.
17. Ohzono A, Tsuruta D, Hashikawa K, et al. Three cases of pseudolymphoma successfully treated with amoxicillin. Eur J Dermatol 2013;23:717-8.
18. Mikasa K, Watanabe D, Kondo C, Tamada Y, Matsumoto Y. Topical 5-aminolevulinic acid-based photodynamic therapy for the treatment of a patient with cutaneous pseudolymphoma. J Am Acad Dermatol 2005;53:911-2.
19. Gosain AK, Drolet BA, Neuburg M, Whittaker MH. Cutaneous pseudolymphoma: an unusual presentation of a deep subcutaneous thigh mass. Ann Plast Surg 1995;35:541-5.
20. Olson LE, Wilson JF, Cox JD. Cutaneous lymphoid hyperplasia: results of radiation therapy. Radiology 1985;155:507-9.
21. Kulow BF, Cualing H, Steele P, et al. Progression of cutaneous B-cell pseudolymphoma to cutaneous B-cell lymphoma. J Cutan Med Surg 2002;6:519-28.