Low Grade Fibromyxoid Sarcoma of the Axillary Fossa and Breast Cancer – A Case Report

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Abstract

Low grade fibromyxoid sarcoma (LGFMS) is a rare tumor, they are usually located in the lower limbs or any other location is possible. Its occurrence has been reported in thoracic wall, axilla, groin, pelvis, abdominal wall, bladder or the palate. Low grade fibromyxoid sarcomas comprise 10% of all soft tissue sarcomas, originate from the deep layers of soft tissues and occur in both sexes with the same frequency, although some report more common occurrence in men.

The goal of this work is to present the diagnostics and therapeutic management in a patient with breast cancer and axillary low grade fibromyxoid sarcoma treated at the Bydgoszcz Oncology Centre.

A 55-year old patient was admitted to the Oncology Centre for the diagnostics of a left-sided breast lesion. A 4 cm movable tumor could be palpated beneath the papilla and an enlarged lymph node, about 7 cm in diameter, was noted in the left axilla. Patient underwent modified simple amputation of the left breast, with sentinel and post sentinel lymph node procedure as well as removal of a tumorous lesion of the left axillary fossa. Patient was re-referred for interdisciplinary medical committee, where based on the breast cancer staging (T2N1micM0) and presence of a sarcoma (LGFMS), despite it being low grade and due to lack of proper surgical margin, she was qualified for 5-years hormonal therapy and radical radiotherapy.

Patient remains in good condition under care of Radiotherapy, Surgery and Rehabilitation Outpatient Clinic. Clinical examination and imaging studies showed no foci of active neoplastic process.

Keywords: Low grade fibromyxoid sarcoma; Breast cancer; Radiotherapy

Introduction

Low grade fibromyxoid sarcoma (LGFMS) is a rare tumor first described by Evans in 1987 [1]. They are usually located in the lower limbs or any other location is possible. Its occurrence has been reported in thoracic wall, axilla, groin, pelvis, abdominal wall, bladder or the palate. Axilla and thoracic wall are the most common locations, while it is rarely found in other areas [2]. Low grade fibromyxoid sarcomas comprise 10% of all soft tissue sarcomas, originate from the deep layers of soft tissues and occur in both sexes with the same frequency, although some report more common occurrence in men. The peak incidence is observed among young and middle-aged individuals [3]. The majority of these tumors are benign, although an aggressive course with recurrences and/or metastases, mainly to the lungs [torriani], is also possible [2,4].

The goal of this work is to present the diagnostics and therapeutic management in a patient with breast cancer and axillary low grade fibromyxoid sarcoma treated at the Bydgoszcz Oncology Centre.

Case Presentation

In October 2015 a 55-year old patient was admitted to the Oncology Centre for the diagnostics of a left-sided breast lesion. Patient had a history of treatment with vitamin B12 for megaloblastic anemia since 1998.
The entire tumor was removed, sparing the vascular, nervous and lymphatic structures of the axillary fossa. Tumor was located beyond the areola. Proximally, on 12 o'clock there was a second focus 9 mm in size was found in the left axillary fossa. No focal lesions were demonstrated in the right breast. Right-sided axillary lymph nodes were unremarkable (BIRADS 5). Considering the result, a core needle biopsy of suspicious lesions was performed, confirming the presence of malignancy: carcinoma lobulare invasivum mammæ, Elston-Ellis G2, receptor status: ER (+), PR (+), HER2 (1+), E-cadherin (+), Ki-67 (+) 3.5%. Imaging studies: chest X-ray and abdominal ultrasound ruled out disease spread and the patient was referred to the interdisciplinary medical committee in order to determine further management. Patient was referred for surgical treatment with a biopsy of left-sided axillary lesion. Further adjuvant treatment was to be decided based on the final result of histopathological examination.

Surgery was performed at the Clinical Department of Breast Cancers and Breast Reconstruction Surgery in December 2015 – patient underwent modified simple amputation of the left breast, lymphoscintigraphy with sentinel and post sentinel lymph node procedure as well as removal of a tumorous lesion of the left axillary fossa, which has been present there for several years. Left axillary lymphoscintigraphy was performed at the Department of Nuclear Medicine for identification of sentinel lymph nodes in the left axillary fossa. In the surgery breast tissue was cut with a transverse incision and dissected from the left pectoralis muscle, resulting in simple amputation. Subsequently, a gamma camera was used to locate the sentinel lymph node (radiation dose: 8000 units) and the post sentinel lymph node (radiation dose: 8000 units) in the axillary fossa. Radiation dose to the place of application: 14000 units. Lymph nodes were excised and sent for intraoperative histopathological examination. Its result indicated reactive lymph nodes. Then, a tumor coming out of the muscles of axillary fossa was exposed. A section was excised and sent for intraoperative histopathological examination. The result showed a benign lesion of non-endothelial origin. The entire tumor was then removed, sparing the vascular, nervous and lymphatic structures of the axillary fossa. Tumor was located beyond the axillary fossa. A titanium clip was inserted in the axillary floor where the tumor had been excised. Because of the anatomical conditions (tumor was located on subcapsular muscles) we were not able to remove a wide margin around the tumor (Figures 1,2 and 3).

