CASE REPORT

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Tongue spindle cell rhabdomyosarcoma: case report in a pediatric patient

Abstract:

Rhabdomyosarcoma (RMS) is an uncommon soft tissue malignant tumor derived from striated muscle tissue. RMS is uncommon in the oral cavity. Herein, we reported the clinicopathological and immunohistochemical features of an RMS case in a 1-year-old female presenting clinically as an asymptomatic nodule on the lateral border of the tongue. The surgical excision of the lesion was performed. Morphologically, spindle cells with elongated nuclei and eosinophilic cytoplasm proliferation in a fascicular pattern was observed, with few tumor cells showing rhabdomyoblastic differentiation. Immunohistochemical analysis showed positivity to vimentin, muscle-specific actin, desmin, MyoD1, and myogenin. Ki-67 proliferation index was less than 10%. The final diagnosis was spindle cell RMS. The patient did not show signs of recurrence after twenty months of follow-up. Because of the unspecific clinical appearance, the clinical diagnosis of RMS is difficult. Therefore, careful histopathological and immunohistochemistry analysis of these tumors is essential for correct diagnosis and classification.

Keywords: Pediatrics; Neoplasm; Rhabdomyosarcoma; Tongue; Case report.

INTRODUCTION

Soft tissue sarcomas represent 7 and 1% of cancers in children and adults, respectively[1]. Rhabdomyosarcoma (RMS) is a malignant tumor originating from striated skeletal muscle tissue and represents about 3-4% of pediatric cancers. Although the head and neck is the most frequently affected region, RMS is uncommon in the oral cavity[2-4]. Although RMS's etiology and risk factors are still unknown, some cases have been associated with heritable syndromes, such as neurofibromatosis type 1, Noonan, and Li-Fraumeni[1,5].

Statement of Clinical Significance
Due to overlapping clinical features with benign oral neoplasms, careful histopathological and immunohistochemistry analysis of oral spindle cell rhabdomyosarcoma is essential for correct diagnosis. Oral spindle cell rhabdomyosarcoma shows a favorable diagnosis in early childhood.

RMS was traditionally classified into three main subtypes: alveolar, embryonal, and pleomorphic[6,7]. Later, the World Health Organization (WHO) grouped the spindle cell and sclerosing RMS morphological variants as a new fourth subtype. All four RMS subtypes present different histological, molecular, and prognosis profiles[3,4]. Spindle cell/sclerosing RMS account for 5-10% of all RMS, usually associated with VGLL2/NCOA2 fusions, and presents a more favorable prognosis in pediatric patients than in adults[7-9]. In this context, this article aims to report a new case of a pediatric patient with spindle cell RMS in the tongue and discuss its clinical and histopathological characteristics.

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CASE REPORT

A 1-year-old female was admitted to the pediatric clinic of the Hospital Batista Memorial (Fortaleza, CE, Brazil) with a 6-month history of a lesion on the lateral border of the tongue. The parents reported that the child was presenting dysphagia, dysphonia, and breathing difficulties. The intraoral examination revealed a well-defined, normal-colored nodular lesion with an irregular surface measuring approximately 3 cm (Figure 1A). Upon palpation, the lesion had a firm consistency and was asymptomatic. No alterations were observed in the other mucosal surfaces, and the teeth were clinically healthy. The past medical history was not contributory. Based on the clinical aspect, the clinical diagnosis hypothesis included benign mesenchymal neoplasia, such as neurofibroma and leiomyoma. Under sedation, a surgical excision with safety margins was performed since the clinical aspect favored a benign lesion. The excisional specimen was sent for histopathological analysis (Figure 1B).

