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CASE REPORT

Extranodal follicular dendritic cell sarcoma involving tonsil

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Abstract

Follicular dendritic cell sarcoma (FDCS) is a rare neoplasm arising from lymph nodes as well as extranodal sites. Despite the characteristic histopathological features and distinctive immunophenotype, extranodal FDCS are often misdiagnosed initially as undifferentiated carcinoma, inflammatory pseudotumour, meningioma, metastatic malignant melanoma, ectopic thymoma, etc., because of its rarity and lack of awareness. Correct diagnosis of this tumour is imperative given its potential for recurrence and metastasis. We report a case of tonsillar FDCS in a 30-year-old lady who presented with slowly progressing throat pain and dysphagia for a duration of one year. Local examination showed an enlarged left tonsil with an ulceroproliferative growth. The right tonsil was normal. There was no regional lymphadenopathy. Histopathological examination of the tonsillectomy specimen showed a 2.2 x 1.5 cm infiltrative tumour composed of ovoid to spindle cells arranged in characteristic storiform, interlacing fascicular and diffuse patterns. The tumour cells were immunopositive for CD21, CD23, CD35, and S-100 protein and negative for cytokeratin. The Ki-67 antigen-labelling index (Ki-67 LI) was 6%. The EBV status was negative. It was classified as a low risk FDCS. The patient was lost to follow-up after 6 months.

Keywords: extranodal, follicular dendritic cell sarcoma, tonsil

INTRODUCTION

Follicular dendritic cells (FDC) belong to the accessory immune system and are normally present in the germinal centre of primary and secondary follicles. They are non-lymphoid, non-phagocytic cells which play major roles in the induction and maintenance of the humoral immune response. They are best visualised by immunostaining with FDC markers such as CD21,CD35, Ki-M4p and Ki-FDC1p.[1] Follicular dendritic cell sarcoma (FDCS) is a neoplastic proliferation featuring morphological and immunophenotypical characteristics of follicular dendritic cells. It is regarded as an indolent tumour with a tendency of local recurrence but low risk of metastasis, behaving like a low grade soft tissue sarcoma.[1] FDCS commonly affects lymph nodes, the involvement of extranodal sites being rare.[2]

CASE REPORT

A 30-year-old female presented with slowly progressing throat pain and dysphagia for a duration of one year. Local examination showed an enlarged left tonsil with an ulceroproliferative growth. The right tonsil was normal. There was no regional lymphadenopathy.

Pathology

We received a left tonsillectomy specimen measuring 2.6 x 1.7 x 1 cm which showed an ulceroproliferative growth measuring 2.2 x 1.5 cm. The cut surface revealed a circumscribed mass with homogenous gray white appearance.

Histopathological examination showed tonsil with an infiltrative tumour composed of ovoid to spindle cells arranged in characteristic storiform, interlacing fascicular and diffuse patterns. Distinct cellular whorls in 360 degree were also observed (Figs. 1 and 2). The individual tumour cells had moderate amount of eosinophilic cytoplasm with indistinct cytoplasmic borders. The nuclei had delicate nuclear membrane with finely dispersed chromatin and distinct nucleoli. The neoplastic spindle cells were intimately admixed with mature lymphocytes with focal perivascular cuffing (Fig. 3). The tumour showed

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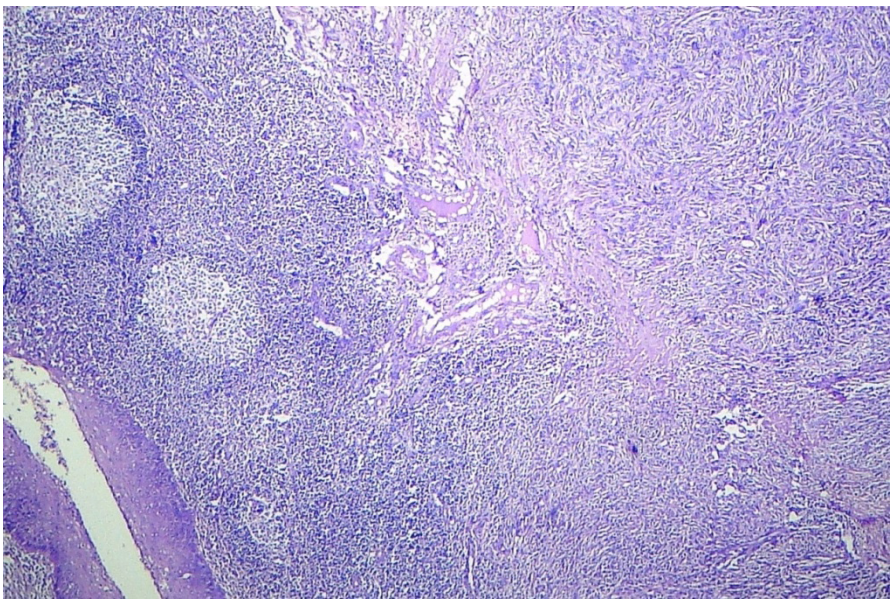

