Follicular Dendritic Cell Sarcoma of the Tonsil: A Rare Entity

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Abstract

Follicular dendritic cells (FDC) are nonlymphoid, nonphagocytic accessory cells in the immune system. They have major roles in antigen presentation and regulation of germinal center reaction. FDC sarcoma is a rare and under-recognized malignancy. Most of the cases are reported in the lymph nodes. The typical morphology is syncytial aggregates of oval/spindly cells with vesicular bland nuclei and small nucleoli. Focal whorling and storiform pattern, multinucleate giant cells, and the presence of small lymphocytes in the background give additional clues for the diagnosis. As spindle cell tumors are rare in the lymph nodes, FDC sarcoma comes under the differential diagnosis of spindle cell neoplasms of the node and an accurate diagnosis is often rendered. However, when the neoplasm occurs in extranodal sites, the diagnosis is often missed because the FDC markers are not routinely used in the immunopanel for undifferentiated neoplasms. Because of its rarity, the extranodal FDC sarcomas pose a great diagnostic challenge and often misdiagnosed initially. Herein, we report a case of FDC sarcoma of the tonsil in a 36-year-old female patient. Biopsy of the lesion showed oval to spindly cells in syncytial sheets and focally in whorled pattern. The individual cells were having plump vesicular nuclei and small nucleoli. Occasional multinucleate cells and sprinkling of lymphocytes within the tumor were also noted. The tumor cells were positive for CD23 and CD35. A diagnosis of FDC sarcoma was given. Greater awareness of the morphologic spectrum of FDC sarcoma and appropriate immunostains for FDC differentiation will help in recognition of this rare neoplasm.

Keywords: *Follicular dendritic cell sarcoma, spindle cell neoplasm, tonsil*

Introduction

Follicular dendritic cell (FDC) sarcoma is a rare and under-recognized malignancy. It is a neoplastic proliferation of spindled to ovoid cells showing morphologic and immunophenotypic features of FDCs. FDCs function as the antigen presenting cells to B lymphocytes provide architectural support to the lymphoid follicles.[1,2] Most cases of FDC sarcoma occur in lymph nodes of the neck, mediastinum, and axilla. Around 30% of cases occur in extranodal sites such as palate, tonsil, pharynx, thyroid, mediastinum, soft tissue, skin, liver, spleen, and gastrointestinal tract.[2,3] When the neoplasm with spindle cells occurs in extranodal sites, this rare entity is often not considered and FDC markers are not included in the immunohistochemical panel of undifferentiated neoplasms. The scarcity of extranodal FDC sarcoma may be due to the under-recognition of this entity. FDC sarcoma has numerous distinctive histological features that should serve as clues to bring the neoplasm into the differential diagnosis and thus prevent misdiagnosis.

Case Report

A 36-year-old female patient presented with on and off throat pain and bleeding from the mouth for 1 year duration. She had a history of parotidectomy and hemimandibulectomy for salivary gland tumor 30 years ago. She had received chemotherapy and radiotherapy for the same at that time, details of which were not available.

On examination, there was 2 cm × 2 cm ulceroproliferative lesion involving the left tonsil. Biopsy of the lesion was taken. Histopathological examination showed a neoplasm composed of syncytial sheets of oval to spindly cells. Focally the cells were arranged in whorls [Figure 1]. Individual cells had plump vesicular oval to spindly bland nuclei and small nucleoli [Figure 2]. Occasional large pleomorphic cells and multinucleate cells were noted [Figure 3]. Small lymphocytes were seen intermingled with the neoplastic cells.

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The differential diagnoses considered were spindle cell carcinoma, melanoma, sarcoma, meningioma, and FDC sarcoma. On immunohistochemical examination, the cells were positive for CD23 and CD35 [Figures 4 and 5] and were negative for cytokeratin, EMA, S100, HMB 45, and vimentin. Based on the morphology and immunoprofile, a diagnosis of FDC sarcoma was given. The patient underwent wide excision of the lesion with negative margins.

Discussion

FDC belongs to the accessory immune system. FDC cells are present in the nodal and extranodal lymphoid follicles and function as antigen presenting cells to B-cell lymphocytes. It plays role in B-cell migration, proliferation and differentiation.[1,2] By the cell-to-cell attachments and desmosomes, FDC cells assist in the architectural support of the lymphoid follicles.[3,4] FDCs are spindle to ovoid cells, with indistinct cell borders and vesicular nuclei.

FDC sarcoma is a rare malignancy showing FDC differentiation. It occurs mainly in the lymph nodes of the neck, mediastinum, and axilla. Spindle cell neoplasms are rare in the lymph node. Hence, the diagnosis of nodal FDC sarcoma is comparatively easier.

