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CASE REPORT

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Aggressive fibromatosis in the submandibular region of a child

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Abstract

Aggressive fibromatosis is proliferation of well-differentiated fibroblasts. Submandibular region is rare location for fibromatosis. We report a case of a rapidly growing mass in submandibular region of 5-year-old girl, excised surgically and ascertained to be aggressive fibromatosis on histological examination. Recovery was uneventful, and she was disease-free in 6-month follow-up.

KEYWORDS

aggressive fibromatosis, desmoid tumor, desmoids, soft tissue tumor

1 | INTRODUCTION

Fibrous tumors and tumor-like conditions are a heterogeneous group of lesions consisting of benign and malignant entities. Aggressive fibromatosis is a locally invasive, non-metastasizing fibrous proliferative disorder that comprises less than 3% of all soft tissue tumors.[1] Etiology of fibromatosis is controversial but genetic abnormalities, trauma, surgery, or endocrine stimulation may be contributory factors. Tumor cells have shown collagen production ability in presence of estrogen.[2,3] There is also a theory suggesting the role of viral infection in formation of this lesion.[4] The lesion has intermediate clinical behavior and histopathological features between benign fibrosis and low-grade fibrosarcoma. As the result of difficulty in classifying these lesions, multiple synonyms are described for this entity by WHO, including infantile fibromatosis (desmoid variant), desmoid tumor, and desmoid type fibromatosis.[5] Most commonly involved sites are abdominal and extraabdominal sites, such as trunk and extremities.[2] The

lesion is not common in head and neck, and involvement of oral cavity and jaw bones may occur very sporadically.[4] Age distribution for oral lesions is from birth to 51 years with average of 11.2 years, and both genders are almost equally affected.[6] Clinically, the lesion often presents as a nonspecific solitary deep, firm mass with or without pain.[2] Ulceration, teeth mobility, intraoral bleeding, trismus, otalgia, dysphagia, and dyspnea are less common reported symptoms.[4] Although imaging appearance of the tumor is nonspecific, imaging is essential to determine the location, extent, and infiltration of adjacent structures for preoperative treatment planning and postoperative follow-ups.[7] Because of nonspecific clinical and radiographic appearances, biopsy and histological examination are essential for diagnosis. On microscopic examination, fascicles of spindle-shaped fibroblast cells are observed in a collagenous matrix. No sign of cellular atypia or hyperchromatic nuclei is expected. However, the tumor frequently invades adjacent tissues.[8] The appearance resembles a borderline lesion microscopically, as more cellular varieties of fibromatosis are identical to well-differentiated fibrosarcoma; therefore, immunohistochemical staining plays an important role in definitive diagnosis.[4] Due to infiltrative nature of the lesion extending beyond the palpable margins and imaging borders, surgical removal with large rim of normal-appearing tissue must be performed. Radiation therapy, whether as a primary or adjuvant, is shown to be effective when resection is not possible.[7] Combination chemotherapy with vinblastine and methotrexate is described as an effective treatment without acute or long-term morbidity in children.[9]

This paper reports a case of aggressive fibromatosis in the submandibular space with a unique radiographic appearance, diagnosed based on immunohistochemical features and rapid growth, treated with surgical removal.

2 | CASE PRESENTATION

A 5-year-old girl presented to Oral and Maxillofacial Surgery department with chief complaint of swelling in the lower jaw of 2 months' duration. The patient did not report any difficulties in swallowing or breathing or symptoms of facial pain and neural alterations in the affected side. History of trauma was negative. Past medical history and familial history of the patient were unremarkable. No abnormal findings were observed in laboratory tests, except low red blood cell mean corpuscular volume (MCV), which was proved to be of iron deficiency origin.

On clinical examination, there was a solitary fixed mass in left submandibular region (measured about 4 × 5 cm in diameter) with resultant facial asymmetry (Figure 1A–B). The covering skin was normal without signs of inflammation. On palpation, the involved region was firm and non-tender. No cervical lymphadenopathy was detected. Mouth opening was within normal range.

Intra-oral examinations revealed intact mucosa with normal color (Figure 1C). Dental carious lesions were present on distal aspect of mandibular primary first molars bilaterally.

