Case Report

An intriguing case report of follicular lymphoid hyperplasia of tongue with the detailed review of literature

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Abstract

Follicular lymphoid hyperplasia is a rare reactive benign lesion of the oral mucosa. This is also known as pseudolymphoma as the features mimic the malignant counterpart Follicular lymphoma. In present case, a 34 year old male patient came with a nodular swelling in the posterior–lateral left side of tongue. Medical or dental history was non contributory. Swelling was painless, well demarcated, and about peanut sized. The swelling was provisionally diagnosed as either neurilemmoma, mucocele, or traumatic fibroma. Complete excision was performed, and tissue was sent to a private laboratory. Histopathological findings seen were germinal centers having a core of monotonous cells of the same size and demarcated mantle area mimicking the lymphoma. Immunophenotyping revealed diffused positivity for kappa and lambda expressions. CD10 was diffusely positive in germinal centers and BCl 2 was positive in the mantle area while negative in germinal centers. The final diagnosis given was follicular lymphoid hyperplasia. The entity mentioned in the present paper is an unusual variant of the benign lymphoproliferative lesion and very few cases are reported in the tongue area. Thus, it is important to understand the nature of this benign lesion in all aspects to avoid diagnostic dilemmas due to its malignant mirroring characteristics.

Keywords: Germinal centres, lymphoid lesion, polyclonal cells, pseudolymphoma

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INTRODUCTION

Follicular lymphoid hyperplasia (FLH), which is also known as benign lymphoid hyperplasia (BLH), reactive lymphoid hyperplasia, nodular lymphoid lesion or pseudolymphoma, is a benign lymphoid tacit entity which resembles the follicular lymphoma.[1] The aetiology of (FLH) could be any unknown antigenic response or a reactive action against chronic irritation.[2] Histopathologically, lymphoid hyperplasia can be seen as a sinusoid, diffuse, follicular, or mixed pattern and amongst these, the follicular pattern is the commonest pattern seen in the head and neck region.[3] The rarity of the lesion in the head and neck region makes its diagnosis difficult. To the best of our knowledge, only 43 cases of FLH have been reported so far [Table 1][4-18]. We hereby present a case report on FLH with a review of the literature.

CASE REPORT

A 34-year-old male patient reported with a complaint of

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swelling on the left posterior–lateral border of the tongue for over one month. There was no significant medical history, family history, or habit history. Extra-orally face was symmetrical, with no changes in vitals. Lymph nodes were nonpalpable. Intra-orally, the swelling was sessile, measuring 0.5 mm × 0.6 mm approximately, red in colour, homogenous, and soft in consistency. The swelling was non-ulcerative and painless. No other similar lesion was seen in the oral cavity or elsewhere. The patient was unable to recollect any history related to trauma. The provisional diagnosis was neurilemmoma, irritational fibroma, benign salivary gland tumour, or mucocele. A total blood count was done and a slight rise in white blood cells was evident. Additional investigations were done like serology to rule out any viral lesion. After receiving an informed consent complete excision with curettage was done under local anaesthesia and tissue was sent to a private laboratory for histopathological investigations. Histopathologically, parakeratinized stratified squamous epithelium was seen with few dysplastic features like altered nuclear/cytoplasmic ratio and hyperchromatic nuclei in 1/3rd of epithelium. In connective tissue, multiple germinal centres with distinct mantle zone were evident. Few histiocytes were observed [Figures 1 and 2]. Immunohistochemistry was conducted for kappa and lambda chains. Kappa and lambda chains showed polyclonality and diffused positivity. Bcl-2 marker was positive in the mantle area and negative in germinal centres [Figure 3]. Diffused positivity was seen with CD10 in germinal centres [Figure 4]. After all investigations, a diagnosis was confirmed as follicular lymphoid hyperplasia. The patient was asked to visit for regular follow-ups after every 6 month interval. A 1-year follow-up was done and no recurrence, no adverse, and unanticipated events were observed or reported to date.

