

# Head and Neck Follicular Dendritic Cell Sarcoma: Disease Associations and Treatment Review

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## SUMMARY

Currently, of less than 50 cases of head and neck follicular dendritic cell (FDC) sarcoma reported in the literature, 5 have been found to occur in the background of Castleman disease. We report another case of head and neck FDC sarcoma with emphasise on its associated lesions and review the outcome of treatment from the existing cases in the literature.

## KEY WORDS:

*Follicular dendritic cell sarcoma, Head and neck, Disease association*

## INTRODUCTION

Follicular dendritic cells (FDCs) are antigen presenting cells found mainly in the germinal centers of primary and secondary lymphoid follicles. A few cases have been reported of FDC sarcoma with Castleman Disease (CD) of the hyaline-vascular type, suggesting a possible link between these two entities. FDC sarcoma has also been associated with other lesions such as human herpes virus 8, Epstein-Barr virus, Kaposi sarcoma, paraneoplastic pemphigus and lymphomas.

## CASE REPORT

A 65 year-old man presented to our clinic with right sided neck swelling for three years. He had no difficulty breathing or swallowing, no changes of voice, and no fever. On examination, the swelling measured 5.0cm x 10.0cm and extended from the upper third of the neck down to the clavicle. Its surface was smooth, with a well defined border, hard in consistency and non tender to palpation. There were no cervical lymph nodes palpable. The full blood count and biochemical profile including hepatic function tests were within the normal range.

Fine needle aspiration cytology (FNAC) of the mass produced cells of mesenchymal origin with marked cellular atypia suggesting a malignancy. Computerized Tomography (CT) scan from skullbase to pelvis showed a well defined heterogeneously enhancing soft tissue density mass with an area of necrosis at the right side of the neck, deep to the sternocleidomastoid muscle. There were multiple small right cervical lymph nodes adjacent to the mass with no lymphadenopathy seen in the axillae, abdomen and pelvis.

The patient underwent excision of the right neck mass with selective posterolateral neck dissection (levels II, III, IV and

V). The tumour appeared well circumscribed and covered by a thin capsule. There were multiple small lymph nodes surrounding the tumour. Microscopically, sections from the tumour showed a markedly variable picture (Figure 1). The stroma showed area of extensive hyalinised collagen with scanty mitotic figures. There were prominent lymphoproliferative features in the stroma throughout the tumour. Immunohistochemical staining was positive for CD 21, CD 68, Ki-67 and vimentin. Microscopic features of the 12 lymph nodes surrounding the tumour showed malignant change in 3 of them. The rest of the nodes showed reactive Castleman-like changes, with abnormal follicles and atrophic germinal centers surrounded by broad mantle zones of small lymphocytes. The definitive diagnosis was follicular dendritic cell sarcoma arising in a lymph node within a background of Castleman disease.

The patient refused chemoradiation post-operatively and was followed-up for two years. He was well during the last visit with no evidence of tumour recurrence clinically and on CT.

## DISCUSSION

A literature search (PubMed) revealed 5 cases of head and neck follicular dendritic cell (FDC) sarcoma occurring in association with Castleman disease (CD) (Table I). From these six cases (including the present case), FDC sarcoma had arisen concomitantly with CD in three of them. When present at the same time, it is very difficult to tell if FDC sarcoma and CD have any clonal relationship with each other. A possible explanation for this transformation is FDC dysplasia in the follicles of CD, probably following a hyperplasia-dysplasia-neoplasia sequence similar to the development of some epithelial neoplasms<sup>1</sup>. In our case, we tried to find a possible link between FDC sarcoma and CD by studying the 3 lymph nodes infiltrated by the malignant tumour. An on-going dynamic process was evidenced by different stages of malignant proliferation (cytological atypia and mitotic activity) from within the follicles to the interfollicular areas of the lymph nodes. This was more likely malignant change within the lymph nodes itself rather than a direct invasion from the main tumour bulk. As sarcoma is more likely to metastasize haematogenously, lymphatic spread is less likely to happen thus further strengthening our suspicion. Unfortunately, we are unable to conclude in this case that clonal progression has taken place from CD to FDC sarcoma, as some authors argue that CD maybe a reactive stage of FDC rather than a precursor lesion<sup>2</sup>. In three cases, FDC sarcoma

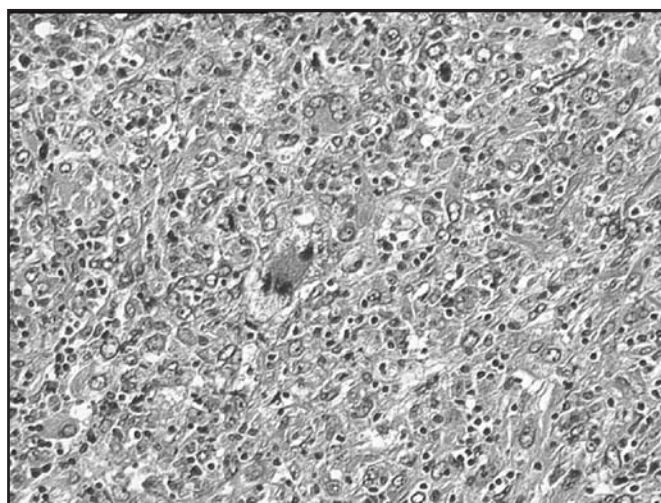
*This article was accepted: 1 February 2010*