The gross examination of the biopsy revealed an irregularly shaped soft tissue fragment with an irregular surface and rubbery consistency, measuring 2.5 × 2.3 × 2.1 cm. Histopathological analysis revealed a mesenchymal neoplasm with atypical spindle cell proliferation forming variable-length interlacing fascicles (Figure 2A-C). Most cells showed spindle morphology and presented eosinophilic cytoplasm with elongated to ovoid, and sometimes vesicular, nuclei (Figure 2D-E). In addition, a few cells presented features of rhabdomyoblastic differentiation with less spindle morphology, large eosinophilic cytoplasm, and slightly hyperchromatic eccentric nuclei (Figure 2F). In addition, it was also observed that the margins of the specimen were free of neoplastic cells. Based on the histopathological findings observed through the hematoxylin and eosin staining, the diagnostic hypotheses of spindle cell rhabdomyosarcoma and infantile fibrosarcoma were established, and an immunohistochemical analysis was performed.

Immunohistochemical analysis revealed that most neoplastic cells presented cytoplasmatic positivity for vimentin, muscle-specific actin (hhf35), and desmin (Figure 3A-C). Scattered cells showed nuclear positivity for MyoD1 and myogenin (Figure 3D-E). The tumor was negative for Pan-cytokeratin AE1/AE3, S-100 protein, H-caldesmon, and anaplastic lymphoma kinase (ALK). Ki-67 positivity was seen in less than 10% of tumor cells (Figure 3F). Given the morphological and immunohistochemical findings, the final diagnosis was spindle cell rhabdomyosarcoma. The patient has been in follow-up for twenty months with head and neck surgery and oral and maxillofacial surgery services. After surgery, the patient showed improvement in dysphagia, dysphonia, and breathing functions. No signs of alterations in other oral and maxillofacial structures and tissues or recurrence have been observed.

