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CASE REPORT - PATHOLOGY

Myxoid liposarcoma in an 11-year-old patient

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Abstract
Myxoid liposarcoma is a mesenchymal malignancy that most commonly presents in young adults, with peak incidence between the ages of 30–50 years. The clinical behavior of myxoid liposarcoma has been well characterized in adults. However, little is known about the clinical features and treatment outcomes of myxoid liposarcoma in child, owing to its rarity. This case report describes an 11-year-old previously healthy female who presented with a painless mass in her right thigh. Ultrasonography, computed tomography, and magnetic resonance imaging demonstrated a soft tissue mass with clear margins in the subfascial plane superficial to the gracilis and sartorius muscles. She was diagnosed with myxoid liposarcoma based on histological and molecular cytogenetic examinations of the core-needle biopsy specimen. The patient subsequently underwent wide resection without any adjuvant treatment. The patient has not experienced any symptoms of local recurrence and metastases as of 2.5 years after surgery.

Keywords Myxoid liposarcoma · Childhood tumors · Sarcoma

Introduction

Liposarcoma is the second most common type of soft tissue sarcoma. In the latest World Health Organization (WHO) Blue Books, there are five subtypes of liposarcoma [1]. Myxoid liposarcoma (MLS) accounts for approximately 20–30% of liposarcomas [2]. The peak incidence of MLS occurs in the fourth and fifth decades. Its clinical behavior has been well studied. On the other hand, MLS in children and adolescents is extremely rare; the clinicopathological and imaging features, optimal treatment strategy, and optimal surveillance after treatment remain unclear [3]. In this article, we report a case of MLS in an 11-year-old girl in detail.

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Case report

An 11-year-old girl with no significant medical history presented with a painless mass over her medial thigh (Fig. 1a). She was referred to our hospital for surgical treatment after several examinations and a core-needle biopsy performed at a nearby hospital. The mass had grown in size over the preceding 2 months. Her height was 146.6 cm and her weight was 39.7 kg. Her body mass index was 18.5 kg/m^2. Physical examination revealed a soft, palpable 5 × 4 cm mass with moderate mobility under the right distal thigh without restriction of the right knee's range of motion. Ultrasonography visualized a homogeneous, slightly hyperechoic, and well-delineated mass with regular contours. Low vascular flow was observed (Fig. 1b and c, respectively). Plain radiographs of the right thigh showed a soft tissue tumor with discoidal morphology in the distal third of the right thigh without calcifications (Fig. 2). Computed tomography (CT) showed a soft tissue mass with slightly lower density than adjacent muscles (Fig. 3) and no apparent lung metastases (data not shown). On magnetic resonance imaging (MRI), the lesion measured 47 × 36 × 10 mm and appeared as a tumor with clear margins adjacent to the gracilis and sartorius muscles. The lesion had low signal intensity on T1-weighted images (Fig. 4a) and very high signal intensity T2-weighted images with and without fat suppression

