Follicular Dendritic Cell Tumour: A Rare But Characteristic Neoplasia

W Back, R Grobholz, F Riedel

Citation

W Back, R Grobholz, F Riedel. *Follicular Dendritic Cell Tumour: A Rare But Characteristic Neoplasia*. The Internet Journal of Pathology. 2003 Volume 3 Number 1.

Abstract

Tumours of the follicular dendritic cells are rare tumours. Therefore, information about adequate treatment and overall prognosis is limited. We report about a 55 year-old patient, who was operated because of a persisting cervical lymph node swelling. The histopathological investigation showed a predominantly fascicular, relatively cell-rich tumour. Immuno-phenotyping of this tumour confirmed the diagnosis of a follicular dendritic cell tumour. Crucial for the correct diagnosis was a positive immunoreaction for CD21 and CD68. Furthermore we could demonstrate positive immunostaining for Fas-ligand in this tumour similar to the immunophenotype of normal follicular dendritic cells. We conclude, that neoplastic lesions in cervical lymph nodes but also unclear tumours of other regions especially if they show fascicular growth patterns should be screened for a FDC tumour immunohistochemically. Immunoreactivity for Fas-ligand - though not being specific - could supplement the diagnostic decision process.

INTRODUCTION

The follicular dendritic cells (FDC) are an important component of the B-cellular lymph follicle building an intricate network (= "reticulum") in germinal centres of lymph follicles. They have been described under the more general heading "dendritic reticulum cells" [1] and are thought to present antigens to immunocompetent cells in the lymphatic tissues just as to regulate the germinal centre reaction [2]. Primarily they promote the humoral response of the immune system. A hyperplastic proliferation of these FDCs can be found in some reactive but also in neoplastic conditions of lymphatic tissues as for instance in lymphofollicular hyperplasia, different lymphomas of Non-Hodgkin as well as of Hodgkin type [3]. Tumours of follicular dendritic cells are very rare. Only some 40 cases of FDC tumours have been reported in the literature. Most of these tumours of follicular dendritic cells were found in lymph nodes [4,5]. But also extranodular localizations of FDC tumours have been described. These include the oral cavity, the thyroid, the nasopharynx, the gastrointestinal tract, the spleen and the liver [5,6,7,8,9]. The normal phenotype of FDCs recently has been reported to include expression of Fas ligand [10], so we questioned whether this is also true for a FDC tumour.

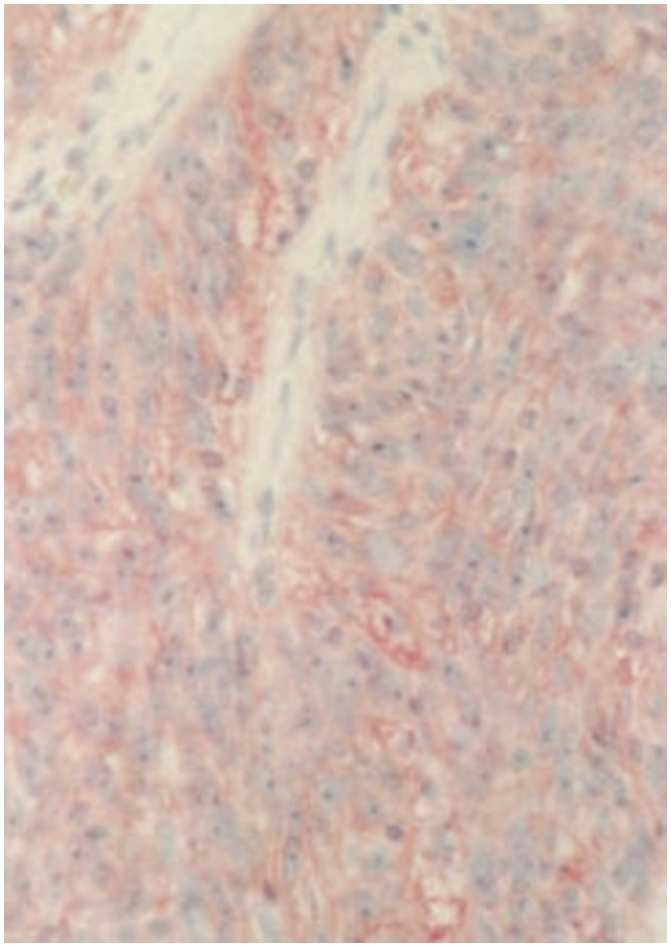
CASE REPORT

A 55 year-old patient was seen in the outpatient clinic of the ENT department because of a persistent swelling of cervical lymph nodes. He was in good general condition. The patient reported a history of affective depression for one year. For 12 years he suffered from tinnitus. In earlier years an allergic asthma had been present. His mother died at the age of 73 years from a bronchial carcinoma and his father at the age of 75 years from a kidney tumour.

