Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology 31 (2019) 406–409

Contents lists available at ScienceDirect

Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology

journal homepage: www.elsevier.com/locate/jomsmp

Case Report

Low-grade myofibroblastic sarcoma of mandible in an infant

Ryo Miyazaki, Takaaki Ogawa, Kenjiro Takao, Yuuri Houchi, Mao Tanaka, Fumi Nakai, Akinori Iwasaki, Yumiko Ohbayashi, Minoru Miyake*

Department of Oral and Maxillofacial Surgery, Faculty of Medicine, Kagawa University, 1750-1 Ikenobe, Miki-cho, Kita-gun, 761-0793, Japan

ARTICLE INFO

Keywords:
Low-grade myofibroblastic sarcoma
Infant
Chemotherapy
Radiotherapy
Surgery

ABSTRACT

Low-grade myofibroblastic sarcoma (LGMS) is a rare sarcoma characterized by myofibroblastic differentiation. LGMS can occur at various sites on the body but frequently occurs in the head and neck region, particularly the tongue. LGMS occurs in younger individuals compared to other tumors, but few LGMS cases have developed in early childhood. Wide excision is the first choice; there are a few reports of cases treated by chemotherapy and radiation therapy. Here we describe an extensive LGMS centering on the mandible of a Japanese male who was 1 year and 9 months old at his presentation. We successfully treated his LGMS by a combination of chemotherapy, radiotherapy and surgery.

1. Introduction

Myofibroblasts are altered fibroblasts and were first discovered in granulation tissue in 1971; they have since been detected in normal, granulation tissue and benign, malignant tumors [1]. Myofibroblasts are spindle-shaped, stellate or bipolar cells with elongated, tapered or wavy nuclei [2]. Under mechanical stress or with the application of transforming growth factor-beta (TGF-β) and extra domain-A of cellular fibronectin, fibroblasts transform to myofibroblasts [3].

Myofibroblastic sarcoma is a rare sarcoma tumor that must be differentiated from other diseases such as benign myofibroblastoma, spindle cell cancer, osteosarcoma, and leiomyosarcoma. However, it is often difficult to make a conclusive diagnosis. We describe a case of myofibroblastic sarcoma in an infant which was difficult to diagnose but was treated successfully with a combination of surgery and chemoradiotherapy.

2. Case report

In 2006, a Japanese boy who was 1 year and 9 months old was referred to our Department of Oral and Maxillofacial Surgery at Kagawa University Hospital. He needed a close examination of a swollen lesion of the left lower jaw that had first been noted 3 months earlier. An oral examination revealed a soft 40 × 30 mm mass pressing on the patient' tongue (Fig. 1). CT and MRI exhibited a 90 × 83 × 55-mm tumor spread around the mandible. FDG-PET confirmed the absence of metastasis (Fig. 2). The tumor had shown rapid growth, and we performed a tumor biopsy and emergency debulking surgery because obstruction of the airway had occurred.

The pathological examination indicated spindle-shaped tumor cells with nuclei of different sizes and mitotic figures (Fig. 3). Immunohistochemistry revealed that most of the spindle cells were positive for vimentin and alpha-smooth muscle actin (α-SMA) and slightly positive for muscle actin (HHF35) (Fig. 4) but negative for S-100 and CD34. Taking into consideration the spontaneous site and the patient's age, we initially suspected an embryonal rhabdomyosarcoma. Therefore, following the Japan Rhabdomyosarcoma Study Group (JRSG) protocol, we administered VAC therapy (vincristine 0.62 mg/body, actinomycin D 0.55 mg/body, and cyclophosphamide 1000 mg/body). However, after six courses of this chemotherapy the tumor continued to grow and interfere with the patient's breathing; we therefore performed another tumor biopsy and additional debulking surgery.