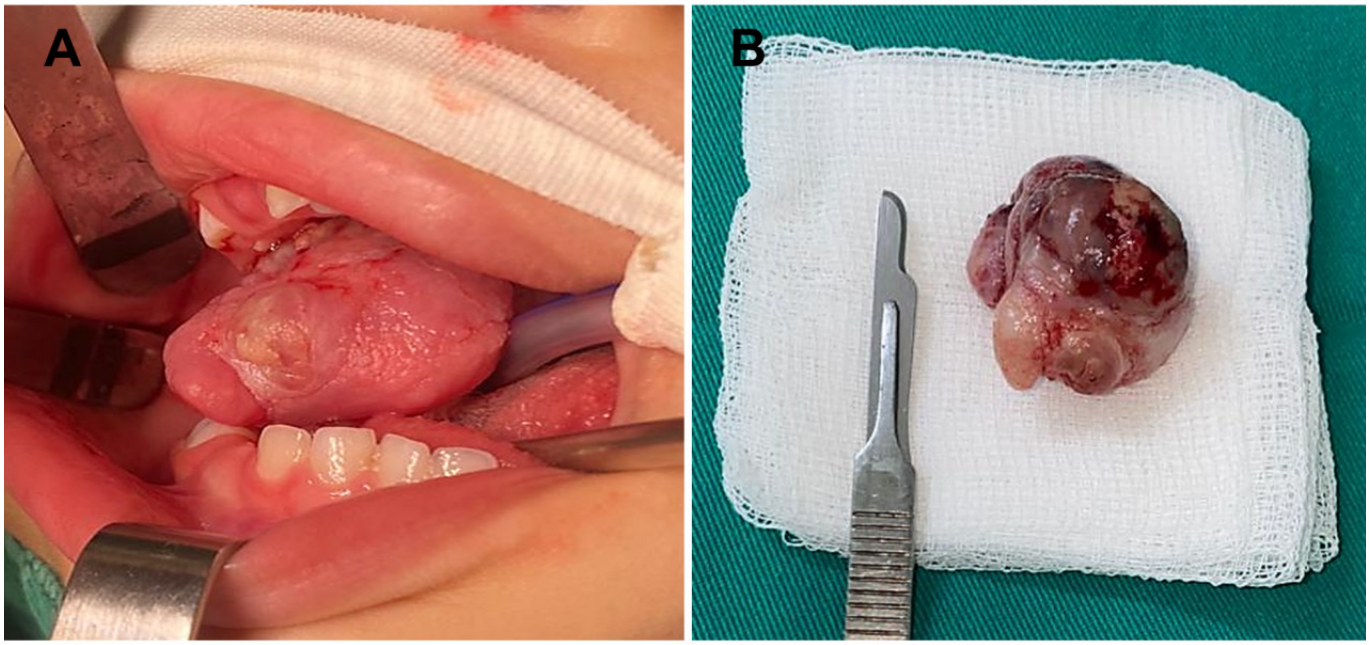

Figure 1. Clinical appearance of the spindle cell rhabdomyosarcoma. (A) Intraoral clinical aspect of the lesion. Note a normal-colored nodular lesion with an irregular surface affecting the lateral border of the tongue. (B) Gross aspect of the specimen.

