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Short Communication

Soft Tissue Sarcoma in a Malignancy Prone Patient: An Update

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Abstract

It is possible to encounter a patient who might have more than one type of a primary malignant tumor. The literature supports increasing tendencies for subsequent development of malignancies within same individual. A case example of a young woman is given who was diagnosed with a pleomorphic Liposarcoma, while she is been followed up for metastatic ductal breast carcinoma and with a past history of treated acute lymphoblastic Leukemia. As per our review, various associations of malignant conditions are encountered, but are more likely to be metachronous rather than synchronous. The duration between diagnosing a second and third malignancy tends to be relatively short. Soft tissue sarcoma as a synchronous malignancy has been shown to be associated with breast cancer more often. Patients diagnosed with new subsequent malignancy including soft tissue sarcomas must be managed holistically and with full measures; as per current data, their prognosis is not necessarily poorer than regular cancer patients.

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Keywords

Multiple; Malignancy; Cancer; Metachronous; Synchronous Soft tissue; Sarcoma; Liposarcoma

Abbreviations

MPM: Multiple Primary Malignancies; STS: Soft Tissue Sarcoma; LPS: Liposarcoma; MDT: Multidisciplinary Tumor Board; LFS: Li-Fraumeni Syndrome

Introduction

When a patient with more than one type of malignant condition is diagnosed and with history of prior anti-cancer therapy, the complexity involved in treating such an individual can only be left for imagination. The obvious challenge in achieving a diagnosis and differentiating a new entity from a secondary lesion is one side of the coin. The other challenge would be to find an appropriate holistic approach to the patient rather than applying multiple regimens of therapies. The oncology literature has already shown, the risk of developing second primary tumor are on the increase; this is due to:

1. Persisting effects of genetic and behavioral risk factors
2. Long term sequelae of chemotherapy and Radiation
3. Increased diagnostic sensitivity
4. Therapeutic possibilities in the field of oncology

Multiple Primary Malignancies (MPM) at different sites in a patient can be either defined as “Synchronous” when diagnosed in an interval of 6 months, or as “Metachronous” when diagnosed more than 6 months apart. MPM was further elaborated, each tumor must present definite picture of malignancy; must be distinct and the probability of one being metastasis of the other must be excluded [1-4].

Soft Tissue Sarcomas (STS) are reported to account for approximately 1% of all malignant tumors. Consequently, they are thought to be less common type of malignancies in humans. Some types are known to present at older age but others are more common in younger age and children. STS have such a variable spectrum of manifestations, as an example ranging from a slowly growing swelling with a pseudo-capsule or with inflammatory manifestations besides a swelling and in other cases the tumor may even simulate a vascular malformation. Generally, their mode of spread is more of hematogenous, to lesser extent via lymphatics. STS in an extremity have a special mode of spread along fascial planes and tendons.

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Liposarcoma (LPS) is one of the most common STS and accounts for approximately 15-20% of all mesenchymal malignancies. It is a malignant tumor derived from primitive mesenchymal cells that undergo adipose differentiation. The extremities are the most common site, accounting for about 40% of the cases.

In LPS, an association between site of primary tumor and histologic subtypes has been shown. Although all the subtypes occur most commonly in the extremities, a significant proportion of pleomorphic and well-differentiated tumors arise in the retroperitoneum and in other visceral spaces. Histologic grade is one of the most important predictors of outcome. Complete surgical resection remains the mainstay of local therapy, but adjuvant radiation therapy is effective at controlling microscopic residual disease following surgical resection [5-7].

While there have been several reports about the influence of multiple primary malignancies on overall prognosis. However, there have been very few reports about the relationship between one or more preceding primary malignancy and a new primary STS. A case example is presented and relevant significant data are discussed.