Because of the VAC therapy's lack of effect and the α-SMA immunostaining positivity, we made the diagnosis of low-grade myofibroblastic sarcoma (LGMS). According to the protocol for non-round cell sarcomas (ARST0332 protocol), we administered chemotherapy: four courses of ifosfamide 1.6 g/body ×3 days and doxorubicin 20 mg × 2 days, and then two courses of ifosfamide alone. The tumor shrank remarkably, and a tumor resection could be performed (Fig. 5). As a postoperative treatment, chemotherapy (two courses of ifosfamide alone) and radiotherapy (two orthogonal gate irradiations at 1.6 Gy/day; total 56 Gy) was carried out. Twelve years later, the patient's healing course is good and there has been no recurrence (Fig. 6).

* Corresponding author.
E-mail address: dentmm@med.kagawa-u.ac.jp (M. Miyake).

https://doi.org/10.1016/j.ajoms.2019.06.008
Received 27 March 2019; Received in revised form 17 June 2019; Accepted 23 June 2019
Available online 05 September 2019

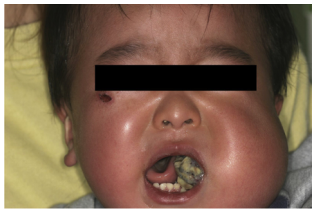

Fig. 1. The patient at his first visit, at the age of 1 year and 9 months. The tumor was 40 × 30 mm, and his tongue was pressed by the tumor.

3. Discussion

Myofibroblasts exhibit characteristics of both fibroblasts and smooth muscle cells and are first observed in the granulation tissue of a healing wound. They also play a role in the production of contractile force [1,4]. Myofibroblastic sarcoma was first reported as a tumor representing differentiation to myofibroblasts, and these sarcomas are classified into three categories: low-, intermediate-, and high-grade [2,5]. This tumor is prevalent in the head and neck, and it is more likely to develop in young people compared to other tumors. The ages of the reported myofibroblastic sarcoma patients range from 1 to 85 years; the median age is 42.3 years old [6]. However, it is very rare for a

