Solitary Breast Metastasis of the Lower Extremity Malignant Fibrous Histiocytoma: Report of a Case and Review of the Literature

Alt Ekstremite Yerleşimli Malign Fibröz Histiositomanın Soliter Meme Metastazı: Olgu Sunumu ve Literatür Derlemesi

Mustafa ADLI, MD,[a]
H. Mehmet TÜRK, MD,[b]
Mehmet E. KALENDER, MD,[b]
Ediz TUTAR, MD,[c]
Ahmet DİRİER, MD[a]

[a]Department of Radiation Oncology,
[b]Division of Medical Oncology,
Department of Internal Medicine,
[c]Department of Pathology,
Gaziantep University Faculty of Medicine, Gaziantep

This case was presented in the 9th National Breast Diseases Congress; 5-8 September 2007, Ankara, Turkey

Geliş Tarihi/*Received:* 13.06.2008
Kabul Tarihi/*Accepted:* 22.09.2008

Yazışma Adresi/*Correspondence:*
Mustafa ADLI, MD
Gaziantep University
Faculty of Medicine
Department of Radiation Oncology,
Gaziantep,
TÜRKİYE/TURKEY
adli@gantep.edu.tr

ABSTRACT Malignant fibrous histiocytoma (MFH) is the most common soft tissue sarcoma in adults and its distant metastases most commonly occur in the lung, bone and liver. However, breast metastases of this tumor are extremely rare. A 67-year-old woman presented with a single left breast mass as the only metastasis two years after the initial surgery of the MFH of lower extremity. A mass had appeared below her right knee 32 months before she recognized her breast mass, and she had undergone surgery for it 8 months later. The patient is alive and disease-free 59 months after the lower leg surgery and 31 months after the breast surgery. Despite several reports of primary breast MFH cases, only three cases of breast metastasis have been reported in the literature. Breast metastases from extra mammary malignancies are also rare. However, no report of isolated breast metastasis is present in the medical literature. This is the first case of solitary breast metastasis of the MFH, reported with all clinical, radiological and histological details, in English literature to our best knowledge. Malignant fibrous histiocytoma may present as a solitary breast metastasis as the first site of metastasis. Breast metastasis should be kept in mind in a patient with MFH diagnosis presenting with solitary breast mass.

Key Words: Sarcoma; histiocytoma, malignant fibrous; breast; neoplasm metastasis; solitary fibrous tumors

ÖZET Malign fibröz histiositoma (MFH), erişkinlerde en sık görülen yumuşak doku sarkomu alt grubudur ve sırasıyla en sık akciğer, kemik ve karaciğere metastaz yapar. Bununla birlikte, bu tümörün meme metastazı çok nadir görülür. Altmış yedi yaşında bir kadın hasta, alt ekstremitede MFH nedeni ile yapılan operasyondan 2 yıl sonra sol memede kitle şikâyetiyle bize başvurdu. Hasta, memedeki kitle saptanmadan 32 ay önce sağ diz altında bir kitlenin ortaya çıktığını ve kitle saptadıktan 8 ay sonra opere olduğunu belirtti. Hasta son takibinde; ilk ekstremite operasyonundan itibaren 59 ay ve meme operasyonundan itibaren 31 ay sonra, hastalıksız olarak hayattadır. Primer meme MFH olguları çok sayıda bildirilmekle birlikte, MFH'nin meme metastazı literatürde sadece 3 olgu ile sınırlıdır. Meme dışı malignitelerin memeye metastazları da çok nadirdir. Bununla birlikte, izole meme metastazı tıbbi literatürde bildirilmemiştir. Bu vaka tüm klinik, radyolojik ve histolojik detayları ile bildirilen ilk MFH'nin meme metastazı olgusudur. MFH'nin ilk metastazı solid meme metastazı şeklinde saptanabilir. MFH tanısı konmuş ve memede kitle saptanan hastalarda MFH'nin meme metastazı olabileceği akılda tutulmalıdır.