Case Presentation

A 31 years old female developed Acute Lymphoblastic Leukemia (ALL) at age of 20. She was treated with allogenic stem cell transplant, the donor being her sister. Apparently, she was considered cured. 8 years later, patient developed an invasive right-side Ductal Breast carcinoma with a relatively large mass and metastases to the ipsilateral axillary nodes, liver, bone, mediastinal nodes and chronic pleural effusion. Patient received multimodality treatments, was regularly followed by medical oncology and considered to be in stable condition. One year later, patient complained of a swelling over her left shoulder which has been very gradually enlarging for about one year (or from the time she was diagnosed with breast cancer) but she did not give much attention initially. However, the swelling accelerated in growth in last few months. In fact, patient was initially only seen by a dermatologist due to overlying dermatitis like condition. Family history did not reveal similar tumors in close relatives.

At her visit to Plastic and reconstructive surgery, the young woman generally seemed doing well, history also revealed secondary amenorrhea, hypothyroidism and backpain. The swelling was about 6x7 cm overlying an area posterior to left deltoid. The overlying skin had intense telangiectasia as well as atrophy but was not tethered to the lesion. The lesion was non-tender, soft, smooth, easily mobile and not attached to muscles (Fig. 1). Axillary lymph nodes were not palpable.

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The ultrasound showed a solid heterogenous lesion with peripheral vascularity, measuring 6.6 x 4.3 x 5.3 cm. The initial impression was that of a lipoma, apart from the patient's positive history of metachronous tumors and the skin changes over the swelling.

It is of significance to add, the fact this patient was seen in July 2020 at the peak of COVID-19 global pandemic, the medical or surgical interventions were quite restricted everywhere. We managed to book an excisional biopsy in about 6 weeks from time of presentation, this was done with a lazy s incision under a local anesthetic. Even intraoperatively, the tumor did not look any different from a routine and common lipoma. Pathologic testing unfortunately came as a high-grade sarcoma, consistent with pleomorphic Liposarcoma.

The case was discussed by the Multidisciplinary Tumor Board (MDT), the consensus was to consider conservative surgical resection, no chemotherapy was advised. Consideration for any radiation was left to be re-evaluated according to postoperative status. Patient already had radiologic finding of metastases from her breast cancer, therefore the MDT did not recommend chasing any mets related to the sarcoma in this metachronous lesions patient.

Within 3 weeks post excisional biopsy, tumor regrowth was evidenced at the scar site as a nodule (Fig. 2) and progressed to a full evolution of the initial mass and beyond within 7 weeks (Fig. 3). MRI could not be done within reasonable time frame due to the pandemic situation, patient was considered to be taken for wide regional resection.

As a Subcutaneous, extra-compartmental and still freely mobile lesion, a wide resection including skin and deep fascia with preservation of Deltoid and Triceps muscles compartment was considered. The defect was reconstructed with a thick split thickness skin graft following a circumferential recruitment of soft tissues (Fig. 4). All margins came as free and final pathologic diagnosis remained same in terms of subtype and grade. Lympho-vascular invasion was not identified.

Patient's early postoperative course was complicated with respiratory failure and need for assisted ventilation, this was related to her pleural effusions, which were treated with chest tubes under suction and monitoring for several days.

Thoracocentesis cytology showed hemorrhagic exudates but repeatedly negative cytology. She was eventually discharged home in stable condition. Patient did receive a course of radiotherapy with interruptions due to her recurrent pleural effusions and she mostly followed pulmonology service. She unfortunately did not survive more than one year following her third primary malignancy and deceased of her pulmonary metastatic disease.

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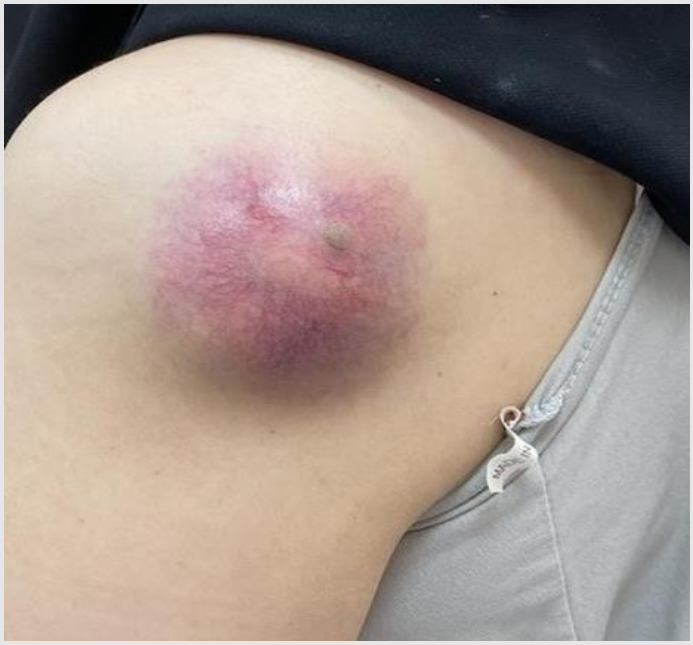

