



**ORIGINAL RESEARCH PAPER**

**Otorhinolaryngology**

**FOLLICULAR VARIANT OF PRIMARY CUTANEOUS FOLLICLE CENTRE LYMPHOMA OF INFRAORBITAL REGION**

**KEY WORDS:** Cutaneous lymphoma, Infraorbital region, Follicle centre cell, Immunohistochemistry.

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**ABSTRACT**

Primary cutaneous lymphomas are one of the extra nodal types of Non-Hodgkin's Lymphoma. Primary cutaneous lymphomas are mainly divided into B-cell and T-cell. B-cell Follicle centre Lymphoma is most common of all B-cell lymphomas. We present a 38 year old lady who came with an erythematous firm swelling in the right infra orbital region. FNAC showed features of acute and chronic inflammatory cells. The lesion was excised and histopathology showed features of lymphoid follicle formation with centrocytes and centroblasts in dermis and subcutaneous tissue. Immunohistochemistry showed neoplastic nodules positive for CD20, Mum-1, BCL-6 and negative for BCL-2, CD79a, CD10 and CD43. All these features were consistent with follicular variant of follicle centre lymphoma, which is rare. Postoperative PET-CT didn't show any uptake elsewhere. The patient was disease free and was on regular follow up since 2 years. Cutaneous lymphomas are rare and have an indolent course when compared with nodal lymphomas. Primary cutaneous Follicle centre B-cell lymphoma has a good prognosis with a 5-year survival rate up to 95% but do have local recurrences.

**INTRODUCTION:**

Non-Hodgkin's lymphoma (NHL) may be nodal or extra nodal. After GI tract, skin is the most common site for extra nodal lymphomas. WHO and EORTC classified cutaneous lymphomas in 2005 [1]. A new WHO classification showed cutaneous lymphomas as a separate entity. Revised European American classification of Lymphoid neoplasms does not classify it as a separate entity but included in broader classification of follicle centre lymphomas [2]. B-cell lymphomas constitute 25% of all cutaneous lymphomas and are categorised into marginal zone B-cell, follicle centre, large B-cell leg and large B-cell intravascular types [1]. Primary cutaneous follicle centre lymphomas (PCFCL) constitute 55% of all cutaneous B-cell lymphomas (CBCL) [3]. PCFCL is further divided into follicular, diffuse and follicular & diffuse varieties histologically. We report a case of follicular type of PCFCL in the infraorbital region, which is a rare variant of PCFCL.

**CASE REPORT:**

A 38 year old lady presented with history of swelling below right eye since 1 year, which was associated with redness since 3 months. On examination it was a single, globular, erythematous, ill defined, 3x4 cms, firm, immobile, nodular swelling in the right infraorbital region (Fig.1). There was no cervical lymphadenopathy. CT scan showed ill-defined mildly enhancing soft tissue density infiltrating the preaural fat space without erosion of maxilla. Complete blood picture was normal and serology for HbsAg, HCV and HIV was negative. FNAC from the lesion showed features of chronic inflammatory lesion. Excision biopsy was done along with periosteum and the defect was reconstructed with glabellar flap (Fig.2). On histopathology the dermis showed lymphoid follicles with germinal center containing centrocytes and centroblasts, interfollicular region showed plasma cells and histiocytes (Fig.3,4). Sub cutis showed mature adipose tissue and few lymphoid follicle formations (Fig.5). On Immunohistochemistry the neoplastic nodules were positive for CD20, Mum-1 and BCL-6, negative for BCL-2, CD79a, CD10 and CD43. The morphology and IHC features were consistent with primary cutaneous follicle centre B-cell lymphoma. PET-CT done 2 months after surgery showed no uptake elsewhere (Fig.6). Our tumor board deferred adjuvant treatment and advised only regular follow up. The patient was disease-free for 2 years after surgery.