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**Table I: Reported cases of follicular dendritic cell sarcoma associated with Castleman disease in the head and neck**

Authors	Sex/age	Tumor location	Type of associated CD	Interval between diagnosis of CD and FDC sarcoma	Treatment and outcome
Chan <i>et al.</i> Histopathology 2001	M/23	Nasopharynx	HV	10 years	Chemotherapy (CHOP regime) followed by nasopharyngectomy (maxillary swing approach). Disease free at 3 years follow-up
Farah <i>et al.</i> Oral Oncol Extra 2006	F/62	Right infratemporal fossa	HV	0	Wide excision followed by radiotherapy. Recurrence in right submandibular region after 9 months, subsequently had further radiotherapy. Disease free at 2 years.
Lin <i>et al.</i> Am J Surg Pathol 1997	F/76	Left neck	HV	0	Surgical excision. Local recurrence and chest wall metastases at 3.5 years, death at 4 years.
Chan <i>et al.</i> Cancer 1997	F/33	Left cervical lymph node	HV	5.5 years	Surgical excision. No documented follow-up.
Katano <i>et al.</i> Pathol Int 1997	M/30	Left cervical lymph node	HV	14 years	Surgical excision. Well at 4 months.
Current case	M/65	Right cervical lymph node	HV	0	Surgical excision with selective posterolateral neck dissection. No recurrence at 2 years.

CD: Castleman disease, FDC: Follicular dendritic cell, HV: Hyaline vascular



**Fig. 1:** Section of the tumour showing area of lymphoplasmic infiltration with scattered macrophages and eosinophils within the hyalinised stroma. (H&E stain, X 200 magnification)

was discovered in the same anatomic site years after a diagnosis of CD was made (Table I). These cases provide further evidence that there may be some evolutionary process that turns CD into FDC sarcoma. One study clearly demonstrated, through sequential biopsies, the progression of FDC proliferation in the setting of hyaline vascular CD over a 10 year period<sup>1</sup>.

CD and FDC sarcoma has been associated with vascular lesions such as Kaposi sarcoma, particularly in the HIV-positive population<sup>1,2</sup>. Epstein-Barr virus and Human Herpes Virus 8 (HHV-8) infections are associated with malignant transformation of CD to FDC sarcoma<sup>2</sup>. FDC sarcoma and CD are the commonly associated tumours in paraneoplastic pemphigus, a life-threatening autoimmune blistering skin disease<sup>3</sup>. FDC sarcoma may be mistakenly diagnosed as lymphoma or inflammatory pseudotumour in certain cases as these diseases mimic each other in the behavior and pathological findings<sup>1,2</sup>. It is necessary to perform an

immunohistochemical study to confirm FDC sarcoma. The immunophenotype of FDC sarcoma is positive for CD21, CD35, Ki-M4p, and Ki-FDC1p; and variably positive for vimentin, S-100 protein, CD68, and specific muscle actin<sup>2</sup>. It has recently been found that chemokine CXCL13 and podoplanin (D2-40) produced by the neoplastic FDC sarcoma cells can potentially be used as a biomarker to diagnose this tumour<sup>4,5</sup>.

Surgery is the mainstay treatment for FDC sarcoma. Some authors advocate surgical removal of the regional lymphatic drainage system if metastasis is suspected on imaging<sup>1</sup>. In this present case, CT showed evidence of lymph node involvement, thus a selective neck dissection was included with the tumour excision. Among the 5 head and neck FDC sarcomas with CD previously reported, none had documented neck dissection performed (Table I). This is because none of the authors reported any neck node involvement in their cases. All cases had surgical excision of the tumour, with two given additional chemotherapy and radiotherapy. For the three patients who underwent surgery alone, only one had local recurrence after 3 years. In the present case, no recurrence was noted 2 years after surgery. Nevertheless, the follow-up period for all these cases ranged from 4 months to 4 years, and one patient was lost to follow-up. Given the small number of cases reported, surgical treatment of the lymphatic drainage areas may need further evaluation.

The role of adjuvant treatment in the management of FDC sarcoma remains uncertain. Some authors suggest postoperative radiotherapy and some recommend chemotherapy or radiotherapy only when the tumour is aggressive, high volume and surgically unresectable<sup>1,2</sup>. In the present case, the patient refused postoperative radiotherapy. Nevertheless he was disease free after 2 years follow-up. Local recurrence has been reported in a patient who received postoperative radiotherapy, but subsequently cured with an additional course of radiotherapy (Table I). This suggests that the tumour is somewhat radiosensitive. Another patient with nasopharyngeal FDC sarcoma was treated with chemotherapy to shrink the tumour followed by surgery, and this patient

was disease free for 3 years<sup>1</sup>. All these patients have not been uniformly treated because of the retrospective nature of the reports and many reported cases have short or no follow-up. As there are no large series in the literature of this disease so far, the best treatment option is still debatable.

In conclusion, this report further reaffirms the association of FDC sarcoma with hyaline vascular CD within the same lesion in the head and neck. A strong index of suspicion is essential for the diagnosis of these types of lymphoproliferative tumours and immunohistochemical study is necessary to confirm the diagnosis. Surgical excision with neck dissection alone has provided good outcome in our case. However, optimal treatment has yet to be defined and larger case series are required.

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