CASE REPORT

Follicular dendritic cell sarcoma of the tonsil: A case report of uncommon tumor displaying diagnostic features and review of the literature

Morgan Sly, Emily Wichelt, Jamie Spears, Kiley Clark, Mohamed Aziz

ABSTRACT

Introduction: Follicular dendritic cells are non-hematopoietic cells that are found in germinal centers and function in the differentiation and development of activated B cells. Follicular dendritic cell sarcoma is a rare neoplasm, typically, located in lymph nodes throughout the body. Follicular dendritic cell sarcomas can also be found in extranodal sites. Follicular dendritic cell sarcomas located in extranodal sites are underdiagnosed due to the rarity and lack of consideration in differential diagnoses. Additionally, up to one-third of extranodal cases are misdiagnosed. Case Report: We are presenting a case of follicular dendritic cell sarcoma located in the tonsil of a 73-year-old male. Examination revealed a tonsillar mass suspicious for squamous cell carcinoma, malignant melanoma, or anaplastic lymphoma. Biopsy of the tonsil was performed and the patient was diagnosed with a low-grade malignant tumor exhibiting morphologic and immunohistochemical features indicative of dendritic/reticulum cell origin. Conclusion: The reporting of this case aims to increase knowledge and awareness regarding the morphologic and immunohistochemical features of rare and often misdiagnosed extranodal follicular dendritic cell sarcomas. Heightened awareness of this tumor will lead to inclusion as

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Received: 14 May 2019 Accepted: 25 June 2019 Published: 01 August 2019 a differential diagnosis of the initial evaluation of biopsy with this tumor features and avoid misdiagnosis.

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INTRODUCTION

Follicular dendritic cells (FDCs) are immune cells that play a direct role in the differentiation and development of activated B cells [1]. They are found within both germinal centers and in close proximity to areas of B cells that have had antigen stimulation [1]. Follicular dendritic cells differ from dendritic cells in that they are not derived from the bone marrow [2]. Follicular dendritic cell sarcomas (FDCSs) were first distinguished in 1986 [3]. It was not until nine years later, in 1997, that the entity was given the name FDCS [4]. As of 2012, there were only 200 cases of FDCSs reported in the English literature [5]. These neoplasms are found predominantly within lymph nodes but have been found to occur in extranodal sites. A review published by Youens and Waugh presented 46 cases of extranodal FDCSs with 10 of the 46 located in the tonsil [6]. Additional extranodal locations included the gastrointestinal (GI) tract, nasopharynx, palate, liver,

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and soft tissue of the neck [6]. Approximately one-third of reported extranodal follicular dendritic cell sarcomas are misdiagnosed, namely due to the lack of consideration as part of the differential diagnosis [7]. If FDCS is considered, there are pathological features and immunohistological stains that are specific to the neoplasm that can aid in a proper diagnosis [7]. Reporting cases of FDCSs are imperative in order to bridge the gap between the known pathological features of this tumor and the consideration of this neoplasm in differential diagnoses. The ultimate intent of reporting cases is to reduce the number of misdiagnoses [8].

CASE REPORT

A 73-year-old male presented with dysphagia and pain in the tonsillar area. Initial examination revealed a tonsillar mass with differential diagnoses including squamous cell carcinoma, malignant melanoma, or anaplastic lymphoma. Biopsy of the right tonsil revealed a malignant tumor consisting of a nesting arrangement of medium-sized cells (Figure 1A). The cell membranes were ill-defined resulting in a syncytial appearance and abundant cytoplasm. Throughout the tumor there were scattered lymphocytes extending into the tumor cells (Figure 1B). There was low mitotic activity, minimal atypia, and pleomorphism, with absence of necrosis. Histological features of the tumor indicated possible dendritic cell origin.

The tumor cells were negative for desmin, common muscle actin, smooth muscle actin, pan-melanoma, CD31, CD34, CD68, cytokeratin, and factor XIIIa. A positive immunoreactivity for both CD21 and CD35 (Figure 1C) suggested that the tumor originated from FDCs. The tumor cells were also positive for S100 and vimentin (Figure 1D). The predominant function of these



Figure 1: Pathological analysis of the mass with H&E staining and immunohistochemistry studies. (A) Section from the mass stained with H&E showing nesting and grouping of tumor cells; x40. (B) Section from the mass stained with H&E showing low grade atypical cells associated with scattered lymphocytes. No mitosis and no necrosis identified; x60. (C) Immunohistochemistry studies positive for CD35. (D) Immunohistochemistry studies positive for vimentin.

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immune response cells is to interact with lymphocytes to provide significant information regarding the tumor cells to aid in the lymphocytes cytotoxic effect. The diagnosis following biopsy and immunohistochemistry revealed a low-grade malignant tumor with morphologic and immunohistochemical features indicative of dendritic/ reticulum cell origin. Following diagnosis of follicular dendritic cell sarcoma, the patient underwent a wide tonsillectomy with radical neck dissection revealing a 4-cm tumor with 32 lymph nodes negative for metastasis. The patient was then treated postoperatively with chemotherapy. There was no evidence of disease (recurrence or metastasis) with five years follow-up. The patient was subsequently lost for follow-up.

DISCUSSION

Follicular dendritic cells are immune cells that display antibody-antigen complexes on their surface and act as key regulators in activated B cell differentiation and growth [1]. They are located within both activated B cell areas and germinal centers [1]. Additionally, FDCs are located in acquired lymphoid tissue throughout the body where extranodal FDCSs may occur [5].