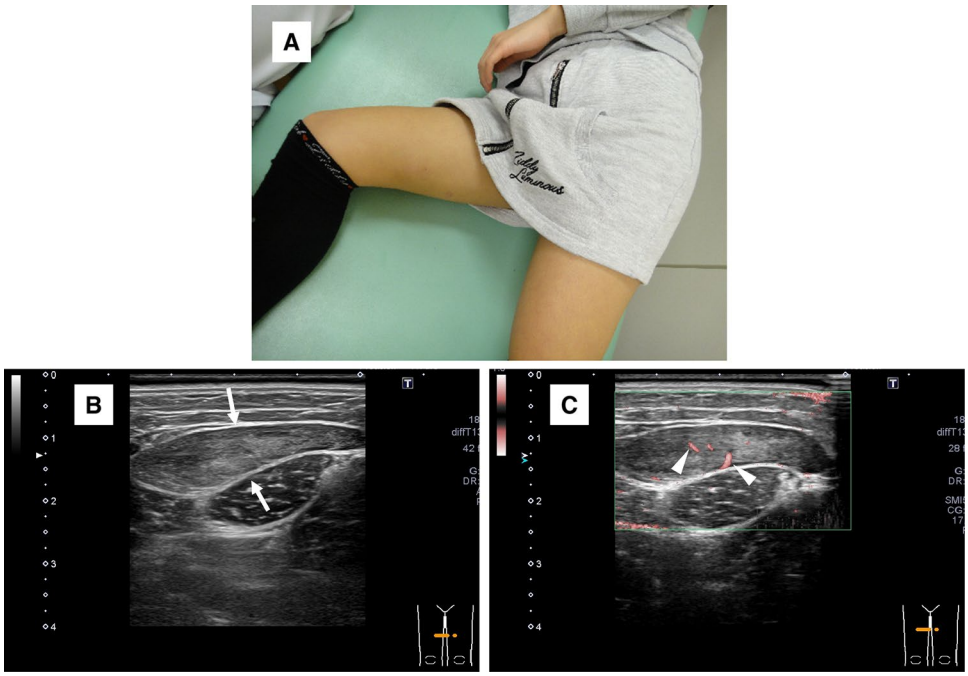

Fig. 1 **a** Photograph of the right thigh lump at the first visit. Ultrasonography: **b** A homogeneous mass (arrows), slightly hyperechoic relative to the adjacent muscle, is seen in the right medial thigh, mainly in the subfascial plane superficial to the gracilis muscle. Margins are well-defined. **c** A low level of internal vascularity is observed (arrowheads)

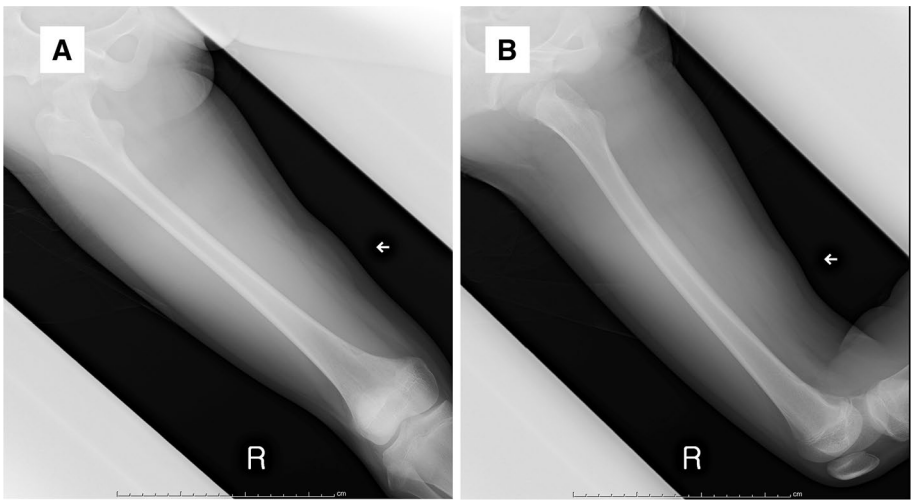

Fig. 2 **a** Anteroposterior and **b** lateral views on plain radiographs show a soft tissue tumor with discoidal morphology in the distal third of the right thigh (arrow)

(Fig. 4b and c). Diffuse homogeneous internal enhancement was observed on gadolinium-enhanced T1-weighted images with fat suppression (Fig. 4d). Core needle biopsy was performed. Histopathologically, the specimens of the biopsy showed a proliferation of atypical short-spindle or oval cells having hyperchromatic nuclei and eosinophilic cytoplasm admixed with mono- or multi-vacuolated lipoblasts arranged in a haphazard fashion embedded in an abundant myxoid stroma containing delicate arborizing vascular channels (Fig. 5a). Mitotic figures were few. Reverse transcription-polymerase chain reaction (RT-PCR) was performed using total RNA extracted from the formalin-fixed and paraffin-embedded tumor tissue specimens, and *FUS-DDIT3* fusion gene transcript was detected (Fig. 5b). Histopathological features and molecular analysis were compatible with MLS. A 18F-fluorodeoxyglucose-positron emission tomography/computed tomography (FDG-PET/CT) scan was performed. Faint FDG uptake was detected in the standard field of imaging (SUVmax 1.76) (Fig. 6). The patient underwent wide resection with sacrifice of the sartorius and gracilis muscles. The postoperative clinical course was uneventful.

