Head and Neck Pathol (2015) 9:269–272
DOI 10.1007/s12105-014-0555-3

CASE REPORT

Malignant Rhabdoid Tumor of the Floor of Mouth: First Reported Case in the Oral Cavity of an Adult

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Received: 3 June 2014 / Accepted: 22 June 2014 / Published online: 6 July 2014

Abstract Malignant rhabdoid tumors (MRTs) are exceedingly rare lesions. To our knowledge, only 2 cases have been reported in the oral cavity, with both examples occurring in infants. The current case is the third reported case of MRT of the oral cavity and the first reported case to occur in an adult at this location. The following report describes the clinical, histologic and immunohistochemical features of this tumor.

Keywords Malignant rhabdoid tumor · INI1 · Floor of mouth

Introduction

Malignant rhabdoid tumor (MRT) was first described in 1978 by Beckwith and Palmer [1]. Initially, cases of MRT were reported as renal tumors occurring in children and were thought to be a variant of Wilms tumor [1]. Rhabdoid tumors present with unique histologic and molecular characteristics. The tumors are composed of large polygonal cells with eccentrically placed nuclei, and demonstrate an intracytoplasmic paranuclear eosinophilic condensation which compresses the nucleus [2]. Electron microscopy and immunohistochemical analysis has confirmed that these eosinophilic paranuclear condensations are composed of intermediate filaments [3]. Uncondensed chromatin and prominent nucleoli can often be found within the nuclei of the tumor cells [2, 3].

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Molecular studies of MRT illustrate alterations of chromosome 22 which result in a lack of SMARCB1 (INI1/BAF47/SNF5) gene expression [4–8]. This can also be demonstrated by immunohistochemical studies in which a loss of INI1 expression is seen within the lesional cells [4, 8, 9]. However, the lack of INI1 expression is not unique to MRT.

Subsequent studies have reported MRT in extra-renal sites. These sites include the mediastinum, retroperitoneum, leg, bladder, liver, lung, abdomen, chest, foot, pelvis, parotid gland, central nervous system, parapharyngeal space, tongue, and gingiva [5, 6, 10–13]. Tumors exhibiting rhabdoid differentiation act in an aggressive fashion and are correlated with a poor prognosis [5, 6, 12, 13].

Case Report

A 51 year old female presented with a swelling of the left floor of the mouth (Fig. 1). The mass was pink–red and exophytic. The surface of the swelling demonstrated a linear leukoplakic area adjacent to the mandibular molar teeth. The leukoplakia was assumed to represent frictional keratosis as a result of contact with the occlusal surface of the mandibular teeth. The patient's medical history was non-contributory. An incisional biopsy of the tumor was performed.

Microscopically, the biopsy showed fibrous connective tissue and hemorrhagic foci containing a tumor composed of sheets of polygonal cells (Fig. 2a). The cells contained hyperchromatic and eccentrically placed nuclei. Paranuclear eosinophilic condensations were noted within the cytoplasm of the lesional cells. Nucleoli were indistinct (Fig. 2b).

Immunohistochemical studies revealed positivity for vimentin and neurofilament (Fig. 2c). The tumor lacked expression of INI1 (Fig. 2d). The tumor cells were negative for CD20, CD3, CD45, calponin, PAX8, p63, WT-1, CK7, CK20, AE1/AE3, CK5/6, CAM 5.2, Epithelial membrane antigen, e-cadherin, pan-melanoma, smooth muscle actin, synaptophysin, mammaglobin, myogenin, desmin, S100 protein, TTF-1 and CDX2. The Ki67 was estimated to be 80 %.

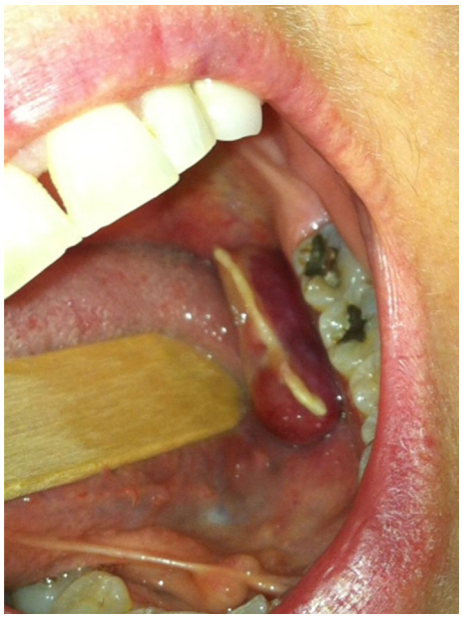

Fig. 1 Nodule of the left floor of the mouth with a linear leukoplakia caused by frictional keratosis from the adjacent mandibular molars

After the diagnosis was obtained from the incisional biopsy, the patient underwent evaluation. No other lesions were found. The tumor in the floor of the mouth was determined to be the primary lesion. A resection of her tumor and subsequent neck dissection was performed. The excisional specimen was composed of tan-pink to tan-yellow soft tissue. The tumor measured 5.0 × 3.8 × 1.5 cm and 1.9 cm in thickness. The surface mucosa was ulcerated. The midline and lateral margins were positive. Lymphovascular and perineural invasion were not identified. The tumor was noted to be of high histologic grade. All lymph nodes were negative for metastasis (0/23). The diagnosis of MRT was rendered for both the incisional and excisional specimens.

