CASE REPORT

Follicular dendritic cell sarcoma of the tonsil

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SUMMARY

Follicular dendritic cell sarcoma (FDCS) is an uncommon tumour within the spectrum of histiocytic and dendritic cell neoplasms that can occur at nodal and extra-nodal sites. Besides being rare, these tumours are difficult to diagnose. A 72-year-old man with a painless mass in the right tonsil was admitted to the Mersin University Hospital. Tonsillectomy was performed. Microscopically, the tumour consisted of spindle-shaped cells with large oval to polygonal nuclei. Lymphocytes were scattered among the tumour cells. Immunohistochemically, the cells were positive for CD23 and vimentin. The tumour was diagnosed as FDCS with histological and immunohistochemical findings. Recognition of extranodal FDCS requires knowledge of this entity and to consider it during the diagnosis. Confirmatory immunohistochemical staining is essential for diagnosis. Correct characterisation of this neoplasm is important because of its potential for recurrence and metastasis.

BACKGROUND

Follicular dendritic cells (FDC) are antigen-presenting immune accessory cells thought to be derived from local stroma and therefore are of mesenchymal origin rather than haematopoietic.¹ They form a stable meshwork within lymphoid follicles, and activate B-cells in the follicle.² FDC sarcoma (FDCS), first described by Monda *et al*³ in 1986, is a rare neoplastic proliferation showing morphological and immunophenotypic features of FDC. It can occur at nodal and extra-nodal sites, which were first described by Chan *et al*^{4 5} in the oral cavity. Metastatic disease has also been observed in the lymph nodes, lung and liver.² To date, approximately 70 cases of FDCS have been reported in the literature, 24 of which were localised in the head and neck region, eight of them being located in the tonsil.^{6 7}

CASE PRESENTATION

A 72-year-old man with a 4 cm×3 cm painless mass located in the right tonsillar region was admitted to the Mersin University Otorhinolaryngology clinic with a 2-month history of discomfort during swallowing food and 1-month history of respiratory distress. Physical examination showed a swollen, enlarged, indurated right tonsil that featured necrotic ulcerative areas. The mass showed extensions to the nasopharynx and hypopharynx. MRI showed a 5 cm×3 cm mass which began from the right tonsillar region and extended inferiorly to the parapharyngeal soft tissue plans and obliterated lateral pharyngeal recess. There was no enlarged lymph node in the neck. After the injection of a contrast agent, contrast enhancement was detected

in the lesion. Tumour resection with tonsillectomy was planned under general anaesthesia. Total resection was not possible, hence piecemeal tumour resection was performed. Intraoperative frozen consultation was requested in order to exclude epithelial tumours. Macroscopically, two tumour masses, one 2 cm in diameter and the other 1.5 cm in diameter, were evaluated. Cytologically, the imprints revealed large epithelioid to spindled cells, both in loosely cohesive and syncytial groups as well as single cells with oval-shaped to cigar-shaped nuclei, vesicular chromatin and distinct nucleoli. Another feature was a prominent lymphoplasmacytic cell component intimately admixed with tumour cells (figure 1). The histological examination of frozen sections showed a tumour comprising of oval to spindle-shaped cells that were arranged in solid sheets and diffusely sprinkled with small mature lymphocytes and plasma cells. These findings did not lead to a definitive diagnosis during frozen section evaluation.

In the sections obtained from paraffin blocks, the tumour was characterised by a proliferation of spindle to ovoid cells which formed fascicles, storiform patterns and whorls. Individual cells tended to become plump, with slightly eosinophilic, fibrillary cytoplasm and indistinct cell borders. The nuclei were elongated and had vesicular or granular chromatin, small but distinct nucleoli and a delicate nuclear membrane. Small lymphocytes were scattered throughout the tumour (figure 2). The tumour cells showed positive immunohistochemical staining for CD23 (figure 3) and vimentin, and negative staining for cytokeratin, LCA, S100, CD31, CD34, HMB-45 and desmin. Based on these histopathological and immunohistochemical findings, the patient was diagnosed with FDCS of the tonsil.

Figure 1 Loosely cohesive groups of spindle cells with lymphocytes (H&E, ×200).

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Figure 2 Fascicles of spindle cells admixed with lymphocytes (A: H&E, $\times 100$; B: H&E, $\times 40$).

TREATMENT

The patient had left the treatment on his own will after receiving one dose of the planned postoperative adjuvant chemotherapy. The hospital records show that the patient did not participate in the routine follow-up either. During the preparation of this article, the relatives of the patient were reached and it was found out that the patient died 1 year after the first dose of chemotherapy, and the cause of death is unknown since an autopsy was not performed.