The provisional clinical diagnosis was inflammatory lesion associated with left mandibular primary molar tooth, although there was no sign of inflammation. Because of progressive nature and fast growth pattern, malignant lesions of mesenchymal origin were also included in the possible diagnoses.

On panoramic radiograph (Figure 1D), a poorly defined radiolucency was observed in the left mandibular body with some spicules of bone emanating from the inferior mandibular border. Compared to the unaffected side, left second premolar tooth crypt was not detectable. Cone-beam CT scan was obtained for further investigations. Cross-sectional images of the radiolucent area revealed destruction of the alveolar bone from the lingual aspect. Diffuse spicules of periosteal bone were also detected on buccal and lingual cortices (Figure 2A–B). On axial views, soft tissue swelling overlying the bone was apparent. Delicate and sclerotic spicules of bone were also detected (Figure 2C). Based on the radiographic appearance of destruction, soft tissue mass, and periosteal reaction, sarcomas were the most possible differential diagnoses, including Ewing sarcoma, Osteosarcoma, and Fibrosarcoma, with Hemangioma and Desmoplastic fibroma ranked next. Incisional biopsy was performed under general anesthesia. Histopathological examination of the biopsy specimen revealed soft tissue tumor composed of haphazardly arranged bland spindle cells with wavy nuclei in collagenous to myxoid stroma which infiltrated to striated muscle fibers. Scattered slit-like vascular spaces, many capillaries, small nerve bundles, and hemorrhage were seen (Figure 3). For definitive diagnosis, immunohistochemical (IHC) staining was performed (Figure 4). Ki-67-labeled tumor cells were less than 10% in cellular areas. Tumor cells were stained for b-catenin. The specimen was negative for desmin, S-100, CD 34, and bcl-2 stains. Diffuse positive reactions to SMA stain were observed. Diagnosis was compatible with fibromatosis. In presurgical visit, the lesion had enlarged and therefore medical CT was obtained for further evaluation of soft tissue extension (Figure 5). Surgical treatment was planned based on the histopathological report of fibromatosis. After providing general anesthesia, excision was performed using an apron flap incision. Invasion of the left submandibular region and bony spicules observed on CBCT images were also detected surgically. The tumor was dissected from vital structures on medial aspect. The