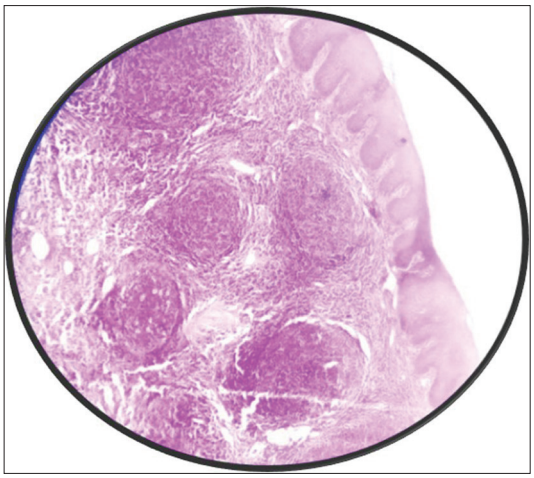

Figure 1: Mildly dysplastic epithelium with germinal centres and mantle area (4× view)

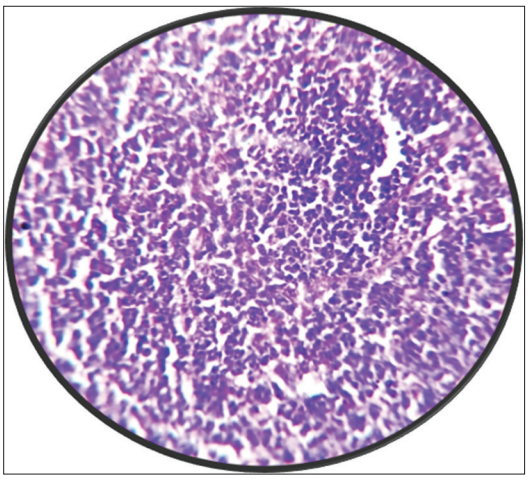

Figure 2: Inflammatory cells, majorly lymphocytes are seen. (40×)

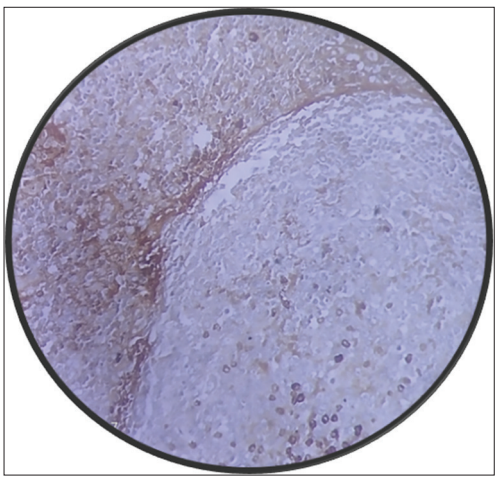

Figure 3: BCL-2 showing demarcated positivity for the mantle area and negativity for germinal centres. (40×)

DISCUSSION

The first case of lymphoid hyperplasia was reported by Adkins in 1973. He explained a lesion with lymphoid hyperplasia which was seen commonly in the hard palate.[10] FLH can be seen on the hard palate, tongue, and oral mucosa in the age range 38–79 years.[1] As per the present literature, females are more commonly affected than males.[1,3] It is a painless, slow-growing, mucosa-coloured nonulcerated hard swelling. After a meticulous search of PubMed database and Google Scholar, we found that to date only 43 cases have been reported [Table 1] The aetiology of FLH is not explained but there are cases which may occur due to some antigenic response, chronic irritation, Epstein–Barr virus association, etc.[18] Lymphoid hyperplasia can be divided into two variants, namely, benign lymphoid hyperplasia and atypical lymphoid hyperplasia.[1]

Radiographical features are quite variable. Some cases exhibit no bone involvement, while others reveal prominent radiolucency mimicking malignancy.[1]

Table 1: List of cases reported in present literature (except case reported by Adkins *et al.*)