Figure 1: Initial presentation, 31 years old female, with one-year history of a swelling over shoulder, with accelerated growth in last 6 months. One year earlier, patient was diagnosed with metastatic breast cancer. She also had a history of ALL treated at age 20.

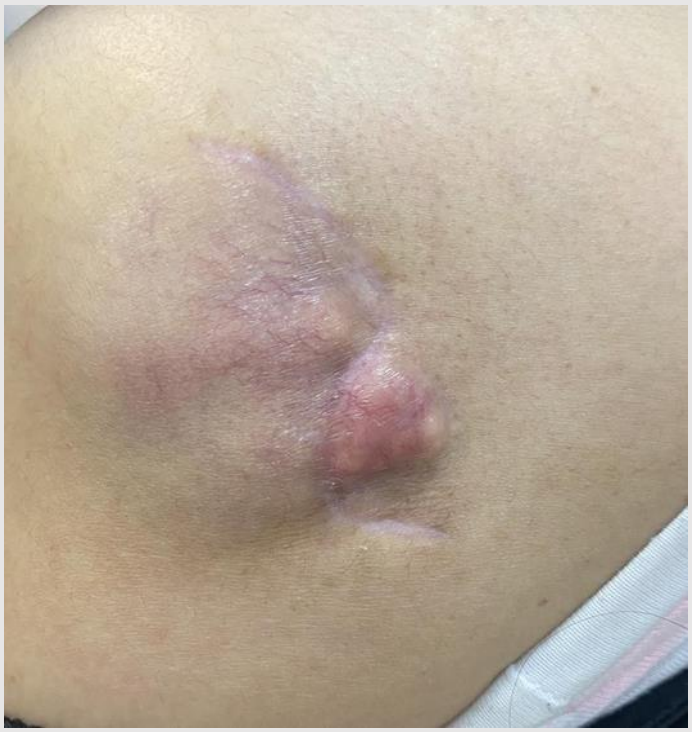

Figure 2: 3 weeks following excisional biopsy and confirmation of Liposarcoma, nodule recurrence within the scar.

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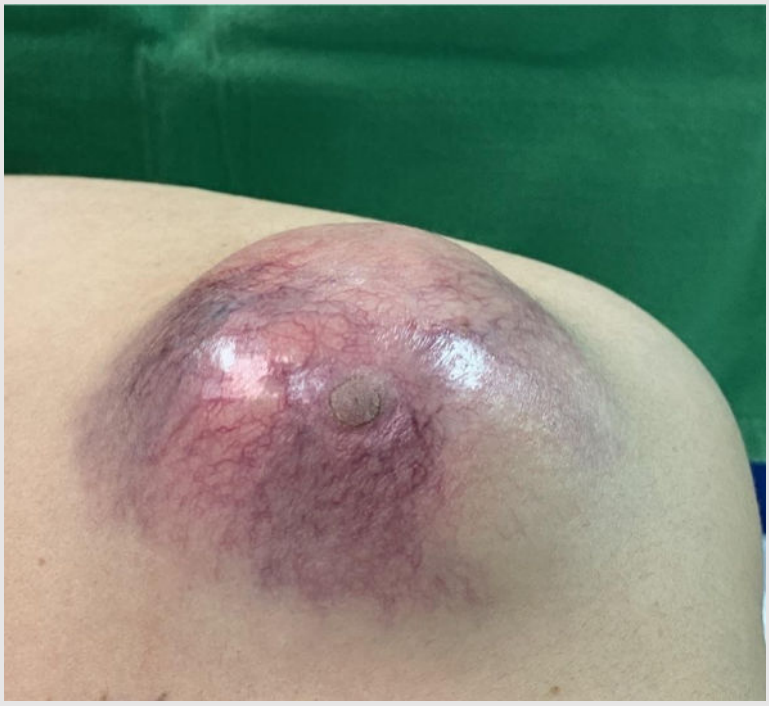