The patient received post operative proton radiation at a dose of 66 Gy to the oral cavity. At 6 months a PET scan was performed and the patient had no evidence of disease.

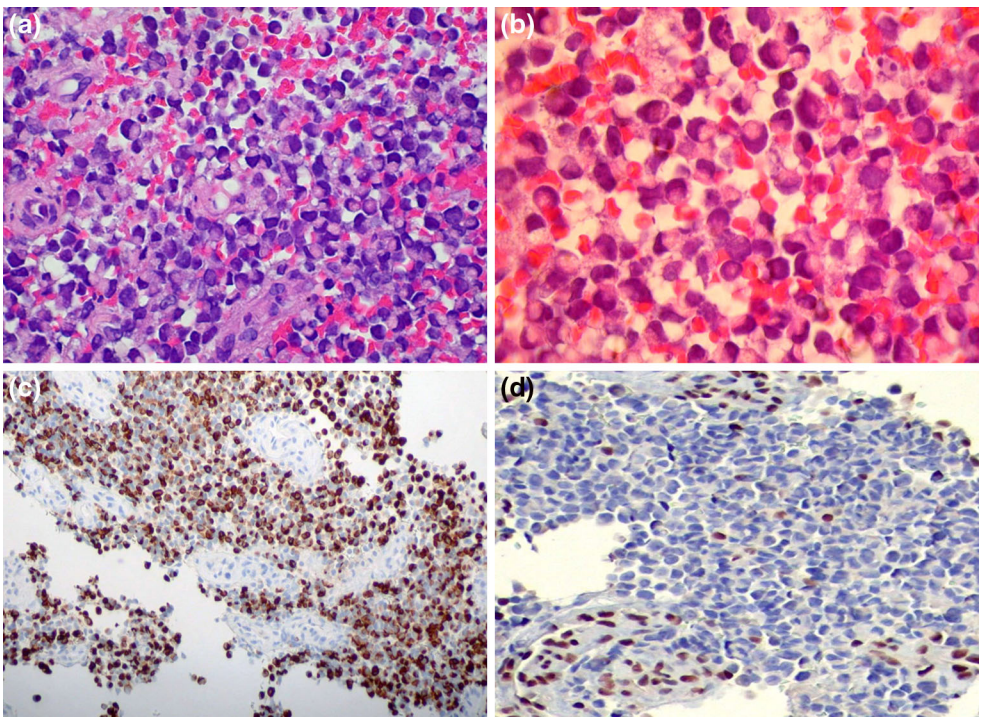

Fig. 2 **a** The incisional biopsy showed a tumor composed of sheets of polygonal cells set in a background of hemorrhage (H&E stain). **b** A paranuclear eosinophilic condensation which is causing indentation of the nucleus is noted in the tumor cells (H&E stain). **c** The paranuclear condensation showed reactivity for neurofilament. **d** Loss of INI1 expression was seen within the tumor cells but not the endothelial cells of the blood vessel

Table 1 Reported cases of MRT of the head and neck

	Age at diagnosis	Gender	Site	Treatment	Survival
1. Patron et al.	10 days	Male	Tongue	Partial resection	days
2. Dominey et al.	2 days	Female	Soft tissue of face	None	days
3. Roy et al.	3 days	Male	Soft tissue of the neck	Unknown	Unknown
4. Pizer et al.	1 day	Female	Gingiva	None	35 days
5. White et al.	33 weeks	Female	Face and neck	None	Few minutes
6. White et al.	1 day	Female	Face and neck	Chemotherapy	1 month
7. White et al.	3 months	Female	Cervical epidural and paraspinal soft tissue	Debulking, chemotherapy	2 months
8. White et al.	1 week	Male	Thyroid and submandibular gland	Surgery, chemotherapy brachytherapy	3 months
9. Gottlieb et al.	28 days	Male	Orbit	Exteneration of the left orbit	42 days
10. Mahmood et al.	11 years	Male	Oropharynx	Chemotherapy	Unknown
11. Sparano et al.	2 years	Female	Parapharyngeal space	Resection, chemotherapy, radiation	No evidence of disease at 9 months
12. Garces-Inigo et al.	1 month	Female	Neck	Unknown	Alive at 12 months (lung and CNS metastases on recurrence)
13. Cobb et al.	2 months	Female	Scalp	Resection, chemotherapy	10 months
14. Ramieri et al.	1 day	Male	Frontonasal–orbital region	Resection, chemotherapy	No evidence of disease at 3 years