Author	Year	Cases	Age/ Sex	Site	Provisional diagnosis	Investigations	IHC markers	Final diagnosis	Treatment	Recurrence and follow-up (years)
Harsany D L *et al.*[4]	1980	4	60/F	HP	–	–	NS	FLH	Excision	12
			47/M	HP, SP				FLH	radiotherapy	4
			72/F	MF				FLH	Excision	9
			70/F	HP				FLH	Excision radiotherapy	7
Wright and Dunsworth[5]	1983	1	72/F	HP	NS	Peripheral blood smear–normal, CT scan, bone marrow biopsy	NS	FLH	Excision	2 NR
Bradley *et al.*[6]	1986	7	76/F	HP	NS	H	NS	BLH	Excision	4 NR
			73/F	HP	NS	H	NS	BLH	No treatment	8 NR
			62/F	HP	NS	H	NS	BLH	No treatment	3.5 NR
			57/F	SP	NS	IP for kappa and Lambda	NS	BLH	Excision	3 NR
			41/M	SP	NS	H	NS	BLH	Excision	3.3 NR
			51/F	HP	NS	H	NS	BLH	Excision	RSL and after
			60/F	HP	NS	H, CBC, ESR, FR, ANR, SIEP, Qlg,	NS NS	BLH	No treatment	3 years NR of SL 12 presences of PL
Davila and Thomson[7]	1988	1	49/F	HP	NS	Liver scan CT scan Bone marrow biopsy, Serology for various titres		RLH	Excision	7 NR
Napier and Newlands[8]	1990	2	38/F	JHPSP	Salivary adenoma	H immunoperoxidase staining	NS	BLH	Excision	NS
			79/F	JHPSP	Salivary Adenoma	H immunoperoxidase staining	NS	BLH	Excision	NS
Mopsik *et al.*[9]	1992	1	63/M	HP	Lymphoma	CBC, ESR, cholesterol, TAP, ECG, Radiograph, Chest X-ray, CT scan	NS	FLH	Excision	NS
Menasce *et al.*[10]	2001	3	51/M	JHPSP	Salivary gland tumour	H, Immunostaining	BCL-2 +ve MA and –ve GC kappa and lambda were equivocal	FLH	Excision	4 NR
			75/M	HP		H, Immunostaining		FLH	Excision	2 NR
			61/F	V and T	Pleomorphic adenoma, lymphoma	H, Immunostaining serology	BCL-2 +ve MA and –ve GC BCL-2 –ve GC Light chains polytypic	FLH	Excision	12 RSL
Kolokotronis *et al.*[11]	2003	1	74/F	HP	NS	H, Panoramic and occlusal radiograph, IHC	CD20, CD45RO, BCL-2 –ve lymphoid cells	FLH	Excision	1.5 NR
Carnelio *et al.*[12]	2005	1	36/F	T	Malignancy of T	Hemogram, serology, chest X-ray	NS	BLH	Excision	4 NR
Kojima *et al.*[13]	2005	1	49/F	BM	NS	H, IHC, ISH	CD20 +ve, IgM , IgD+ve in GC , MA, CD 10 +ve and BCL-2 –ve in GC, CD3, CD45RO scattered in lymphocytes of nodule, CD57 +ve, CD30 +ve IFA, EMA –ve, CD 15 –ve in IFA, CAN.42 follicular dendritic cells	FLH	Excision	1.3 NR
Jham *et al.*[14]	2009	1	55/F	HP	Mesenchymal tumour, lymphoma, salivary gland tumour	H, Panoramic and occlusal radiograph, IHC	CD 10 +ve LF, CD21, BCL-6 CD20 +ve/CD79α, +ve -LF, CD3 +ve/CD5 +ve PFA, CD45 + PFA and LF, BCL-2 – ve LF, CD30 PFA immunoblasts, CD 15 +ve granulocytes	FLH	No treatment	0.25 NR

Contd...

Table 1: Contd...