Figure 3: Significant regrowth within 7 weeks and at time of definitive surgical resection.

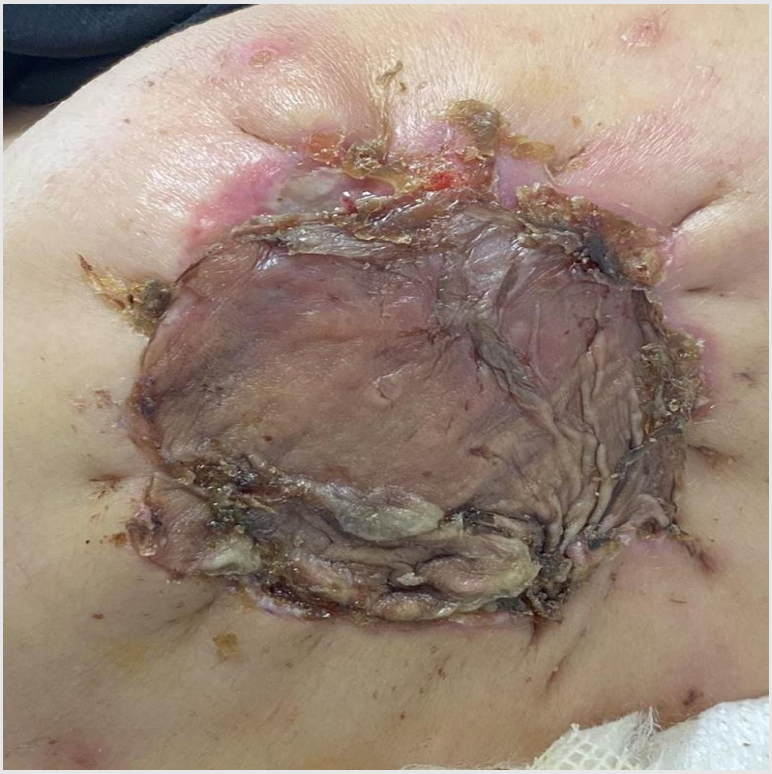

Figure 4: 2 weeks following surgical treatment and coverage with skin graft.

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Discussion

Several factors play a role in the above presented case example and scenario. These include: Genetic aspects; Correlation between multiple primary malignancies and sarcomas; Soft tissue sarcomas; Liposarcoma; and prognostic factors including surgical and other intervention.

1. Genetic aspects

Li and Fraumeni in 1969 described a rare autosomal dominant condition which is usually associated with abnormalities in the tumor suppressor protein P53 gene (TP53) located on chromosome 17p13. The syndrome usually presents with multiple cancers as sarcoma, breast, leukemia and adrenal gland [6,7]. Three genes identified with Li-Fraumeni Syndrome (LFS) Tp53 17p13, 1q23 and checkpoint kinase two genes CHEK2 locus at 22q12.1. In these three genes, TP53 mutations were found to be most common [8]. It is not necessarily that all patients with LFS must have TP53 mutations, it can be due to an alteration in gene promoter which causes defective protein expression. And also, could be due to new mutations that have not been described yet. The criteria for establishing the diagnosis of LFS includes:

1. A sarcoma diagnosed before age 45
2. A first-degree relative, parent, sibling, or child with any cancer before age 45
3. Any cancer before age 45 or a sarcoma at any age in first-degree or second-degree relative (grandparent, aunt/uncle, niece/nephew, or grandchild) [8,9]