The resected tumor was well-circumscribed and lobulated gelatinous tumor and located in the subfascial plane superficial to the sartorius and gracilis muscles (Fig. 7a and b). Histological findings of the resected specimen were similar to those of the needle biopsy. Mature-appearing larger fat cells and mucous pools were also seen. Mitotic figures were few. Areas with round cells or necrosis were

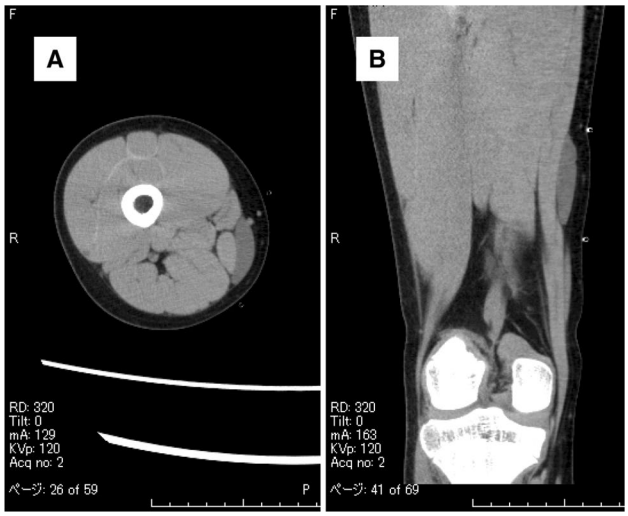

Fig. 3 Computed tomography shows a soft tissue mass with slightly lower density than adjacent muscles (arrow)

absent. Immunohistochemically, the tumor cells are positive for DDIT3 (Fig. 7c). The tumor was diagnosed as MLS. Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) was Grade 1 (score 2 + 1 + 0 = 3) and the surgical margins were negative.

No adjuvant treatment such as radiation therapy or chemotherapy was administered. The patient did not experience any symptoms of local recurrence or metastasis as of 2.5 years after surgery.

Discussion

Pediatric soft tissue sarcomas are a heterogeneous group of malignant tumors that originate from primitive mesenchymal tissue. Rhabdomyosarcoma is the most common soft tissue sarcoma in children aged 0–14 years, accounting for 50% of tumors in this age group [4]. Liposarcomas are extremely rare in childhood, representing about 2% of all childhood soft tissue sarcomas. MLS is the most common liposarcoma subtype in children and adolescents [5]. In doubtful cases, detection of the typical chromosomal translocation is the best diagnostic tool. The detection of *FUS-DDIT3* fusion leads to a definite diagnosis in the majority of patients with MLS [6].

The clinicopathological and imaging features, optimal treatment strategy, and prognosis of MLS have been well studied in adults. For example, age, presence of tumor necrosis, size (> 10 cm), and presence of a round cell component comprising more than 5% of the tumor have been reported as prognostic factors [2]. Surgical resection with adjuvant radiotherapy and possible chemotherapy is the primary management option for MLS in the extremities [7]. However, data on pediatric MLS are limited. A couple of case series