Author	Year	Cases	Age/ Sex	Site	Provisional diagnosis	Investigations	IHC markers	Final diagnosis	Treatment	Recurrence and follow-up (years)
Sands *et al.*[15]	2011	1	64/F	OP	Lymphoma	Immunohistochemical markers for lymphoma, CT scan, HIV serology	NS	BFLH/ Intrafollicular lymphoid hyperplasia	Adenotonsillectomy along with a tapering dose of prednisolone for 3 weeks	NS
Gordon-Nunez *et al.*[16]	2012	1	70/F	SP	NS	H, IHC	BCL-2+ve in MA, –ve in GC	FLH	Excision	1.8 NR
Anjomshoaa *et al.*[17]	2013	1	46/F	HP	Pleomorphic adenoma, mucoepidermoid carcinoma	Immunohistochemistry, situ hybridization for kappa and lambda chains showed polyclonality	CD20 +ve GC, MA and IFA, BCL-2++ in MA and IFA, –ve for GC, CD3 and CD5 diffused +ve in GC and IFA and – ve MA, BCL-6++ MA, CD10 ++ve GC, Cyclin D+ve scatter at few cells	Florid FLH with mild atypia	Intralesional steroid injections	0.7 NR
Watanabe *et al.*[1]	2017	1	61/M	BM	Granuloma	Biochemical tests, haematological tests,	L-26, LCA, CD79α, UCHL-1 +ve, CD10, CD56 –ve, BCL-2 +ve MA, CD23 +ve MA	BLH	No treatment	2 NR
Watanabe *et al.*[18]	2019	1	51/F	Maxilla	Castleman's disease	MRI, CT	CD20, Cd79a +ve LF, CD10 -ve GC, BCl-6 +ve GC, Ki67 +ve GC, BCL-2 No expression, CD3 +ve inPFA, CD5 +ve PFA, CD45RO +ve GC and MA, CD15 -ve GC and MA	FLH	Excision	1 NR
Luana *et al.*[3]	2021	15	36/F	SR	HLN/LH		CD3+ve MA, IFA	FLH	Excision	10 NR
			15/F	BM	NS	Panoramic	CD20++ve MA, + GC	FLH	Excision	7 NR
			30/F	BM	LNS	US	CD68+ve macrophages in GC, IFA	FLH	Excision	12 NR
			08/F	PR	LN	H, IHC for all cases	BCL-2+ve MA, PFA, –ve GC	FLH	Excision	08 NR
			38/M	T	FH			FLH	NS	17 NR
			44/F	BM	NF/L			FLH	NS	07 NR
			34/M	BM	FL/NF			FLH	Excision	06 NR
			41/F	T	PH			FLH	Excision	05 NR
			39/M	SG	SGA			FLH	Excision	05 NR
			NS/F	HP	Hg/PG			FLH	Excision	20 NR
			NS/F	SP	FH/M			FLH	NS	13 NR
			43/F	T	FH			FLH	Excision	09 NR
			NS/F	BM	NF/L			FLH	Excision	06 NR
			10/F	BM	R			FLH	Excision	02 NR
			39/F	T	OEC			FLH	Excision	0.7 NR
Present case	2022	1	34/M	T	M	H and IHC	Kappa and lambda chains, BCL-2+ve for mantle area and–ve in germinal centres, CD10 diffused+ve in GC	FLH	Excisional	1 NR

HP—Hard palate, SP—soft palate, MF—multifocal, OP—oropharynx, v—vallecula, T—tongue, BM—buccal mucosa, SR—submentonian, PR—parotid region, SG—salivary gland, NS=Not stated, H—histopathology, IHC—immunohistochemistry, + ve—positive, ++—strongly positive, ISH—in situ hybridization, GC—germinal centres, MA—mantle area, LF—lymphoid follicles, IFA—intrafollicular area, PFA—parafollicular area, CBC—complete blood count, ESR—erythrocyte sedimentation rate, Rf—rheumatoid factor, ANR—antinuclear rate, serum immunoelectrophoresis—SIEP, CT scan-computed tomography scan, MRI—magnetic resonance image, ECG—electrocardiogram, quantitative immunoglobulins—QIg, transaminase alkaline phosphatase, NR—no recurrence, PL—primary lesion, RSL—recurrence into secondary lesion. SL—secondary lesion, HLN—hyperplastic lymph node, LH—lymphoid hyperplasia, LNS—lymph node swelling, LN—lymph node, FH—fibrous hyperplasia, NF—neurofibroma, L—leiomyoma, FL—fibrolipoma, PH—papillary hypertrophy, SGA—submandibular gland alteration, Hg—haemangioma, PG—pyogenic granuloma, M—mucocele, R—rhabdomyoma, OEC—oral epithelial cyst

