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CLINICAL REPORT

Low-Grade Fibromyxoid Sarcomas with the Maxillary Sinus Localization: A Case Report and Review of the Literature

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Abstract A low-grade fibromyxoid sarcoma (LGFMS) is an extremely rare tumor first described by Evans in 1987. LGFMS is a type of soft tissue sarcoma characterized by a deceptively benign histological appearance but completely malignant behavior. LGFMS is usually seen in the deep soft tissues of the extremities and trunk. We have examined many reviews, case reports and case series previously published in PubMed and Google Scholar. To date, only five cases have been reported in the maxilla. LGFMS generally affects young adults, but it can also be seen in children and older adults. A radical surgical approach is the most recommended treatment option. LGFMS has a very low mitotic activity; therefore, it is considered that neither chemotherapy nor radiotherapy has a significant effect on long-term LGFMS prognosis. However, to date, there has been no study suggesting any protocol for the follow-up of patients with LGFMS. In this report, we present a case with LGFMS located in the maxillary sinus, in which despite radiotherapy following extensive surgical excision, the tumor recurred in a short period of three months and reached its former size.

Keywords Low-grade fibromyxoid sarcoma · LGFMS · Sarcoma · Maxillary sinus · Paranasal sinus sarcoma

Introduction

Low-grade fibromyxoid sarcoma (LGFMS) is a variant of fibrosarcoma that usually occurs in the deep soft tissues of the extremities in young or middle-aged adults [1]. Primary sarcomas of the head and neck region are very rare and constitute approximately 1% of malignancies in this region [2]. Although LGFMS acts like a benign tumor with a slow growth pattern, it has very high potential for local recurrence and distant metastasis [3]. The incidence of LGFMS is very similar between men and women, and it is a tumor that can be seen at all ages [4, 5]. LGFMS is primarily seen in the deep soft tissues of the extremities and trunk, and a small number of cases have been reported in the head and neck region [3, 4]. It is genetically characterized by translocation on chromosomes 7 and 16 [6]. Immunohistochemically, most cells of this sarcoma are strongly positive for vimentin but are generally negative for α-actin, desmin, S-100 protein, cytokeratin, CD34, and CD56 [7]. LGFMS typically appears as a well-circumscribed, encapsulated mass without necrosis or bleeding foci [8]. We aimed to obtain a more accurate idea of LGFMS by reviewing the literature and examining relapse, recurrence, gender and affected areas in cases reported to date. As a result of this detailed literature review, we summarized the data obtained in a table, which constitutes the most comprehensive list of LGFMS cases with the head and neck localization in the literature (Table 1).

Case

A 56-year-old male patient presented to our clinic with a painless swelling growing slowly in the right malar region. On his physical examination, there was a swelling

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Table 1 List of all case reports obtained after a comprehensive review of the literature (PubMed and Google Scholar)

Case	Age	Sex	Location	Outcome (If Known)	References
1	26	M	NECK	Multiple recurrent, alive at 44 years	Evans [9]
2	3y 10 m	M	JAW	Local recurrence after 3 months; local recurrence and concomitant lung metastasis after 15 years with surgery and radiation; NED 2.5 years later	Papadimitriou et al. [10]
3	36	M	NECK	NED at 55 mo	Lane et al. [11]
4	N/A	N/A	HEAD/NECK	N/A	Folpe et al. [12]
5	N/A	N/A	HEAD/NECK	N/A	Folpe et al. [12]
6	N/A	N/A	HEAD/NECK	N/A	Folpe et al. [12]
7	N/A	N/A	HEAD/NECK	N/A	Folpe et al. [12]
8	41	M	LEFT SUPRACLAVICULAR REGION	N/A	Zamenik and Michal [13]
9	57	F	CHEEK	N/A	Botev et al. [14]
10	22	M	NECK	NED at 38 months	Guillou et al. [15]
11	40	F	SCM	NED at 12 months	Marglani et al. [16]
12	57	M	THYROID	NED at 13 months	Merchant [17]
13	1Y 10 M	M	CHEEK	NED after 6 months	Tang et al. [18]
14	57	M	NECK	N/A	Viswanathan et al. [19]
15	27	M	JAW	NED after 22 months	Rekhi et al. [20]
16	31	M	FACE	N/A	Rekhi et al. [20]
17	69	M	NECK	2 recurrences after 10 years	Rekhi et al. [20]
18	26	M	NECK	Multiple recurrences treated with excision, NED at 44 years	Evans [3]
19	9	M	NECK	Multiple recurrences, followed by radiation after last; lung and chest wall metastases at 25 years treated with multiple resections; died of metastatic tumor at 42 years	Evans [3]
20	84	F	RIGHT FOREHEAD	After resection with a 1-cm skin margin, recurrence occurred at 15 months postoperatively. Additional wide excision was subsequently performed with a 2-cm skin margin. Recurrence and metastasis have not been observed for 1 year after the second excision	Abe et al. [7]
21	53	F	NECK	NED after 91 months	Maretty-Nielsen et al. [21]
22	35	M	NECK	NED after 63 months	Maretty-Nielsen et al. [21]
23	N/A	N/A	THYROİD	N/A	Dong and Zhang [22]
24	14	M	CHEEK	NED after 12 months	He et al. [23]
25	41	M	NECK	LUNG MET 48 MONTH 271 MONTHS DİED OF DİSEASE	Prieto-Granada et al. [24]
26	40	M	HARD PALATE	NED after 4 months	Soma et al. [25]