DISCUSSION

FDCS is an extremely rare malignant neoplasm.⁸ This tumour primarily affects young or middle-aged adults. No gender predilection has been reported; however, a slight female predominance (1.2:1) with a median age of 41.5 years has been determined.⁹ Patients often present with a slow-growing, painless mass. Abdomen, including the spleen, liver, pancreas and small intestine, and tonsils are the most common sites of extranodal FDCS. Although the pathogenesis of this neoplasm remains unknown, it occurs in association with Castleman's disease in a small portion of cases, usually the hyaline vascular type.³⁻⁹ Epidermal growth factor receptor (EGFR) expression has been investigated as another shared feature of both entities. In addition, overexpression of the p53 protein is noted in FDCS. Proliferations of FDC occurring in a subset of inflammatory pseudotumours, most commonly in the liver and spleen, have been associated with Epstein-Barr virus.²⁻¹⁰ Recent research studies have demonstrated that HIV infection may also play a role in the formation of FDCS.¹¹

Figure 3 Positive staining of tumor cells with CD23 (CD23, $\times 200$).

Several reports discuss the usefulness of fine-needle aspiration (FNA) for the pre-surgical diagnosis of FDCS.¹² To date, 12 cytology cases have been reported in the literature. Ten of these cases involved peripheral lymph nodes and the remaining two were intra-abdominal masses.¹¹⁻¹³ Although FDCS demonstrates characteristic cytological features on FNA specimens, the diagnosis can be challenging when aspiration cytology is the sole diagnostic modality.¹² Although the cytomorphological features of FDCS can overlap with those of many other tumours, FNA with a biphasic cellular population composed of large cells with mild-to-moderate atypia and small lymphocytes should direct the cytopathologist to the appropriate confirmatory algorithms.¹³⁻¹⁴

It has been reported in several studies that as many as one-third of previously reported cases were misdiagnosed at initial evaluation, mainly because FDCS was not considered in the differential diagnosis.¹⁵ Recognition of extranodal FDCS requires the awareness and knowledge of this entity, especially when they occur in the head and neck region.⁸ Misdiagnoses have included reactive response, inflammatory pseudotumour, malignant fibrous histiocytoma, meningioma, mesenchymal tumour with neural differentiation, schwannoma, stromal tumour and carcinoma. In addition to the aforementioned list of misdiagnoses, thymoma, gastrointestinal stromal tumour, and interdigitating reticulum cell sarcoma can also be considered in the differential diagnosis.¹⁵ Once morphologically suspected based on cytological features, the diagnosis of FDCS is confirmed by the use of an appropriate panel of immunohistochemical markers and, in difficult cases, by the ultrastructural demonstration of desmosomes.⁵⁻¹⁵⁻¹⁶ CD21 and CD35, directed against the C3d and C3b receptors, respectively, and CNA.42 are the most widely used markers demonstrating FDC differentiation. Other FDC-specific markers useful for confirming a diagnosis of FDCS include Ki-M4, Ki-M4p, R4/23, Ki-FDC1p, clusterin, fascin and podoplanin.²⁻¹⁶ Noticeably, reactivity for CXCL13 is highly specific for FDCS.¹⁵ This chemokine is normally expressed on a major subset of FDCS and is retained during their transformation in FDCS and Castleman's disease.

Although it was originally known as *follicular dendritic cell tumour*, Chan *et al*¹⁵ proposed the name *follicular dendritic cell sarcoma* to emphasise the clinical behaviour of the neoplasm as a sarcoma rather than a lymphoma. Until recently, FDCS was considered as an indolent tumour with a tendency for local recurrence, but with a low risk of metastasis. Recent reports with longer follow-up data of larger patient numbers have concluded that FDCS is more aggressive and should be considered at least as an intermediate-grade malignancy.¹⁶ Recurrence occurs in more than 50% of cases and metastases occur in about 25% of patients; such occurrences may be delayed for many years. However, owing to the short-term follow-up periods in the reported cases, the local recurrence and metastatic rates might be underestimated.¹ At least 10–20% of patients die because of the disease, often after a long period of time. Poor prognostic factors for this tumour include intra-abdominal location, size ≥ 6 cm, and mitotic count $\geq 5/10$ HPF, extensive coagulative necrosis, significant nuclear pleomorphism and lack of adjuvant therapy.⁸⁻¹⁷

The most effective treatment is complete surgical excision and should include diligent control of surgical margins.¹⁸ Adjuvant radiotherapy or chemotherapy appears to be indicated in cases having adverse pathological features in recurrent or incompletely resected lesions.⁸ However, the role of adjuvant therapy (chemotherapy or radiation) is unclear because of the rarity of the lesion and the retrospective nature of the published reports.

In addition, demonstration of EGFR expression in FDSC brings out the possibility of using antibodies and inhibitors targeting EGFR as adjuvant agents.⁶

Learning points

- In summary, follicular dendritic cell sarcoma (FDSC) is an uncommon tumour with characteristic but not specific morphological features.
- Accurate diagnosis, which requires awareness of this entity, knowledge of its cytomorphology and appropriate differential diagnostic considerations, is critical due to its significant recurrence and metastatic potential.

Competing interests None.

Patient consent Obtained.

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