2. Multiple primary tumors and Sarcomas

A large-scale and quite a significant study published by Bittorf et al. from Germany in 2001, looked into the data of patients with at least 3 primary malignancies; it included 52,398 cases. In their population, 3.8% of all tumor patients developed at least one further primary. 1% of their patients developed a third primary which corresponded to 2.8% of the 2 tumor patients. The mean age for the first primary was 59 years. The sex predilection was that for males, which was different from other parallel investigation. Synchronous tumors were less common than Metachronous. The interval of 4 years between first and second primary was, on average longer than that between second and third primaries (2.5 years). Types of tumors were mostly urogenital, gynecological and of GI tract [3].

A different large scale review revealed higher incidences of a second new primary in certain kinds of tumors, these included premenopausal women with breast cancer, melanomas, bladder and head and neck cancer patients [10]. Another general review has shown about 17% prevalence of developing further primary malignancy, these patients are usually of Caucasian ancestry, present at earlier stages, they frequently have strong family history of similar cancer and their cancers tend to have an indolent clinical behavior with longer survival rates [11].

Breast ductal cancer has been reported as a metachronous 3- primary tumors in a male patient, with renal cell carcinomas and prostate carcinoma as well [12].

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In terms of hematologic malignancies and granulocytic sarcomas association, a Japanese study looked into adults with acute myeloid leukemia, where an association of 10.4% was found. The remission post therapy and survival rates did not differ but the granulocytic sarcoma patients had much higher relapse rates [13]. Similarly, a vulvar myeloid sarcoma has been reported to be as a presenting picture for an acute myeloid leukemia, a quite rare occurrence [14].

Immunosuppression as results of medical treatment is generally a well- known risk factor for inducing malignancies. One would assume, organ transplanted patients, such as renal transplants on immune suppressants are a high-risk group for developing multiple primary malignancies. In one study, 24 out of 1200 patients developed multiple cancers, the authors indicated these patient's life span was not long enough due to other comorbidities to prove whether they are in high risk for such multiple primaries. [15].

3. Soft Tissue Sarcomas (STS) and Liposarcoma (LPS)

STS in general is such a large and a complex area of research and findings. Unlike carcinomas, the guidelines seem to be much more variable depending on the subtypes and pathological details.

However, they are literally quite malignant set of entities probably more so than carcinomas and requiring much more aggressive resections and other interventions. Ramanathan, et al., proposed a modification to the AJCC staging system for STS of extremities, more importance and details were given to the tumor size:(T1:<5 cm, T2: 5-10 cm, T3: 10-15 cm, T4: > 15 cm) as well to a stage grouping.

An equal significance on the grade and size was shown, which correlated well with prognosis. [16,17]. In a recent review of long- term outcome in LPS of extremity and truncal wall, Goertz et al. indicated that, only the histologic grade was found to be an independent prognostic factor and not the negative margins for overall survival [18].

LPS represents the most common group of all STS in adults. Complete surgical resection remains the mainstay of local therapy, but adjuvant radiotherapy is effective in controlling microscopic residual disease. In the well differentiated LPS, radiation was found ineffective in reducing the time to recurrence but it has been recommended for a patient with recurrent disease [19]. The use of chemotherapy in LPS is more controversial. WHO divides LPS into 5 histologic subtypes: Atypical; Well differentiated; Dedifferentiated; Myxoid; and Pleomorphic. The Atypical and dedifferentiated LPS comprise 50% of all LPS. They are mostly locally aggressive but lack metastatic potential. Pleomorphic LPS on the other hand is the least common, it exhibits an aggressive behavior and significant metastatic potential [20]. Myxoid LPS in extremities, where they tend to be deep seated and when with larger diameters, were found more likely to present with distant metastases [21]. In a large cohort of patients, with extremity LPS, Wortman, et. al., made correlations of MRI findings with pathologic types.

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Among their findings was that Atypical LPS occasionally contained no or little fat on imaging. [22].

