**Scholars Journal of Medical Case Reports**
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

**Radiotherapy**

# Follicular Dendritic Cell Sarcoma of the Tonsil: A Case Report with Review of the Literature

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**DOI:** 10.36347/sjmcr.2024.v12i05.097 | **Received:** 07.04.2024 | **Accepted:** 15.05.2024 | **Published:** 30.05.2024

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**Abstract** **Case Report**

***Introduction:*** Follicular dendritic cell tumors (CDF tumors) are rare, it is an uncommon neoplasm derived from non-lymphoid accessory cells of peripheral lymphoid tissue. FDCS is grouped with histiocytic neoplasms and dendritic cell neoplasms in the World Health Organization tumor classification. ***Observation:*** We report the case of a 37-year-old patient followed for dendritic follicular cell sarcoma of the epithelioid type of the left amygdala. He underwent surgical removal of the left tonsil, followed by chemotherapy such as Cyclophosmide, Doxorubicin, Vincristine, and Prednisolone (CHOP) and radiation therapy at the 60 Gy dose. ***Discussion:*** FDC sarcoma is an uncommon neoplasm of antigen-presenting cells of B-cell follicles of lymphoid organs. According to the World Health Organization's classification of hematopoietic and lymphoid tumors, FDCS belong to histiocytic and dendritic cell neoplasms. The appearance of follicular dendritic cell sarcoma of the amygdala, in an extra lymph node site, as occurred in our patient has rarely been observed. Histologically, FDCT cells appear as strands with a storiform, verticillated, and prominent pattern. On the immunohistochemistry level, we note the positivity of antibodies CD21, CD23 or CD35. Treatment is based on broad surgical excision followed by adjuvant chemotherapy and radiotherapy. However, these complementary treatments have not contributed to long-term survival. The evolution is marked by local or metastatic recurrences. ***Conclusion:*** Although rare, dendritic follicular cell sarcomas of epithelial type may have as a starting point the head and neck region, lymphoid, and extra ganglion sites.

**Keywords:** Sarcoma, Follicular, Dendritic, Tonsil.



## INTRODUCTION

Follicular dendritic cells (FDCs) are non-lymphoid, non-phagocytic accessory cells of the immune system that are essential for antigen presentation and regulation of the germinal center response [1]. They are present in lymph nodes and extra ganglionic lymphoid tissue [2]; mainly in the germinal centers of primary and secondary lymphoid follicles, where they form a very tight meshwork [2]. Their dendritic nature is best demonstrated by the different FDC markers, such as CD21 (C3d receptor), CD23, CD35 (C3b receptor), R4/23, Ki-M4, Ki-M4p and Ki-FDC1p [1]. Follicular dendritic cell sarcoma (FDCS) is a tumor derived from non-lymphoid accessory cells in the peripheral lymphoid tissue. There are 3 main subtypes of accessory cells, including follicular dendritic cells, interdigitated dendritic cells, and fibroblastic reticular cells [3]. First described by Monda *et al.*, in 1986, follicular dendritic cell sarcomas (FDCS) are very rare [4]. Approximately 70 cases have been reported, including 24 extra ganglionic cases in the head and neck [5]. Eleven cases of tonsillar FDCS have been reported [6]. We report the case of a 37-year-old patient by analyzing the pathological features, immunophenotypic profile, and clinical features of the disease and by reviewing the treatments, responses, and outcomes.

## OBSERVATION

A 37-year-old patient with no specific pathological history was consulted in December 2019 for the appearance of a left tonsillar mass. A radiological workup done by magnetic resonance imaging noted a left tonsillar process of 39.2 x 24 x 23.7 mm with minimal extension to the skull base (Figure 1). Anatomical pathology and immunohistochemistry examination of the biopsy noted a granulocytic sarcoma. The patient underwent surgical removal of the left tonsil. Anatomical pathology and immunohistochemistry of the surgical

specimen showed a dendritic follicular cell sarcoma of epithelioid type, which came in contact with the limits of the excision (Figure 2). Two months after surgery, the patient presented with continued local progression and confirmed mediastinal and pulmonary lymph node metastasis. He received 6 courses of CHOP chemotherapy with a good clinical and radiological response of about 50% according to the RECIST criteria, and radiotherapy at a dose of 60 Gy.