Final histopathological examination confirmed the diagnosis: carcinoma lobulare invasivum mammæ, Elston-Ellis G2, PT2. A poorly demarcated tumor, 3.5 cm in diameter, was located under the breast papilla. High grade fibrosis within the tumor and mild peripheral lymphocytic infiltration were noted. A second cancerous lesion 1.5 cm × 1.0 cm × 0.8 cm was also found within breast tissue. A single reactive lymph node was dissected from the border of the axillary floor. Intraoperative examination of the sentinel (I) and post sentinel (II) left axillary lymph node revealed: I – reactive, partially infiltrated by adipose tissue, 1.0 cm in diameter, II – reactive, partially infiltrated by adipose tissue, 1.2 cm in diameter. However, final pathomorphological diagnosis stated as follows: I – a cancer micrometastasis was identified in the deeper slices using immunohistochemical techniques CK7 (+), AE1/AE3 (-); lesion did not exceed beyond the node capsule – pN1mic (SN). Histopathological examination yielded the following result: specimen consisted of a tumor fragment 5.0 cm × 4.0 cm × 3.8 cm in size.

A 4-cm movable tumor could be palpated beneath the papilla and an enlarged lymph node, about 7 cm in diameter, was noted in the left axilla. Patient reported having this lesion for over 20 years; it never changed in size and has never been verified. No other suspicious, enlarged lymph nodes have been found. The right breast did not contain any pathological masses, axillary and supraclavicular lymph nodes were not palpable. Mammography was performed, revealing fatty and glandular mammary glands. A hypoechogetic, poorly demarcated tumor, 17 mm × 13 mm × 12 mm in diameter, was identified in the left breast, at 3 o'clock beyond the outer margin of the areola. Proximally, on 12 o’clock there was a second focus 9 mm × 6 mm × 6 mm in diameter. Malignant tumor was suspected. Skin thickening was noted. An enlarged, hypoechogetic, 51 mm × 50 mm in size was found in the left axillary fossa.
Pas (-), Pas + amylase (-/-), Caldesmon (-), Calponin (-), CD34 (-), CKAE1/AE3 (-), EMA (-), Ki67 (+) in a few single cells, MDM2 (+), S100 (-), SMA (-/-+) focally, Vimentin (+), (Figures 4 and 5).

Patient was re-referred for interdisciplinary medical committee, where based on the breast cancer staging (T2N1micM0) and presence of a sarcoma, despite it being low grade and due to lack of proper surgical margin, she was qualified for 5-year hormonal therapy and radical radiotherapy.

She was referred to the Department of Radiotherapy at the Oncology Centre for further treatment. Since this disease is extremely rare, patient’s case was discussed at a radiotherapeutic medical committee. Due to the histopathological result, tumor size exceeding 5 cm and lack of surgical margin patient was qualified for adjuvant radiotherapy, where irradiated field should encompass both incision sites – one after excision of the sarcoma as well as the breast cancer excision scar. The radiotherapy planning system was used to draw out the postoperative site, including the titanium clip and the contents of the axillary fossa as well as the surgical scar with a 2 cm to 3 cm margin and to adapt it to anatomical structures. We consulted contouring of those areas with the operating surgeon to indicate tumor location and relation to the surrounding tissues. We planned and executed radical radiotherapy with IMRT using X-rays of 6/15 mV energy to the surgical site including the titanium clip and contents of the axillary fossa as well as the surgical scar with a margin and adjusted it to anatomical structures in DC of 50Gy in 25 fractions and boost to the axillary fossa in DC of 10Gy in 5 fractions up to a total of 60Gy in 30 fractions (Figures 5, 6 and 7). In weekly follow-up we observed mild post-irradiation reaction manifesting as erythema of the irradiated region. The maximal score obtained at the end of treatment was: RTOG/EORTC skin reaction – ½, esophagus – 0, heart – 0, lungs – 0.

Patient remains in good condition under care of Radiotherapy, Surgery and Rehabilitation Outpatient Clinic. Clinical examination and imaging studies showed no foci of active neoplastic process.