Discussion

Malignant rhabdoid tumor (MRT) of the kidney has been well established as a unique entity. Recently, numerous reports of MRT appearing in extra renal sites have been reported [5, 6, 10–21]. In a review of the English literature, 14 cases of primary MRT involving the soft tissues of the head and neck were identified [11–21] (Table 1). Of the 14 reported cases, 12 occurred in infants under 1 year of age and 2 occurred in children under 12 years of age (cases 10 and 11) [11, 18]. To our knowledge, a case of primary MRT occurring in the soft tissue of the head and neck of an adult has not been described. Furthermore, only 2 (cases 1 and 4) of the 14 cases occurred in the oral cavity [12, 13]. The current case is only the third reported case of MRT in the oral cavity and the first reported case to occur in the floor of the mouth. Only two patients (case 11 and 14), in addition to the current case, showed no evidence of disease at follow up appointments [11, 21].

The origin of rhabdoid cells remains unclear [23]. Some consider rhabdoid cells to be pluripotent cells which can differentiate along various cell lines. This leads to polyphenotypia among lesions diagnosed as MRT [23]. Therefore, the diagnosis of MRT is based on the histological appearance and the unique immunohistochemical profile. In the current case the presence of large polygonal cells with eccentrically placed nuclei and intracytoplasmic paranuclear eosinophilic condensations were observed. This appearance is characteristic of rhabdoid cell morphology.

The presence of rhabdoid differentiation can be seen in a variety of tumors. Notable examples include rhabdomyosarcoma, epithelioid sarcoma, myoepithelial carcinoma and Wilms tumor of the kidney [4]. Although these tumors can contain foci of rhabdoid cells, the diagnosis of MRT is reserved for tumors that consist solely of rhabdoid cells without further differentiation [4]. The incisional biopsy in this case consisted of sheets of rhabdoid cells. Evidence of specific differentiation was not present.

Furthermore, immunohistochemical studies can aid in the confirmation of a diagnosis of MRT. More specifically, the loss of INI1 expression is a hallmark of MRT. Absence of INI1 has been reported in a variety of tumors including synovial sarcomas, proximal type epithelioid sarcoma, myoepithelial carcinoma, renal medullary carcinomas, epithelioid malignant peripheral nerve sheath tumor, and extraskeletal chondromyxoid sarcomas [4, 8]. The lack of rhabdoid cells in these tumors is crucial to distinguishing MRT from other INI1 negative tumors.

The intracytoplasmic paranuclear condensations present in the rhabdoid cells are composed of intermediate filaments [3]. Most commonly, these are keratin filaments and can be highlighted by low and high molecular weight keratin immunohistochemical stains [24, 25]. In rare instances, such as this case, the intermediate filaments are highlighted by neurofilament markers [9, 26].

Interestingly, the proximal type of epithelioid sarcoma has many overlapping features with MRT. The "proximal type" of epithelioid sarcoma shows a predominance of polygonal cells with intracytoplasmic hyaline inclusions consistent with rhabdoid cell morphology [14, 22]. Similar to MRT, the tumor cells exhibit a loss of INI-1 expression. Immunohistochemical studies of "proximal type" epithelioid sarcoma are similar to conventional epithelioid sarcoma with the tumor cells demonstrating reactivity for epithelial membrane antigen (EMA), low and high molecular weight keratins, and vimentin [8]. In addition, some examples of "proximal type" epithelioid sarcoma show positivity for desmin and smooth muscle actin [14, 22]. The current case lacked reactivity for EMA and cytokeratin markers. In addition, the tumor cells showed positivity for neurofilament which is not a feature of "proximal type" epithelioid sarcoma. Therefore, the immunohistochemical profile of the current case distinguishes this tumor from epithelioid sarcoma and supports a diagnosis of MRT.

Due to the rarity of MRT, few investigations have been done to determine the efficacy of different treatment modalities and overall outcome of patients with MRT. One study by Sultan et al. [10] found that radiation therapy, age at diagnosis (with children under 2 showing the worst prognosis) and tumor stage to be the most significant prognostic factors. Reports of overall survival rates of patients with MRT range from 20 to 33 % [5, 10]. Distant metastasis has been reported and is more common in renal MRT [5, 10]. Interestingly, increased survival rates have been noted in children who received radiation therapy following resection of their tumor [5, 10]. However, very few cases of MRT occurring in adults have been reported in the literature.

Further investigation of the behavior and clinical outcomes of MRT in adults is warranted to produce definitive conclusions regarding these exceedingly rare tumors.

Acknowledgments The authors thank these clinicians who kindly provided case material and clinical follow up when available: Dr. Dennis Kraus MD, FACS (New York, NY) and Dr. Deborah F. Rosin MD (Edison, NJ).

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