Follicular dendritic cell tumor of tonsil—is it an underdiagnosed entity?

Departments of Surgical Oncology and Pathology, Tata Memorial Hospital, Mumbai, India.

Correspondence to: P. S. Pai, E-mail: drpai@vsnl.com

Abstract

Neoplasms of follicular dendritic cells are uncommon and while majority of them occur in lymph nodes, they are increasingly recognized at varied sites such as abdominal viscera. Tonsil is the most common extra nodal site for occurrence of follicular dendritic cell tumor in the head and neck region. We describe three cases of follicular dendritic cell tumour occurring in the tonsil.

Key Words: Follicular dendritic cell tumor, Tonsil

Follicular dendritic cells (FDCs) participate in the immune system by presenting and retaining antigens for B cells and stimulating B-cell proliferation and differentiation. World Health Organization classifies tumors with FDC in the group of haematopoietic and lymphoid tissues, which are further subclassified into histiocytic and dendritic cell neoplasms. The designation tumor/sarcoma is used because of variable cytologic and unpredictable clinical behavior in many cases.

FDCT of tonsil is extremely rare and so far only ten cases have been reported in English literature. The diagnosis of FDCT is established on basis of histological findings, immunohistochemistry, and electron microscopy. The neoplastic cells display the characteristic features of normal FDC namely, spindle to ovoid shape plump cytoplasm with indistinct cell borders storiform and fascicular pattern. Ultrastructurally, the long cytoplasmic processes and desmosomal junctions are noted. The neoplastic cells are positive for at least one of the follicular dendritic cell markers, as stained by immunohistochemistry (IHC), including CD21, CD23, CD35, and other monoclonal FDC specific markers.

The great majority of patients have been treated surgically, often followed by radiotherapy or adjuvant chemotherapy, but such adjuvant treatments are still to be proven to contribute towards long-term survival. The FDC tumour should be differentiated from nasopharyngeal carcinoma, ectopic thymoma, meningioma, malignant fibrous histiocytoma, large cell lymphoma, and melanoma. Our aims are to complement the current understanding of this rare disease and to alert histopathologists and clinicians to this rare entity occurring at extranodal site, which is well treated with surgical excision.

Case report

Two males aged 40 and 45 presented to us with a tonsillectomy done elsewhere and diagnosed as undifferentiated carcinoma. The blocks were sent to us for histopathologic examination. The first patient had no residual disease. The second patient had residual induration in the right tonsillar fossa, which was treated by wide intra oral excision. Both cases were free of disease with a follow-up of 1 year. Recently, blocks and slides of a 34-year-old male were referred to us who had right tonsillar fossa swelling. This patient had history of right-sided tonsillectomy 10 years back and previous histopathology report was not available.

Histopathology review

In the first patient, left tonsil showed multinodular tumour composed of tissue with an ovoid to spindle cells arranged in storiform, and interlacing fascicular
growth pattern (Figure 1). Tumour cells revealed oval nuclei with dispersed chromatin and small but distinct nucleoli. The cytoplasm was fibrillary and moderate in amount. The cell border was indistinct imparting the characteristic syncytial look. There was cellular atypia with mitosis in the background of lymphoid aggregate. On IHC tumour cells were strongly positive for vimentin, CD21, CD35, were focally positive for CD23 and S100, and were negative for cytokeratin (CK), epithelial membrane antigen (EMA), leukocyte common antigen (LCA), and CD20.

In the second patient, gross examination revealed a greyish white firm tumour with few haemorrhagic areas. Microscopically tumour was composed of neoplastic cells arranged in sheets and nests, separated by scanty fibrovascular stroma, lymphocytic sprinkling was noted all throughout the tumor (Figure 2). The tumour cells had large round to oval vesicular nuclei having nucleoli and irregular nuclear membrane, moderate amount of cytoplasm, with indistinct cytoplasmic border. The tumour was covered by stratified squamous epithelium showing an area of ulceration. Few mitotic figures were seen. Tumour cells were immunoactive for CD 21, CD23, and vimentin and were negative for CK, EMA, α-feto protein (AFP), LCA, CD30, ALK1, S100, HMB 45, carcino-embryonic antigen (CEA), and CD35 (Figure 3).