Anahtar Kelimeler: Sarkom; malign fibröz histiositoma; meme; metastaz; soliter

Turkiye Klinikleri J Med Sci 2009;29(5):1320-5

Soft tissue sarcomas (STSs) are rare tumors, accounting for less than 1% of all cancers.[1] MFH is the most common STS in older adults and its distant metastases most commonly occur in the lung, bone and liver.[2] Although it is rare, breast metastases of the MFH were reported before.[3,4]

However any report of solitary breast metastasis is not present in the literature.

A case of isolated metastatic breast MFH is presented with all clinical, radiological, and histological details.

CASE REPORT

A 67-year-old woman who had been treated for malignant fibrous histiocytoma of the lower leg more than two years ago, presented to the hospital with a painful mass in her left breast for a month. She had undergone coronary angiography a couple of months ago for coronary artery disease. She had no family history of breast cancer or any other malignancies.

She had felt a mass below her right knee 32 months before she recognized a mass in her breast, and had undergone surgery for it 8 months later. Her right leg MRI reported, "50 x 30 mm contrast enhanced solid mass with well-defined lobulated contours, located in proximal antero-medial part of the right tibia" (Figure 1). Exploration had revealed a capsulated, highly vascularized mass invading the periosteum and eroding the bone and total excision had been performed. Pathological examination showed a 5 x 4 x 4 cm gray-brown and in many areas yellow-white solid mass with cystic formation. Histological examination showed atypical, pleomorphic spindled cells and bizarre giant cells with high mitotic activity, necrosis and in some areas myxoid degeneration (Figure 2). Surrounding fat tissue was infiltrated by the tumor. The pathological diagnosis was "pleomorphic malignant fibrous histiocytoma". Surgical margins were not reported. She had received 50 Gy postoperative radiotherapy to the right lower leg, but no adjuvant chemotherapy.

The patient was free of local recurrence and there was no evidence of distant metastases at her abdominal CT and bone scans, which were performed at postoperative 14 months.

The patient admitted to the hospital with a mass in her left breast 14 months after the operation for pleomorphic malignant fibrous histiocytoma. Physical examination showed a 3 x 3 cm, painful, firm mass located in the sub-areolar area of the left breast. Left nipple was minimally retracted at inspection. There was no palpable axillary lymph node. Right breast examination was normal.

Mammography revealed a 3.5-4 cm, lobulated, high density mass located in the lower-outer quadrant of the left breast, close to the midline (Figure 3). Middle border of the mass was well circumscribed; however, other borders were ill defined. Microcalcifications were not observed. No abnormalities were reported in the right breast.

Breast ultrasonography (US) showed a 33 x 17 x 35 mm hypoecoic solid lesion with macro- and micro-lobulation located in the lower-outer quadrant of the left breast. No lymph nodes were defined in either mammogram or the US.

Fine needle aspiration biopsy and incisional

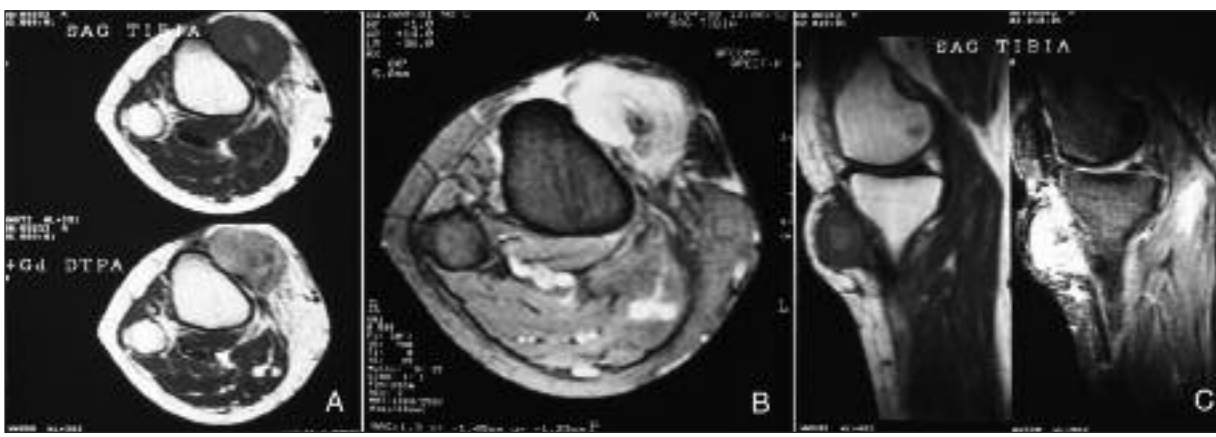

FIGURE 1: MRI of the leg mass (A, B: axial, C: sagittal views).