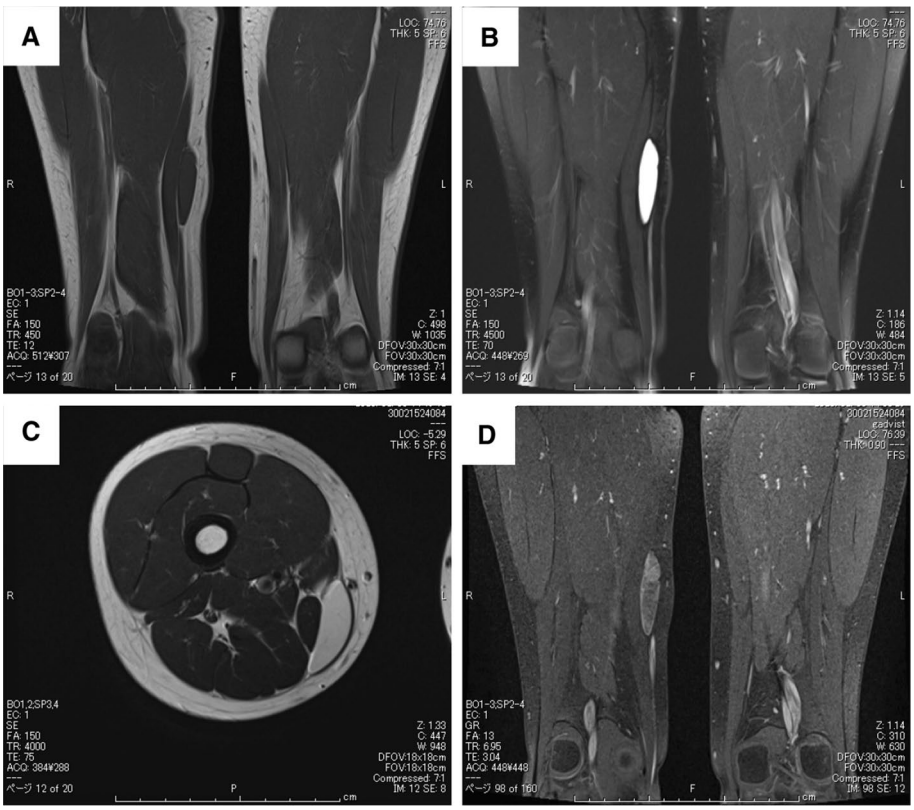

Fig. 4 Magnetic resonance imaging shows a tumor with clear margins adjacent to the gracilis and sartorius muscles. **a** T1-weighted coronal image. **b** T2-weighted coronal image with fat suppression. **c** T2-weighted axial image. **d** Gadolinium-enhanced T1-weighted coronal image with fat suppression

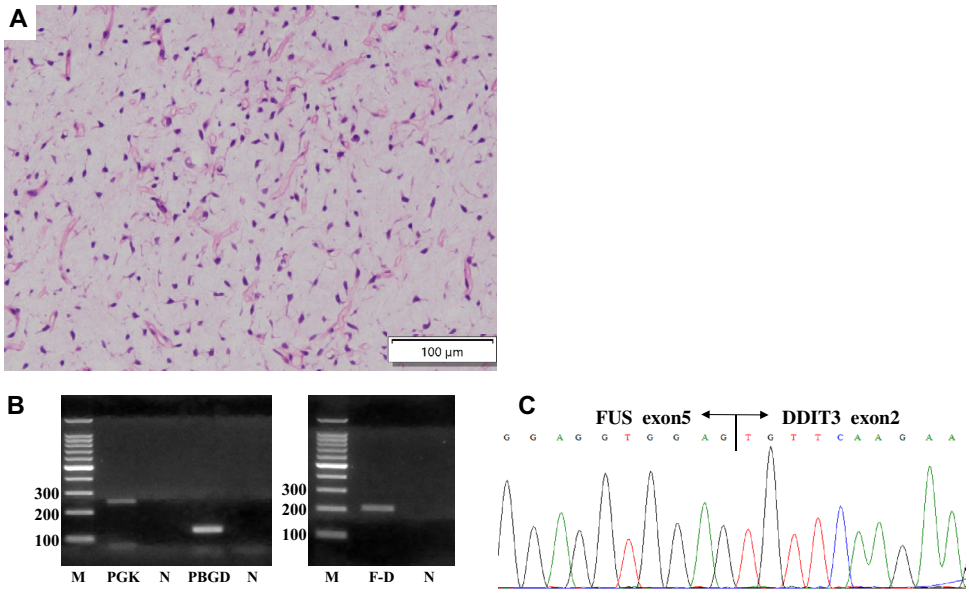

Fig. 5 **a** Microscopic image of the biopsy specimen with hematoxylin–eosin staining shows a proliferation of atypical short-spindle or oval cells admixed with mono- or multi-vacuolated lipoblasts arranged in a haphazard fashion embedded in an abundant myxoid stroma containing delicate arborizing vascular channels. RT-PCR (**b**) and subsequent sequencing analysis (**c**) detected a transcript of the FUS-DDIT3 fusion gene. *M* size marker, *F-D* FUS-DDIT3, *N* negative control, *PGK/PBGD* housekeeping genes as internal positive controls