Discussion

Low grade fibromyxoid sarcoma was first described by Evans and was classified by the WHO as a fibroblastic/myofibroblastic tumor. Imaging studies are generally not very specific for this disease, but MRI, CT, and USS of the area may be of help. Magnetic resonance imaging studies are characterized by low to high uptake in T1-weighted images and heterogeneous uptake in T2-weighted images, as well as variable uptake in post-contrast sequences [5].

The gross findings of LGFMS include a well circumscribed oval to round mass in size from 10 cm to 20 cm in diameter (median size, 5 cm). The cut surface shows white-gray appearance [6-10]. Microscopically, LGFMS typically shows an admixture of heavily collagenized, hypocellular zones and more cellular myxoid zones with vascular arcades. There is a proliferation of bland-appearance spindle tumor cells with a whorled or linear arrangement. Mitotic figures tend to be absent or sparse [6,8,9,11]. Immunohistochemistry, the neoplastic cells of LGFMS are consistently positive for vimentin only and negative for variety of antibodies. Occasional cells are positive for SMA, which is attributed to focal myofibroblastic differentiation.
Mucin4 (MUC4) is highly sensitive and specific immunostaining marker for LGFMS [13]. Immunohistochemical staining has been reported by a number of authors, with some conflicting results [6].

The heterogeneous histological and immunohistochemical appearance makes the diagnosis of LGFMS challenging. LGFMS is characterized by its relatively benign histological appearance with spindle cells as well as collagenized and myxoid areas. In spite of low-grade and benign histological appearance, studies of retrospectively diagnosed LGFMS have shown a distinct biological behavior, with a relatively high and atypical metastasizing potential, making the correct diagnosis of LGFMS important [14]. Differential diagnosis of LGFMS includes lesions showing spindle cell proliferations with myxoid pattern with or without fibrous component. There are several related neoplasms that are more commonly observed, including low grade myxofibrosarcoma, perineuroma, myxoid neurofibroma, myxoid solitary fibrous tumor, and fibromatosis. Low grade myxofibrosarcoma exhibits a more uniform myxoid stroma and more cellular atypia, but lacks areas of fibrous stroma or a whorled arrangement of tumor cells. Perineuroma may have fibrous and myxoid areas and is diffusely positive for EMA. Neurofibroma shows more slender wavy nuclei and expresses S100. Myxoid solitary fibrous tumor is uniformly immunoreactive for CD34. Fibrosis has a more fascicular architecture and is immunoreactive for β catenin [6,7,10,15].

In the recent years genetic studies have played an important role in the diagnostics of LGFMS. Cytogenetically, this tumor is characterized by translocation (t(7;16)(q33;p11) or, less often, t(11;16)(p11;p11), resulting in gene fusions FUSFig, CREB3L2, or FUS-CREB3L2. An endothelial glycoprotein MUC4 has been recently discovered - a sensitive and specific marker for LGFMS enabling differential diagnostics [5].

If high mitotic indexes are identified, these rare tumors should be diagnosed and treated with radical surgery as soon as possible, as only such treatment improves survival time and reduces the risk of recurrence. Little is known about the effectiveness of other forms of therapy, including chemo- and radiotherapy [3].

During surgery, tumors separate easily from the surrounding tissue and can be removed without problems, except for those in difficult locations or large tumors, where total resection may be difficult or even impossible. Enneking et al. reports that 5-year survival following surgical treatment reaches 90% for patients with small tumors and positive prognostic factors. Disease relapses occur in intervals ranging from several months to 15 years from initial treatment, while distant metastases may appear up to 45 years after treatment [2]. In 2011 Evans demonstrated results showing that in long term patient follow-up tumors with high mitotic indexes are associated with 63% risk of local recurrence and 45% risk of disease spread [1,16]. The most frequent locations of distant metastases include lungs, pleura, thoracic wall and bones [16]. Nielsen et al. presented an interesting work analyzing a database of Danish patients from the last 30 years. Results from 30 patients with low grade fibromyxoid sarcoma (LGFMS) were evaluated. These patients have been in follow-up over a period ranging from 2.5 years to 24.3 years, with a median of 5.0 years. During fibromyxoid sarcoma (LGFMS) cases [14].

Radio- and/or chemotherapy may be the treatment of choice for patients with disease recurrence and/or metastasis. The role of adjuvant treatment is still controversial, although adjuvant radiotherapy is indicated in case of incomplete tumor resection [4].

Our patient remains under care of the Oncology Center in Bydgoszcz and shows no signs of recurrence in current imaging studies.

**Conclusion**

Diagnosis of low grade fibromyxoid sarcoma must be taken into consideration in unusual locations and the diagnostics requires application of immunohistochemical techniques. With proper diagnostics and treatment patients have a great chance to gain control over the disease. Surgical resection with negative margins is the basis for treatment. Further studies are required to form a consensus of multidisciplinary diagnostic and therapeutic management.

**References**