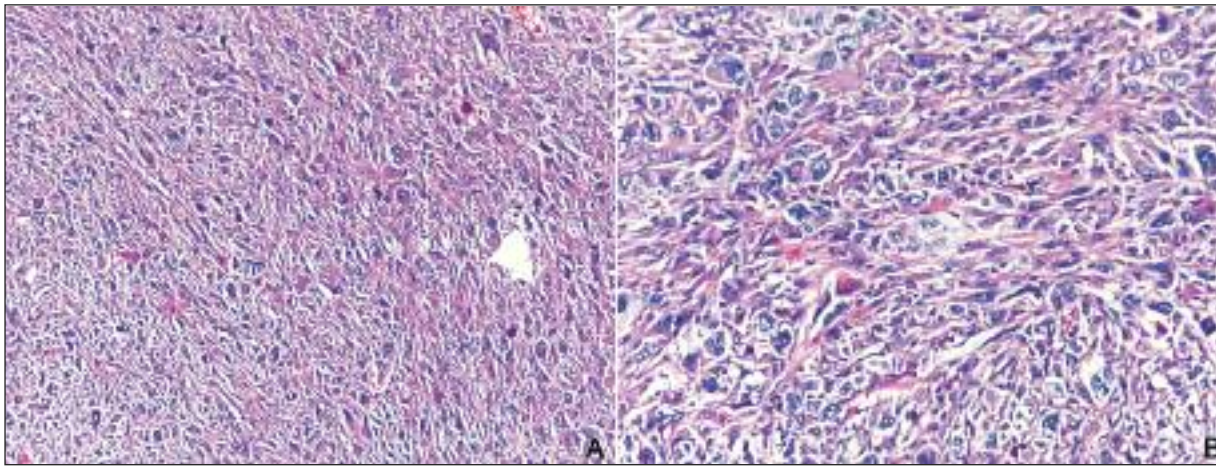

FIGURE 2: Microscopic findings of the leg mass. Low power (A, HE, x 100) and high power (B, HE, x 200) examinations.

biopsy of the breast mass revealed malignant tumor. No metastases were detected with chest X-ray or abdominal US. Modified radical mastectomy and axillary dissection was performed. Pathology reported a capsulated 2.7 x 2.2 x 3.5 cm white-gray mass. Histological examination showed pleomorphic round and spindled cells, with high mitotic activity and necrosis, reported to be consistent with leiomyosarcoma (Figure 4). No tumor was detected in any of the 28 axillary lymph nodes dissected.

Histopathological examination revealed spindle cells forming giant cells with high mitotic activity and necrosis consistent with high-grade malignant fibrous histiocytoma.

The results of the pathological examination of the masses were similar for breast and lower leg masses. No local or distant recurrences were detected by physical examination and radiological imaging. The patient was free of any other metastases with chest and abdominal-pelvic computed tomography scans and right breast US.

She received six cycles of adjuvant chemotherapy consisting of ifosfamide (5000 mg/m²), mesna (5000 mg/m²) and adriamycine (50 mg/m²) for "solitary breast metastasis of malignant fibrous histiocytoma".

The patient is alive and disease-free 59 months after the lower leg surgery and 31 months after the breast surgery at the last follow-up visit.

