Primary Spindle Cell Sarcoma of the Breast

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Key Words

Breast tumor · Spindle cell sarcoma · Breast sarcoma, primary

Summary

Background: Primary pure breast sarcoma is a rare disease and constitutes 0.2–1.0% of all mammary malignancies. The establishment of a diagnosis of soft tissue sarcoma is difficult in adults. Immunohistochemical analysis usually proves to be helpful in indistinguishable cases. The simplistic step is to classify sarcomas on a simple descriptive basis as spindle cell sarcomas, myxoid sarcomas, pleomorphic sarcomas, and small round cell sarcomas. **Case Report:** Here, we present a rare case of primary spindle cell sarcoma of the breast. A 43-year-old woman was admitted to our clinic with a 2-month history of a left breast lump. Histopathological examination showed a tumor of 2.5 cm in diameter and of nuclear and histological grade 2. In the immunohistochemical examination, vimentin positivity, high nuclear overexpression of P53, high Ki-67 and S-100, desmin, leukocyte common antigen, keratin, and smooth muscle antigen, CD34, HMB45 and EMA negativity were detected. **Conclusion:** Most invasive breast neoplasms are epithelial tumors, and mesenchymal breast tumors are rarely seen. In primary breast sarcoma, adequate surgical tumor excision, tumor grade, and tumor diameter seem to be the most important prognostic factors.

Schlüsselwörter

Mammatumor · Spindelzellsarkom · Mammasarkom, primäres

Zusammenfassung

Background: Das primäre reine Mammasarkom ist eine seltene Erkrankung und macht 0.2–1.0% aller Mammatumore aus. Bei Erwachsenen sind Weichteilsarkome schwierig zu diagnostizieren. Die immunhistochemische Analyse ist bei nicht zu unterscheidenden Fällen zumeist sehr hilfreich. Am einfachsten ist es, Sarkome auf einer schlichten beschreibenden Basis in Spindelzellsarkome, myxoide Sarkome, pleomorphe Sarkome und klein/ runde Sarkome einzuteilen. **Fallbericht:** Hier stellen wir den seltenen Fall eines primären Spindelzellsarkoms der Brust vor. Eine 43-jährige Patientin stellte sich mit einem Knoten in der linken Brust in unserer Klinik vor. Die histopathologische Untersuchung ergab einen Tumor mit einem Durchmesser von 2.5 cm und nuklearem und histologischem Grad 2. Die immunhistochemische Untersuchung ergab einen positiven Befund für Vimentin, starke nukleare Überexpression von P53, hohe Werte für Ki-67 und S-100, Desmin, LCA, Keratin und einen negativen Befund für smooth muscle Antigen, CD34, HMB45 sowie EMA. **Schlussfolgerung:** Die meisten invasiven Neoplasien der Brust sind epitheliale Tumoren, während mesenchymale Mammatumoren sehr selten sind. Bei primären Mammatsarkomen scheinen die angemessene operative Entfernung des Tumors, Tumorgad und Tumordurchmesser die bedeutendsten prognostischen Faktoren zu sein.

Introduction

Primary pure sarcomas occurring in breast are rare and constitute 0.2–1.0% of all mammary malignancies [1]. Only a few hundred cases of breast sarcoma have been reported in the lit-

erature, but the number of reported cases and clinical experience are increasing. In most cases, breast sarcomas are secondary to radiotherapy [2]. Diagnosis of soft tissue sarcoma in adults is difficult. Certain tumors such as biphasic synovial sarcomas have characteristic aspects, but most do not. The sim-

plistic step is to classify them on a simple descriptive basis as spindle cell sarcomas, myxoid sarcomas, pleomorphic sarcomas, and small round cell sarcomas [3]. Herein, we present a rare case of primary spindle cell sarcoma of the breast.