In the third patient also tumour was composed of fascicles of spindle cells with elongated plump nuclei and mild pleomorphism. Cytoplasm showed eosinophilic and fibrillary appearance. Scanty mitosis was present. On IHC vimentin and CD23 were strongly positive and CD21 was focally positive. Based on these findings confident diagnosis of follicular dendritic cell tumour of tonsil was made.

**Review of literature**
The existence of FDC tumors was first characterized by Monda et al.\textsuperscript{[4]} Since then, only few studies based on a limited number of cases have been reported. Chan et al.\textsuperscript{[5]} summarized the clinical features of previously reported cases to evaluate clinical behavior of the patients of FDCT. They found that FDCT is predominantly a disease of young-to-middle-aged adults with no gender predilection. They described predominant site of tumor involvement as the lymph nodes in cervical region. The intra-abdominal organs and tonsils were the most frequently involved extranodal sites.

Only ten cases of FDC tumour of the tonsil have been reported in English literature to date. We reviewed all ten cases. First case of FDC tumour of tonsil was...
reported by Nayler et al.\(^6\) in an 18-year-old girl of the ten cases reported earlier there were five males and five females. Age ranged from 16 to 77 years with average of 45.5 years. In nine cases tonsillectomy was performed. In two cases radical neck dissection was done along with tonsillectomy whereas in one case parapharyngeal space resection was done along with tonsillectomy. In three cases tonsillectomy was the only treatment. Amongst the remaining three cases; one case received chemotherapy, another received radiotherapy whereas the third case received combined chemotherapy and radiotherapy as adjuvant treatment. Of these nine cases only one case recurred after 4.5 years, which was treated with wide excision and neck dissection. Follow up information was present from 0 to 60 months with average of 28 months.

One interesting case described by Idress et al.\(^7\) was 77-year-old female presented with mediastinal and hilar lymph nodes which on biopsy were reported as metastasis of FDCT. She had history of tonsillar enlargement 8 years back, which was diagnosed as poorly differentiated squamous cell carcinoma. She had received neo-adjuvant radiotherapy and thereafter underwent tonsillectomy with parapharyngeal resection and radical neck dissection. Idress\(^7\) reviewed these blocks and slides and finally diagnosed her as having had FDCT of tonsil. Review of FDCT of tonsil is summarized in following (Table 1).

### Discussion

FDCT a kind of dendritic cells, constitute a component of secondary lymphoid follicles, serving the functions of antigen presentation. Tumours arising from FDC are known to be rare. One possible explanation for rarity of this tumour is that FDC markers are not routinely applied in the immunohistochemical evaluation of poorly differentiated neoplasms\(^5\) occurring at extranodal sites as liberally as they are at nodal sites.

During immunohistochemical staining, the neoplastic cells generally retain the phenotype of the normal FDCs. Fascin though sensitive, is not specific marker for FDCT as it stains many other neoplasms of dendritic cell origin.\(^10\) CD21, CD35, and FDC (CAN