FIG. 1: Tonsil with tumour (H&E x100)

few multinucleated tumour giant cells, areas of necrosis and occasional mitotic figures.

Immunohistochemistry revealed that the tumour cells were positive for CD21, CD23, CD35, and S-100 protein. The cells were immunonegative for cytokeratin. The Ki-67 antigen-labelling index (Ki-67 LI) was 6% (Fig. 4). Based on the characteristic histological and immunohistochemical findings, a diagnosis of tonsillar FDCS was rendered.

Clinical course

The patient was lost to follow up. Hence details about any treatment other than surgery and clinical course are not known.

DISCUSSION

Proliferation of follicular dendritic cells occurs in a number of reactive and neoplastic conditions such as reactive follicular hyperplasia, follicular

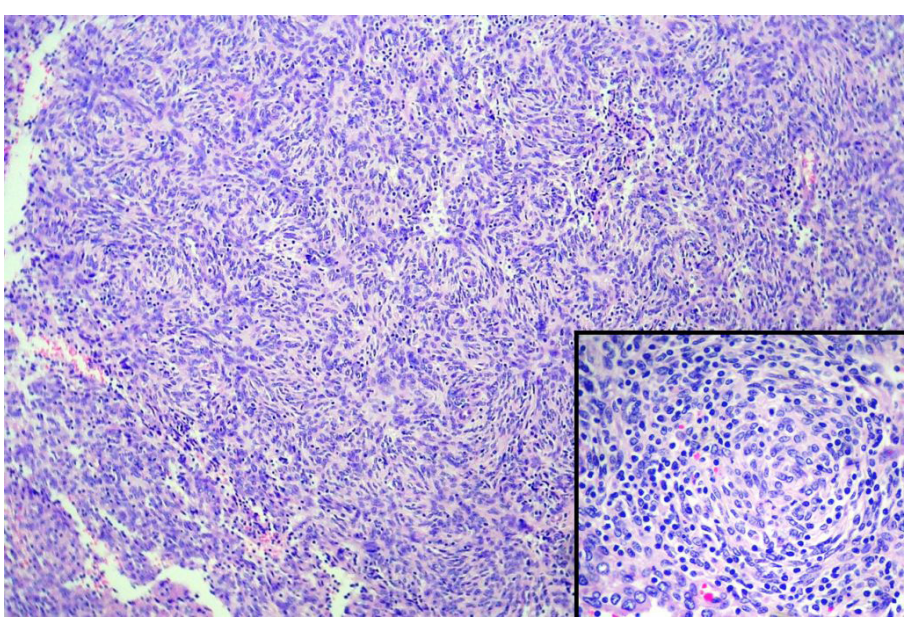

FIG. 2: Tumour cells arranged in characteristic storiform, interlacing fascicular and diffuse patterns. Inset showing distinct cellular whorls in 360°. (H&E, x100)