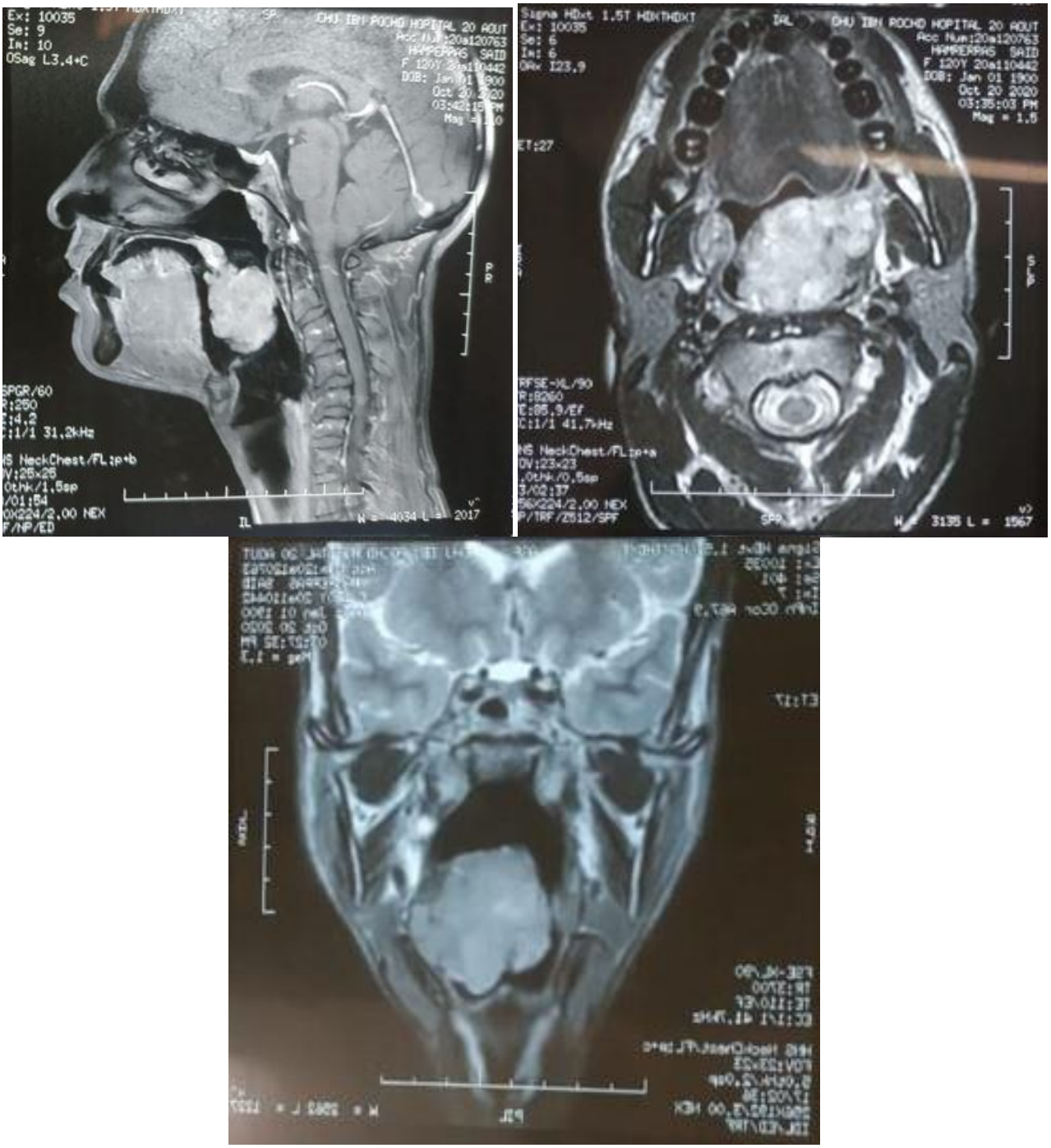

**Figure 1: Magnetic Resonance Imaging of the OtoRhinoLaryngology sphere showing my left amygdala mass**

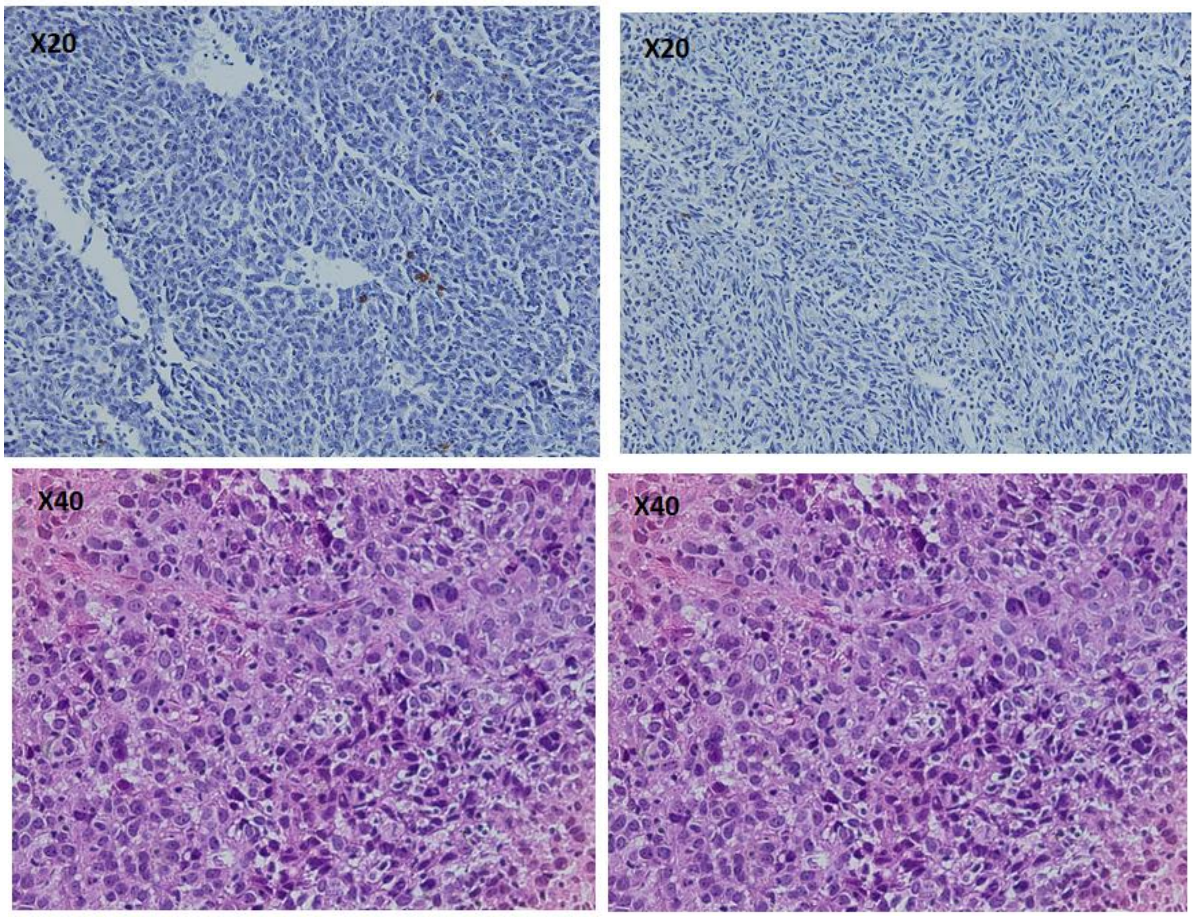


**Figure 2: Histological appearance of follicular dendritic cell sarcoma of the amygdala**

## DISCUSSION

FDCs are non-lymphoid elements of the lymph node that play an important role in immune regulation and antigen presentation in primary lymphoid follicles and the follicular center. FDCs form a tight meshwork with numerous cytoplasmic processes and extensive gap junctions between adjacent cells. The cytoplasmic processes contain complement receptors, which bind and present antigens to B cells and form a complex part of the B cell immunoregulatory system. 14 Various cytokines and cell surface receptors play a role in these functions. FDCs are an integral part of lymphoid tissue, whether it is an acquired tissue (e.g., lymphoid tissue associated with the gastric mucosa) or a structural component of the organ (e.g., lymph nodes and spleen). This explains the development of extranodal FDCT. Ultrastructurally, FDCs have relatively few organelles; their most prominent features are long, thin, and complex interdigitated cellular processes that are attached by tight junctions [5].

FDC sarcoma is an uncommon neoplasm of antigen-presenting cells in B-cell follicles of lymphoid organs. Follicular dendritic cells are required for the germinal centers of B-cell follicles, which are present not only in lymph nodes but also extraganglionally, either as