When reviewing prognosis of LPS, obviously there are numerous factors need to be taken in consideration [23]. Generally speaking, in an advanced LPS a retrospective study has shown the median survival from diagnosis of inoperable or metastatic LPS was 13 months. In addition, the Myxoid LPS had significantly better overall survival.

Metastectomy of lung lesions when complete excision is possible has also been advocated [24]. LPS in children has a quite different spectrum of presentation compared to adults, the Myxoid type is more common, usually in extremities and has excellent prognosis.

4. Surgical prognostic factors in STS

Surgical treatment of a LPS in extremities follows oncologic principles. Measurable distance guidelines that could be followed do not truly exist, the extent of resection remains controversial. Surgical treatment should be aimed at minimizing local recurrence and to preserve function. A functional compartmental resection in STS when tumor is limited within one compartment has been advocated, particularly in quadriceps and buttocks. Encouraging results with such approach were reported in terms of ability to return to work [25].

In cases of atypical lipomatous tumors, which are often intra- muscular, the resection is usually un-complicated. Higher grade Myxoid round cell type and Pleomorphic liposarcomas might require resection of entire muscle groups to ensure adequate margins.

Pleomorphic LPS entity is an uncommon, the median age for it is 54 years, with predilection in lower extremity followed by upper extremity followed by other sites. Its median size at presentation is about 8 cm. Majority were identified as Sub-facial followed by Sub- cutaneous or dermal location, in which case the metastases were found only in 3.5% [26].

Whether antecedent primary malignancy has an impact on the prognosis of STS, Torigoe, et. al., in a recent study, studied 21 cases of extremity STS in association with an antecedent tumor of solid organs, 6 of which were breast cancers (the most common). These were compared with170 cases of STS only. The 5-year survival was not significantly different and overall, they concluded, an antecedent primary tumor in STS patients would not be considered a negative prognostic factor in their practice [27].

The unfortunate young female patient presented above with the uncommon pleomorphic type LPS was our trigger behind this review. Oncologic and Reconstructive surgeons are prone to confront such an occasional scenario, we felt the need for update was there. It is obvious, the review is quite diverse in terms of pathologies, prognostic factors and in terms of geographical, ethnic and practice related elements. Denial and or neglect with late presentation (which was noted with the 2nd and 3rd primaries in our case) is probably a common and expected

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phenomenon. We believe each patient must be given full attention with involvement of MDT and plans tailored accordingly. Soft tissue tumors with otherwise classic benign physical features in a patient with history of antecedent malignancy, must be biopsied on urgent basis.

Conflict of Interest

It is stated that there are no conflicts of interest.