| Table 1: Summary of all reported cases of FDCT tumor of tonsil |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| **Author** | **Age/sex** | **Treatment** | **Status at last follow up (FU)** | **Remark** |
| Nayler et al.\(^6\) | 18/F | T + CT | NED, no follow up | Total 13 cases of FDCT reported out of which one of tonsil |
| Perez–Ordonez et al.\(^6\) | 62/F | T | NED at 12 months FU | |
| Chan et al.\(^9\) | 44/M | T | NED at 36 months FU | Describe two cases of extranodal FDCT one of tonsil other one from palate |
| Chan et al.\(^5\) | 32/M | T + RT | Loco-regional recurrence after 4.5 years (treated with surgery) | Reviewed 17 cases of FDCT in which one case from tonsil |
| Biddle et al.\(^10\) | 48/F and 48/M | T + RND | NED after 3 months FU | Reported three cases of FDCT (two from tonsil, one from pharynx) |
| Vergas et al.\(^11\) | 54/F | T + RND | NED after 8 months FU | Review 35 cases of FDCT in head and neck and report one case of FDCT of tonsil |
| Satoh et al.\(^12\) | 16/M | Palatopharyngeal resection + tonsillectomy + CT + RT | NED after 24 months FU | Reported a case of large FDCT tumour in tonsil, RMT and parapharyngeal space |
| Tisch et al.\(^13\) | 51/M | T + RT | NED after 5 years FU | Reported case of FDCT tonsil and review literature |
| Idress et al.\(^7\) | 77/F | Preop RT + composite medial and hilar nodes recurrence after 8 years | Case report of a patient who misdiagnosed as squamous cell carcinoma and 8 years later |
| Present case | 45/M | T | NED after 1 year FU | Retrospectively diagnosed as FDCT of tonsil |
| Present case | 45/M | T | NED after 1 year FU | |
| Present case | 34/M | T | Local recurrence after 10 years | Tonsillectomy was done 10 years back now present with local recurrence |

Abbreviations: T, tonsillectomy; CT, chemotherapy; RT, radiotherapy; RND, radical neck dissection; NED, no evidence of disease; FU, follow up; FDCT, follicular dendritic cell tumour
markers work well on formalin-fixed, paraffin-embedded tissue.[10] CD21 is reported to be expressed strongly in approximately 96% of cases of FDCT, but occasionally the staining can be patchy or weak. The immunoreactivity for CD35 is also present in most FDCT, but the intensity of staining with CD35 is generally weaker than CD21.[14] Since FDCs have a variable immunophenotype depending on their location and on the stage of germinal center reaction,[15] staining with the normal FDC markers, such as CD21, CD35, can be focal and the FDC specific markers (R4/23, Kim4, Kim4p, and KiFDC1p) may not be completely immunoreactive. The specificity of the various FDC markers is reported to be 63–94%.[13] Results of these immunological tests are less specific because the results are based on the materials prepared by the different methods and different type of antibodies. Monoclonal antibodies which can specifically identify FDCs in routinely processed paraffin-embedded tissue have only recently become available.[16]

The differential diagnoses of FDC tumor at extranodal sites, particularly in the tonsil, is large cell lymphoma, and undifferentiated carcinomas of nasopharyngeal type. Both these tumors have characteristic morphological features and immunoreactivity with lymphoid and epithelial markers respectively besides they lack immunoreactivity for CD21, CD35, and other FDC specific markers. The storiform pattern, syncyitial and spindloid cells, bland nuclei with small but distinct nucleoli are diagnostic clues.

After reviewing 17 cases occurring at all sites in the body, Chan et al.[5] described six features associated with bad prognosis. (1) Large tumor (size more then 6 cm), (2) intra-abdominal location, (3) presence of coagulative necrosis, (4) high mitotic count (more then five per ten HFP), (5) significant cellular atypia, and (6) lack of adjuvant therapy. None of our cases showed any of the above features.

In FDC tumours at extranodal sites the major problem is the diagnostic recognition and the distinction from the more aggressive neoplasms. Interpretation of FDC as undifferentiated carcinoma or lymphoma may lead to a completely different line of treatment with its attendant morbidity. We opine that FDC tumour remains under diagnosed mostly due to ignorance on the part of pathologist caused by the rarity of the lesion and non-availability of IHC markers in all pathology labs. The appropriate application of the monoclonal specific FDC markers for any poorly differentiated neoplasm at extranodal sites would be helpful to identify the tumor. Since an isolated lesion in the tonsil would rarely have the poor prognostic features as highlighted by Chan et al.[5] tonsillectomy may be the only treatment required. Adjuvant treatment should be offered only in cases with poor prognostic features.

FDCT merits recognition of its wide morphological spectrum and also extra nodal occurrence. More cases need to be studied for larger follow up in view of its tendency to recur after a latency of several years, to better define its true nature. Accurate diagnosis will obviate unnecessary morbid treatment.

References