A diagnostic lymph node excision was done in general anasthesia. Several little lymph nodes as well as an easily movable tumour measuring 2,5 cm were removed from the left side of the neck. Histologically this tumour mass showed a predominantly spindle cell pattern and a compactly growing tumour. Residual lymph node tissue was only sparsely present. Besides the spindle-cell tumour also showed small whirl-like aggregates of tumour cells (figure 1).

Figure 1

Figure 1: Fascicular tumour cell architecture of the FDC tumour with whirl formation. H&E, x 175.



Other tumour areas showed enhanced nuclear pleomorphism of the tumour cells. Tumour necrosis was not present, the mitotic rate was about 4 - 6 mitotic figures per 50 high power fields.

The differential diagnosis of this neoplasm first had to rule out a metastatic lesion especially a metastasis of a so-called spindle cell carcinoma. This kind of tumour is especially prevalent in the mucosa of the pharynx, larynx and esophagus. Clinically a microlaryngoscopy and a panendoscopy was performed, followed by a tonsillectomy, by several biopsies from different other mucosal regions and a bilateral selective neck dissection. The histopathologic examination showed no further tumour and did not reveal dysplastic or neoplastic mucosa in any location.

A general medical examination did not find any other pathological conditions, especially no lymph node enlargements at other sites. By ultrasonography the abdomen was normal. The general urologic examination was inconspicious. A nuclear magnetic resonance tomography of the head, neck and upper mediastinum showed no other suspicious lesions.

The immunohistological phenotyping of this tumour was done using immunohistochemical routine procedures ("avidin labelled biotin" system with alkaline phosphatase, Dako, Germany) for paraffin sections. The most important antibodies are summarized in table 1.

Figure 2

Table 1: Immunophenotyping of the FDC tumour

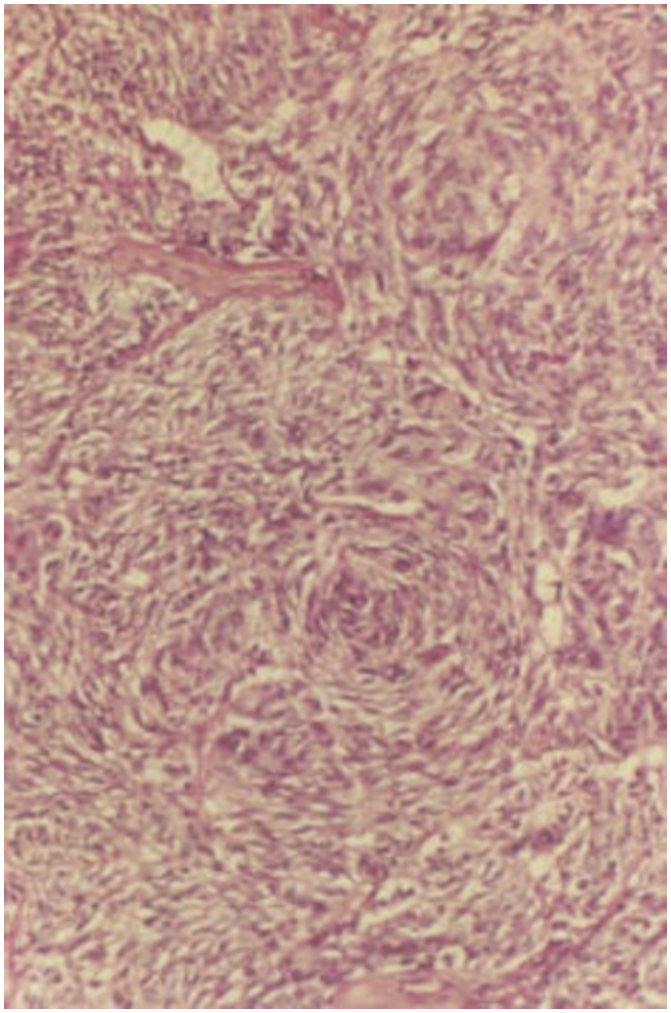
Antibody		Source	Result
Vimentin	mc*	Dako, Hamburg, Germany	positive
S100-Protein	pc*	Dako, Hamburg, Germany	positive in some areas and some tumour cells
EMA (epithelial membrane antigen)	mc*	Dako, Hamburg, Germany	negative
SMA (smooth muscle actin)	mc*	Novocastra, Newcastle, UK	negative
CD 21	mc*	Dako, Hamburg, Germany	**positive**
CD 23	mc*	Novocastra, Newcastle, UK	negative
CD 35	mc*	Serotec, Düsseldorf, Germany	**positive**
CD 68	mc*	Dako, Hamburg, Germany	**positive in some areas**
Fas (CD 95) ligand	mc*	Novocastra, Newcastle, UK	**positive**
Fas (CD 95) ligand	pc*	Santa Cruz, Heidelberg, Germany	**positive**

* mc = monoclonal, pc = polyclonal

The immunoreactions with epithelial markers (different cytokeratins, EMA, HEA 125), neuroendocrine markers (chromogranin A, synaptophysin, NSE), vascular markers (CD 34, FVIIIrA), muscular markers (desmin, smooth muscle actin, HHF1) and lymphatic markers (CD 20, CD 3, CD30, CD23, LCA) were found to be negative. In the tumour cells specific positive immunostaining was present for vimentin, for the macrophage marker CD 68, for CD 21, CD 35 and for Fas ligand (figure 2).