Table 1 continued

Case	Age	Sex	Location	Outcome (If Known)	References
27	63	F	MASSETER MUSCLE	NED after 12 months	Lee et al. [26]
28	16	M	MAXILLA	NED after 6 months	Spalthoff et al. [27]
39	6	M	PESTERİOR CERVİCAL SPİNE	One patient was disease-free at 12 months post-excision. The other patient was alive 10 months after surgery with multiple sub-centimeter pulmonary nodules too small to biopsy and enlarged posttracheal and jugular chain lymph nodes (up to 1.4 cm) suggesting disseminated disease	Cowan et al. [4]
30	43	F	FACİAL SKİN	One patient was disease-free at 12 months post-excision. The other patient was alive 10 months after surgery with multiple sub-centimeter pulmonary nodules too small to biopsy and enlarged posttracheal and jugular chain lymph nodes (up to 1.4 cm) suggesting disseminated disease	Cowan et al. [4]
31	45	M	MANDİBLE	One patient was disease-free at 12 months post-excision. The other patient was alive 10 months after surgery with multiple sub-centimeter pulmonary nodules too small to biopsy and enlarged posttracheal and jugular chain lymph nodes (up to 1.4 cm) suggesting disseminated disease	Cowan et al. [4]
32	73	M	LARYNX	One patient was disease-free at 12 months post-excision. The other patient was alive 10 months after surgery with multiple sub-centimeter pulmonary nodules too small to biopsy and enlarged posttracheal and jugular chain lymph nodes (up to 1.4 cm) suggesting disseminated disease	Cowan et al. [4]
33	35	M	MANDİBLE	N/A	Chaudhuri et al. [28]
34	61	M	MANDİBLE	NED after 24 months	Kargahi et al. [29]
35	2 M	M	NECK	NED after 4 months	Zakiyah [30]
36	40	F	POSTERIOR NASAL CAVITY	NED after 60 months	Sohn et al. [31]
37	N/A	N/A	TONGUE	N/A	Pellini et al. [32]
38	18	F	BUCCAL MUCOSA	NED after 18 months	Kanato et al. [33]
39	44	F	EXTERNAL AUDITORY CANAL	NED after 18 months	Kumari et al. [34]
40	57	F	PARAPHARYNGEAL SPACE	NED after 24 months	Toro et al. [35]
41	N/A	N/A	MAXİLLARY SINUS	NED after 148 months	Koucky et al. [36]
42	N/A	N/A	MAXİLLARY SINUS	NED after 148 months	Koucky et al. [36]
43	N/A	N/A	NASAL CAVİTY	NED after 148 months	Koucky et al. [36]
44	45	M	MAXILLA	NED after 12 months	Flores et al. [1]
45	78	M	NECK	NED after 12 months	Park et al. [8]

M male, *F* female, *N/A* information was not available, *NED* no evidence of disease

extending to the right upper hard palate. The endoscopic examination revealed a soft tissue mass filling the middle meatus in the right nasal passage. The nasopharynx was natural, and all routine blood tests were normal. Contrast-enhanced paranasal sinus, neck and thorax tomographies were taken. Diagnostic imaging revealed a contrast-enhancing soft tissue mass in the right maxillary sinus, which had eroded the bone structures of the sinus. The mass extended into the right nasal passage and filled the middle meatus (Figs. 1, 2). However, no signs of invasion or metastasis were detected. A punch biopsy was performed from the part of the mass extending to the nasal passage under local anesthesia. Histologically, the mass was characterized by epithelioid cells with a fibrotic basis. In the immunohistochemical examination, vimentin and MUC4 were positive while S100, CD34, desmin, actin, keratin,