Extranodal FDC sarcomas are less well recognized although its occurrence has been noted since 1994.[5] One-third of cases of FDC sarcoma occur in extranodal sites which include pharyngeal region, mediastinum, liver, spleen, and gastrointestinal tract. In the pharyngeal region, FDC sarcomas have been reported in the tonsil, nasopharynx, parapharyngeal space, palate, pharynx, and hypopharynx.[6] Extranodal FDC sarcomas are challenging because of the broad differential diagnoses which include undifferentiated carcinoma, spindle cell carcinoma, sarcoma, melanoma, fibrohistiocytic neoplasms, meningioma, and inflammatory pseudotumor. FDC sarcomas arising in extranodal sites are often misdiagnosed and picked up only in recurrence or

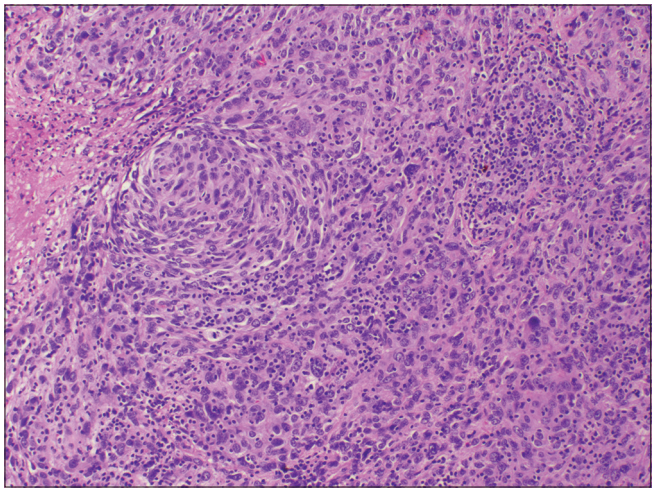

Figure 1: Microscopy showing the neoplastic cells arranged in syncytial pattern with focal whirling (H and E, ×100)

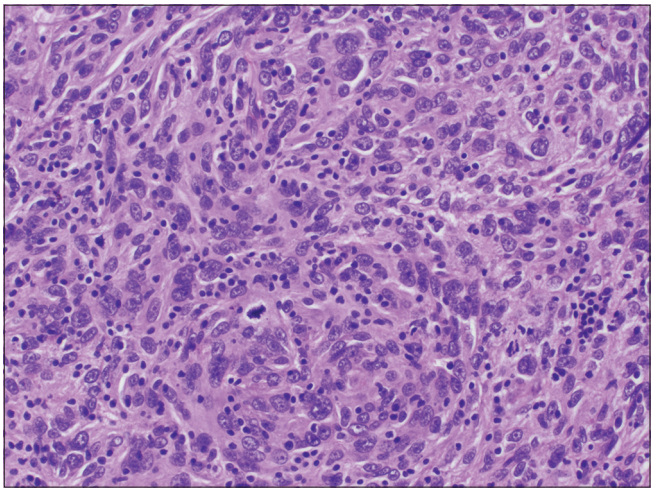

Figure 2: Higher power showing cells with indistinct cell borders, plump vesicular nuclei with sprinkling of lymphocytes in between the tumor cells (H and E, ×200)

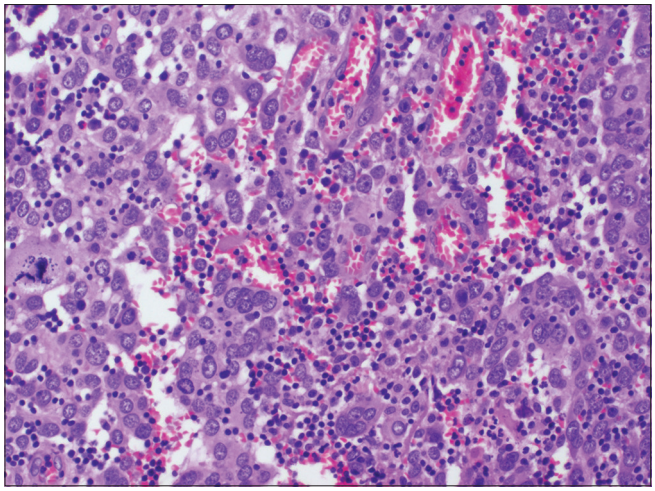

Figure 3: Pleomorphic and multinucleate cells (H and E, ×200)

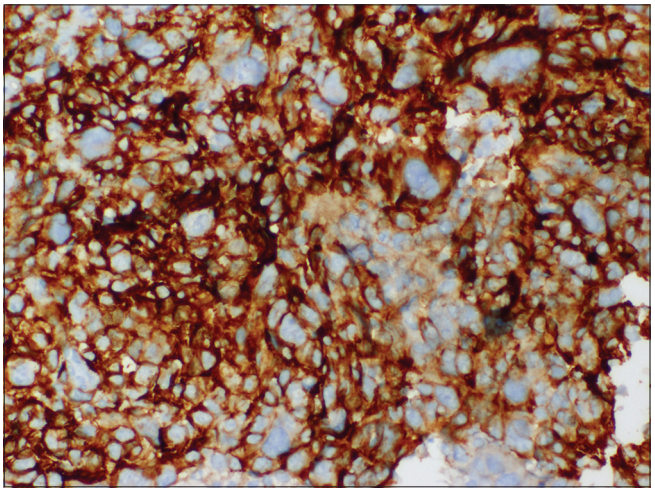

Figure 4: Tumor cells showing positivity for CD23 (IHC, ×400)