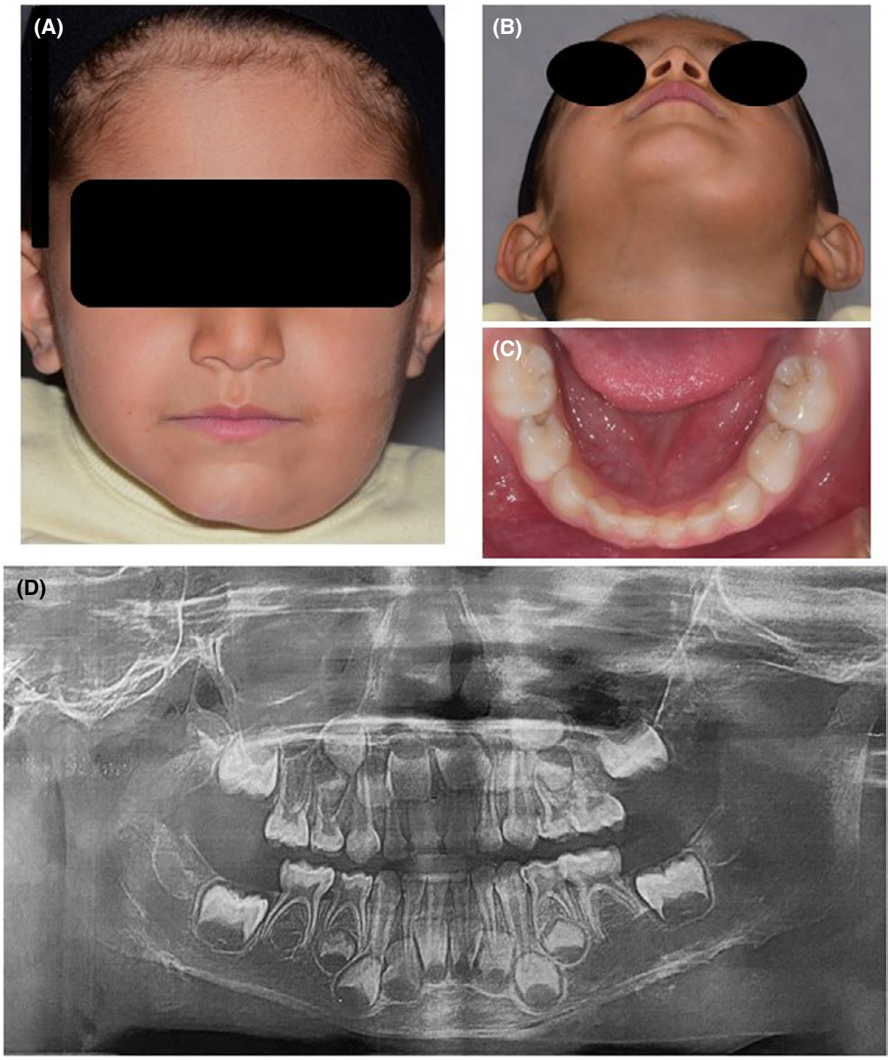

FIGURE 1 (A and B) Extra-oral views demonstrating the swelling in submandibular region with normal covering skin. (A) Frontal view (B) Submental view. (C) Intra-oral occlusal view of mandible showing intact oral mucosa. (D) Panoramic view showing poorly-defined radiolucency in the left mandibular body with some spicules of bone from the inferior border

involved soft tissue lateral to the tumor and bony spicules extending from mandible into the lesion were resected with tumor. After surface smoothening, wound closure was performed in layers and vaccum-drain was placed. The recovery process was uneventful. Before discharging, patient was under medical care in hospital for 2 days. Sutures were removed in the first follow-up visit, 1 week postoperative. Patient is now under regular follow-up, and no recurrence was observed on clinical and radiographic examination in 6 months (Figure 6).

3 | DISCUSSION

Aggressive fibromatosis is a soft tissue neoplasm that presents as a mass within skeletal muscles or in the adjacent fascia, aponeurosis, or periosteum.[7] Usually, the tumor is oriented with its long axis parallel to the muscle bundles in which it is found.[10] Secondary bony involvement, presumably because of mass effect, can range from cortical remodeling to destructive lesions. Bone erosion, periosteal thickening, and even lateral bowing of mandibular ramus are reported radiographic appearances.[6] Involvement of head and neck is not common, and there are case reports of infantile fibromatosis involving the submandibular space.[3,11] Clinical presentation of the lesion as a rapidly growing swelling was consistent with the reported cases of aggressive fibromatosis.[3,12–14] Despite negative sexual predilection, most of the reported cases of aggressive fibromatosis of the mandible were young females.[3,11,12,14–17] In the current case, lesion was mainly located in buccal and inferior portions of mandible and lingual vestibule showed normal depth, while bone destruction was observed in lingual aspect of the alveolar process away from the main tumor mass. This kind of extension could be explained by periosteal extension of the lesion. Shuker et al.[11] and Roychoudhury et al.[3] also reported spicules of periosteal layer of bone. To the best of our knowledge, simultaneous bone erosion and periosteal bone deposition are reported in only one study, in which there was erosion of the mandibular angle and body in the affected side.[3] Destruction of cortical bone with adjacent soft tissue mass