acquired lymphoid tissue or as part of the organized constitutive lymphoid tissue [7]. According to the World Health Organization classification of tumors of hematopoietic and lymphoid tissues, these tumors belong to histiocytic and dendritic cell neoplasms [2]. Follicular dendritic cell tumors are very rare. In 1978, Lennert [8] identified reticular cells in lymph nodes. He suggested that neoplasia could originate in the lymph nodes and yet be histologically different from lymphoma. Monda *et al*., [4] described the characteristic features of FDCT in 1986 and reported a small series of lymphoid FDCT. The designation tumor/sarcoma is used to reflect the variable cytologic and clinically indeterminate behavior of FDCT in many cases and to emphasize that they are distinct from lymphomas [2].

A literature review was performed to find published articles on FDC tumors/sarcomas; approximately 80 cases of FDC tumors/sarcomas were documented [9]. Chan *et al*., [10] summarized the clinical characteristics of the 17 previously reported cases. The patients, 7 males, and 10 females, ranged in age from 17 to 63 years, with a mean of 37.6 years and a median of 40 years. These tumors occurred with more or less equal frequency in both sexes [11]. The occurrence of a primary tumor in an extra-nodal site, as it happened in our patient, has been rarely observed. Soriano *et al*., [12], six patients had extra-nodal disease, including disease involving the intestine, nasopharynx, liver,

