AXILLA LEIOMYOSARCOMA IN PATIENT WITH BREAST CANCER AND LEIOMYOSARCOMA OF THE LEG. CASE REPORT

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Abstract

We report a case of a woman, 46 years old with leiomyosarcoma of the axilla.

In the 2006 the patient was underwent to left breast quadrantectomy and axillary dissection for cancer, chemotherapy and radiotherapy.

In the 2010 the patient was underwent to excision of the primary leiomyosarcoma in the hid left leg.

The histological diagnosis of a cutaneous leiomyosarcoma was established.

In the 2015 the patient presented with a painful nodule in the left axilla increasing in size for few months.

Introduction

Cutaneous soft-tissue sarcomas are rare tumors and account for fewer than 1% of all soft-tissue malignancies. They most commonly affect Caucasian men, with a peak incidence in the 5th and 6th decades of life. These tumors present as solitary, erythematous, or brownish well-circumscribed dermal nodules ranging in size from 0.5 to 3 cm. Because they are dermal-based tumors, they may appear fixed to the epidermis and ulceration may be present.20 The lower extremities and head and neck locations are the most common sites of involvement as identified in the literature. Preoperative staging with cross-sectional imaging (CT of the thorax, PET imaging, or both) appeared to add minimal clinical impact as more than one-half of the patients in this series underwent imaging. Imaging results for all patients were negative. The utility of preoperative staging for cutaneous leiomyosarcoma has not been previously described in the literature. (1)

Case report

A 46 years old woman patient presented with a painful in the left axilla.

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In the 2010 the patient was underwent to excision of the primary leiomyosarcoma in the hid left leg. The histological diagnosis of a cutaneous leiomyosarcoma was established.