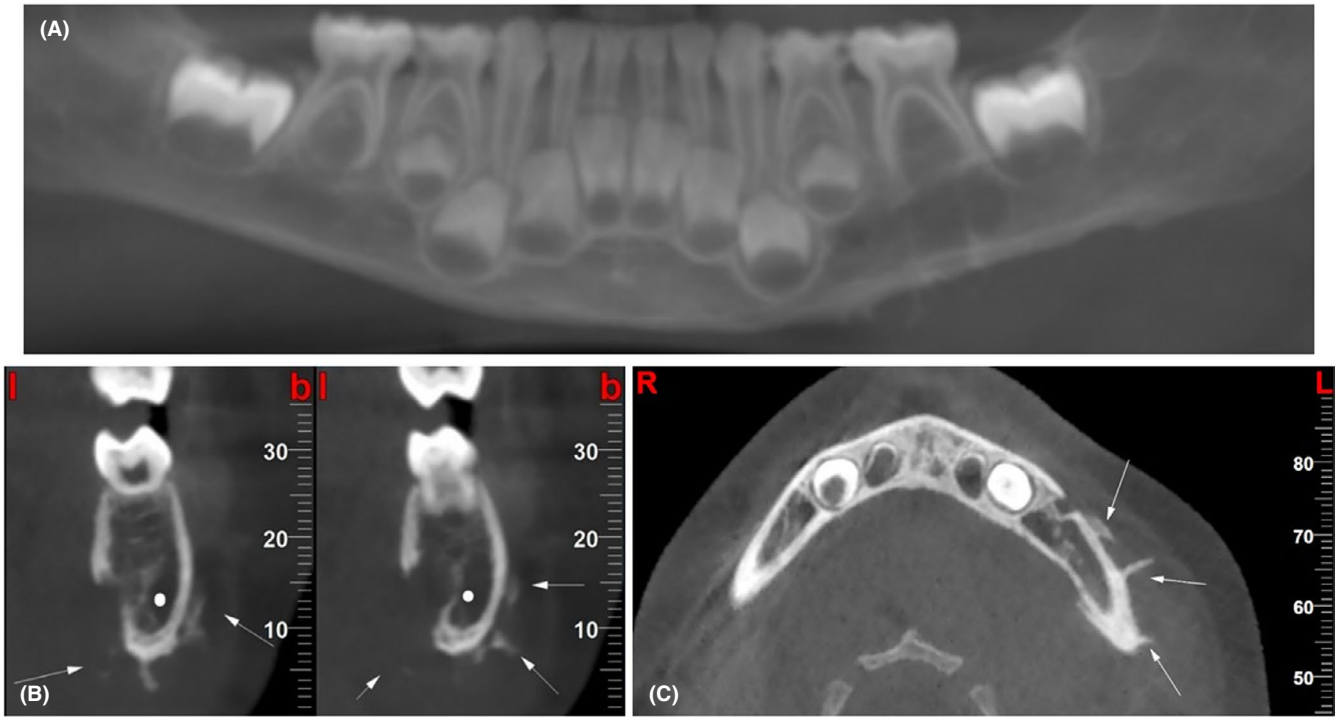

FIGURE 2 CBCT reformatted images. (A) Multiplanar reformatted panoramic image (thickness = 10 mm) (B) Cross-sectional views from left second primary molar region demonstrating destructive lesion extending from the lingual aspect. (C) Axial view at hyoid bone level demonstrating soft tissue mass overlying the bone. Sclerotic and delicate spicules are indicated by arrows

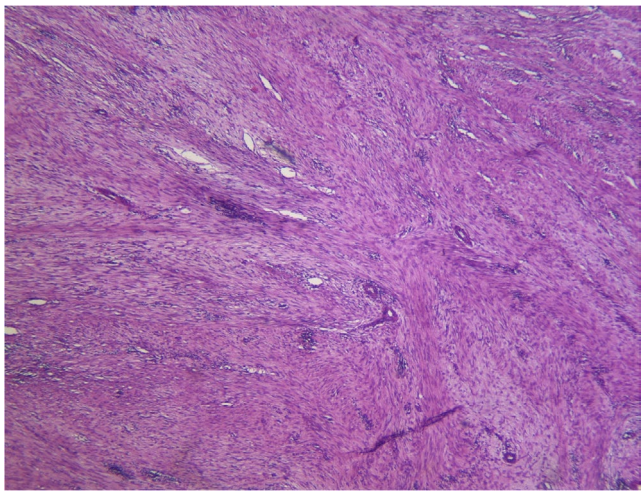

FIGURE 3 Photomicrograph showing proliferation of spindle cells with wavy nuclei in collagenous to myxoid stroma (Hematoxylin and Eosin staining, 40×)

is considered to be highly suggestive of malignancy. This also increased the susceptibility to mesenchymal malignancies as radiologic differential diagnoses.