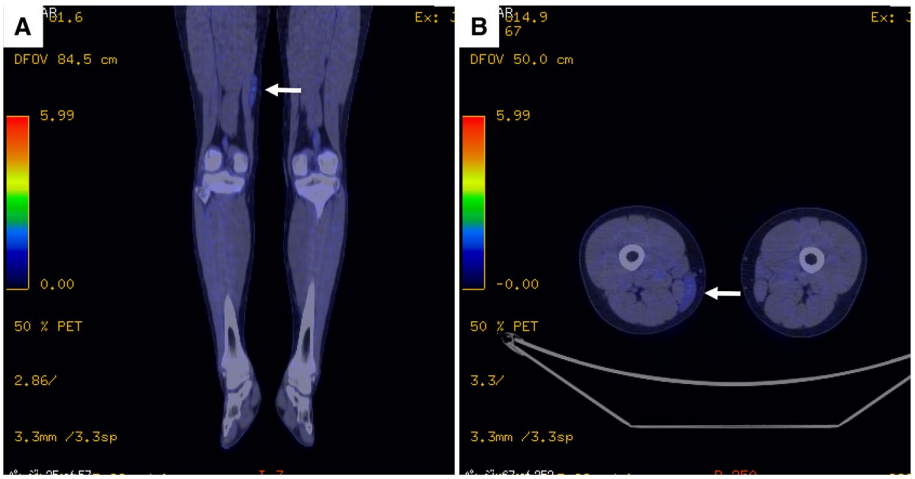

Fig. 6 Representative **a** coronal and **b** axial images of 18F-fluorodeoxyglucose (FDG)-positron emission tomography/computed tomography show faint uptake of FDG in the lesion (arrow)

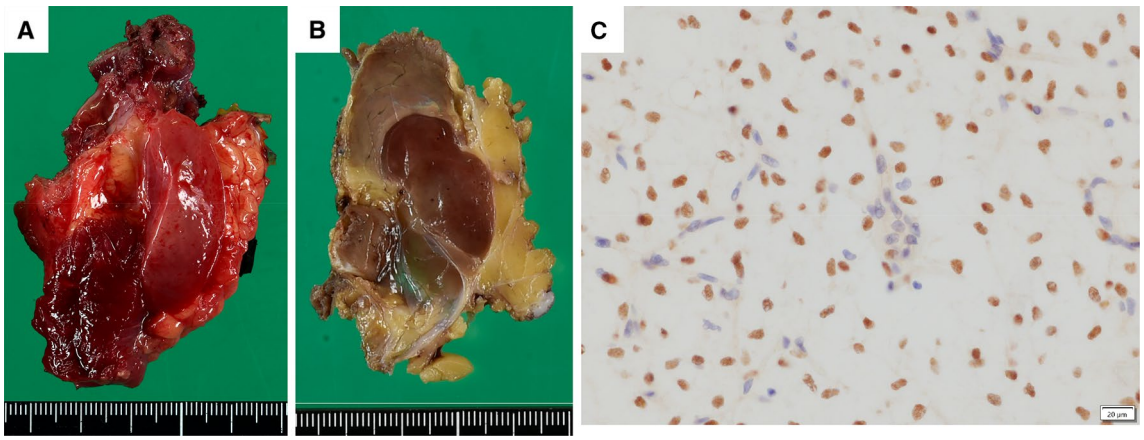

Fig. 7 Macroscopic appearance of the tumor with a gelatinous cut surface **a** before and **b** after formalin fixation. The tumor is well-circumscribed and lobulated tumor and located in the subfascial plane superficial to the sartorius and gracilis muscles. **c** Immunohistochemically, the tumor cells are positive for DDIT3, but vascular endothelial cells and inflammatory cells are negative

have shown that pediatric liposarcoma has a different spectrum of presentation than in adults and MLS has excellent prognosis [3, 5, 8]. Baday et al. performed a literature review investigating the treatment and prognosis of pediatric MLS. They revealed that none of the patients had distant metastasis at presentation, 72.8% of patients underwent resection only, and 6.5% of patients died of disease, which generally occurred in the abdominal and pelvic regions and primary lesions were greater than 5 cm in size [3].

