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Case study

Cytokeratin-positive epithelioid angiosarcoma presenting in the tonsil: a diagnostic challenge ☆

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Summary Primary oral cavity sarcomas are exceedingly rare and may pose a great diagnostic challenge. A 71-year-old woman without history of malignancy or radiation to the head and neck presented with an antibiotic-refractory diffuse painful swelling of the right tonsil necessitating tonsillectomy. Histologic evaluation revealed subtotal replacement of the right tonsil by a high-grade epithelioid neoplasm displaying extensive ulceration, necrosis, and primitive vasoformation. Immunohistochemistry showed strong/diffuse expression of pancytokeratin antibodies KL-1 and Lu5, cytokeratin 8, cytokeratin 18, cytokeratin 19, vimentin, CD31, ERG, and Freund leukemia integration site 1 (FLI-1). High-molecular-weight cytokeratins (cytokeratin 5, 34βE12), cytokeratin 7, cytokeratin 13, and cytokeratin 20 were not expressed. Within months, the patient underwent surgical resection of multiple bleeding intraoral and gastrointestinal metastases. She is currently alive with disease 9 months from diagnosis. To our knowledge, this case represents the first well-documented primary epithelioid angiosarcoma of the tonsil. The strong cytokeratin expression in epithelioid angiosarcomas represents a diagnostic pitfall. Thus, awareness of this rare and highly aggressive neoplasm is necessary for distinguishing it from poorly differentiated and acantholytic squamous cell carcinoma and diffuse large cell lymphoma.

1. Introduction

Most of the malignant neoplasms of the head and neck represent squamous cell carcinomas, whereas sarcomas are rare in this anatomical region [1]. Although approximately 60% of cutaneous angiosarcomas arise in the skin of the head and neck area, noncutaneous sarcomas of the head and neck are exceptionally rare, accounting for approximately 4% to 10% of all sarcomas and less than 1% of all head and neck cancers [1]. In an extensive review of 11 250 head and neck cancers by Gorsky and Epstein [1], sarcomas constituted 1.24% of head and neck cancers. Because of their rarity, head and neck sarcomas have been the subject of case reports and a few case series [2,3]. Only a few larger series have been reported from large specialized centers [4-6]. Furthermore, sarcomas arising in the soft tissue of the oral cavity are vanishingly rare; they represented only 0.14% of head and neck malignancies in the review by Gorsky and Epstein [1]. Of 214 head and neck sarcomas reported from a sarcoma registry, only 5% affected the oral cavity [2]. Among the different histologic subtypes, head and neck angiosarcoma was less common in previous series. In the series by Yamaguchi et al [6], only 2 of 32 oral and maxillofacial

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sarcomas were histologically angiosarcomas. The largest series on head and neck angiosarcoma (n = 22) has been published from the Armed Forces Institute of Pathology [5]. The tongue seems to be a predilection site for intraoral angiosarcoma, whereas the palate was rarely involved [2,3,5,6]. We herein report on the first well-documented case of an epithelioid angiosarcoma arising in the palatine tonsil and following an aggressive course. This case illustrates the potential pitfall related to the epithelioid morphology and common cytokeratin (CK) expression in epithelioid angiosarcomas and the caution needed to distinguish them from poorly differentiated squamous cell carcinoma and lymphoma.

2. Case history

A 71-year-old woman without a previous history of malignancy or radiation in the head and neck area presented with a diffuse painful swelling of the right tonsil that was initially thought to represent acute tonsillitis. However, symptoms did not resolve upon antibiotic treatment, and the patient was referred to our hospital for further treatment. A bilateral tonsillectomy was then performed. Based on the histologic findings with positive resection margins, a re-resection was performed followed by radiation therapy (total dose: 70 Gys) and 5 cycles of chemotherapy with taxol (70 mg/m^2). Seven months later, a small metastasis was excised from the right buccal mucosa. There was no evidence of another primary tumor in the skin or the soft tissue, and no regional cervical lymph node metastasis was detected clinically. Nine months from initial surgery, the patient presented with features of upper and lower gastrointestinal bleeding suggestive of metastasis. Imaging procedures showed multiple metastases in the duodenum, small bowel, and the uvula. A total of 8 metastatic deposits have been removed via multiple segmental resections and full-thickness bowel excisions to prevent further life-threatening gastrointestinal bleeding. In addition, a new small oral metastasis was excised from the uvula. The patient was then referred to palliative medical care. All of the excised metastatic deposits were minute lesions compatible with metastatic disease. No other primary tumor was detected on last follow-up.