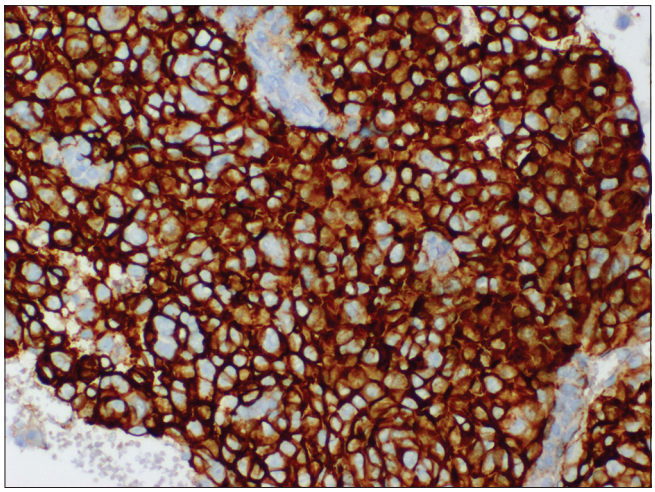

Figure 5: Tumor cells showing positivity for CD35 (IHC, ×400)

metastasis. The misdiagnosis can lead to unnecessary treatment and associated mortality.

On microscopy, the neoplastic cells are spindle/ovoid cells arranged in fascicles, whorls, diffuse sheets, vague nodules, and storiform arrays. Individual cells will have abundant cytoplasm without distinct cell borders forming a syncytial appearance. The cells will have plump oval or elongated vesicular bland nuclei with small nucleoli. Multinucleate giant cells and scattered pleomorphic cells can also be present. Sprinkling of small lymphocytes within the tumor with formation of perivascular cuffing is another characteristic feature.[7]

Extranodal FDC sarcoma should come in the differential diagnoses when we encounter an unusual appearing cytokeratin–negative neoplasm, thymoma-like tumor present outside the mediastinum, meningioma-like tumor outside the dura, and gastrointestinal stromal tumor-like tumor rich in lymphoid cells.[5,8]

On immunohistochemistry, FDC sarcoma will show positivity for one or more of the FDC markers such as CD21, CD23, CD35, and KiM4p.[7] Podoplanin (D 2-40) and CXCL13 are the other two markers for FDC tumors.[9,10] Clusterin is almost always strongly positive and clusterin expression help to differentiate FDC sarcoma from other dendritic cell neoplasms.[11] The tumor cells are usually positive for vimentin, epidermal growth factor receptor, desmoplakin, fascin, and HLA-DR. Variable expression of epithelial membrane antigen, CD68, and S 100 protein is documented. Expression of cytokeratin, CD45, and CD20 is exceptionally rare. CD3, CD30, CD34, CD31, myeloperoxidase, CD1a, lysozyme, and HMB 45 are always negative.[7] Electron microscopy will show the cells containing numerous long interwoven cytoplasmic processes joined by well-developed desmosomes.

FDC sarcomas are indolent tumors with a tendency for local recurrence but with a low risk of metastasis. The management includes complete surgical excision with or without adjuvant radiotherapy or chemotherapy. In their clinicopathologic analysis of 17 cases of FDC sarcomas, Chan *et al*. described poor prognostic factors in FDC sarcoma which included large tumor size (more than 6 cm), intra-abdominal location, coagulative necrosis, high mitotic count (more than 5/10 hpf), and significant cellular atypia.[7,12] The recommended management for isolated lesions in the tonsil is tonsillectomy. Adjuvant treatment should be offered in cases with poor prognostic features.

Extranodal FDC sarcoma of the pharyngeal region is challenging and is often missed especially in small biopsies and picked up only on wide excision or on recurrence. Recognition of this rare tumor requires a high index of suspicion. FDC sarcoma should be considered when we encounter syncytial sheets of cytokeratin negative undifferentiated epithelioid/spindle cell tumor arranged focally in storiform pattern and centripetal whorls, lymphocytic infiltration, low mitosis, lack of crowded/overlapping nuclei, and the presence of multinucleate giant cells. The awareness of the occurrence of FDC sarcoma in extranodal sites and its histological features along with the use of immunohistochemistry will help in rendering an accurate diagnosis.

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Conflicts of interest

There are no conflicts of interest.

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