**DISCUSSION:**

Cutaneous lymphoma can be primary or secondary manifestation

of NHL. Primary cutaneous lymphoma was defined as presence of cutaneous lesions without nodal or visceral involvement for a period of at least 6 months after complete staging [4]. The etiology of PCFCL is unknown, but association with Borrelia Burgdoferi, HHV 8 and hepatitis C has been reported [5]. PCFCL occurs rarely in chronic lymphocytic leukemia. It has predilection for males around 60 years of age. Our patient was a 38 year old lady. The lesions are seen mostly in the head & neck and trunk. Lesions in the legs which are rare carry a poor prognosis.

Lesions present as solitary or grouped, erythematous to violaceous papules or pustules which rarely leads to ulceration [6]. In our case there was a solitary erythematous nodular swelling in the right infraorbital region. The lesions mimic rosacea, folliculitis, acne, insect bites and rhinophyma. Histology, immunohistochemistry and a newer technique UV laser beam micro dissection which is more specific are used to categorise cutaneous lymphomas [4]. In PCFCL dermis and subcutaneous tissue contain neoplastic follicles with germinal centers having centrocytes (cleaved cells), centroblasts and interfollicular region having reactive T-lymphocytes. Follicular variant is predominant in head & neck and diffuse type is predominantly seen in trunk [4]. Prognosis does not differ between diffuse and follicular variants, but few studies have shown that cases with diffuse growth, BCL-2 expression and histological large cleaved cells have guarded prognosis [7]. As the tumor increases in size, B-cells also grow and replicate, but T-cells decrease. The tumor expresses B-cell markers like CD20, CD79a, CD10. Follicular variant of PCFCL expresses CD10 and BCL-6 [4]. Diffuse variety is CD10 negative and do not have CD21 dendritic cell network [8]. Our case expressed CD20 and BCL-6, so diagnosed as follicular variant of PCFCL, which is rare. MUM-1 is expressed in <30% of PCFCL cells, this was positive in our patient. BCL-2 positivity and t(14:18) are rare [4]. For single isolated lesions the choice of treatment is surgery or low dose radiotherapy [9, 10]. Superficial fractionated radiotherapy around 1400-1500 cGy has been used [10]. Radiotherapy is also treatment of choice in multiple lesions, histologically predominant large cleaved cell lesions and skin relapses without disease progression. Chemotherapy is indicated in extensive skin lesions and patients with extra cutaneous manifestations [4]. Rituximab and interferon alpha - 2a are used as alternate treatment options if surgery or radiotherapy is not feasible. Systemic and intralesional Rituximab given over 1-8 cycles achieves complete remission in cases of CBCL. Rituximab (anti CD20) is used in combination with

cyclophosphamide for refractory and relapsed cases. The 5-year survival rate for PCFCL is 95% [3]. It rarely affects lymph nodes and internal organs, but cutaneous recurrences are common up to 53.3% [4]. Our patient underwent wide excision only and was disease-free for 2 years after treatment.

**CONCLUSION:**

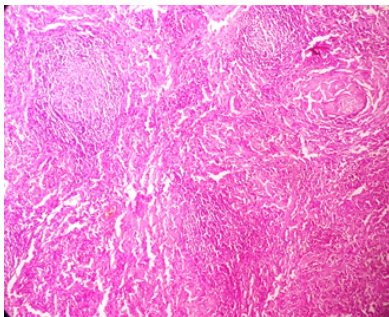
Cutaneous lymphomas are rare and have an indolent course when compared with nodal lymphomas. Primary cutaneous Follicle centre B-cell lymphoma has good prognosis with 5-year survival rate of 95% but can have local recurrences.



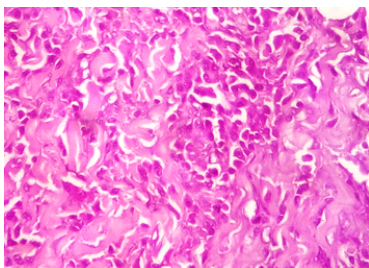
**Fig 1: single globular erythematous lesion in the right Infraorbital region.**