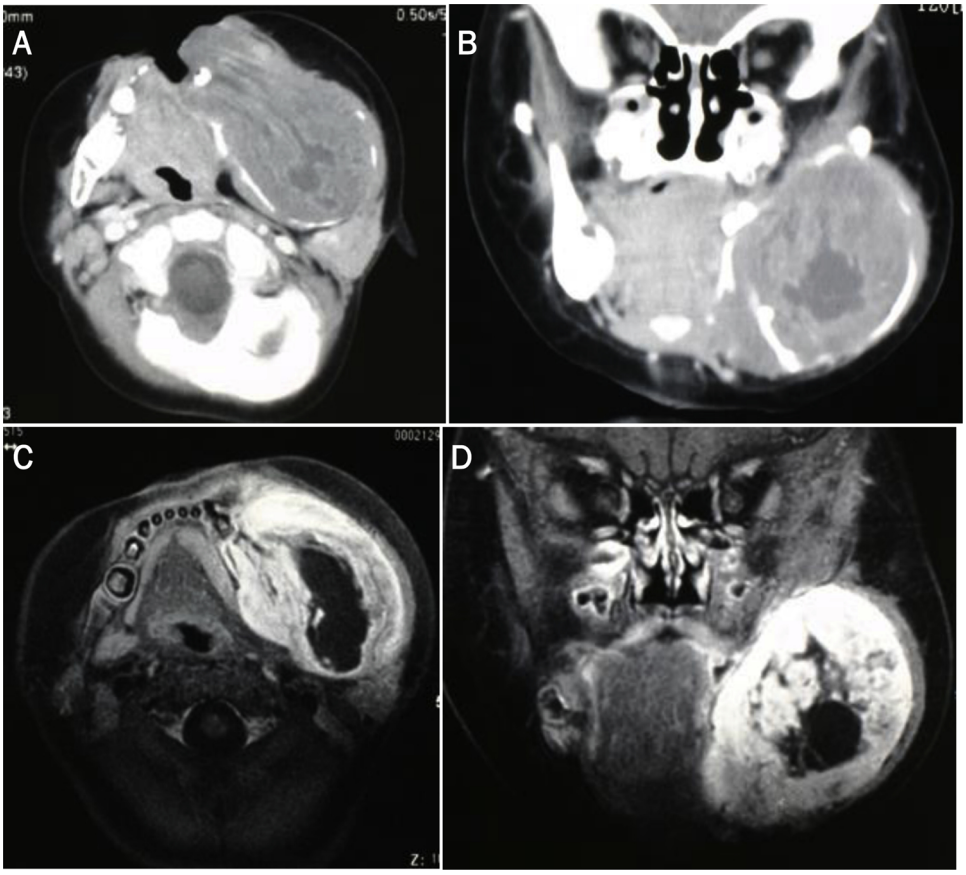

Fig. 2. A,B: Pretreatment CT. **C,D:** Pretreatment MRI. The tumor grew to 90 × 83 × 55 mm around the lower jawbone.

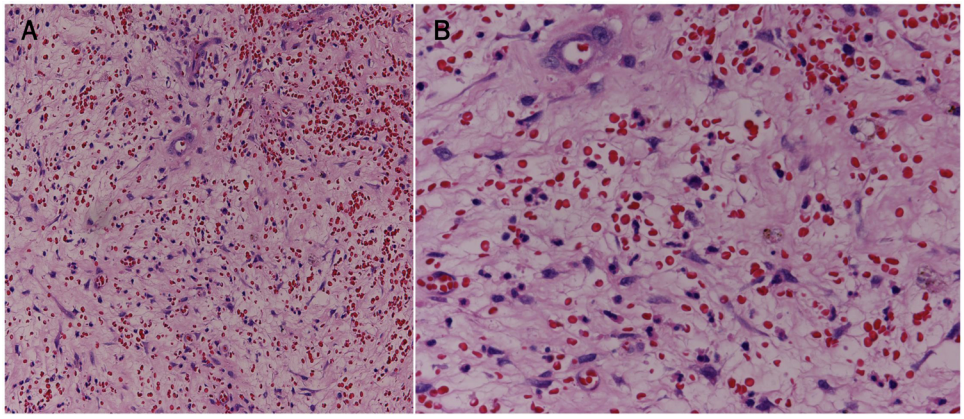

Fig. 3. Hematoxylin and eosin stain revealed spindle-shaped cells with nuclei of different sizes, accompanied by inflammation. **A:** ×50, **B:** ×200.

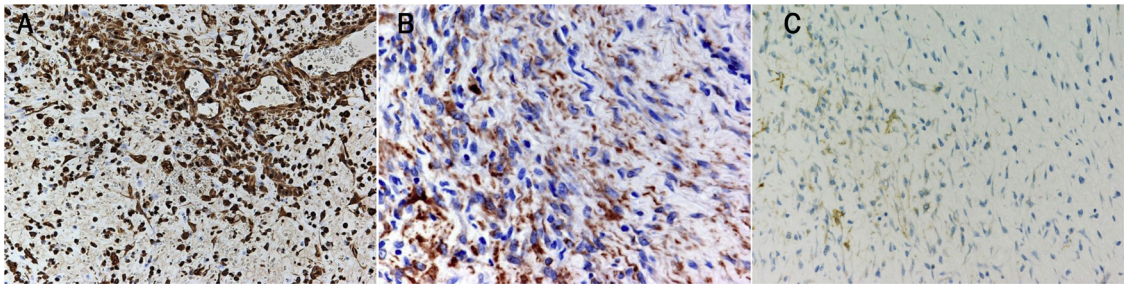

Fig. 4. Immunohistochemical staining. **A:** Spindle cells positive for vimentin (×50). **B:** Spindle-shaped cells positive for α-SMA (×200). **C:** Spindle-shaped cells slightly positive for muscle actin (HHF35) (×50).