MRI is considered as imaging technique of choice for extremity fibromatosis.[7] Because of heterogenous composition on histology and depending on the collagen content and cellularity of the lesion, fibromatosis shows variable signal intensities on MR imaging which makes it nonspecific for diagnosis.[18] Claustrophobia is an important consideration especially when children are examined. Moreover in order to reduce the risk of patient movement and image distortion, moderate to deep sedation is required during MRI procedures, which is accompanied by potential complications.[19] Unenhanced and contrast-enhanced CT scans most accurately show the extent and anatomic relations, but there is no consistent relationship between CT appearance and histology. Bone involvement is more accurately assessed by CT using bone window settings compared to conventional radiography or MR imaging.[7] Cone-beam CT can provide similar information with shorter scanning time and lower radiation dose.[20] A technical consideration in imaging soft tissue lesions of jaws is to use cotton rolls to separate the lesion from adjacent soft tissues and better define the outline of the mass. Thinning and perforation of buccal cortical plate can also be detected using CBCT images more precisely.[21] Sonographic appearance is also nonspecific, but it is helpful to perform biopsy of superficial lesions under sonographic guidance.[7]

Fibromatosis might occur as superficial or deep form (also called desmoid form). Superficial lesions usually remain small, whereas deep fibromatoses often display locally invasive characteristics clinically. Alterations in the WNT signaling pathway occur in both superficial and deep forms, which share histologically similar features. Mutations in b-catenin or the adenomatous polyposis coli (APC) gene are exclusively observed in deep form.

SMA	Desmin	CD-34	Bcl-2	S100	Ki-67	β catenin
Diffuse positive	Negative	Negative	Negative	Negative	<10%	Positive

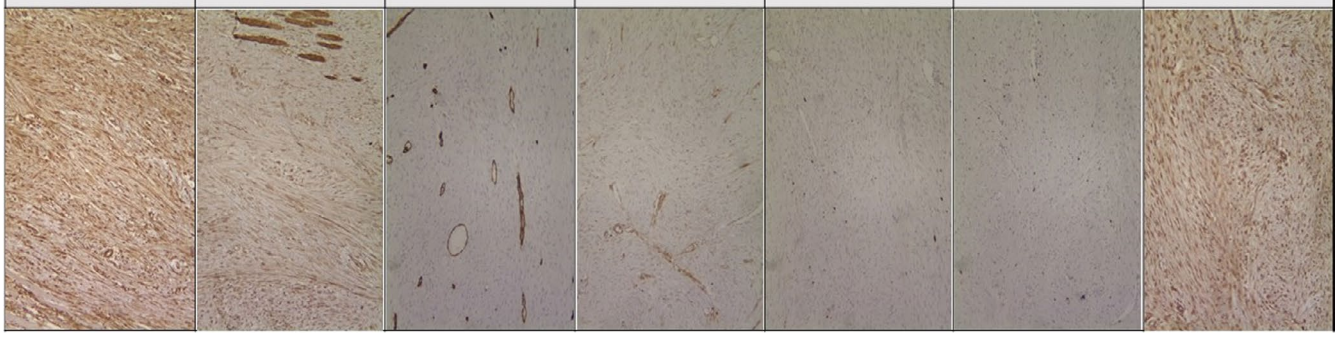

FIGURE 4 IHC staining results (magnification 100×)