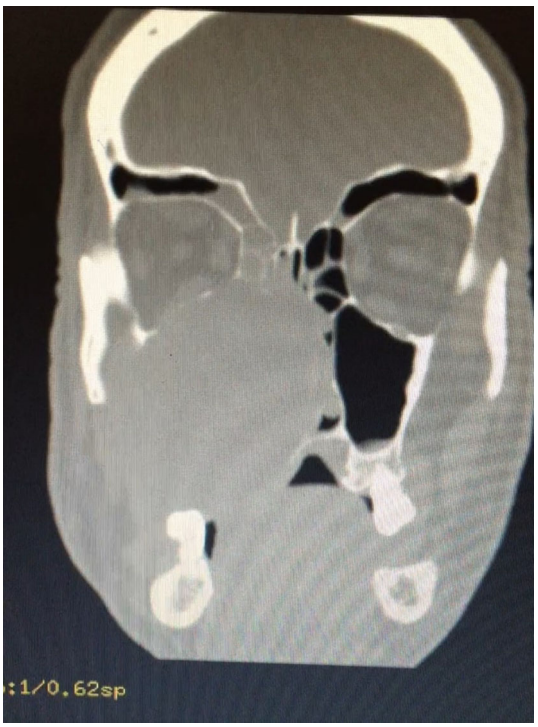

Fig. 1 Preoperative computed tomography image in the coronal plane

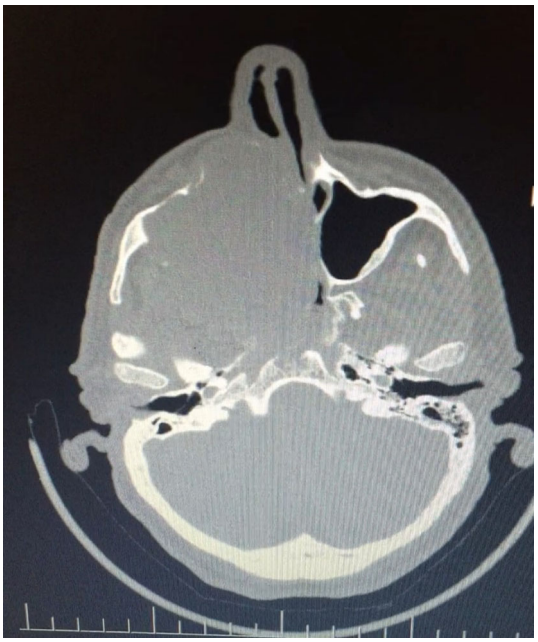

Fig. 2 Preoperative computed tomography image in the axial plane

and epithelial membrane antigens (AE1/AE3, LMWK, and HMWK) were negative. Thus, we planned the excision of the entire tumor, including the surrounding soft tissue, under general anesthesia. We made a Weber-Ferguson incision to reach the tumor (Fig. 3). After flap elevation, it