To further investigate the clinicopathological features, treatment strategies, and oncological prognosis of pediatric MLS, we conducted a literature search of articles about MLS in patients aged 12 years or younger published after 1990 [8–18] (Table 1). We identified 2 case series and 9 case reports in which 30 cases of MLS originated in an extremity (n = 22, 73.3%), trunk (n = 3, 10%), omentum (n = 1, 3.3%), or head and neck (n = 4, 13.3%). All patients had low-grade MLS, except for 6 patients for whom histological grade was not described. All but 1 underwent surgery as the primary treatment.

Regarding (neo) adjuvant radiotherapy, recent studies have shown that MLS is more sensitive to radiotherapy than other histological soft tissue sarcoma subtypes [19]. On the other hand, Nishida et al. reported that good local control could be achieved with wide surgical margins without radiotherapy in MLS of the extremity and superficial trunk [20]. Our literature review showed that surgical resection with wide negative margins achieved good local control in children aged 12 years or younger. In addition, a case series reported by Stanelle et al. showed that among 25 pediatric and adolescent patients with MLS, only 8 patients received radiation therapy [21]. A multi-institutional retrospective analysis by Huh et al. showed that among 24 children and young adults with MLS, only 10 received radiation therapy and only 2 out of 24 patients developed recurrence that originated in the abdomen [5]. In another case series by Baday et al., none of the 8 pediatric patients with MLS received radiation therapy [3]. In order to avoid serious late radiation complications, especially in young patients, we recommend that (neo)adjuvant radiotherapy should be used only in patients with unresectable disease, positive margins, or incomplete resection.

The role of chemotherapy as (neo)adjuvant treatment in the management of resectable pediatric MLS has not been clearly defined. Very recently, results of the prospective ARTS0332 study have been reported. The 551 patients with non-rhabdomyosarcoma soft tissue sarcoma younger than 30 years (which included 25 patients with liposarcoma) had undergone risk-based treatment [22]. They defined non-metastatic R0 tumors, low-grade R1 tumors, or high-grade R1 tumors ≤ 5 cm as low risk. It is recommended that most low-risk patients can be cured without adjuvant therapy, thereby avoiding known long-term treatment complications. We considered our patient to be at low risk because she had no metastatic lesions, a small tumor (< 5 cm), and no round cell components. Our patient did not undergo adjuvant therapy. Taking into consideration our patient and those described in other case series, surgical resection without any adjuvant treatment would be recommended, especially in pediatric MLS defined as low risk. Further studies are required to develop the optimal treatment strategy for MLS in children.

Regarding patient surveillance after treatment for MLS, we should take consideration that MLS has a higher propensity for extrapulmonary metastasis [23]. As MLS in our patient had faint FDG accumulation, it has been reported that MLS might present with low FDG uptake [24]. In addition, Sakamoto et al. reported a case of a MLS patient with multiple vertebral metastases not detected with FDG-PET/CT [25]. Taken together, FDG-PET/CT surveillance would be inappropriate for the detection of pediatric MLS, while FDG-PET/CT was ordered and performed by the previous hospital in the current case. We should be concerned about radiation risks to children from medical imaging. Kleinerman reported that we should pay close attention to the possible risk of secondary cancer following diagnostic radiation exposure in children [26]. Stevenson et al. reported whole-body MRI in MLS to detect extrapulmonary metastatic disease [23]. Currently, we have used a surveillance protocol consisting of whole-body MRI and chest x-ray every 6 months.

In conclusion, the present article reports a rare case of MLS in an 11-year old female. MLS typically presents in young adults. However, this tumor can affect younger individuals. Molecular cytogenetic studies to detect *FUS-DDIT3* gene rearrangement are helpful for the diagnosis of MLS. Surgical resection with negative margins is the mainstay of treatment for pediatric patients with MLS. We should be concerned about radiation risks to children from medical imaging and consider a posttreatment surveillance strategy based on a risk-based approach, such as whole-body MRI.

