Quiz

Correct answer to the quiz. check your diagnosis

High-risk follicular dendritic cell sarcoma of the tonsil mimicking nasopharyngeal carcinoma

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Follicular dendritic cell sarcoma (FDCS) is often misdiagnosed as a carcinoma or malignant lymphoma due to morphological variability. In FDCS application of routine antibody panels without CD21 and CD23 increases the misdiagnosis rate, because the tumor cells often show focal positivity for usual immunohistochemical markers.
Our new case showed a distinct picture due to the uncommon tumor architecture, with extensive areas of necrosis and hemorrhage, the presence of nuclear atypia, and an increased mitotic count and Ki-67 index. These features suggest the classification of this tumor in the category of high-risk malignancies, with uncommon features of FDCSs.

Key words: follicular dendritic cell sarcoma, immunohistochemical markers, high-grade.

Introduction

Follicular dendritic cell sarcoma (FDCS) is a rare tumor that is often mistakenly diagnosed as carcinoma or lymphoma due to the varied morphological appearance. Application of routine antibody panels without CD21 and CD23 increases the rate of misdiagnosis, because other usual immunohistochemical markers (panCK, CD45) often show focal positivity in FDCS. Therefore, it is important to avoid erroneous diagnosis of nasopharyngeal carcinoma and lymphoma. In this paper, we present an uncommon form with nuclear atypia, and increased mitotic count and Ki-67 index, prognostic factors questioning the inclusion of our tumor in the intermediate-risk malignancies, characteristic for FDCSs.

Case presentation

An otherwise healthy, heavy smoker, 55 years old, was admitted to the ENT Clinic due to painless swelling of the left tonsil associated with odynophagia, repeated bleeding and hemoptysis, symptoms occurring for a few weeks.

Intraoral local examination revealed an enlarged left tonsil with elastic consistency but increased in volume, covered by ulcerated epithelium. The ENT examination of the right tonsil, head, ears, and nose was unremarkable without enlarged cervical lymph nodes. Routine biochemical and hematological investigation results were within normal limits. Computed tomography (CT) scan confirmed an expansive, non-infiltrative process without another tumor mass in the head-neck region or the thorax. Based on the

general systemic examination and lack of inflammatory markers, the preliminary clinical diagnosis of a tonsillar malignant tumor, suspected to be a carcinoma or lymphoma, was made.

The patient underwent bilateral classical tonsillectomy under general anesthesia, without postoperative complications. The histopathological analysis of both tonsils was performed and the patient was discharged the following day. Macroscopic examination showed preserved morphological structure of the resected right tonsil. The left tonsil was covered with partially ulcerated epithelium sprinkled with hemorrhagic foci, measuring 35/30/25 mm. On the cut surface, centrally, a 16 mm, relatively well-circumscribed, white-yellow, soft tumor mass was seen, impregnated with multiple hemorrhagic foci.

Histopathological examination of the right tonsil showed normal architecture. The left tonsil tissue presented partial replacement with an infiltrating tumor mass, composed of a diffuse proliferation of medium- to large-sized individual and grouped oval cells with many admixed small lymphocytes, but no stromal reaction (Fig. 1A). They showed indistinct cell borders and slightly eosinophilic cytoplasm, oval and elongated variable nuclear size, with granular, finely dispersed chromatin and small but distinct nucleoli (Fig. 1B). The mitotic rate was 8/10 high-power fields. The maximum diameter of tumor tissue measured 18 mm without infiltration of the lateral and deep resection margins. Infiltrative growth pattern, multifocal coagulation necrosis, high mitotic index and moderate cytonuclear pleomorphism suggested an undifferentiated nasopharyngeal carcinoma, but the first immunohistochemical panel showed vimentin (cloneV9, Dako) positive and pancytokeratin (clone AE1/AE3, LabVision) negative atypical cells. The immunophenotype of suspicious cells was further characterized by a large primary antibody panel, applying the DAKO EnVision Flex, High pH immunodetection system (K 8010) for all antibodies: CD45 (clone 2B11), CD20 (clone L26), CD3 (clone SP7), CD21 (clone 2G9), CD23 (clone 1B12), Epithelial Membrane Antigen/EMA (clone E29), CD68 (clone KP1), Polyclonal Rabbit Anti-S100 protein and Ki67 (clone MIB-1). The reaction product was visualized using DAB chromogen.