Follicular dendritic cell sarcomas are rare neoplasms. From 1986, when FDCSs were first recognized [3], to 2014, there have been more than 200 cases reported, with 116 being located in the head and neck [9]. However, FDCS located in the tonsil were first reported in 1994 [10]. As of 2017, there were 49 reported cases of FDCS of the tonsil [11]. Follicular dendritic cell sarcomas are identified histomorphologically as neoplastic proliferations of spindled to ovoid-shaped cells that take formation as whorls, storiform arrays, and/or fascicles [12]. The FDCs in the neoplastic proliferation exhibit phenotypic features of FDC [13]. The original name for the neoplasm was FDC tumor [4]. However, a name change to FDCS was proposed by Chan et al. [4] to demonstrate the tumors clinical features and similarities to a sarcoma in contrast to a lymphoma [14]. Due to decreased awareness of this rare neoplasm, it is reported that approximately onethird of extranodal FDCS cases can be misdiagnosed initially [6]. Misdiagnoses of FDCS include reactive response, malignant fibrous histiocytoma, meningioma, schwannoma, carcinoma, inflammatory pseudotumor, mesenchymal tumor with neural differentiation, and stromal tumor [6]. The misdiagnoses were predominantly due to lack of consideration of this neoplasm in the differential diagnosis [6]. Despite this long list, FDCS has a distinct immunophenotype that can aid in an accurate diagnosis [6]. This case report adds further information to the literature with regard to presentation, diagnosis, histological features, and immunohistochemistry of a rare extranodal FDCS of the tonsil. Follicular dendritic cell sarcomas are located primarily in lymph nodes with less than one-third of cases found in extranodal sites [5]. Extranodal sites of FDCs include the tonsil, oral cavity, GI

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tract, liver, spleen, soft tissue, skin, and the mediastinum [12].

Follicular dendritic cell sarcoma often presents as an indolent growing, painless mass [13]. The extranodal FDCSs have a median size of 6 cm [6]. Rarely, the tumor may cause paraneoplastic pemphigus and in the classical FDCS systemic symptoms of disease are uncommon [12]. Histopathologically, the neoplasm exhibits a proliferation of spindle to ovoid type cells that form storiform patterns and whorls [6]. The whorled pattern may direct differential diagnoses toward meningioma [6]. The tumor often presents with small lymphocytes dispersed throughout the proliferating cells [6]. The cells have abundant, eosinophilic cytoplasm with ill-defined cell borders [6]. In some cases there may be presence of multinucleated giant cells and dispersed pleomorphic cells [8]. Follicular dendritic cell sarcomas typically show mild to moderate atypia and are classified as low grade [6]. Contrastingly, a recent study concluded that FDCS is more aggressive than previously indicated, and it should be graded as an intermediate grade malignancy [4]. Immunohistochemical features of FDCSs are positive for at least one follicular dendritic marker; CD21, CD35, and CD23. Additionally, FDCSs are positive for epithelial membrane antigen, desmoplakin, vimentin, and HLA-DR. CD1a, lysozyme, CD34, CD3, HMB-45, and cytokeratin stains are negative with this type of tumor [13]. Interestingly, recent research has concluded that the markers clusterin, fascin, and podoplanin are almost consistently positive in FDCSs [6]. Of these three markers, clusterin has been deemed a specific marker for FDCS due to its constitutive expression in spindle cell tumors [15, 16]. Follicular dendritic cell sarcoma can be diagnosed based on its unique immunophenotype. It can be distinguished from other dendritic cell neoplasms based on its unique positive clusterin marker [15, 16]. The negative cytokeratin stain removes carcinoma from the differential diagnoses [6]. Furthermore, meningioma, malignant fibrous histiocytoma, interdigitating dendritic cell sarcoma, and thymoma are all negative for both CD21 and CD35 [6]. This suggests that FDCSs have a unique immunophenotype of their own that can be used to make an accurate diagnosis.

Follicular dendritic cell tumors mimic low grade soft tissue sarcomas in their slow progressive growth [13]. Due to the lack of FDCS cases reported in the literature, there is lack of information and consensus on appropriate treatment regimens for this neoplasm. Currently, the recommended treatment is to follow the treatment course for a soft tissue sarcoma of high grade [6]. The treatment includes surgical removal of the tumor with postoperative chemotherapy or radiotherapy being administered in some instances [6, 13]. The likelihood of metastasis is approximately 25% [13] with the most common sites including the lung, liver, peritoneum, and lymph node [4]. In addition, it is reported that 40–50% of tumors recur [13]. Factors that often lead to a poorer prognosis include high levels of cytologic atypia, coagulative necrosis, high cellular proliferation, and tumors greater than 6 cm in size [13]. The mortality rate is 10–20% [13].

CONCLUSION

The intent of reporting this case is to increase awareness of extranodal follicular dendritic sarcomas as a differential diagnosis. This is of paramount importance in providing patients with a proper initial diagnosis considering a significant number of these neoplasms are initially misdiagnosed. The aforementioned discussion of the unique immunophenotype of FDCS provides a distinct and clear pathway to an accurate diagnosis.

Author Contributions

Morgan Sly – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Emily Wichelt – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Jamie Spears – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Kiley Clark – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Mohamed Aziz – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related

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Guarantor of Submission

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Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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