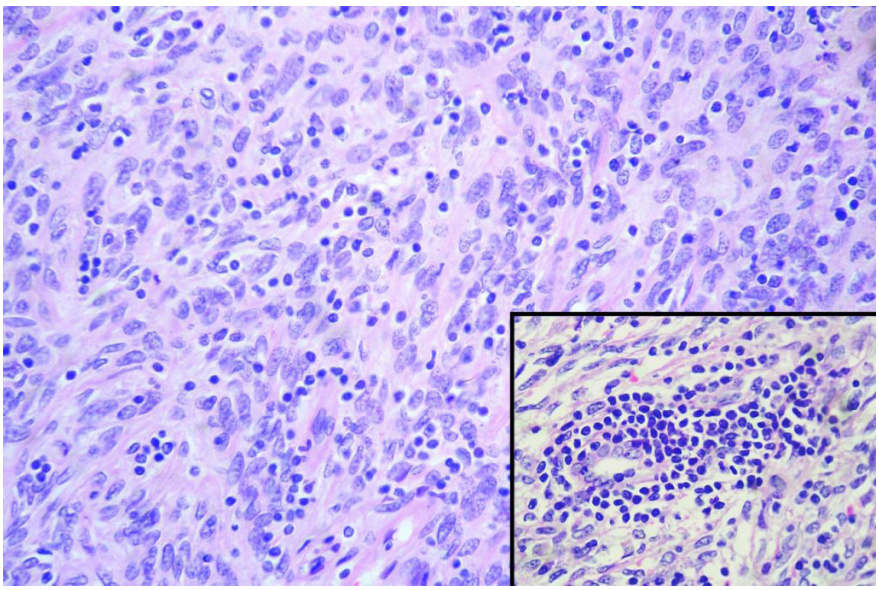

FIG. 3: Neoplastic spindle cells with delicate nuclear membrane, finely dispersed chromatin and indistinct cytoplasm with sprinkled mature lymphocytes. Inset showing perivascular cuffing. (H&E, x400)

lymphoma, mantle cell lymphoma, nodular lymphocytic predominant Hodgkin lymphoma and angioimmunoblastic T cell lymphoma.[3] The existence of FDC tumours was predicted by Lennert in 1978 but it was not until 1986 that the tumour was first characterised by Monda *et al*.[4] Extranodal FDCS account for one third of cases and involve liver, tonsil, head and neck, gastrointestinal tract, skin, lung and breast.[2] Only 30 cases of FDCS of tonsil have been reported in the English literature till date.[5-30] These are summarised in Table 1. As evident from the table, metastases of FDCS has been reported as late as 8 years after surgery, underscoring the pivotal role of the correct diagnosis.

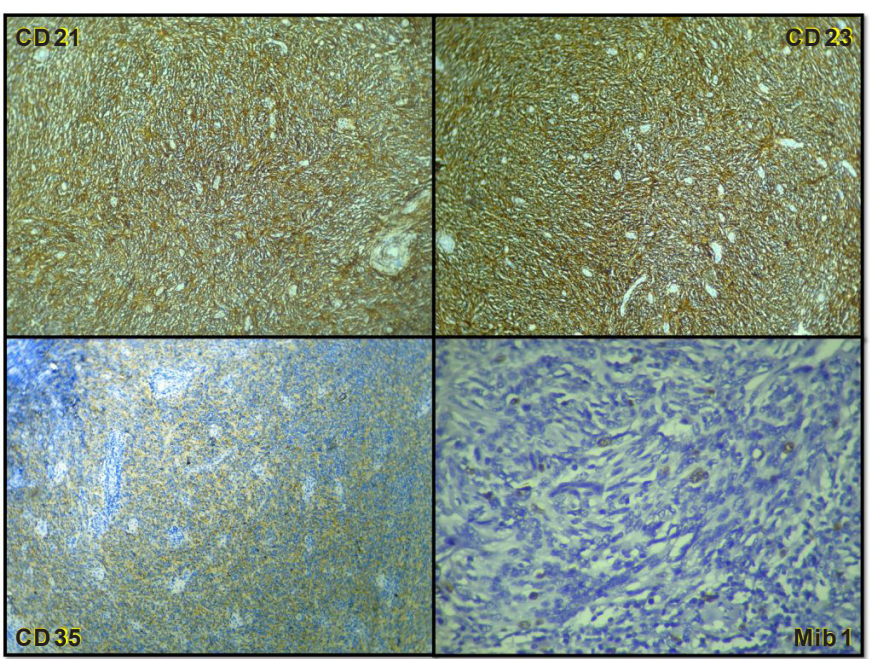

FIG. 4: Immunohistochemistry showing tumour cells expressing CD 21, CD23 and CD 35 Mib1 labelling index is 4-6%.