The epithelial and lymphoid components of the remaining tonsil tissue were used as an endogenous positive control for most antibodies, and resolved the

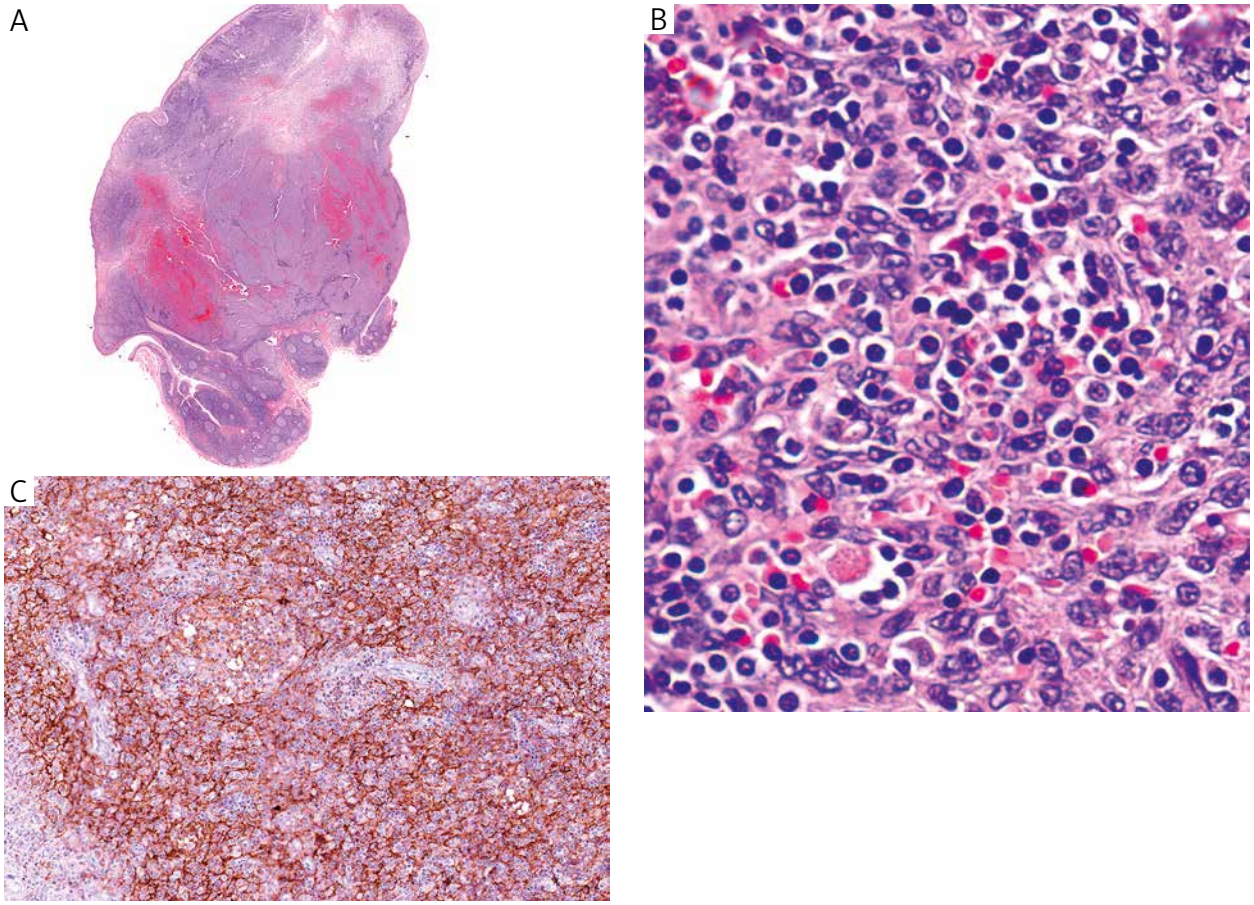

Fig. 1. HE stain: low-power view of a transversal section cut along the left tonsil, presenting an infiltrative tumor mass (A). HPF showing oval and spindle cells with many admixed small lymphocytes and no stromal reaction (B). These neoplastic cells present strong immunoreactivity for CD21 (C), (DAB chromogen, 40×)

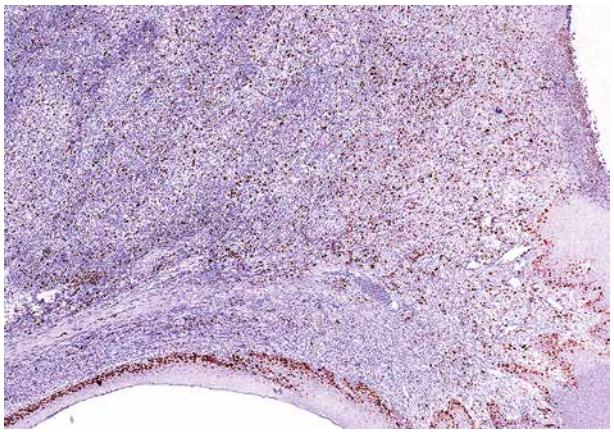

Fig. 2. The Ki-67 proliferative index is approximately 20% (DAB chromogen, 10×)

diagnostic dilemma: the tumor cells showed strong positivity for CD21 (Fig. 1C) and CD23. In addition, the expression of CD45, EMA and S-100 protein was focally observed. The Ki67 index was approximately 20% (Fig. 2). The cells did not show expression of CD20 and CD3. Based on histopathologic and immunohistochemical findings, the diagnosis was completed to FDCS of the tonsil. Despite the small size of the tumor (less than 2 cm), the high mitotic rate associated with increased Ki-67 index, nuclear pleomorphism, and multifocal coagulation necrosis are criteria for a poor prognosis; therefore the patient was considered to have a high-risk malignancy. The bilateral tonsillectomy was followed by radiotherapy (applied to the left tonsillar region) and after a 3-year follow-up period the patient was disease-free.