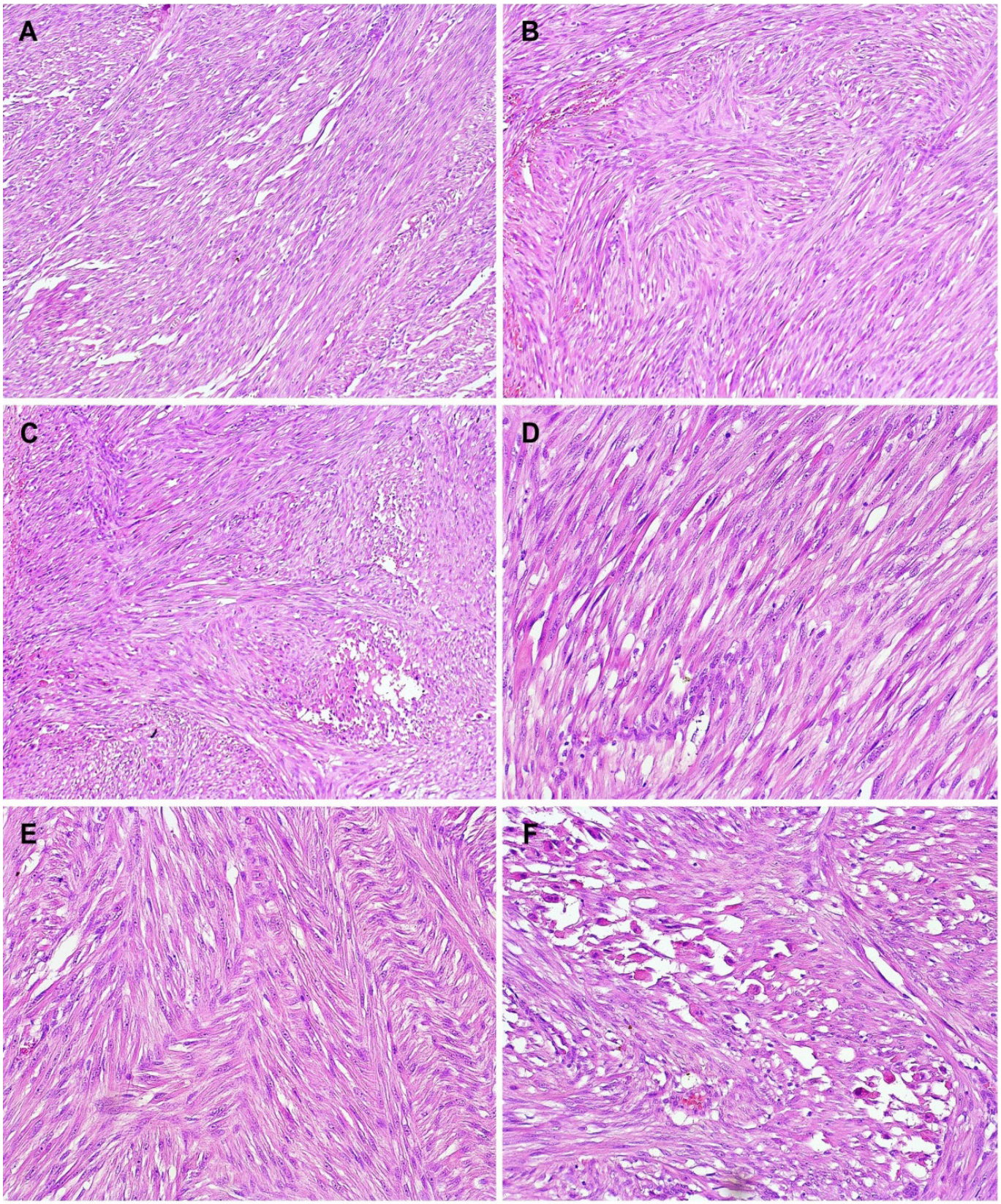

Figure 2. Histopathological aspects of spindle cell rhabdomyosarcoma. (A-C) A low-power view shows monomorphic, undifferentiated spindle cell proliferation in interlacing fascicles or haphazard arrangements. (D-E) Spindle cells present eosinophilic cytoplasm. The nuclei show elongated to ovoid morphology and, sometimes, vesicular aspect. (F) Presence of cells with rhabdomyoblastic differentiation exhibiting significant eosinophilic cytoplasm with slightly hyperchromatic and eccentric nuclei (Hematoxylin and eosin stain. Magnification: A-C, 100×; D-F. 200×).