TABLE 1: Summary of cases of tonsillar FDCS in English literature

Author (year)	Age (yrs)/ Gender	Side of tonsil	Symptoms	Tumour size (cm)	Metastasis	Recurrence	Status	Follow up (months)
Chan *et al*[5] (1994)	44/F	Left	NA	1.5	No	No	NED	36
Perez-Ordonez *et al*[6] (1996)	62/F	Tonsil	NA	NA	No	No	NED	12
Nayler *et al*[7] (1996)	18/F	Tonsil	Enlarged bilateral tonsil	4x2x2	NA	NA	NA	Lost to FU
Chan *et al*[8] (1997)	32/M	Right	Enlarged right tonsil	Weight 8gm	Cervical LN metastasis 4.5yrs postsurgery	Yes, 4.5yrs postsurgery	AWD	54
Vargas *et al*[9] (2002)	54/F	Left	Neck mass, weight loss	3	No	No	NED	8
Biddle *et al*[10] (2002)	48/M	Right	Pain in tonsillar area	3.5x2x2	No	No	NED	8
	48/F	Left	Enlarged hard lymph node in submandibular region	3.5x3.5x2	No	No	NED	6
Tisch *et al*[11] (2003)	51/M	Left	Globus sensation	NA	No	No	NED	60
Grogg *et al*[12] (2004)	57/F	Tonsil	NA	NA	NA	No	AWD	8
Idress *et al*[13] (2004)	70/F	Tonsil	A tonsil mass	NA	Yes	Yes	Lung & hilar LN	96
Dominguez-Malagon *et al*[14] (2004)	48/M	Left	Dysphagia	1.5x1.5	No	No	NED	36
Bothra *et al*[15] (2005)	34/M	Right	NA	NA	Yes	No	AWD	120
	45/M	Right	NA	NA	No	No	NED	12
	40/M	Left	NA	NA	No	No	NED	12
Shia *et al*[16] (2006)	69/F	Tonsil	NA	NA	Lung & hilar LN 8 yrs postsurgery	No	AWD	108
Clement *et al*[17] (2006)	27/F	Right	Dysphagia	4x3x2	No	No	NED	6
Aydin *et al*[18] (2006)	76/F	Left	A mass in tonsil	3.5x3.5x1.5	No	No	NED	48
Fan *et al*[19] (2007)	48/F	Right	Tonsillar swelling & weight loss	NA	Yes	Yes 15 years	AWD	
Mcduffie *et al*[20] (2007)	59/F	Right	A mass in tonsil& OSA	4	No	No	NED	18
Vaideeswar *et al*[21] (2009)	50/M	Left	Dysphagia	2x2	No	No	NED	48
Suchitha *et al*[22] (2010)	63/M	Left	Dysphagia, Blood tinged sputum	4.2x4x2	NA	NA	AWD	8
Li *et al*[23] (2010)	60/M	Tonsil	NA	5	No	No	NED	86
Duan *et al*[24] (2010)	41/M	Left	Hypertrophy of tonsil	3x3x2	No	No	NED	9

Author (year)	Age (yrs)/ Gender	Side of tonsil	Symptoms	Tumour size (cm)	Metastasis	Recurrence	Status	Follow up (months)
Suhail *et al*[25] (2010)	52/F	Right	Swelling in the throat & dysphagia	2.5x2	No	No	NED	12
Eun *et al*[26] (2010)	65/M	Right	Discomfort during swallowing	1x1	No	No	NED	24
Mondal *et al*[27] (2012)	27/M	Left	Difficulty in swallowing	2.8x2.6x2.3	No	No	NED	6
Kara *et al*[28] (2013)	72/M	Right	Painless tonsillar region mass, Discomfort during swallowing, respiratory distress	5x3	NA	NA	Died after 1st dose of chemo-therapy	24
Hu *et al*[29] (2013)	59/F	Left	Oropharyngeal mass, dysphagia, dyspnoea	4.5x4x2	No	17 months	DOD	24
	36/F	Left	Oropharyngeal mass, dysphagia	3x2.5x1.5	No	Yes 6 months	AWD	15
Lu *et al*[30] (2015)	59/M	Right	Globus sensation	4.6x2.5x2.5	No	No	NED	32
Present case	30/F	Left	Throat pain, dysphagia	2.2x1.5	No	No		Lost to FU after 6 months

NA- not available, NED - no evidence of disease; AWD - alive with disease; DOD- died of disease; F- female; M- male; OSA- obstructive sleep apnoea; FU- follow up

FDCS is a painless, slow growing, well-circumscribed mass. Tonsillar involvement clinically manifests as an irregular tonsillar growth with or without ulceration of the overlying mucosa and/or associated lymphadenopathy. Patients usually present with dysphagia or pain in the tonsillar region. Our patient presented with dysphagia and throat pain.