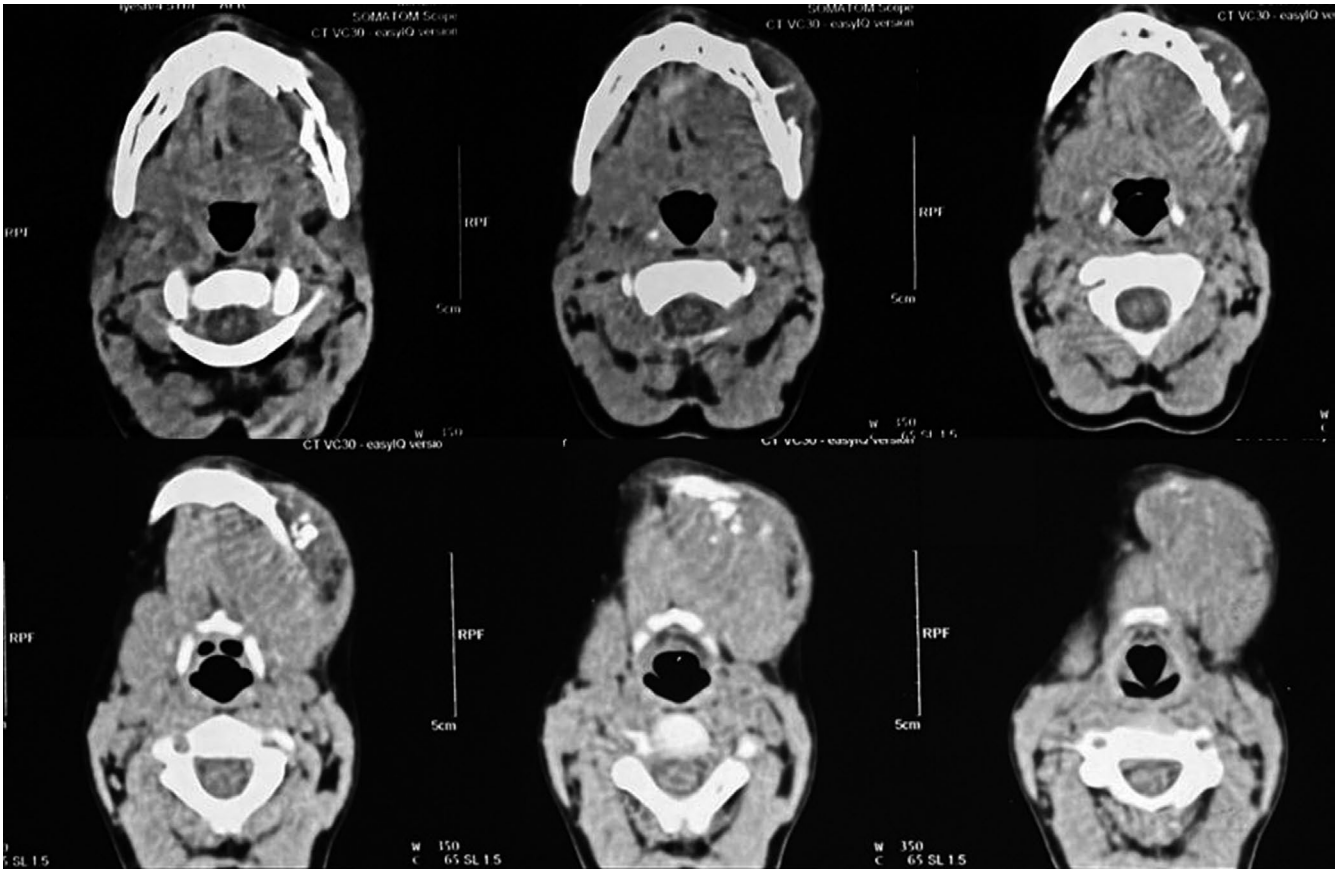

FIGURE 5 Serial axial CT (narrow window setting) demonstrating the soft tissue mass in the submandibular region, extending from skull base to the level of hyoid bone, and occupying the left buccal space and floor of the mouth without altering the airway

Involvement of head and neck occurs in extraabdominal fibromatosis, which is a subclass of deep form.[22]

Based on the histopathologic findings, some lesions were possible for differential diagnosis. Different IHC staining was applied in the reported cases of fibromatosis. The tumor cells were reported to be negative for S-100 and CD 34 stains.[4,8] Results of desmin and vimentin staining were controversial, that could be a result of myofibroblastic differentiation in cases that were positive for desmin and vimentin stains.[4,16] Despite similar appearances, desmoplastic fibroma (which is the osseous counterpart of fibromatosis) is less cellular and shows less infiltration.[4] In IHC staining results, proliferation index (Ki-67) was less than 10% in cellular areas, ruling out the malignant nature