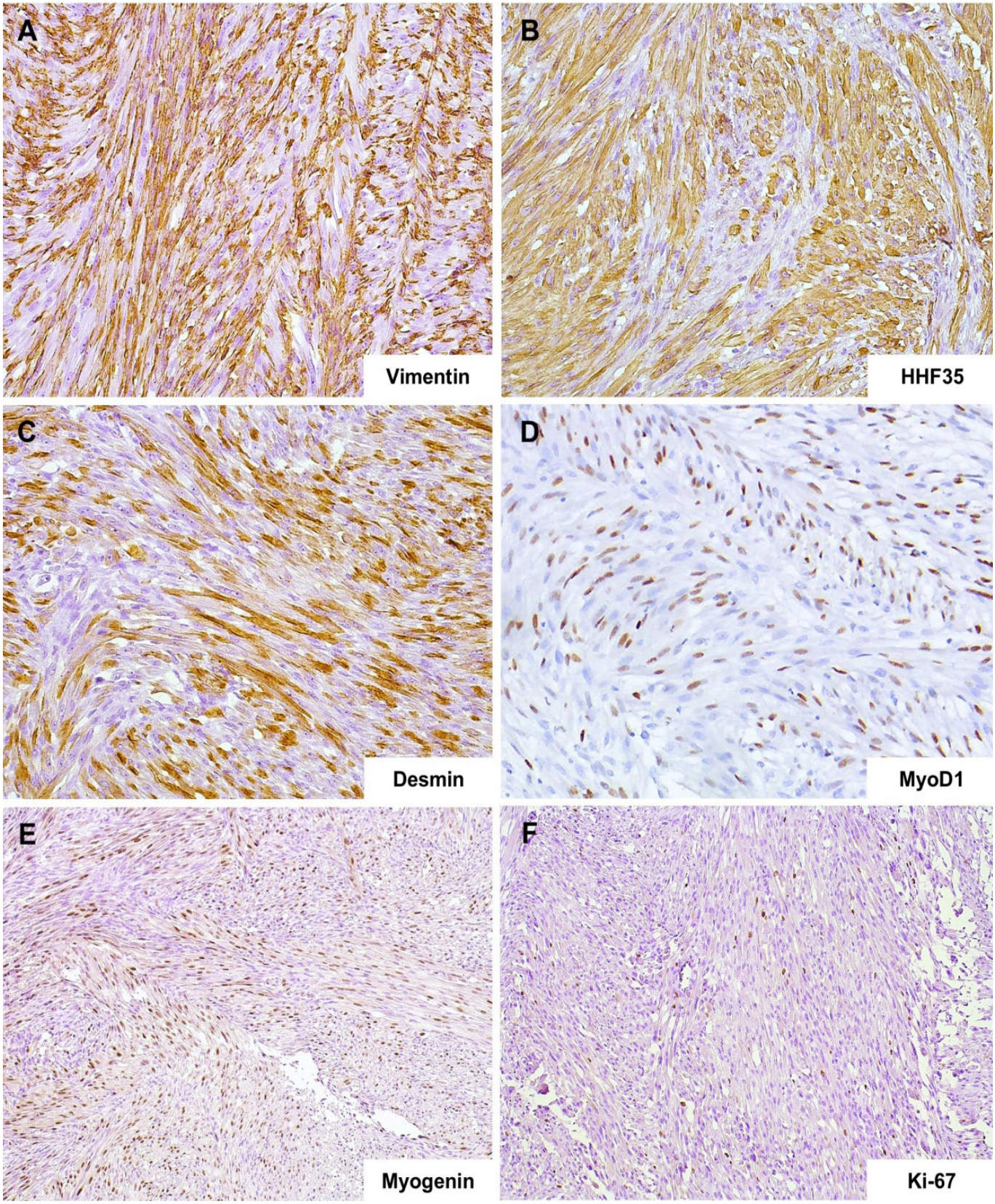

Figure 3. Immunohistochemical characteristics of spindle cell rhabdomyosarcoma. Most neoplastic cells show strong and diffuse cytoplasmic labeling for (A) Vimentin, (B) Muscle-specific actin (HHF35), and (C) Desmin. Some neoplastic cells exhibit positive nuclear reactivity to (D) MyoD1 and (E) Myogenin. (F) Ki-67 proliferation index was less than 10% (Magnification: A-D, 200×; E-F. 100×).

DISCUSSION

A broad spectrum of oral and maxillofacial non-neoplastic and neoplastic lesions can affect the pediatric population[10,11]. Soft tissue sarcomas arise in the head and neck in 35–40% of the cases, and only 10% occur in the oral cavity[12]. RMS shows an incidence of six cases per 1,000,000 population, leading to 250 new cases in the pediatric population every year[5]. Two age intervals have been described as the most prone lifetime to RMS occurrence, between 2 and 6 years and between 10 and 18 years. These two age intervals generally reflect the occurrence of two histologic subtypes of RMS: embryonal (2–6 years) and alveolar (10–18 years)[5]. RMS rarely affects children under 2 years of age, especially in the oral cavity. Despite this, the tongue is the most common intraoral site for RMS in children[4]. Interestingly, in the case described here, a spindle cell RMS was diagnosed in the lateral border of the tongue of a 1-year-old patient.

In the present report, RMS affected a female child; however, there is no consensus regarding the sex predilection of RMS in children. Some authors[13,14] have reported a slight male predilection for oral RMS in children, which has been related to different gene expression patterns due to unknown sex-specific factors that increase the risk for cancer in the male pediatric population. Additionally, it was shown that male children show a slightly increased incidence of embryonic RMS than females in the same age group (male:female ratio: 1.51)[1]. In contrast, a recent scoping review[4] synthesized the clinic-demographic characteristics of RMS in children between 0 and 2 years old, and it showed that oral RMS in young children does not present gender predilection.

As in the present case, RMS affecting children between 0 and 2 years often causes airway obstruction, impacting breathing function, and it is clinically described as an asymptomatic nodular mass affecting the tongue[4,5]. Indeed, the clinical aspect of RMS in early childhood is similar to a wide variety of non-neoplastic and neoplastic oral lesions with a benign background. Thus, due to its nonspecific clinical appearance, microscopical analysis is essential to RMS diagnosis and histological classification to help establish its prognosis[4].