3. Material and methods

Tumor specimens were fixed in buffered formalin and embedded routinely for histologic evaluation. Immunohistochemical stains were performed on 5-μm sections cut from paraffin blocks using a Ventana automated system (VANTAGE; Ventana, Tucson, AZ, USA) and the following antibodies: vimentin (clone V9, 1:100; DakoCytomation, Hamburg, Germany), CD31 (clone JC70A, 1:20; DakoCytomation), factor VIII (clone F8/86, 1:100; DakoCytomation), CD34 (clone QBEnd10, 1:200; Immunotech, Krefeld, Germany), pancytokeratin (clone KL-1, 1:200; Beckmann-Coulter, Krefeld, Germany), pancytokeratin (clone Lu5, 1:300; BMA Biomedicals, Augst, Switzerland), CK 5 (clone XM26, 1:50; Zytomed, Berlin, Germany), CK7 (clone OV-TL12/30, 1:1000; DCS, Hamburg, Germany), CK8 (clone C51, 1:200; Biogenex, Fremont, CA, USA), CK13 (clone KS-1A3, 1:1000; Sigma, Diesenhofen, Germany), CK18 (clone CY-90, 1:500, Sigma), CK19 (clone RCK108, 1:300; DakoCytomation), CK20 (clone Ks20.8, 1:50; DakoCytomation), high-molecular-weight CK (clone 34βE12, 1:50; DakoCytomation), p63 (clone 4A4, 1:100; Zytomed), anti-ERG (clone EPR3864, prediluted/ready to use; Ventana Medical Systems), FLI-1 (clone G146-222, 1:200; BD Pharmingen, Heidelberg, Germany), prodoplanin/D2-40 (clone D2-40, 1:50; Zytomed), protein S100 (polyclonal, 1:2500, DakoCytomation), desmin (clone D33, 1:250; Dako, Hamburg, Germany), α–smooth muscle actin (clone 1A4, 1:200, DakoCytomation), CD30 (clone HRS-4, 1:250, Immunotech) and Ki-67 (clone MiB1, 1:100; DakoCytomation). Heat-induced antigen retrieval was performed for all antibodies using either protease 1 or a Cook buffer CC1 (retrieved from Ventana Medical systems, Inc).

4. Results

Grossly, the right tonsil showed extensive necrosis and ulceration (Fig. 1A). Histologic evaluation revealed subtotal replacement by a frankly malignant high-grade neoplasm showing extensive ulceration of the surface epithelium and hemorrhagic necrosis with fibrinopurulent exudate (Fig. 1B, C). The tumor cells were arranged into gaping vessel-like spaces (Fig. 1D), anastomosing sinusoid-like spaces (Fig. 1E) as well as cords and solid sheets with anaplastic high-grade nuclear features. The latter were composed of large epithelioid cells with vesicular nuclei, prominent nucleoli, and pale to basophilic copious cytoplasm (Fig. 1F). The surface epithelium in nonulcerated areas showed no evidence of dysplasia or carcinoma in situ. The resection specimens from the metastatic deposits showed essentially similar histologic features, but the vascular nature of the neoplasms was more obvious than in the primary tumor. The gastrointestinal metastases were predominantly located in the mucosa and the submucosa and were associated with prominent bleeding. There were no spindled areas or features suggestive of a true epithelial (squamous) differentiation.

Immunohistochemistry showed strong diffuse expression of vimentin and the pancytokeratin antibody KL-1 (Fig. 2A, B). In addition, a diffuse but less strong immunostaining was seen for the pancytokeratin antibody Lu5, CK8, CK18, and CK19. The tumor cells did not stain with high-molecular-weight CKs (CK5 and 34βE12; Fig. 2B inset), CK7, CK13, and CK20. CD31 was strongly expressed in almost all tumor cells (Fig. 2C). Furthermore, the tumor cells displayed strong