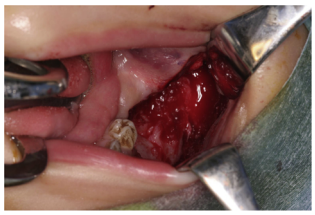

Fig. 5. Oral photo after the tumor excision. The mandibular canal was also excised with the tumor.

myofibroblastic sarcoma to occur in an infant or child under 1 year old. Only one such case in the temporal fossa was reported [7]. Clinically, LGMS is a painless slow-glowing tumor and rarely metastasizes even after a number of years. In our patient's case, the tumor presented aggressive local invasion, but distant metastasis did not occur.

Histologically, LGMS is composed of mostly bland stellate and spindle cells with tapered or ovoid nuclei with small nucleoli, plus scant or moderate amounts of eosinophilic cytoplasm with variably distinct cell boundaries. These cells are arranged in a storiform or herring bone growth pattern [2]. Immunohistochemically, myofibroblastic sarcoma is strongly positive for vimentin and α-SMA and partially positive for desmin and muscle-specific actin and negative for EMA, AE1/AE3, and CD34 [2,8]. As diseases to be differentiated, the following tumors should be considered: benign myofibroma, as well as malignancies such as spindle cell carcinoma, malignant melanoma, osteosarcoma, leiomyosarcoma, and fibrosarcoma. Benign myofibroma was denied in our patient's case because of the rapid growth of the tumor and the histologically nuclear variation of the tumor cells. Spindle cell carcinoma, and malignant melanoma were also denied based on the negativity for AE1/AE3 and S-100. Osteosarcoma was denied based on the histologically osteoclastic formation. Leiomyosarcoma was contradictory without acidophilic cells in hematoxylin/eosin staining. Fibrosarcoma was excluded due to the positivity for α-SMA. Myofibroblastic sarcoma is a difficult disease to diagnose because there are no deterministic diagnostic criteria. It was difficult to obtain a definite diagnosis in the present case.

We initially suspected an embryonal rhabdomyosarcoma in our patient, but the VAC therapy was not effective. Immunohistochemically, α-SMA-positivity contributed to the final diagnosis of LGMS. Regarding LGMS treatment, wide excision with tumor-free margins is required, and post-operative radiotherapy or chemotherapy is added if needed [9]. However, in our patient's case, the lesion was huge (90 × 83 × 55 mm) and the excision was performed after the chemotherapy led the tumor to shrink. Standard chemotherapy is not established for LGMS, and we thus applied the non-round cell sarcoma protocol.

The reported recurrence rate (RR) for low-grade myofibroblastic sarcoma is 28.6%–38.2%; the use of radiotherapy and > 3-cm tumor size were reported to increase the RR [6,10]. Considering these points, our patient's case was at high risk for recurrence. Ifosfamide induces tooth agenesis if used in childhood [11]. Recurrence has not been observed in our patient since his treatment over 12 years ago, but he has lost several adult teeth and has shown poor growth of the left mandible. Careful observation is thus important, and when our patient completes his growth to adulthood, a mandibular osteoplasty and prosthetic including implant therapy should be considered.