Since 2013, the WHO classification has recognized the spindle cell/sclerosing variant as a new RMS subtype. This classification suggested that the spindle cell and sclerosing histological variants represented a morphological spectrum of RMS due to their overlapping histopathological features[6]. Similar to our case, spindle cell RSM is microscopically characterized by the proliferation of nonpleomorphic cells exhibiting spindle-to-ovoid morphology and light eosinophilic cytoplasm. The cells are commonly arranged in intersecting long fascicles, and cells with a rhabdomyoblast appearance were also described[6,12].

Immunohistochemical analysis also helps to shed light on diagnosing spindle cell RMS cases that resemble neoplastic lesions of smooth muscle and connective tissue origin[12]. Similar to the present case, positivity to Vimentin usually demonstrates the mesenchymal origin of this neoplasm[12]. HHF35 can help differentiate neoplasms of muscle origin from connective tissue neoplasms, such as fibrosarcoma. Since HHF35 is not specific for striated skeletal muscle, positivity to desmin, MyoD1, and myogenin are reliable markers for analyzing rhabdomyoblastic differentiation. However, desmin expression may vary depending on tumor differentiation. In contrast, although showing heterogenous positivity, MyoD1 and myogenin are considered reliable markers for skeletal muscle differentiation.[6,12,15]. Our immunohistochemical analysis showed positivity for muscle markers, especially the striated skeletal muscle ones. In this way, our results helped confirm the diagnosis of spindle cell rhabdomyosarcoma.

There is no consensus about the optimal type of treatment for spindle cell RMS[7]. It has been reported that, in children between 0 and 2 years, most RMS cases are stage I in the TNM clinical grading system, surgical excision is the most common treatment, and 53.6% of the patients survive without recurrence signs[4,7]. A recent systematic review of RMS in toddlers showed that adjuvant treatment, such as chemotherapy and radiotherapy, is performed in only ~12% of the cases[4]. In addition, molecular analysis has shown that congenital and early childhood spindle cell RMS are frequently associated with NCOA2 and VGLL2 gene fusions, which are related to muscle tissue development. In this context, NCOA2- and VGLL2-associated spindle cell RMS presents a significantly more favorable prognosis than spindle cell RMS with MYOD1 mutations that occur in later childhood and adulthood[6,7,12]. In the present case, the patient was in early childhood and did not present signs of recurrence after twenty months of the surgical excision of the lesion.

CONCLUSION

Oral spindle cell RMS seems to show a favorable prognosis in children under 2 years old. As shown in the present case, since RMS shows unspecific clinical features, careful histopathological and immunohistochemistry analysis is critical for correctly diagnosing and classifying these tumors.

AUTHORS' CONTRIBUTIONS

ILC: conceptualization, data curation, writing – original draft. CCSB: conceptualization, data curation, writing – original draft. HCCJ: data curation, investigation, writing – review & editing. AFMA: data curation, investigation, writing – review & editing. PAV: investigation, formal analysis, writing – review & editing. RBC: investigation, formal analysis, writing – review & editing. BABA: investigation, formal analysis, writing – review & editing.