Discussion

FDCs are antigen-presenting and -processing non-migratory, non-lymphoid and non-phagocytic accessory cells found in primary and secondary follicles of the B cell areas of lymph nodes, spleen, and mucosa-associated lymphoid tissue (MALT). They form a stable network due to intercellular connections between FDC processes and interact intimately with follicular B cells, that are essential for the germinal center reaction regulation [1]. Their transformation into tumor cells leads to an uncommon neoplasm -Follicular Dendritic Cell Sarcoma (FDCS), representing less than 1% of lymphoid tumors with nodal or extranodal origin (WHO 2008) in adult patients [2]. The existence of a primary tumor of the follicular dendritic cell was first described in 1986 by Monda *et al*. [3]. Although lymph nodes are the most common origin of FDCS, many extranodal sites (especially pharyngeal location) have been identified as possible origins [4]. At present, 52 pharyngeal FDCS cases (27 of them with tonsillar location) have been reported in the literature [5].

The etiology and pathogenesis of FDCS are unknown. So far, cytogenetic abnormalities characteristic of this tumor have not been demonstrated, and the clonal relationship between hyaline-vascular Castleman disease and FDCS suggests the possibility of an increased incidence of FDCS in these patients [6, 7, 8]. It is possible that the tumor has a racial or geographic correlation, because most cases have been reported from the Eastern Asian area [9]. A similar prevalence was seen between male and female patients, almost all being adults, with average age between 40 and 50 years [10].

Due to the numerous distinctive morphological features, the tumor can mimic different histopathological entities – NHL, lymphoepithelial carcinoma, carcinosarcoma, interstitial reticulum cell sarcoma – or may be misinterpreted as a reactive response (inflammatory process), documented by a high misdiagnosis rate (57%) according to the reviewed cases [4]. So, morphologic criteria alone are not enough to designate a tumor as FDCS, especially when lymphoid cells, admixed with clusters and single tumor cells, obscure the morphology of the tumor. Large panels of antibodies, but without CD21, CD23 or CD35, increase the rate of misdiagnosis because the tumor cells can be focal positive for epithelial, mesenchymal and neural routine immunohistochemical markers (LCA, CD68, EMA, S-100). The tumor cells were also positive for HMW-CK squamous epithelium marker [11]. All authors agree that the final diagnosis can be rendered only after immunohistochemical examination with follicular dendritic cell (FDC) markers [12]. These markers work well on formalin-fixed materials and are commercially available [7].

Idress et al. recommend the use of these antibodies for any undifferentiated epithelioid cell or spindle cell tumor to avoid misdiagnosis, especially in preoperative nasopharynx biopsy specimens [13].

For a long time the FDCS was considered an indolent tumor with a low tendency of recurrence and low metastatic capacity, being underestimated due to a short follow-up period for most patients [14]. However, recent studies with longer follow-up have suggested that FDCS is a more aggressive tumor and should be considered an intermediate-grade sarcoma.

Li *et al*. (2010) proposed a prognostic assessment system for FDCS: Tumor size ≥ 5 cm associated with mitotic count over 5/10 HPF, high-grade histology and Ki-67 proliferative index (≥ 10%) increase the likelihood of tumor recurrence. Based on the recurrence potential, this tumor can be graded as a low-, intermediate- and high-risk FDCS, but the prognosis also depends on the location, as the tumors in the various anatomical regions show distinct prognoses [15].

In conclusion, our patient requires strict oncological follow-up. Despite its small size, the presence of nuclear atypia, increased mitotic count, and Ki-67 index ≥ 10% classify this tumor in the category of high-risk malignancies. FDCS is an uncommon tumor of the tonsil, but in spite of its rarity it should be considered for differential diagnosis of any unilateral tonsillar swelling and head and neck tumor biopsies, especially in small (needle biopsy) specimens with an incomplete storiform or syncytial morphological pattern rich in lymphocytes. An erroneous diagnosis can be avoided by using a well-designed immunohistochemical panel. Although FDC markers are not available in most routine laboratories, we suppose that FDCS in reality is far more frequent than is known.

The authors declare no conflict of interest.

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