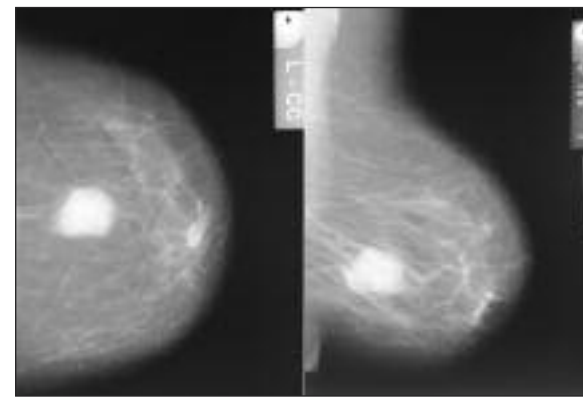

FIGURE 3: Left breast mammography images (L-CC: Left cranio-caudal, L-MLO: Left medio-lateral oblique).

REVIEW

The current case, a 67-year-old woman, presented with a solitary breast mass as the only metastasis of the lower leg MFH, two years after the surgery for leg mass.

Non-mammary breast metastases are very rare, accounting for less than 0.5% of total breast malignancies.[5] STSs are the third most common source of blood-borne metastases to the breast, following melanoma and lung cancer.[6] MFH is the most common STS in late adult life and it most commonly affects the lower extremity.[7] Distant metastasis rate is high and most commonly occurs in the lung, bone and liver.[2,7] Breast metastasis of the MFH is extremely rare. Despite several reports

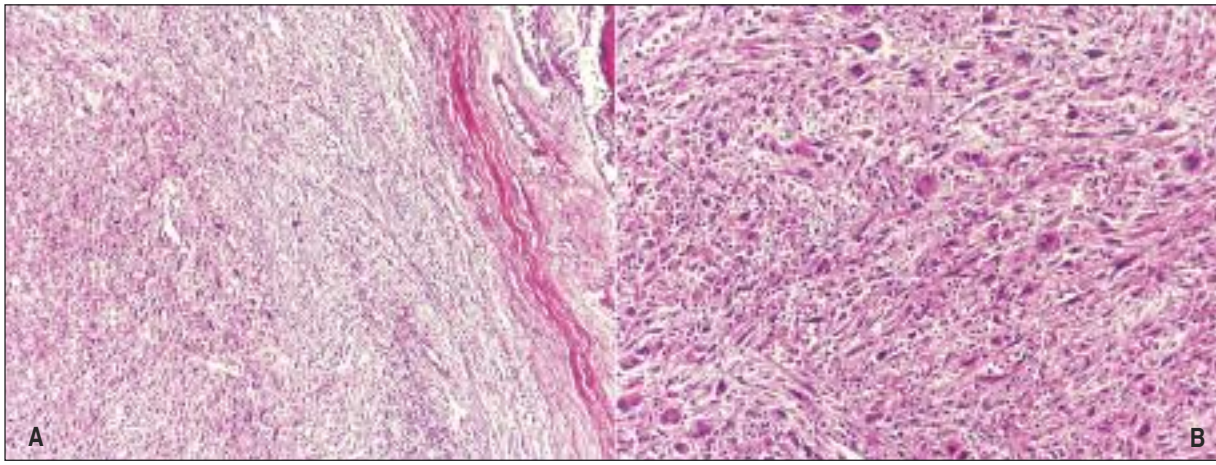

FIGURE 4: Microscopic findings of the breast mass. Low power (A, HE, x 100) and high power (B, HE, x 200) examinations.

of primary breast MFH cases only three cases of metastatic breast MFH were reported.[3,4,8-12] However, no report of isolated breast metastasis is present in the medical literature. One of the three metastatic breast MFH cases found in the literature was reported by Rao et al, a 41-year old female with MFH of the buttock with pulmonary and breast metastases.[3] The other two cases were reported by Shukla et al, a 45-year old female with MFH of the thigh with a 4 cm, and a 39-year old female with MFH of the hip with a 2 cm metastatic breast mass.[4] No further clinical detail on whether any of these metastases was isolated was available in the study published by Shukla et al.

