CASE REPORT

Follicular dendritic cell sarcoma associated with Castleman’s disease presenting in the oral cavity

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Summary Follicular dendritic cell sarcoma (FDCS) is a rare intermediate grade malignant neoplasm of reticular dendritic origin. Castleman’s disease (CD) represents a non-neoplastic lymphoproliferative disorder with various clinical and morphological features. FDCS has been reported to be associated with CD. In this article, we describe the first case of follicular dendritic cell sarcoma associated with Castleman’s disease presenting in the oral cavity.

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Introduction

Follicular dendritic cell sarcoma (FDCS) is a rare intermediate grade malignant neoplasm of reticular dendritic origin, first described by Monda et al. in 1986. This entity frequently develops in the lymph nodes of the cervical, axillary, and supraclavicular region. The tonsil is one of the more common extranodal sites that has been involved.

Castleman’s disease (CD) represents a non-neoplastic lymphoproliferative disorder with various clinical and morphological features. Its clinicopathologic features depend on various etiologic factors such as Kaposi sarcoma herpesvirus, over secretion of IL-6, and follicular dendritic cell dysplasia. Clinically, solitary Castleman’s disease presents as a single mass, often in the mediastinum or the pulmonary hilum, and occurs in a young population. Generalized involvement of nodes in several centers accompanied by systemic involvement is manifested in the multicentric type of Castleman’s disease.

Approximately 22 of the 55 cases of follicular dendritic cell sarcoma in the head and neck region that have been reported to date have been extranodal. In the literature, 14 examples of FDCS have been reported to be associated with Castleman’s disease. In this article, we describe the first case of follicular dendritic cell sarcoma associated with Castleman’s disease presenting in the oral cavity.

Case report

A 62-year-old Caucasian female was referred in December 2003 for assessment of a soft tissue swelling in the right maxillary buccal sulcus in the region of the missing 16. The patient wore a complete maxillary acrylic denture,
and had experienced a sore denture hyperplasia with some mucosal ulceration which had previously resolved following adjustment of the denture by her dentist. Her past medical history was significant for osteoarthritis, one total knee replacement, and a transient ischaemic attack.

Clinical examination confirmed the presence of a large soft tissue mass measuring approximately 2.0 cm in greatest dimension, located in the reflection of the sulcus in the 16 region. The lesion could not be visualized intra-orally or extra-orally, but was easily palpable intra-orally. There was no evidence of ulceration, or epithelial hyperplasia.

An incisional biopsy was performed under local anesthesia and microscopic examination revealed a lymphoid nodule with a hyalinised connective tissue background. Molecular analysis showed a monoclonal B-cell population associated with a bcl-2 \[t (14;18)\] chromosome translocation, suggestive of an inconclusive presentation of follicular lymphoma, although there were no constitutional symptoms of lymphoma.

Subsequently, a deeper biopsy was performed one month later on which extensive immunohistochemical and molecular studies were performed. Bcl-2 translocation was not detected, and TCR gene rearrangement studies showed polyclonal beta and gamma chains.

A working diagnosis of follicular dendritic cell sarcoma in association with extranodal Castleman’s disease was made. The patient was referred to the Oncology Clinic at the Princess Alexandra Hospital, Brisbane, Australia. A CT and MRI scan of the head and neck revealed a slightly lobulated but well-defined right infra-temporal fossa mass lesion marginating the anterior aspect of the right coronoid and mandibular ramus, with some erosion of the adjacent bone (Fig. 1). The cortex was absent on the posterior zygoma, but the tumour did not extend beyond its immediate margins.

There was no evidence of any involvement in the neck, chest, abdomen or pelvis. There was no lymphadenopathy or hepatosplenomegaly. A wide operative excision was performed which included a close normal margin, and this was followed with radiotherapy to the surgical site only. Nine months later the patient presented with a submandibular lymph node enlargement, which was confirmed on CT, and she underwent subsequent irradiation to the ipsilateral neck. The patient is now disease free.

**Histopathologic examination**

Haematoxylin and eosin stained sections revealed two morphologically distinct areas. In one area, there were germinal centres with prominent mantle zones, many of which contained regressed follicles. Interfollicular sclerosis and lymphoid infiltrate were also evident (Fig. 2). The other distinctive area of abnormality was a monomorphic spindle cell proliferation containing admixed lymphocytes and scattered plasma cells (Fig. 3).