spleen, pancreas, pleura, and pulmonary parenchyma. In the series of Fonseca *et al*., [13] extra-nodal involvement was found in 33% of cases, most commonly in the oral cavity, spleen, liver, small intestine, pancreas, and peritoneum [12]. Pileri *et al*., reported extra-nodal disease in 6 (46%) of 13 patients [14]. Other authors reported extra-nodal involvement in the oropharyngeal region, head and neck, neck, thyroid, abdominal wall, mediastinum, skull, and colon [12]. In the head and neck, these masses were remarkable for their slow growth and absence of pain.

Histologically, FDCT cells may appear in strands with a storiform, whorled, prominent pattern. Tightly nested processes may give a fibrillated appearance. Nuclei are usually oval or rounded, show some degree of pleomorphism, may have an irregular outline, and may be serrated or grooved [10]. The nuclear chromatin is finely dispersed, so the nucleus may appear clear. Distinct pink nucleoli are invariably present. Nuclear inclusions are usually present and may vary in size and color. The cytoplasm is markedly eosinophilic without cellular boundaries [5]. Small to medium-sized vessels are scattered throughout the tumor and a large perivascular cuff of lymphocytes is frequently seen. A pseudoangiomatous pattern has been observed in many cases, including the present case [5]. Mitosis rates are typically 0 to 10 per 10 fields at high power. High-grade histologic features such as high mitosis counts (>5 per 10 HPF), coagulative necrosis, and significant cellular atypia have been described and may be associated with an adverse outcome [10].