Case Report

A 43-year-old woman was admitted to our clinic with a 2-month history of a left breast lump without any known personal or family history of cancer. Physical examination revealed a mass of 2.5 cm in diameter in the left breast. Mammography showed dense breast parenchyma. A focus of increased density of approximately 12 × 10 mm was noted central to the left breast. Excisional biopsy was performed, and histopathological examination of the biopsy specimen revealed a cellular composition with a predominance of atypical elongated to plump spindle-shaped cells with complete microscopic resection (fig. 1). The patient underwent modified radical mastectomy, and we did not detect any residual tumor tissue. Axillary lymph node negativity was determined during surgery. In the pathological examination, a tumor of 2.5 cm in diameter and of nuclear and histological grade 2 (graded with Fédération Nationale des Centres de Lutte Contre le Cancer), with 5 mitoses per 10 fields was detected, and a tumor necrosis rate lower than 5% was determined for all the examined tumor surface. Surgical excision borders were negative for tumor cells, and there was no neural, vascular, and capsular invasion. In the immunohistochemical examination, vimentin positivity, high nuclear overexpression of P53, high Ki-67 and S-100, desmin, leukocyte common antigen, keratin, and smooth muscle antigen, CD34, HMB45, and EMA negativity were detected (figs. 2 and 3). These established histological features of a malignant spindle cell tumor as well as the immunohistochemical results led to the diagnosis of intermediate-grade spindle cell breast sarcoma. Routine hematological and biochemical examinations, Ca15-3, and CEA were found to be normal. A bone scan and computed tomography (CT) scans of the thorax, abdomen and brain were negative for metastases.

Discussion

Sarcomas can occur anywhere in the body. 43% of sarcomas occur in the extremities with two-thirds of the extremity lesions occurring in the lower limb. 34% of sarcomas are intra-abdominal, consisting of visceral (19%) and retroperitoneal (15%) lesions [4]. Breast sarcomas are rarely seen. Those that are seen are primary pure breast sarcomas or advanced breast sarcomas secondary to radiotherapy. The former is a rare disease, while the latter forms the majority of cases of breast sarcoma. The reported 5-year survival rates for patients with breast sarcoma range from 40 to 91% [5–7]. Higher rates were determined in the series of Christensen et al. [8] and in Zelek et al. [9], however, 57/83 women in their series had malignant fibrous histiocytoma. In the study of Pandey et al. [10], the overall 3-year disease-free survival (DFS) was 39%. There were no failures beyond the third year in this series. Similar to these studies, 4 years after treatment, our patient is in complete clinical and radiological remission.

As in the case of sarcomas of other body parts, treatment of breast sarcoma depends on the histological type, degree of differentiation, tumor size, and advancement of disease. Sec-

Fig. 1. Spindle cell sarcoma well demarcated from normal fibro-adenomatous breast tissue (H and E staining, magnification ×100).

Fig. 2. Smooth muscle antigen negativity in spindle cells (SMA staining, magnification ×100).

Fig. 3. Desmin positivity is only seen around vascular structures (Desmin staining, magnification ×100).

ondary breast sarcoma is usually diagnosed at an advanced stage; therefore treatment is generally not successful. In local disease such as primary early breast sarcoma complete microscopic resection of the primary tumor is an important factor for local disease control, overall survival (OS), and DFS [5, 10]. In the Pandey et al. [10] study, the margin of surgical resection was found to be the most important prognostic indicator. The 3-year survival was 33.3% in patients with negative margins, 57% in patients where margins were not known, and 0% in patients with positive margins ($p = 0.05$). However, in the retrospective analysis by Zelek et al. [9] of primary breast sarcomas, the 10-year OS and DFS rates were 62 and 50%, respectively. For Fédération Nationale des Centres de Lutte Contre le Cancer grade 1, 2, and 3 tumors, the 10-year OS and DFS rates were 82 and 61%, 62 and 51%, and 36 and 25%, respectively ($p = 0.00007$ and 0.004, respectively). For tumors measuring less than 5 cm, 5–10 cm, and more than 10 cm, the 10-year OS and DFS rates were 76 and 66%, 68 and 55%, and 28 and 15%, respectively ($p = 0.002$ and 0.009, respectively). In the multivariate analysis, the tumor size and histological

grade were correlated with the 10-year DFS rate ($p = 0.04$ and 0.01 , respectively), but only the histological grade was correlated with OS ($p = 0.01$). Additionally, our patient who had grade 2 sarcoma with negative margins and a 2.5-cm diameter has been in complete remission during a more than 4-year follow-up.