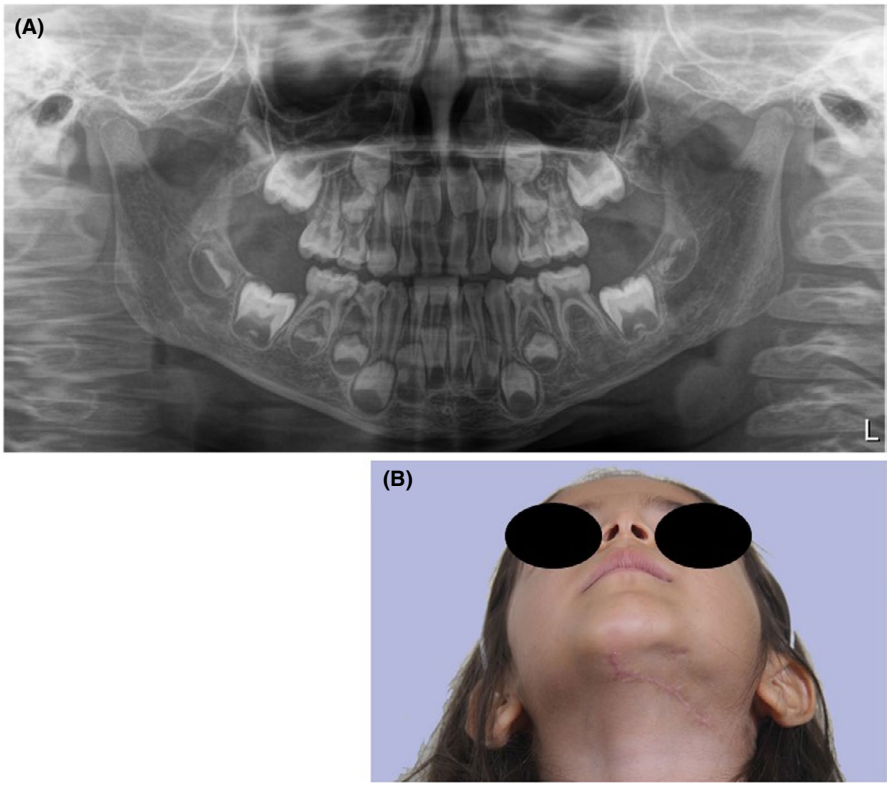

FIGURE 6 Clinical and Radiographic follow-up images showing no evidence of recurrence

of the lesion. Therefore, fibrosarcoma, the most significant differential diagnosis, can be ruled out based on this staining. Neurofibroma, which is considered as a differential diagnosis, can be distinguished using S-100 staining, in which the neurofibroma is positive while the specimen was negative for this stain.[4] Malignant peripheral nerve sheath tumor presents higher mitotic rate, and half of the cases are positive for S-100 staining.[4,23] Hemangiopericytoma and solitary fibrous tumors (SFT) are mesenchymal neoplasms of fibroblastic origin that must be differentiated from fibromatosis. CD 34 and bcl-2 stainings are sensitive markers of solitary fibrous tumor which could be applied to separate SFT from histologically similar neoplasms.[24]

Fibromatosis is benign histologically, but local aggressiveness and high recurrence rate (20%–70%) may result in associated morbidity and mortality.[15] Recurrence is more commonly reported in the first year, but there are reports of lesion recurrence even 5 years after treatment. A duration of at least 3 years is recommended for follow-up in the literature.[3] Although some histopathological features have been described as predicting tools for higher recurrence rates, neither histopathological appearance, nor enhancement pattern are reliable factors of tumor recurrence.[3,7]

4 | CONCLUSION

Fibromatosis is a histologically benign soft tissue tumor with nonspecific clinical features, which is not common in head and neck. Radiographic appearance of bony involvement, secondary to mass effect, ranges from cortical remodeling to areas of bone erosion. Periosteal reaction, as observed in the current case, might be present due to periosteal origin of the lesion. Histopathological examination and IHC staining play an important role in definitive diagnosis. Surgical removal with large rim of normal-appearing tissue is advised. Because of local aggressiveness and high recurrence rate, long-term follow-up is necessary.

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None.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

All authors involved in preparing the case report. Mostafa Alam involved in patient treatment, obtaining informed consent, and manuscript revision. Hassan Mir Mohammad Sadeghi involved in conception and design of the study. Fatemeh Mashhadiabbas involved in histopathological diagnosis, article revision, and approval of the final version for submission. Mina Iranparvar Alamdari involved in data collection, radiographic interpretation, and writing manuscript.

ETHICAL APPROVAL

Ethics approval is waived because this report does not involve any experiment.

CONSENT

Written informed consent was obtained from the parent to publish this report in accordance with the journal's patient consent policy.

DATA AVAILABILITY STATEMENT

The data are available from the corresponding author upon request.

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