On palpation, an irregular, firm, tender exphthitic swelling, measuring 6 cm x 5 cm x 3.5 cm with overlying skin showing ulcerations. There were no signs of infection and the overlying skin was normal. The remainder of the clinical examination was normal. Lymph nodes were not palpable. A surgical resection with wide margins of at least 2 cm was performed. Histopathological examination revealed a leiomyosarcoma G2-G3. The surgical margins were free of disease. On a detailed immunohistochemical analysis, the tumor cells were intensely positive for smooth muscle actin (SMA), moderately positive for desmin, vimentin and CD68. (Fig. 1-2)
Discussion
Cutaneous leiomyosarcoma (CLM) is a very rare smooth muscle tumor arising from the dermis or subcutaneous tissue in the skin. Generally, superficial leiomyosarcomas occur as a solitary, slowly growing lesion most commonly on proximal extremities, which coincide with the hair bearing areas. It may also occur anywhere on the body, the existing cases being reported on the face and trunk. Only 10-15% of the subcutaneous leiomyosarcomas arise in the trunk. CLM presents in persons of all ages but with a peak between 60-70 years old. Preoperative misdiagnosis is common because it is a rare malignant tumor. The etiology of these tumors is relatively unknown, although ionizing radiation, sunlight, antecedent traumatic injury, chemicals and lupus vulgaris have been associated with this type of tumor. (2)
Currently, there exist limited therapeutic options for patients diagnosed with leiomyosarcoma, and the lack of actionable prognostic markers and a limited understanding of the biological mechanisms underlying LMS complicate the clinical management of these tumors. The rate of metastatic relapse for these tumors following local treatment is about 40% at 5 y, leading to, in most cases, an incurable condition. Previous work in experimental models of bladder cancer, leukemia, and lymphoma has demonstrated that inhibiting the interaction between CD47 and SIRPα using anti-CD47 monoclonal antibodies (mAbs) allows for increased phagocytosis of cancer cells by macrophages in vitro and a decrease in tumor burden in vivo. (3)
Grade and size are the most important prognostic factors for disease-specific survival and distant recurrence in patients with primary leiomyosarcoma. Site is not an important independent prognostic factor for local recurrence in this series; however, size and margin are. Long-term follow-up of leiomyosarcoma patients is important as late local or distant recurrence occurs in 9% of abdominal/retroperitoneal patients and 6% of extremity patients. (4)
Radiation-induced leiomyosarcoma of the breast seems to become increasingly common, with patients being diagnosed years after the radiation therapy, as survival of these women is enhanced because of multimodal treatment. (5)
Histologically, the tumor is composed of highly cellular fascicles of spindle-shaped cells. The fascicles are arranged in irregular interlacing bundles, often intersecting at right angles. The cells have nuclei that are elongated and blunted giving a “cigar” appearance. The degree of differentiation may vary within a single tumor differentiated areas, the cells resemble the typical smooth muscle cells of leiomyomas. Other areas may be poorly differentiated, with extensive cellular atypia and prominent nuclei and nucleoli. Mitotic figures are seen throughout the lesion. Criteria for malignancy remain controversial. Generally accepted, features of malignancy, include the presence of mitosis of the least one per 10-high-power fields, high cellularity, significant nuclear atypia and tumor giant cells. Classical immunophenotyping of leiomyosarcoma comprises positive vimentin, desmin and smooth muscle actin (SMA) staining. (6)
Adjuvant radiotherapy (RT) to the breast plays a significant role in preventing local disease recurrence in women treated for early stage breast carcinoma. This fact is supported by multiple clinical trials demonstrating that adjuvant RT
In this study the authors reviewed the records of 16,705 patients with breast carcinoma. Of these, 13,472 (81%) were treated with megavoltage radiotherapy and 3233 were treated without at the Institute Curie (Paris, France) between 1981 and 1997. Median doses of 50–55 Gray (Gy) in 25–27 fractions were delivered to the whole breast over a period of 5–5.5 weeks (2 Gy/day, 5 weekly fractions) followed, when indicated, by a 16–26-Gy boost to the tumor or tumor bed. Treatment of radiation induced sarcomas (RIS) consisted mostly of radical surgery and chemotherapy. Overall, 35 patients developed sarcomas. Of these, 27 fulfilled the Cahan criteria. The median follow-up was 9.3 years (range, 1–22.4 years). The latency period ranged from 3 years to 20.3 years. Thirteen sarcomas were located in the breast, 5 in the chest wall, 3 in the sternum, 2 in the supraclavicle, 1 in the scapula, and 3 in the axilla. Histologic evaluation identified 13 angiosarcomas, 3 osteosarcomas, 5 undifferentiated sarcomas, 1 malignant fibrous histiocytoma, 2 leiomyosarcomas, 1 fibrosarcoma, 1 rhabdomyosarcoma, and 1 myosarcoma. The cumulative RIS incidence was 0.07% at 5 years, 0.27% at 10 years, and 0.48% at 15 years. Standardized incidence ratios were 10.2 (95% confidence interval, 9.03–11.59) for irradiated patients and 1.3 (0.3–3.6) for nonirradiated patients. Of the 27 patients, 15 died of sarcoma within 1 month to 14.5 years (mean, 34.2 months). The 5-year actuarial survival rate after diagnosis of RIS was 36%. The current study confirmed the rarity of Radiation induced sarcoma. However, it showed that the risk increased with time. Therefore, careful, long-term follow-up of patients treated with radiotherapy is needed for early detection and efficacious treatment of these malignancies. Radiotherapy in the treatment of breast cancer is associated with an increased risk of subsequent sarcoma, but the magnitude of this risk is small. Angiosarcoma is significantly more prevalent in cases treated with radiotherapy, occurring especially in or adjacent to the radiation field. The small difference in risk of subsequent sarcoma for breast cancer patients receiving radiotherapy does not supersede the benefit of radiotherapy. (8)

Appropriate treatment begins with appropriate staging studies followed by a carefully planned and well-executed biopsy. The biopsy and subsequent treatment should ideally be carried out at a sarcoma center. Treatment plans should be made in an multidisciplinary setting involving input from the surgeon, medical oncologist, radiation oncologist, radiologist and pathologist. Limb salvage surgery is the standard of care; however, there are circumstances in which amputation is necessary or preferred. Radiation therapy in combination with surgical resection is highly effective at achieving local control. The use of chemotherapy is evolving but currently is not well-defined. Patients should be monitored closely after resection of their disease for local recurrence and metastatic spread. (9)