**Immunohistochemistry**

The described lymphoid area of proliferation showed follicles to be CD20+, CD79a+, CD3, CD43 and CD5 negative within the follicles, but were positive within interfollicular small regular lymphoid cells. The follicles showed weak positivity for CD10, but were negative for BCL-2. Kappa Lambda stains showed apparent polyclonal cytoplasmic immunoglobulin. BCL-6 was restricted to the germinal centres.

The spindle proliferation was strongly positive for CD21 (FDC marker) (Fig. 4). The spindle cell proliferation was

Figure 1 MRI showing large mass lesion in right infra-temporal fossa. The tumour appears to displace but not invade adjacent structures. The mass measured approximately 4.5 cm in the supero-inferior plane, 3.0 cm in the coronal plane, and 3.0 cm in the antero-posterior plane.

Figure 2 Castleman’s disease showing germinal centres with prominent mantle zones, many of which contain regressed follicles. Interfollicular sclerosis and lymphoid infiltrate are also evident (H & E × 100).
negative for CD34, CD31, and SMA, but showed focal positivity for S-100.

Discussion

Follicular dendritic cell sarcomas primarily affect the young or middle-aged adult with a median age of presentation of 43 years, with no gender predilection. In approximately 50% of cases, the lesion presents as a solitary, slow-growing, and painless lymphadenopathy.7

Histologically, the neoplastic cells of FDCS display a characteristic oval or spindle shape showing a syncytial and often fibrillary cytoplasm. The nuclei are oval, with smooth contours, vesicular or granular chromatin, and distinct nucleoli. They are arranged in sheets, interleaving fascicles, or storiform or whorled patterns. Two of the most characteristic features of these neoplasms are the intimate admixture of tumour cells and small lymphocytes throughout the tumour, and the presence of perivascular lymphocytic cuffing.7,8

The pathologic diagnosis of FDCS is often challenging and requires immunophenotyping as confirmatory, although there is significant overlap with interdigitating dendritic cell sarcoma. CD21 recognizes the C3d receptor and has been demonstrated to be expressed in approximately 96% of cases investigated.2,7 Variable expression is shown with S-100 protein, EMA, CD68, MSA, and desmoplakin.

Rare cases of Castleman’s disease have been associated with FDCS but no clonal correlation has been demonstrated. In the literature, 14 examples of FDCS have been reported to be associated with Castleman’s disease; the majority involving the hyaline vascular (HV) type. The possible basis of the association is the observed aberrations in FDC networks as well as FDC dysplasia in some follicles of Castleman’s disease.6 The presumption is that a FDC tumour develops in Castleman’s disease through a hyperplasia–dysplasia–neoplasia sequence, similar to that documented for epithelial neoplasms, however firm evidence of a clonal relationship between Castleman’s and FDCS is scarce. Based on all the documented cases, FDCS have arisen concomitantly with or after a diagnosis of Castleman’s disease, suggesting the existence of a pathogenetic link between these conditions.6,7,9,10 It has been hypothesized that abnormalities of FDC play a pivotal role in the pathogenesis of Castleman’s disease of the hyaline vascular type.11

In cases that the two lesions were discovered in the same anatomic site, it has been argued that the Castleman’s disease lesion was only a reaction to the FDC tumour rather than a precursor lesion. On the contrary, Chan and colleagues clearly demonstrated, through three sequential biopsies, the progression of FDC proliferation in the setting of Castleman’s disease-HV.6 Additionally, they also found some expression of p53 protein in the FDCS, and small numbers of p53 positive cells in the interfollicular zone of CD-HV, suggesting a role for this tumour suppressor gene in the transformation process. In our case, we could not demonstrate any evolution of FDCS from Castleman’s disease, and also can not exclude that the abnormalities of FDCS play a pivotal role in the pathogenesis of Castleman’s disease. There was also no evidence of any association of Castleman’s disease with human herpes virus 8 (HHV8).

Spindle cell proliferation has been well documented with Castleman’s disease.9 The spindle cell proliferation may either be correlated to vascular proliferation or follicular dendritic cell proliferation.4 In our case, the vascular markers were negative. Immunoglobulin heavy chain and T cell receptor gene rearrangement studies showed a germline configuration, providing no evidence for specific monoclonal B or T lymphocyte differentiation. These results are in concordance with genotypic studies performed in two other cases.12,13

In summary, this report documents the first case of follicular dendritic cell sarcoma occurring concomitantly with Castleman’s disease presenting in the oral cavity. The finding of these two distinct lymphoid processes within the same lesion has become more recognizable, though rarely arising within the oral cavity.
References