Although most are sporadic, some STSs may develop after radiation therapy.[13] Breast/chest wall sarcomas are slightly more common in patients treated with radiation for breast cancer.[14] Taghian et al reported 11 sarcomas following irradiation of breast, five of which were MFH.[15] Radiation induced MFH of the breast following breast conserving therapy was also reported.[16-18]

Patients with breast metastasis may present with various symptoms. Presentation with pain, tenderness, and discharge is unusual.[19] Toombs et al in a large series of metastatic breast tumors, which includes 43 sarcoma cases, reported that most of the patients with breast metastasis presented with solitary discrete lesions.[19] They did not describe nipple retraction in any of the patients. The present case presented with a painful solitary breast mass and nipple retraction was noted in the affected breast, although it was not infiltrated by the tumor histologically.

Radiologic imaging of metastatic breast tumors may show variations and may not represent characteristic features of the primary breast tumors. Bohman et al reported that metastatic breast tumors were well circumscribed, not associated with microcalcifications or secondary skin or nipple changes in mammography and exhibited unusual rapid growth.[20] Lee et al concluded that metastatic tumors to the breast appeared as relatively small, superficially located, poorly defined, irregular nodules without calcification on mammography and US.[21] Yao et al reported US findings of a primary breast MFH case; the tumor was well demarcated with cystic and solid components.[11] Mammographic imaging of the present case showed a lobulated, high-density mass with some ill-defined borders. There was no associated microcalcification. Breast US showed a hypoecoic solid lesion with macro- and micro-lobulations.

MFH shows a broad range of histologic appearances and is divided into storiform-pleomorphic, myxoid, giant cell and inflammatory subtypes.[22,23] Most MFHs are descriptively termed as storiform-pleomorphic type.[23] Histologically, MFH consists of spindly fibroblasts with bizarre, multi-nucleated giant cells.[24] The cells are typically

arranged in a storiform pattern radiating out from a central point.

MFH histologically can resemble a pleomorphic variant of leiomyosarcoma in some cases, as in the present case.[24] Alvegard and Berg in their series of 240 high-grade STSs, reclassified three cases of leiomyosarcoma as MFH and indicated that the myofibroblastic parts of an MFH tumor might be similar to a leiomyosarcoma; thus, the differential diagnosis might be difficult.[25] Breast mass of the present case was diagnosed initially as leiomyosarcoma; however, review of the pathology revealed malignant fibrous hystiocytoma.

Pathological review of the leg and breast masses of the present case revealed similar histologies and both tumors were considered identical. However, since the breast mass was solitary and no other metastatic lesion was detected elsewhere, it is impossible to rule out primary breast MFH in this case.

Several factors such as large tumor size (≥5 cm), presence of necrosis, high grade, deep tumor location, and non-myxoid histology were shown to be adverse prognostic factors in patients with MFH.[26-29] The present case had a 5 cm, deeply located, high-grade initial tumor with necrosis and myxoid histology.

Although no data is available for breast metastases, treatment of the isolated pulmonary STS metastases is excision of the metastasis if the primary tumor is controlled.[30-32] Gadd et al reported a median survival of 19 months and a 3-year survival rate of 23% after complete resection in their study with 65 extremity STS patients with isolated pulmonary metastases treated surgically.[31] If adequate margins are achieved, local control is possible with mastectomy alone for primary breast sarcomas.[33] Although it is higher in some histologic types, such as epitheloid sarcoma and rhabdomyosarcoma, at presentation overall only 2.7% of the sarcomas metastasize to the lymph nodes.[34] Thus, lymph node dissection increases morbidity and is not suggested in sarcoma patients with clinically negative lymph nodes.

The role of chemotherapy is not well established in metastatic MFH. Chemotherapy is palliative for most patients with unresectable or metastatic STS. Response rate of advanced STS to chemotherapy was reported to be not more than 30%.[35,36] Edmonson et al in their randomized study of 279 advanced STS patients treated with chemotherapy reported an objective regression rate of 33% in 36 MFH cases.[35] However, less than 20% of the MFH patients survived more than 18 months in this study. In a large European Organization for Research and Treatment of Cancer (EORTC) study, Santoro et al reported an overall response rate of 25% and a 2-year survival rate of around 20% for single agent and combination chemotherapy arms in advanced STS patients.[36]

CONCLUSION

Soft tissue sarcomas of the breast are very rare and many of them are primary tumors. Breast metastases from extra mammary malignancies are also rare. Breast may be the first and the only site of metastasis in patients with MFH. Breast metastasis should be kept in mind in a patient with MFH diagnosis presenting with solitary breast mass.