CONFLICT OF INTEREST STATEMENT

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REFERENCES

1. Skapek SX, Ferrari A, Gupta AA, Lupo PJ, Butler E, Shipley J, et al. Rhabdomyosarcoma. Nat Rev Dis Primers 2019;5(1):1. https://doi.org/10.1038/s41572-018-0051-2
2. Cavalcante IL, Cunha JLS, Silva CCB, Nonaka CFW, Cavalcante ER, Almeida OP, et al. Gingival rhabdomyosarcoma mimicking a non-neoplastic proliferative lesion: a diagnostic challenge. Oral Oncol. 2023;137:106281. https://doi.org/10.1016/j.oraloncology.2022.106281
3. Cunha JLS, Cavalcante IL, Barros CCS, Alves PM, Nonaka CFW, Albuquerque AFM, et al. Intraosseous rhabdomyosarcoma of the maxilla with TFCP2 fusion: a rare aggressive subtype with predilection for the gnathic bones. Oral Oncol. 2022;130:105876. https://doi.org/10.1016/j.oraloncology.2022.105876
4. Nunes MM, Costa AAS, Tavares TS, Aguiar MCF, Martins CC, Caldeira PC. Rhabdomyosarcoma of the oral cavity in children aged 0–2 years: a scoping review. J Oral Pathol Med. 2023;52(6):468-75. https://doi.org/10.1111/jop.13411
5. Dasgupta R, Fuchs J, Rodeberg D. Rhabdomyosarcoma. Semin Pediatr Surg 2016;25:276–83. https://doi.org/10.1053/j.sempedsurg.2016.09.011.
6. Agaram NP. Evolving classification of rhabdomyosarcoma. Histopathology. 2022;80(1):98-108. https://doi.org/10.1111/his.14449
7. Yasui N, Yoshida A, Kawamoto H, Yonemori K, Hosono A, Kawai A. Clinicopathologic analysis of spindle cell/sclerosing rhabdomyosarcoma. Pediatr Blood Cancer. 2015;62(6):1011-6. https://doi.org/10.1002/pbc.25367
8. Leiner J, Le Loarer F. The current landscape of rhabdomyosarcomas: an update. Virchows Arch. 2020;476(1):97-108. https://doi.org/10.1007/s00428-019-02676-9
9. Dehner CA, Broski SM, Meis JM, Murugan P, Chrisinger JSA, Sosa C, et al. Fusion-driven spindle cell rhabdomyosarcomas of bone and soft tissue: a clinicopathologic and molecular genetic study of 25 cases. Mod Pathol. 2023;36(10):100271. https://doi.org/10.1016/j.modpat.2023.100271
10. Barros CCS, Silva LP, Gonzaga AKG, Medeiros AMC, Souza LB, Silveira EJD. Neoplasms and non-neoplastic pathologies in the oral and maxillofacial regions in children and adolescents of a Brazilian population. Clin Oral Invest 2019;23(4):1587-93. https://doi.org/10.1007/s00784-018-2581-0
11. Barros CCS, Silva Júnior CLPS, Moreira DGL, Oliveira AEG, Silveira EJD, Freitas RA, et al. Children and adolescents assisted in a referral oral medicine diagnostic service: 20 years of experience in Brazil. Int J Paediatr Dent. 2024. Online ahead of print. https://doi.org/10.1111/ipd.13269.
12. Jariod-Ferrer UM, Trigo-Cebrian MA, Pantilie B, Simon Sanz MV, Esparza Lasaga L, Gavin-Clavero MA, et al. Tongue spindle cell rhabdomyosarcoma: a rare case report and literature review. J Maxillofac Oral Surg. 2021;20(3):464-9. https://doi.org/10.1007/s12663-020-01447-3
13. Radzikowska J, Kukwa W, Kukwa A, Czarnecka A, Krzeski A. Rhabdomyosarcoma of the head and neck in children. Contemp Oncol (Pozn). 2015;19(2):98-107. https://doi.org/10.5114/wo.2015.49158
14. Williams LA, Richardson M, Kehm RD, McLaughlin CC, Mueller BA, Chow EJ, et al. The association between sex and most childhood cancers is not mediated by birthweight. Cancer Epidemiol. 2018;57:7-12. https://doi.org/10.1016/j.canep.2018.09.002
15. Jain E, Munjal G, Sharma S, Brar Z, Bhardwaj N, Dewan A, et al. Multifaceted spindle cell/sclerosing rhabdomyosarcoma with role of immunohistochemistry in avoiding misdiagnosis: a multi-institutional study of 45 distinct tumors. Int J Surg Pathol. 2024;32(3):496-506. https://doi.org/10.1177/10668969231188422