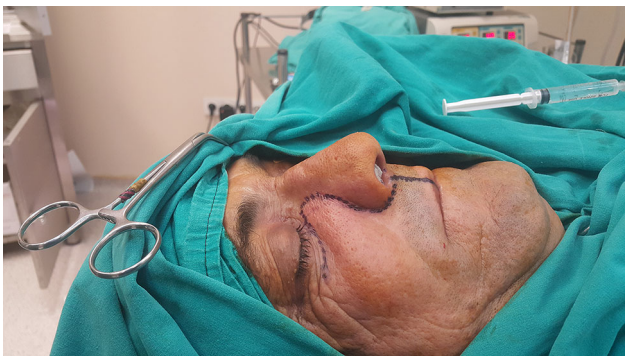

Fig. 3 Weber-Ferguson incision

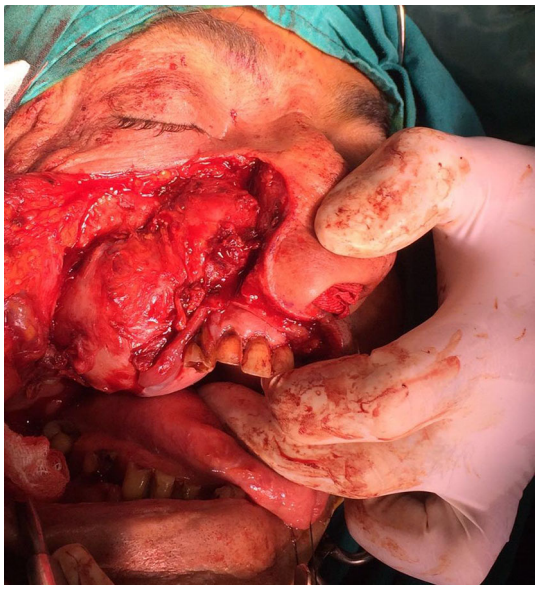

Fig. 4 Appearance of the mass after flap elevation revealing the defect on the anterior wall of the maxilla

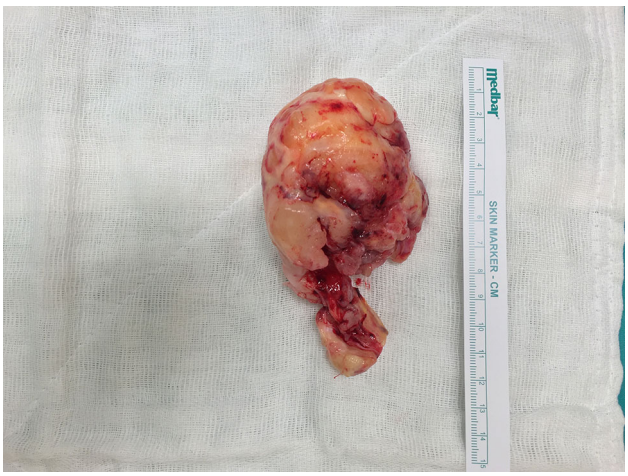

Fig. 5 Macroscopic image of the mass that was removed en-block together with the part extending into the nasal passage

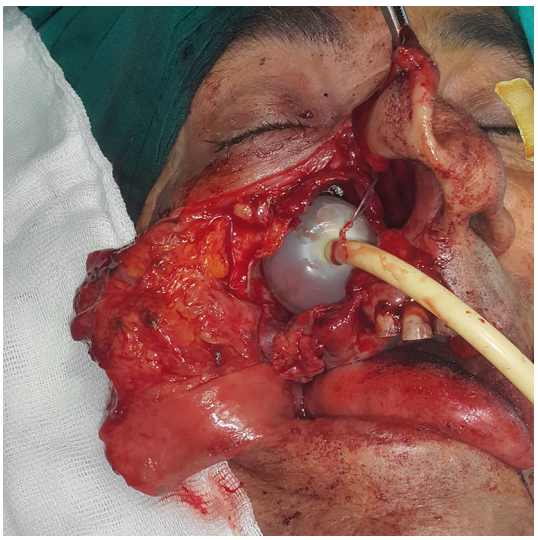

Fig. 6 A Foley catheter inserted in the sinus cavity and inflated to 15 cc sf after the removal of the mass in order to provide support for the eroded maxillary sinus bone structure during healing and prevent cosmetic deformity

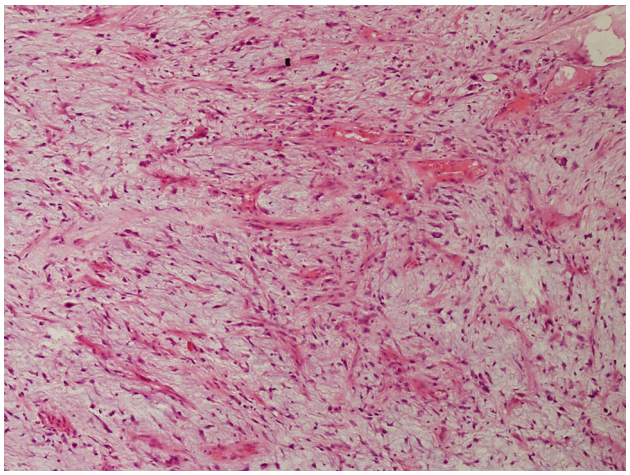

Fig. 7 Low cell rate and dense vascular network tumor morphology in diffuse myxoid focal collagenized stroma (H & E × 100)