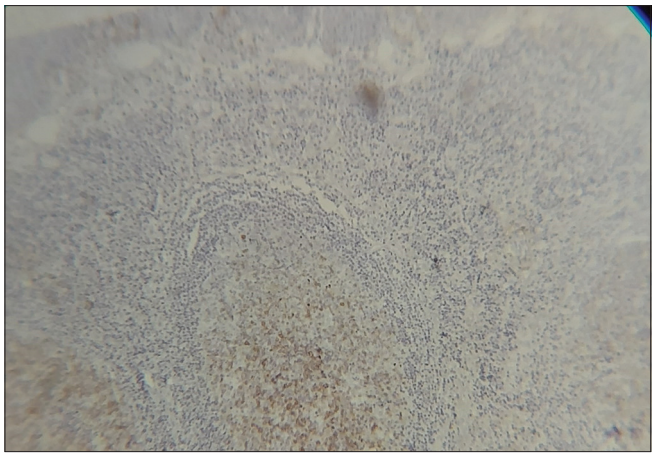

Figure 4: CD10 showing diffuse positivity in germinal centres and negative for the mantle area

Histopathologically, the characteristic feature is the presence of germinal centres with diffused lymphocytes, and macrophages, along with distinct mantle areas in the submucosa and lamina propria. There are two types of follicles seen in FLH. Primary lymphoid follicles where distinct germinal centres are seen and mantle zone is not evident and secondary lymphoid follicles where germinal centres are surrounded by a peculiar mantle zone. In the present case, we observed secondary lymphoid follicles. Many cases do represent epimyoepithelial cell islands.[10] FLH can show lymphoid follicles, diffuse inflammatory infiltrate, focal inflammatory infiltrate, macrophages with apoptotic bodies and mitotic figures.[3] Immunohistochemistry (IHC) plays an important role in differentiating FLH and FL. There is a panel of IHC markers [Table 1]. In our case, we found that kappa and lambda chains showed diffused positivity, whereas CD10 was diffusely positive in germinal centres, while BCl-2 was positive for the mantle zone and negative for germinal centres as seen in many other studies mentioned in Table 1.

Differential diagnosis of FLH includes lymphoma, mesenchymal tumours, neoplasm of the salivary gland and adenomatoid hyperplasia.[15] Differentiating points of FLH and follicular lymphoma is given by Nathwani *et al*.[19] in 1981. They stated four characteristic features. The first being a follicular pattern which is uniform irrespective of size and shape and a little interfollicular tissue zone. Second is the number of follicles which is more in FL and the third criterion is interfollicular cells showing resemblance with follicular cells and is seen in FL. The fourth characteristic feature which differentiates FL and FLH is the presence of histiocytes and the absence of phagocytic activity. All above-mentioned criteria were considered and detected in a present case like the presence of few follicles, interfollicular cells were not resembling germinal centre cells, and the presence of histiocytes. A major difference was BCL-2 marker which was negative in germinal centres and positive for the mantle area led us to the present diagnosis. A few other lesions like mucosa-associated lymphoid tissue-like lymphoma, immunoglobulin G4 disease, Sjogren's syndrome, Castleman's disease, human immunodeficiency virus-related lesion, and diffuse infiltrative lymphocytosis syndrome are the differential diagnosis of the present entity.[3,10,17]

In most cases, surgical excision followed by deep curettage is the treatment of the choice.[10] There is also evidence of remission were corticosteroid injections. The recurrence rate of FLH is 16.7%, and the prognosis is different than that of malignant tumours.[1] It has been stated that multiple-site involvement may lead to mucosa-associated lymphoid tissue-like lymphoma.[10] Contradictory to the same in a published case report, after follow up author saw that there is no involvement of the disease.[10]

CONCLUSION

Follicular lymphoid hyperplasia is a benign entity simulating malignant lesion follicular lymphoma. Very few cases of FLH have been reported to date. Hence along with the help of histopathology and immunohistochemistry, a clinician can draw a definite treatment plan distinguishing the nature of the lesion. Such cases do require follow-ups for a longer period of time to attain a record of no recurrence of primary or secondary lesions. More studies should be conducted to understand the clinical features, histopathology, nature of the lesion and prognosis. We recommend this lesion be involved in the differential diagnosis of lymphoproliferative tumours.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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