Monda *et al* have reported a size range of 1-20 cm for extranodal FDCS in their series. While intra-abdominal tumours had a median size of 11 cm, tumour size outside the abdominal cavity was 3 cm. Grossly, the tumours were well-circumscribed, fleshy masses with solid tan cut surface. Larger tumours showed areas of haemorrhage and necrosis.[4] In our case the tonsil was enlarged and showed an ulceroproliferative growth with homogenous gray tan cut surface. Typical tumours are composed of oval to spindle cells arranged in whorls, fascicular or storiform pattern showing mild nuclear atypia and sparkled small lymphocytes. Epithelioid and pleomorphic patterns suggest anaplastic phenotype. On the basis of histopathological features, Li *et al* defined the criteria for low and high grade tumours using six parameters. Of these, architectural patterns, cellular features, Ki-67 LI and mitoses are the four decisive parameters and regarded as major factors for grading. Lesions with typical architectural and cellular features, mitotic count <5/10 high power fields (HPF) and Ki-67 LI up to 10%, as in our case, were classified as low grade tumours. Those with anaplastic morphology, mitotic count more than or equal to 5/10 HPF and/or Ki-67 LI>10% were classified as high grade tumours. Necrosis and loss or reduction of infiltrating lymphocytes was found to be useful adjuvant factors but not prerequisites for establishing the diagnosis of high grade lesions. These two groups behave as low and high grade soft tissue sarcomas.[23]

Our case revealed typical features with a few scattered multinucleated tumour giant cells which have also been described by Perez-Ordonez *et al*.[6]

The differential diagnoses include ectopic meningioma, ectopic or orthotopic thymoma, malignant melanoma, malignant fibrous histiocytoma and large cell lymphoma. All these tumours lack immunoreactivity for CD21, CD35, Ki-M4p and Ki-FDC1p.[4]

Diagnosis of a spindle variant of squamous cell carcinoma was also considered in our case. However, the overlying mucosa did not show features of carcinoma *in situ*. Also, negative cytokeratin staining ruled out the possibility of carcinoma. Tumour cells were positive for CD21 and CD35 confirming FDCS.

At present, there is no established aetiology for FDCS. FDC express the EB virus receptor CD21 and proliferations of FDC occurring in a subset of inflammatory pseudotumors, most commonly in the liver and spleen have been associated with the Epstein-Barr virus (EBV). However, EBV is absent in nodal and most extranodal FDCS.[31-33] Hence the role of EBV is controversial. The EBV status (EBER test) in our case was negative.

Interestingly, hyaline vascular Castleman disease has been identified as a possible predisposing factor in a minority of cases. There are reports of FDCS and hyaline vascular Castleman disease coexisting in a single specimen as well as FDCS occurring at the same site of hyaline vascular Castleman disease on sequential biopsies.[34-36] Epidermal growth factor receptor expression has been investigated as another shared feature of these two entities. The receptor expression is positive in the tumour cells of FDCS and FDC in Castleman disease, whereas it is negative or weakly positive in FDC of reactive lymph nodes, tonsils and FDC networks of lymphomas.[35]

According to Li *et al*,[23] tumour size and histological grade were the most important factors respectively, for recurrence and disease-associated death. The authors have established a model for recurrence risk assessment by combining these two parameters. Recurrence rates of lesions <5cm, larger lesions >5cm with low grade histology and those with high grade histology were 16%, 46% and 73% respectively, indicating significant differences between the groups. Based on the recurrence potential, these three groups were designated as low, intermediate and high risk FDCS respectively. Also a markedly high mortality rate was observed in cases of high risk tumours (45%) compared to those with low (0%) and intermediate risk (4%). In our case, the size of the tumour was <5cm, hence, it was a low risk FDCS.

In conclusion, FDCS should be included in the differential diagnosis of tonsillar masses because interpretation of FDCS as undifferentiated carcinoma or lymphoma may lead to a completely different line of treatment with its attendant morbidity. Also, if the possibility of FDCS is not considered, the diagnosis is not reached because FDC markers are not routinely used in the IHC evaluation of poorly differentiated neoplasms. The diagnosis of FDCS is confirmed on immunohistochemistry but a high index of suspicion is needed.

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