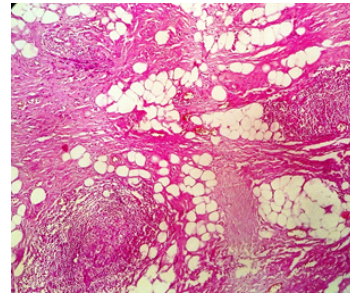
**Fig 2: Post operative picture of patient with excised lesion and reconstructed with Glabellar flap**



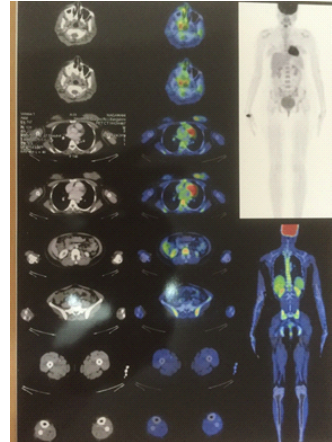
**Figure 3: Dermis shows infiltration by lymphocytes and lymphoid follicles having germinal centre in the reticular dermis H&E (100X)**



**Figure 4 : Interfollicular region showing plasma cells, lymphocytes and histiocytes H&E(400X)**



**Figure 5 : Shows adipose tissue and lymphoid follicle formation in the subcutis H&E(100X)**



**Fig 6: PET-CT showing active focal subcutaneous thickening in the right maxillary region anteriorly with out any other focus.**

**REFERENCES:**

- Burg G, Kempf W, Kazakov DV, Michaelis S, Dummer R, Burg G, Kempt W. Cutaneous lymphomas. Florida: Taylor & Francis Group; 2005. WHO/EORTC Classification of Cutaneous Lymphomas; pp. 91–92.
- Harris NL, Jaffe ES, Stein J, Banks PM, Chan JKC, Cleary ML, et al. A revised European-American classification of lymphoid neoplasms: a proposal from the International Lymphoma Study Group. Blood 1994;84:1361–92.
- Willemze R, Kerl H, Sterry W, Berti E, Cerroni L, Chimenti S, Diaz-Peréz JL, Geerts ML, Goos M, Knobler R, Ralfkiaer E, Santucci M, Smith N, Wechsler J, van Vloten WA, Meijer CJ. EORTC classification for primary cutaneous lymphomas: a proposal from the Cutaneous Lymphoma Study Group of the European Organization for Research and Treatment of Cancer. Blood. 1997 Jul 1;90(1):354-71.
- Cerroni L, Arzberger E, Pütz B, Höfler G, Metzger D, Sander CA, Rose C, Wolf P, Rütten A, McNiff JM, Kerl H. Primary cutaneous follicle center cell lymphoma with follicular growth pattern. Blood. 2000 Jun 15;95(12):3922-8.
- Viguier M, Rivet J, Agbalika F, Kerviler E, Brice P, Dubertret L, Bachelez H: B-cell lymphomas involving the skin associated with hepatitis C virusinfection. Int J Dermatol 2002, 41:577–582.
- Suárez AL, Pulitzer M, Horwitz S, Moskowitz A, Querfeld C, Myskowski PL. Primary cutaneous B-cell lymphomas: part I. Clinical features, diagnosis, and classification. J Am Acad Dermatol. 2013 Sep;69(3):329.e1-13; quiz 341-2.
- Bekkenk MW, Postma TJ, Meijer CJ, Willemze R. Frequency of central nervous system involvement in primary cutaneous B-cell lymphoma. Cancer 2000, 89:913–919.
- Hoefnagel JJ, Vermeer MH, Jansen PM, Fleuren GJ, Meijer CJ, Willemze R: Bcl-2, Bcl-6 and CD10 expression in cutaneous B-cell lymphoma: further support for a follicle centre cell origin and differential diagnostic significance. Br J Dermatol 2003, 149:1183–1191.
- Wanczinski MI, Pinto CAL, Trevisan F, Cunha PR, Grohs LMH. Primary cutaneous follicle center lymphoma simulating basal-cell carcinoma on the nasal ala. An Bras Dermatol. 2015;90(3 Suppl 1):S111-4.
- Ceovic et al.: Radiotherapy of primary cutaneous follicle center lymphoma: case report and review of literature. Radiation Oncology 2013 8:147.