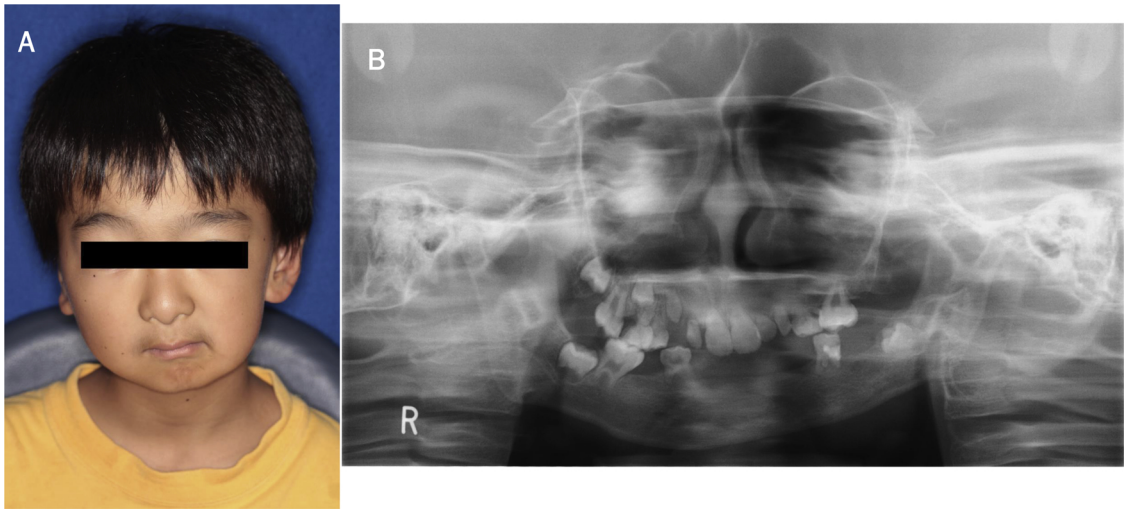

Fig. 6. Facial photo (**A**) and panoramic radiography (**B**) 10 years after treatment. Growth insufficiency and tooth loss are present in the left lower jaw.

Declaration of Competing Interest

The authors have no conflict of interest to declare.

References

[1] Gabbiani G, Ryan GB, Majne G. Presence of modified fibroblasts in granulation tissue and their possible role in wound contraction. Experientia 1971;27(5):549–50.
[2] Fisher C. Myofibroblastic malignancies. Adv Anat Pathol 2004;11(4):190–201.
[3] Gabbiani G. The myofibroblast in wound healing and fibrocontractive diseases. J Pathol 2003;200(4):500–3.
[4] Tomasek JJ, Gabbiani G, Hinz B, Chaponnier C, Brown RA. Myofibroblasts and mechano-regulation of connective tissue remodelling. Nat Rev Mol Cell Biol 2002;3(5):349–63.
[5] Eyden BP, Banerjee SS, Harris M, Mene A. A study of spindle cell sarcomas showing myofibroblastic differentiation. Ultrastruct Pathol 1991;15(4–5):367–78.
[6] Maruyama T, Nakasone T, Nimura F, Matayoshi A, Kawano T, Nishihara K, et al. Indolent growth of low-grade myofibroblastic sarcoma of the cheek mimics benign lesions: a case report and literature review. Oncol Lett 2017;13(6):4307–14.
[7] Keller C, Gibbs CN, Kelly SM, Haller JR, White KS, Coffin CM, et al. Low-grade myofibrosarcoma of the head and neck: importance of surgical therapy. J Pediatr Hematol Oncol 2004;26(2):119–20.
[8] Fletcher C. Bridge JA, Hogendoorn P, Mertens F, editors. WHO classification of tumours of soft tissue and bone. 4th editionIARC Press; 2013. ISBN-13 9789283224341.
[9] Ni C, Xu YY, Zhou SH, Wang SQ. Differential diagnosis of inflammatory myofibroblastic tumour and low-grade myofibroblastic sarcoma: two case reports with a literature review. J Int Med Res 2011;39(1):311–20.
[10] Yamada T, Yoshimura T, Kitamura N, Sasabe E, Ohno S, Yamamoto T. Low-grade myofibroblastic sarcoma of the palate. Int J Oral Sci 2012;4(3):170–3.
[11] Krasuska-Slawinska E, Brozyna A, Dembowska-Baginska B, Olczak-Kowalczyk D. Antineoplastic chemotherapy and congenital tooth abnormalities in children and adolescents. Contemp Oncol (Pozn) 2016;20(5):394–401.