In recent study the authors used gene expression profiling and immunohistochemical assays to demonstrate the existence of 3 distinct molecular subtypes in leiomyosarcoma in two independent sets of cases and showed that they are associated with distinct clinical outcomes. These findings indicate distinct biological subclasses in leiomyosarcoma that may respond differently to novel therapeutic approaches. (10)

For decades, the mainstay of management has consisted of doxorubicin with or without ifosfamide. Trabectedin is a synthetic agent derived from the Caribbean tunicate, Ecteinascidia turbinata. This drug has a number of potential mechanisms of action, including binding the DNA minor groove, interfering with DNA repair pathways and the cell cycle, as well as interacting with transcription factors. Several phase II trials have shown that trabectedin has activity in anthracycline and alkylating agent-resistant soft tissue sarcoma and suggest use in the second- and third-line setting. More recently, trabectedin has shown similar progression-free survival to doxorubicin in the first-line setting and significant activity in liposarcoma and leiomyosarcoma subtypes. Trabectedin has shown a favorable toxicity profile and has been approved in over 70 countries for the treatment of metastatic soft tissue sarcoma. (11)

Significant advances in molecular biology and genetic research have allowed better identification of molecular differences between the types of sarcomas. These molecular signatures are important now not only for appropriate diagnosis but also for identification and use of targeted therapies. mTOR inhibitors, IGFR inhibitors, tyrosine kinase inhibitors, and antiangiogenic agents represent promising drugs for the treatment of sarcomas. (12)

Patients who present to specialized facilities after undergoing apparently total macroscopic resection have a high incidence of positive or undocumented resection margins. Reresection offers a significant improvement in margin status and in local control, even for patients who routinely receive XRT. There is some evidence that inadequate resection margins predispose patients to metastatic recurrence and disease specific death and that this, too, may be ameliorated by...
reresection. However, in the absence of a clear mechanistic relation between positive resection margins and metastatic recurrence, we believe that treatment effects based on this correlation must be considered with circumspection in the clinical setting. (13)

Various different histological subtypes exist that behave similarly regarding their biological characteristics and response to treatment. Soft-tissue sarcomas occur in up to 50% of cases in the extremities, followed by visceral/retroperitoneal and trunk tumors. Primary therapy is predicated on surgical resection with an adequate margin of normal tissue. Limb-sparing surgery for extremity lesions is possible in more than 90% of patients. For high-risk patients, identified by tumor grade, size and site, local control is improved with postoperative adjuvant radiation. Local recurrence rates vary, depending on the anatomic site. In the most common extremity lesions, one-third of the patients develop locally recurrent disease with a median disease-free interval of 18 months. For visceral sarcomas recurrence rates are up to 40-50%. Treatment results for extremity local recurrences may approach those for primary disease. Metastases of extremity sarcomas predominantly spread to the lungs where isolated metastases can be resected with 20-30% 3-year survival rates. Patients with unresectable pulmonary metastases or extra-pulmonary metastatic sarcoma have a uniformly poor prognosis and are best treated with systemic chemotherapy. In general, optimal treatment of soft-tissue sarcoma requires individual care tailored to the single patient. (14)

Conclusion
In summary, we report a case of post-radiation sarcoma after breast cancer treatment. Soft-tissue sarcomas are a relatively rare disease accounting for approximately 1% of adult malignancies. The current study confirmed the rarity of RIS. RT for breast carcinoma can induce malignant sarcoma after a latency period of several years. The risk is extremely low for the individual patient, but is slightly increased as the number of long-term survivors increases. RIS are associated with a poor overall prognosis. The treatment for most patients is late and ineffective. Therefore, careful, long-term follow-up of patients treated with radiotherapy is needed for early detection and efficacious treatment of these malignancies.

References
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