Figure 3

Figure 2: Positive immunoreaction of the tumour cells for Fas ligand (monoclonal). Avidin labelled biotin, alkaline phosphatase detected with Fast Red. Counterstain hematoxylin, x 350.



DISCUSSION

Tumours of follicular dendritic cells are very rare [11]. FDC tumours are mostly diagnosed in young or middle aged adults. Chan and coworkers claimed a 43% risk of local recurrence and a risk for metastasis of 24% deduced from 17 own cases and from cases in the literature [4]. The number of published cases is still too low and the documentation too heterogeneous to give statistically verified therapeutic recommendations for these tumours. In our patient no other metastatic tumour sites could be detected and he is in good health without recurrence for three and a half years now.

FDC tumours are difficult to diagnose clinically and histopathologically. In practical terms it should be kept in mind that in case of an otherwise unspecified and unclear tumour of fascicular architecture not only an extensive tumour search for a primary tumour, but also further immmunohistochemical studies are mandatory. Up to now many aspects of normal follicular dendritic cells, their physiology and their regular immunophenotype are unclear [8]. The expression of Fas ligand in FDCs from the meshwork of lymphonodular germinal centres has been investigated by Verbeke et al. [10]. Also the cells of the reported FDC tumour show an expression of Fas ligand, which could be shown with two different Fas ligand antibodies (table 1, figure 2). Fas ligand is thought to play a role in the selection process of germinal B-cells. There is general consent about the expression of complement-receptor proteins CR1 (CD 35) and CR2 (CD 21) in FDC tumours. In the presented case we found a zonal positivity for CD 68, which has been reported in some FDC tumours. In contrast to other data of the literature no expression of smooth muscle actin and only a weak immunoreaction for S-100 protein in a minority of tumour cells was detected [4,5]. Also the expression of EMA (epithelial membrane antigen), which was negative in our case, is reported to be positive in most cases (85%) of the series of Chan [4], which makes the differential diagnosis to so-called spindle cell carcinomas even more troublesome.

Positivity for Fas-ligand is not a specific finding for FDC tumours. Also other tumours may show expression of Fas-ligand. But in a given setting of other more specific markers a positive reaction for Fas-ligand could aid in the diagnosis of this rare type of tumour. The role of FAS ligand in the development and proliferation control of FDC tumours has to be further elucidated.

References

1. Lennert K. Lymphomas other than Hodgkin's disease. Berlin Heidelberg New York: Springer; 1978:51-68.
2. Tew JG, Kosco MH, Burton GF, Szakal AK. Follicular dendritic cells as accessory cells. Immunol Rev. 1990;117:185-211.
3. Perez-Ordonez B, Rosai J. Follicular dendritic cell tumor: review of the entity. Semin Diagn Pathol. 1998;15:144-154.
4. Chan JK, Fletcher CD, Nayler SJ, Cooper K. Follicular dendritic cell sarcoma. Clinicopathologic analysis of 17 cases suggesting a malignant potential higher than currently recognized. Cancer. 1997 ;79:294-313.
5. Perez-Ordonez B, Erlandson RA, Rosai J. Follicular dendritic cell tumor: report of 13 additional cases of a distinctive entity. Am J Surg Pathol. 1996;20:944-955.
6. Nayler SJ, Verhaart MJS, Cooper K. Follicular dendritic cell tumour of the tonsil. Histopathology. 1996;28:89-92.
7. Galati LT, Barnes EL, Myers EN. Dendritic cell sarcoma of the thyroid. Head Neck. 1999;21:273-5.
8. Beham-Schmid C, Beham A, Jakse R et al. Extranodal follicular dendritic cell tumour of the nasopharynx. Virchows Arch. 1998;432:293-298.
9. Hollowood K, Stamp G, Zouvani I, Fletcher CDM. Extranodal follicular dendritic cell sarcoma of the gastrointestinal tract: morphologic, immuno-histochemical

and ultrastructural analysis of two cases. Am J Clin Pathol. 1995;103:90-97.
10. Verbeke CS, Wenthe U, Zentgraf H. Fas ligand expression in the germinal centre. J Pathol. 1999;189:155-60.
11. Fonseca R, Yamakawa M, Nakamura S et al. Follicular dendritic cell sarcoma and interdigitating reticulum cell sarcoma: a review. AM J Hematol. 1998;59:161-167.

Author Information

Walter Back, MD
Department of Pathology, Theodor Kutzer Ufer, Universitätsklinikum Mannheim

Rainer Grobholz, MD
Department of Pathology, Theodor Kutzer Ufer, Universitätsklinikum Mannheim

Frank Riedel, MD
ENT Department, Theodor Kutzer Ufer, Universitätsklinikum Mannheim