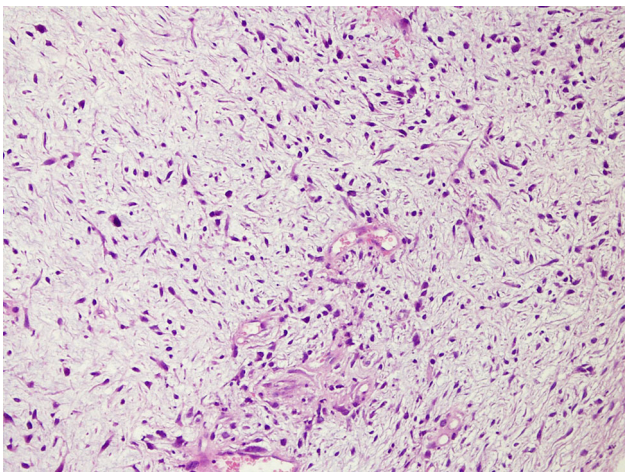

Fig. 8 Spindle cells with mild pleomorphic nuclei in fibromyxoid stroma (H & E × 200). The pathology revealed tumor-cells growing in nests surrounded by partially spindle-like cells and partially myxoid stroma. Some cells were eosinophilic and others showed clear cell-like cytoplasm. Many mitoses were observed with some atypical mitotic figures

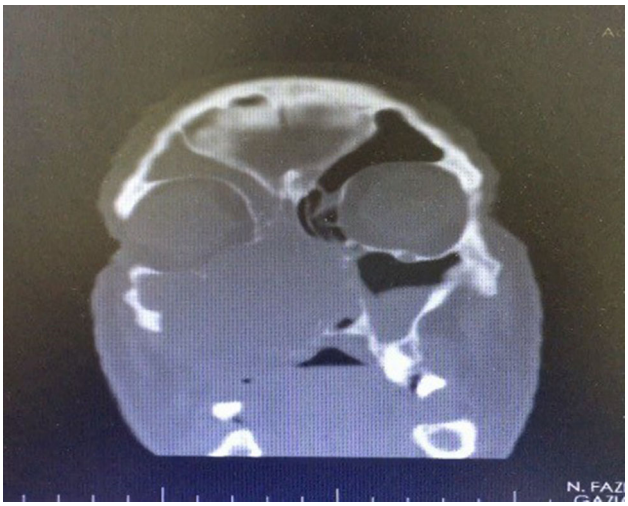

Fig. 9 Postoperative third-month follow-up computed tomography image in the coronal plane

was observed that the maxillary anterior wall bone structure was completely lost. The tumor was seen to have expanded into surrounding tissues (Fig. 4). The tumor was macroscopically removed en-block (Figs. 5, 6). The pathological examination revealed tumor cells growing in nests surrounded by partially spindle-like cells and partially myxoid stroma. Some atypical mitotic figures were also seen (Figs. 7, 8). Immunohistochemically, vimentin was positive in tumor cells, but actin, CD31, CD34, S100, and desmin were negative. The Ki-67 proliferation index was 10–20%. The fluorescent in situ hybridization test was positive for FUS gene rearrangement. Thus, the patient was diagnosed with LGFMS. Radiotherapy was initiated from the third week after surgery. At the end of the postoperative third month, the follow-up computed tomography showed that the tumor had filled the maxillary sinus again and reached its initial size (Figs. 9, 10).

Discussion

LGFMS is a benign tumor rarely seen in the head and neck region. Despite acting like a benign tumor with a slow course, it can exhibit malignant behaviors such as distant

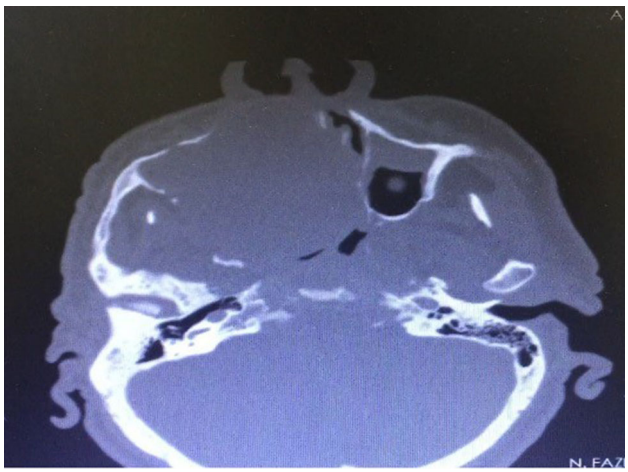

Fig. 10 Postoperative third-month follow-up computed tomography image in the axial plane