REFERENCES

1. Jemal A, Siegel R, Ward E, Murray T, Xu J, Smigal C, et al. Cancer statistics, 2006. CA Cancer J Clin 2006;56(2):106-30.
2. Potter DA, Glenn J, Kinsella T, Glatstein E, Lack EE, Restrepo C, et al. Patterns of recurrence in patients with high-grade soft-tissue sarcomas. J Clin Oncol 1985;3(3): 353-66.
3. Rao UN, Hanan SH, Lotze MT, Karakousis CP. Distant skin and soft tissue metastases from sarcomas. J Surg Oncol 1998;69(2):94-8.
4. Shukla R, Pooja B, Radhika S, Nijhawan R, Rajwanshi A. Fine-needle aspiration cytology of extramammary neoplasms metastatic to the breast. Diagn Cytopathol 2005;32(4):193-7.
5. Georgiannos SN, Chin J, Goode AW, Sheaff M. Secondary neoplasms of the breast: a survey of the 20th Century. Cancer 2001;92(9): 2259-66.
6. Paulus DD, Libshitz HI. Metastasis to the breast. Radiol Clin North Am 1982;20(3):561-8.
7. Weiss SW, Enzinger FM. Malignant fibrous histiocytoma: an analysis of 200 cases. Cancer 1978;41(6):2250-66.
8. Langham MR Jr, Mills AS, DeMay RM, O'-Dowd GJ, Grathwohl MA, Horsley JS 3rd. Malignant fibrous histiocytoma of the breast. A case report and review of the literature. Cancer 1984;54(3):558-63.