Mastectomy was not found to be necessary to improve DFS in the report by Blanchard et al. [11], and wide local excision yielded equally good local control. Axillary dissection is generally thought to be unnecessary for most soft tissue sarcomas, since these tumors rarely metastasize via the lymphatics. After the detection of a mass in the left breast in our patient, we performed an excisional biopsy with intact margins. Then, we performed a mastectomy, but we did not detect any malignant cells in the removed breast tissue. The role of radiation and chemotherapy in the treatment of breast sarcoma is unclear. Some authors [12, 13] suggest that radiation is efficacious after surgical resection, particularly with microscopically involved margins, however, this was not supported by other studies such as that of Blanchard et al. [11].

Sarcoma secondary to radiotherapy is a well known complication of radiotherapy applied for breast carcinoma, and is associated with a poor prognosis. In the study of Kirova et al. [14], most of the examined cases of radiotherapy-induced sarcomas were angiosarcomas located in the primarily radiated areas. The standard and effective treatment for secondary breast sarcoma is surgery, but most cases are diagnosed at an advanced stage which might explain the poor prognosis. Although primary early breast sarcomas such as in our patient are also treated surgically, survival rates are better compared to secondary breast sarcomas.

Distinguishing subtypes of primary breast sarcoma, such as angiosarcomas, from other histological types, is clinically more relevant because some of these subtypes have a dramatically poor prognosis, with lesions exhibiting diffuse and multicentric local extension, rendering surgical resection difficult, and the

majority of patients, if not all, develop early distant metastases [14]. Other therapeutic options such as radiotherapy or chemotherapy will be necessary in these patients [15]. Subtypes of primary breast sarcoma are determined by histopathological examination. The WHO classifies most soft tissue sarcomas according to the presumptive tissue of origin such as liposarcoma, synovial sarcoma, leiomyosarcoma, rhabdomyosarcoma, fibrosarcoma, and angiosarcoma. Immunohistochemistry (IHC) may be useful to rule out other tumors such as non-mesenchymal malignant tumors or sarcomas with a specific line of differentiation. Desmin, vimentin, smooth muscle antigen, keratin, leukocyte common antigen, CD34, HMB45, EMA, and S-100 should all be analyzed in these sarcoma patients. However, some of the subtypes of primary breast sarcoma, such as fibrosarcoma, which have no specific immunological markers for this cell type may be indistinguishable. The simplistic step is to classify sarcomas on a simple descriptive basis as spindle cell sarcomas, myxoid sarcomas, pleomorphic sarcomas, and small round cell sarcomas. In our patient, IHC analysis only vimentin positivity was detected with no specific cell markers for subtypes of primary breast sarcoma.

Pathological prognostic factors play a considerable role in soft tissue sarcomas. Tumor grade is reported to be the single most important pathologic prognostic factor in soft tissue sarcomas [10]. Nonetheless, mutation of P53, nuclear overexpression of P53, and a high Ki-67 proliferation index are also associated with poor prognosis. Our patient had a grade 2 tumor with bad prognostic factors such as high nuclear overexpression of P53 and high Ki-67 proliferation.

In conclusion, most invasive breast neoplasms are epithelial tumors, and mesenchymal breast tumors are rarely seen. Herein, we reported a case of primary grade 2 breast spindle cell sarcoma measuring less than 5 cm in diameter, with complete microscopic resection of the primary tumor. In primary breast sarcomas, adequate surgical excision of the tumor, grade, and tumor diameter seem to be the most important prognostic factors.

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