metastasis and local recurrence [8]. In the head and neck region, the maxillary sinus localization of LGFMS is even rarer, and our literature review revealed only five reported cases in total [1, 9–11]. Although there are many case reports or series about LGFMS in the literature, LGFMS continues to be a challenging and complex clinical entity for surgeons. Since it was first described by Evans in 1987, confusions remain concerning the diagnosis and treatment of LGFMS [12]. Based on our own clinical experience, we can state that unfortunately, it is very difficult to diagnose these patients in centers that are not equipped with molecular, genetic and immunohistochemical laboratories. Even in most experienced clinics, fine needle aspiration biopsy (FNAB), which is the first procedure used for a pathological evaluation in head and neck masses, is insufficient in diagnosing this tumor [13]. In a neck mass that cannot be diagnosed with FNAB, if there is no necrosis or hemorrhage in the mass due to radiological invasion, metastasis or high mitosis, it naturally becomes difficult to make a radical surgery decision. Even if a radical surgery decision is taken, this does not necessarily improve the condition of the patient or the course of the disease. Nevertheless, the radical surgical approach maintains its exaggerated popularity as a treatment method recommended by many surgeons and considered to be the most beneficial for the patient [1, 2, 10, 13–15]. The surgical treatment of LGFMS, which also occurs in the extremities in addition the head and neck region, does not affect the comfort of the patient as dramatically as the large resection of a tumor in the maxillary sinus. Unfortunately, the large surgical excision of LGFMS in the head and neck region, especially in the maxilla, which has been previously described in a few cases in the literature, creates hesitations in the surgical approach due to the possibility of resulting in serious cosmetic deformities [11, 13]. Cosmetic concerns clearly should not change the treatment algorithm of this malignant tumor; however, the literature contains controversial discussions concerning the benefits of radical surgery, with patients often experiencing frequent and short-term recurrences and distant metastases and requiring multiple operations [3, 4, 16, 17]. In the first and longest-term follow-up study, LGFMS was detected in the head and neck region in two patients, one aged 26 and the other nine years, requiring nine and seven operations, respectively after the first excision of LGFMS [3]. Distant metastasis developed in the nine-year-old patient despite radiotherapy application after the last recurrent tumor excision, and the 42-year-old patient died due to distant metastasis after repeated metastasis operations (six operations).

According to Ewans, the mean recurrence time of LGFMS is 3.5 years, while the average duration of distant metastasis is five years. However, such long-term follow-ups are very limited in the literature. In this respect, the literature can be considered insufficient in terms of revealing the true recurrence, distant metastasis capacity and progression rate of the disease. On the other hand, recurrence after surgery is not the only problem caused by the genetic and histological features of LGFMS. Another factor that makes treatment difficult is the low mitosis rate, which is one of the most characteristic features of the tumor [8, 18]. The low mitotic rate and fibrotic background also limit the effectiveness of radiotherapy and chemotherapy, which are highly effective in malignant tumors [19, 20]. This situation leads to the inability to prevent recurrence associated with residual tumor at microscopic level after surgery. As we mentioned in the case we presented, although we were sure of the surgical margins and started radiotherapy immediately after surgery, our patients relapsing in a very short time presented serious evidence for that it is a difficult disease to treat.

Lastly, during the literature review on LGFMS conducted as part of this study, we found 36 cases for which gender and age information was available, and they had a wide age range from two months to 84 years, with the mean value being 38.6 years, which is consistent with previous reviews [4, 15]. However, based on the gender data of 36 patients, among the patients with head and neck involvement, LGFMS was 2.6 times more common in males. In the literature, equal or similar prevalence is generally reported for both genders [4, 5, 15].

In conclusion, LGFMS is a soft tissue tumor that should be diagnosed genetically and immunohistochemically. The benefit of FNAB in diagnosis is very limited. The best option for its treatment is radical surgical excision, although it does not provide a desired satisfaction level in today's conditions. Although the effects of radiotherapy and chemotherapy remain controversial in the literature,

we know that radiotherapy was not beneficial for our patient. We consider that all scientific discussions concerning this issue should continue, and further diagnosis and treatment studies should be conducted on LGFMS.

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