Immunohistochemically, neoplastic FDCs cells generally exhibit the immunophenotype of non-neoplastic follicular dendritic cells and are usually positive for CD21, CD23, or CD35 [12]. CD21 is more reactive than CD35 [5]. Other FDC-specific markers useful for confirming the diagnosis of FDC sarcoma include Ki-M4, Ki-M4p, R4/23, and Ki-FDC1p [7]. CD68, vimentin, S100 protein, and muscle-specific actin are variably expressed [5]. They are also generally positive for desmoplakin, human leukocyte antigen-DR, and EMA. CD20 and CD45 are occasionally expressed, but CD1a, CD3, CD30, CD34, CD79a, HMB-45, lysozyme, and myeloperoxidase are not expressed (12). In 10-20% of cases, FDCs are associated with hyaline-vascular Castleman disease, suggesting a link between these 2 entities [2]. Two other FDCT-specific antibodies are R4/23 and Kim4, but their use is limited to frozen sections [5]. Fascin is also a sensitive marker for FDCT, but it is not specific and stains other neoplasms of dendritic cell origin. The specificities of the different FDCT markers vary from 63% to 94% [5]. Ki 67 varies from 1 to 25% (mean, 13%) [12]. Grogg *et al*., reported clusterin expression in 12 of 12 tumors, two of which were negative for traditional markers (CD21, CD23, CD35) [15]. Their study suggested that including clusterin in the immunohistochemical panel increased sensitivity and specificity in differential diagnosis. Vega *et al*., performed a microarray analysis of lymph node stroma, including follicular dendritic cell tumors, nodal follicular reticular cell sarcomas, and follicular dendritic cells, and found that EGFR transcripts were overexpressed in FDCS [12]. Sun *et al*., found overexpression of EGFR in FDCs, but not in follicular dendritic cells [16]. Thus, EGFR might be an attractive therapeutic target in FDCs [12].

The differential diagnosis is with several tumors: undifferentiated carcinoma, squamous cell carcinoma, malignant melanoma, large cell lymphoma, meningioma, thymoma, malignant fibrous histiocytoma, peripheral nerve sheath tumor, angiosarcoma, and inflammatory pseudotumor [2, 5, 7, 9, 11]. All these tumors lack immunoreactivity for CD21, CD35, and other FDC-specific markers such as Ki-M4p and Ki-FDC1p [9, 11]. Follicular dendritic cell tumors are considered to be of low to intermediate malignancy [5]. Wide excision of the tumor is the primary treatment for FDCTs [2]. Surgery is often followed by adjuvant radiotherapy or chemotherapy, but these additional treatments have not been shown to contribute to long-term survival [5]. The identification of EGFR expression in FDS, as in the present case, may pave the way for the use of EGFR-targeted antibodies and inhibitors as adjuvant agents [2]. To our knowledge, no prospective studies of treatments. Published reports, including our series, are based on retrospective analyses of the data, which makes it difficult to make firm treatment recommendations [12].

The prognosis appears to be good for patients who receive early treatment [11]. The course may be marked by local recurrence and metastasis to sites such as the lungs, liver, and lymph nodes [2]. The local recurrence rate is at least 40% and the metastasis rate is at least 25% [1]. A recent report by Chan *et al*., [3] argued that this tumor appears to act more aggressively than previously described. Their study found an overall recurrence, metastasis, and 3-year mortality rate of 43%, 24%, and 17%, respectively [10].

## CONCLUSION

FDCs are rare tumors. These tumors can occur in the head and neck region in lymphoid and extra-nodal sites. Although the histologic features of FCDs are stereotypical, they are susceptible to misdiagnosis because FDCs-specific monoclonal markers are not routinely used in the immunohistochemical study of poorly differentiated malignancies.

## ACKNOWLEDGMENT

Our sincere thanks to Dr. Pawendtaoré Esdras Zongo for his major contribution and to Professor BOUCHBIKA Zineb for his supervision in the relay of this work.

**Abbreviation**

CDF: Follicular dendritic cell.
FDCS: Follicular dendritic cell sarcoma.
FDCT: Follicular dendritic cell tumor.

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