References

1. Warren S and Gates O. Mutiple primary malignant tumors. A survey of the literature and a statistical study. Am J Cancer. 1932;16:1358-414.
2. Vogt A, Schmid S, Heinimann K, Frick H, Herrmann C, Cerny T, et al. A. Multiple primary tumours: challenges and approaches, a review. ESMO Open. 2017;2(2):e000172.
3. Bittorf B, Kessler H, Merkel S, Brückl W, Wein A, Ballhausen WG, et al. Multiple primary malignancies: An epidemiological and pedigree analysis of 57 patients with at least three tumours. Eur J Surg Oncol. 2001;27(3):302-13.
4. Huh WW, Yuen C, Munsell M. Liposarcoma in children and young adults: a multi-institutional experience. Pediatr Blood Cancer. 2011;57(7):1142-6.
5. Waters R, Horvai A, Greipp P. Atypical lipomatous tumour/well-differentiated liposarcoma and de-differentiated liposarcoma in patients aged ≤ 40 years: a study of 116 patients. Histopathol. 2019;75(6):833-42.
6. Li FP, Fraumeni JF. Soft-tissue sarcomas, breast cancer and other neoplasms. A familial syndrome? Ann Internal Med. 1969;71:747-52.
7. Li FP, Fraumeni JF, Mulvihill JJ, Blattner WA, Dreyfus MG, Tucker MA, et al. A cancer family syndrome in twenty- four kindreds. Cancer Res. 1988;48:5358-62.
8. Doyle MR, Johnston JM. A novel p.Gly187Arg TP53 variant appears to result in Li-Fraumeni syndrome. Pediatr Hematol Oncol. 2018;35(3):203-7.
9. Vogel WH. Li-Fraumeni Syndrome. J Adv Pract Oncol. 2017;8(7):742-6.
10. Coyte A, Morrison DS, McLoone P. Second primary cancer risk the impact of applying different definitions of multiple primaries: results from a retrospective population-based cancer registry study. BMC Cancer. 2014;14:272.
11. Amer MH. Multiple neoplasms, single primaries and patient survival. Cancer Manag Res. 2014;6:119-34.
12. Zargar-Shoshtari MA, Saffari H, Moslemi MK. Metachronous occurrence of triple malignancies of kidneys, prostate and breast. A case report and review of the literature. Case Rep Urol. 2013;2013:194620.
13. Shimizu H, Saitoh T, Hatsumi N, Takada S, Yokohama A, Handa H, et al. Clinical significance of granulocytic sarcoma in adult patients with acute myeloid leukemia. Cancer Sci. 2012;103(8):1513-7.
14. Zhang X, Huang P, Chen Z, Bi X, Wang Y, Wu J. Vulvar myeloid sarcoma as the presenting symptom of acute myeloid leukemia: a case report and literature review of Chinese patients, 1999-2018. Diagn Pathol. 2019;14(1):126.
15. Santangelo ML, Criscitiello C, Renda A. Immunosuppression and multiple primary malignancies in kidney-transplanted patients: a single-institute study. Biomed Res Int. 2015;2015:183523.
16. Ramanathan RC, A'Hern R, Fisher C, Thomas JM. Modified staging system for extremity soft tissue sarcomas. Ann Surg Oncol. 1999;6(1):57-69.
17. Cates JMM. The AJCC 8th Edition staging system for soft tissue sarcoma of the extremities or trunk: a cohort study of the SEER database. J Natl Compr Canc Netw. 2018;16(2):144-52.
18. Goertz O, Pieper A, Lauer H. Long-term outcome of 181 patients with liposarcomas of the extremity and truncal Wall. Anticancer Res. 2019;39(10):5747-53.
19. Fonseca AL, Roland CL, Cormier JN, Torres KE, Hunt KH, Bishop AJ, et al. Radiation and its impact on local recurrence in extremity and trunk well- differentiated liposarcomas. Am Surg. 2019;85(1):52-8.

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20. Hornick JL, Bosenberg MW, Mentzel T, McMenamin ME, Oliveira AM, Fletcher CD. Pleomorphic liposarcoma: clinicopathologic analysis of 57 cases. Am J Surg Pathol. 2004;28(10):1257-67.
21. Zheng K, Yu XC, Xu M, Yang Y. Surgical outcomes and prognostic factors of myxoid liposarcoma in extremities: a retrospective study. Orthop Surg. 2019;11(6):1020-8.
22. Wortman JR, Tirumani SH, Jagannathan JP, Tirumani H, Shinagare AB, Hornick JL, et al. Primary extremity liposarcoma: mri features, histopathology and clinical outcomes. J Comput Assist Tomogr. 2016;40(5):791-8.
23. Goertz O, Pieper A, Lauer H. Long-term outcome of 181 patients with liposarcomas of the extremity and truncal wall. Anticancer Res. 2019;39(10):5747-53
24. Langmans C, Cornillie J, van Cann T. Retrospective analysis of patients with advanced liposarcoma in a tertiary referral center. Oncol Res Treat. 2019;42(7-8):396-404.
25. Pitcher ME, Thomas JM. Functional compartmental resection for soft tissue sarcomas. Eur J Surg Oncol. 1994;20(4):441-5.
26. Nassif NA, Tseng W, Borges C, Chen P, Eisenberg B. Recent advances in the management of liposarcoma. F1000Res. 2016;5:2907..
27. Torigoe T, Imanishi J, Yazawa Y, Kadono Y, Oda H. The impact of antecedent primary malignancy in soft tissue sarcoma patients. J Orthop Surg (Hong Kong). 2019;27(2):2309499019838124.

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