Table 1 Summary of previous cases of patients with myxoid liposarcoma aged 12 years or younger published after 1990

Reference	Year	Age (y)	Sex	Site	Size (cm)	Grade	Surgery	Radiotherapy	CT	Local relapse	Status	Follow-up
Quaglia [15]	1993	0.5	M	Buttock	3	Low grade	Wide local ex	–	–	–	ANED	29.1y
		12	M	Axilla	9	Low grade	Wide local ex	+	for metastases	–	DOD	2y
Miller [16]	1998	9	M	Thigh	10	NA	Complete ex	NA	NA	NA	NA	NA
Ferrari [13]	1999	9	M	Groin	6	Low grade	Radical S	54 Gy	adjuvant	–	CDF	20y
		4	F	Thigh	12	Low grade	Biopsy, non-radical S after CT	–	adjuvant	–	CDF	15y
		5	F	Groin	3	Low grade	Radical S	–	–	–	CDF	12y
		6	F	Thigh	6	Low grade	Radical S	–	adjuvant	–	CDF	11y
		7	M	Thigh	6	Low grade	Radical S	60 Gy	–	Yes, at 43 m	ANED	8y (from 1st S)
		1	M	Groin	3	Low grade	Radical S	–	–	–	CDF	2y
Brookenthal [10]	2003	11	F	Calf	8	Low grade	Wide local ex	–	–	–	CDF	36 m
Alaggio [9]	2009	11	F	Thigh	NA	Low grade	+	NA	NA	–	ANED	24 m
		9	F	Thigh	NA	Low grade	+	NA	NA	–	ANED	120 m
		10	F	Calf	NA	Low grade	+	NA	NA	–	ANED	36 m
		12	F	Inguinal	NA	Low grade	+	NA	NA	NA	Lost	
		7	F	Thigh	NA	Low grade	+	NA	NA	–	ANED	3y
		11	F	Abdomen	NA	Low grade	+	NA	NA	NA	Lost	
		9	F	Tongue	NA	Low grade	+	NA	NA	–	ANED	6y
		11	F	Ankle	NA	Low grade	+	NA	NA	–	ANED	3y
		12	M	Oral cavity	NA	Low grade	+	+	NA	Yes, twice (at 2 and 3 y)	ANED	5y
		12	F	Arm	NA	Low grade	+	NA	NA	–	ANED	1y
		12	M	Leg	NA	Low grade	+	NA	NA	–	ANED	2y
		11	F	Inguinal	NA	Low grade	+	NA	NA	–	ANED	5y
Nichols [17]	2011	9	M	Cheek	3	Low grade	Resection, 5 times	59.4 Gy after 5th surgery	–	multiple	ANED	55 m
De Corti [12]	2012	8	F	Cervicothoracic juncton	NA	NA	Resection	NA	neoadjuvant	–	CR	> 1.5y
Hightower [14]	2014	11	M	Omental	21	NA	+	–	–	NA	Multiple pulmonary nodules, at 6 m	NA
Dall'Igna [11]	2014	12	M	Knee	< 5	NA	+	NA	NA	NA	NA	NA
		12	F	Thigh	> 5, < 10	NA	+	NA	NA	NA	NA	NA
Özşen [18]	2019	12	F	Popliteal fossa	4	NA	+	NA	NA	Yes, at 2y	ANED	NA
Peng [8]	2021	11	F	Waist	NA	Low grade	Complete ex	–	–	–	ANED	32 m
		12	M	Thigh	10	Low grade	Wide ex	–	–	–	ANED	25 m

F Female, *M* Male, *NA* not available, *S* surgery, *ex* excision, *CT* chemotherapy, *y* year, *m* month, *ANED* alive, no evidence of disease, *CDF* continuous disease free, *DOD* dead of disease, *CR* complete remission

Author contributions All listed authors contributed to the original manuscript. TM: is the main orthopaedic oncologist of this case and wrote the manuscript draft. YI: coordinated and completed the manuscript. AM: supported orthopaedic surgical management. YI, KM and MH: supported pathohistological and molecular analyses. All authors have read and approved the manuscript of this case report.

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Data availability The data used to support the findings of this study are available from the corresponding author upon request.

Declarations

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval and consent to participate All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee. For this type of study, formal consent is not required.

Consent for publication Written informed consent was obtained from the patient and her mother. No identifiable information was included in this report.

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