9. Polinari U, D'ugo D, Di Folco S, Scambia G, Sica G. Malignant fibrous histiocytoma. Report of a case and review of the literature. Eur J Gynaecol Oncol 1985;6(2):105-8.
10. Tamir G, Nobel M, Hauben DJ, Sandbank J. Malignant fibrous histiocytoma of the breast. Eur J Surg Oncol 1995;21(2):210-1.
11. Yao MS, Chan WP, Chen CY, Chu JS, Hsieh MC. Malignant fibrous histiocytoma of the female breast: a case report. Clin Imaging 2005;29(2):134-7.
12. De Cesare A, Fiori E, Burza A, Ciardi A, Bononi M, Izzo L, et al. Malignant fibrous histiocytoma of the breast. Report of two cases and review of the literature. Anticancer Res 2005;25(1B):505-8.
13. Brady MS, Gaynor JJ, Brennan MF. Radiation-associated sarcoma of bone and soft tissue. Arch Surg 1992;127(12):1379-85.
14. Huang J, Mackillop WJ. Increased risk of soft tissue sarcoma after radiotherapy in women with breast carcinoma. Cancer 2001;92(1): 172-80.
15. Taghian A, de Vathaire F, Terrier P, Le M, Auquier A, Mouriesse H, et al. Long-term risk of sarcoma following radiation treatment for breast cancer. Int J Radiat Oncol Biol Phys 1991;21(2):361-7.
16. Mason RW, Einspanier GR, Caleel RT. Radiation-induced sarcoma of the breast. J Am Osteopath Assoc 1996;96(6):368-70.
17. Horii R, Fukuuchi A, Nishi T, Takanashi R. A case of malignant fibrous histiocytoma after breast conserving therapy for breast cancer. Breast Cancer 2000;7(1):75-7.
18. Kirova YM, Vilcoq JR, Asselain B, Sastre-Garau X, Fourquet A. Radiation-induced sarcomas after radiotherapy for breast carcinoma: a large-scale single-institution review. Cancer 2005;104(4):856-63.
19. Toombs BD, Kalisher L.Metastatic disease to the breast: clinical, pathologic, and radiographic features. AJR Am J Roentgenol 1977; 129(4):673-6.
20. Bohman LG, Bassett LW, Gold RH, Voet R. Breast metastases from extramammary malignancies. Radiology 1982;144(2):309-12.
21. Lee SH, Park JM, Kook SH, Han BK, Moon WK. Metastatic tumors to the breast: mammographic and ultrasonographic findings. J Ultrasound Med 2000;19(4):257-62.
22. Weiss SW. Malignant fibrous histiocytoma. A reaffirmation. Am J Surg Pathol 1982; 6(8):773-84.
23. Weiss SW, Goldblum JR. Malignant fibrohistiocytic tumors. In: Weiss SW, Goldblum JR, eds. Enzinger and Weiss's Soft Tissue Tumors. 4th ed. St. Louis, MO: C V Mosby; 2001. p. 535-69.
24. Rosenberg AE. Bones, joints, and soft tissue tumors. In: Kumar V, Fausto N, Abbas A, eds. Robbins & Cotran Pathologic Basis of Disease. 7th ed. Philadelphia, PA: W B Saunders, 2004. p. 1273-324.
25. Alvegård TA, Berg NO. Histopathology peer review of high-grade soft tissue sarcoma: the Scandinavian Sarcoma Group experience. J Clin Oncol 1989;7(12):1845-51.
26. Engellau J, Anderson H, Rydholm A, Bauer HC, Hall KS, Gustafson P, et al. Time dependence of prognostic factors for patients with soft tissue sarcoma: a Scandinavian Sarcoma Group Study of 338 malignant fibrous histiocytomas. Cancer 2004;100(10):2233-9.
27. Weitz J, Antonescu CR, Brennan MF. Localized extremity soft tissue sarcoma: improved knowledge with unchanged survival over time. J Clin Oncol 2003;21(14):2719-25.
28. Salo JC, Lewis JJ, Woodruff JM, Leung DH, Brennan MF. Malignant fibrous histiocytoma of the extremity. Cancer 1999;85(8):1765-72.
29. Zagars GK, Mullen JR, Pollack A. Malignant fibrous histiocytoma: outcome and prognostic factors following conservation surgery and radiotherapy. Int J Radiat Oncol Biol Phys 1996;34(5):983-94.
30. Putnam JB Jr, Roth JA, Wesley MN, Johnston MR, Rosenberg SA. Analysis of prognostic factors in patients undergoing resection of pulmonary metastases from soft tissue sarcomas. J Thorac Cardiovasc Surg 1984; 87(2):260-8.
31. Gadd MA, Casper ES, Woodruff JM, McCormack PM, Brennan MF. Development and treatment of pulmonary metastases in adult patients with extremity soft tissue sarcoma. Ann Surg 1993;218(6):705-12.
32. van Geel AN, Pastorino U, Jauch KW, Judson IR, van Coevorden F, Buesa JM, et al. Surgical treatment of lung metastases: The European Organization for Research and Treatment of Cancer-Soft Tissue and Bone Sarcoma Group study of 255 patients. Cancer 1996;77(4):675-82.
33. Pollard SG, Marks PV, Temple LN, Thompson HH. Breast sarcoma. A clinicopathologic review of 25 cases. Cancer 1990;66(5):941-4.
34. Fong Y, Coit DG, Woodruff JM, Brennan MF. Lymph node metastasis from soft tissue sarcoma in adults. Analysis of data from a prospective database of 1772 sarcoma patients. Ann Surg 1993;217(1):72-7.
35. Edmonson JH, Ryan LM, Blum RH, Brooks JS, Shiraki M, Frytak S, et al. Randomized comparison of doxorubicin alone versus ifosfamide plus doxorubicin or mitomycin, doxorubicin, and cisplatin against advanced soft tissue sarcomas. J Clin Oncol 1993;11(7): 1269-75.
36. Santoro A, Tursz T, Mouridsen H, Verweij J, Steward W, Somers R, et al. Doxorubicin versus CyVADIC versus doxorubicin plus ifosfamide in first-line treatment of advanced soft tissue sarcomas: a randomized study of the European Organization for Research and Treatment of Cancer Soft Tissue and Bone Sarcoma Group. J Clin Oncol 1995;13(7): 1537-45.