Case Report

Alveolar soft part sarcoma presenting as a breast metastasis in a patient with a history of thyroid cancer: a case report

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Abstract: Metastases to the breast are uncommon, accounting for 0.5% of breast tumors, and most of them are originated from lymphoma, melanoma and carcinomas of various organs. Alveolar soft part sarcoma (ASPS) is a very rare neoplasm that is usually found in the lower extremities. Lungs are the common site of dissemination and may represent initial manifestation of disease. We report a clinically unsuspected case of ASPS presenting as a breast metastasis in a 25-year-old woman. The patient’s medical history was notable for a thyroid cancer treated by surgery and radioiodine ablation 2 years ago. Core needle biopsy of slowly growing breast mass yielded polygonal cells with abundant eosinophilic cytoplasm arranged into solid pattern. Differential diagnosis between apocrine cell carcinoma, paraganglioma, granular cell tumor, neuroendocrine carcinoma, ASPS and metastatic hepatocellular and renal cell carcinoma was rendered by immunohistochemistry. Strong nuclear TFE3 immunoreactivity confirmed a diagnosis of ASPS. Retrospectively a primary tumor was found in the thigh. Most likely, ASPS and thyroid cancer in the patient were growing synchronously and independently.

Keywords: Alveolar soft part sarcoma, breast metastasis, thyroid cancer, biopsy

Introduction

Metastases to breast are uncommon, and mainly represented in adults by hematological malignancies, melanoma and carcinomas [1]. Alveolar soft part sarcoma (ASPS) is a very rare mesenchymal malignancy accounting 0.5% of all sarcomas [2, 3]. More than third of ASPS cases demonstrates metastasis at initial presentation [4, 5].

We describe a challenging case of metastatic ASPS diagnosed by breast core-needle biopsy in a patient with a history of papillary thyroid carcinoma (PTC).

Case report

A 25-year-old Thai woman presented at local hospital after noticing a painless mass in her left breast, which was slowly progressing over several last months. She had a history of multifocal PTC 2 years ago. The patient underwent a total thyroidectomy followed by radioiodine ablation. There were no signs of thyroid cancer recurrence or nodal disease on follow-up imaging.

On physical examination, a well-circumscribed, mobile, 5×2 cm mass was palpable at 12 o'clock position in the mid-zone of her left breast. There were no nipple discharge, skin changes over the lesion, and associated palpable axillary lymph nodes. Chest X-ray examination revealed micronodular dissemination in basal parts of the lungs. An ultrasound-guided core biopsy of the breast mass was performed.

Histologically, the lesion was composed of large polygonal and rounded cells with abundant acidophilic granular cytoplasm; however some areas showed cytoplasmic vacuolation (Figure 1B). Round vesicular nuclei contained prominent central nucleolus. The predominant pattern of growth was solid with just occasionally observed discohesion (Figure 1A). Numerous sinusoids were interspersed between tumor cells (Figure 1E). Breast tissue appeared intact,
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suggesting expansive growth of circumscribed lesion. Histochemistry revealed that tumor cells contained variable amount of cytoplasmic glycogen and occasional PAS-positive, diastase-resistant rod-shaped crystals (Figure 1C). Immunohistochemistry showed no staining for Pan-cytokeratin, GCDFP-15, Chromogranin, Hepar 1 and S-100 proteins. Positive nuclear staining for TFE3 suggested diagnosis of alveolar soft part sarcoma (Figure 1D).

Figure 1. Metastatic alveolar soft part sarcoma in a 25-year-old woman. A. Low power shows panoramic view of core needle biopsy with solid sheets of tumor cells, Hematoxylin & eosin (HE) staining, ×10. B. Tumor composed of large polyhedral cells with abundant acidophilic cytoplasm and prominent nucleolus, HE staining, ×40. C. PAS-positive, diastase-resistant crystalline material in the cytoplasm of sarcoma cells, PAS-D, ×100. D. Strong nuclear immunoreactivity to transcription factor E3, TFE3 immunohistochemistry, ×40. E. Prominent vascular network, CD34 immunohistochemistry, ×20. F. Moderate proliferative activity of tumor cells detected by Ki-67 labeling index (10%), MIB-1 monoclonal antibody, ×40.
Retrospectively was found that the patient had deep painless mass over the lateral part of her right thigh, did not affecting any movement function, and very slowly enlarging for the past six months. Recent MRI revealed 14×6.9×5.6 cm lesion involving three vastus muscles of the right thigh.

Discussion

ASPS rate is estimated at 0.5-1% range in large series of soft tissue sarcomas [4, 6]. Picci et al. could identify only 24 cases out of 4430 soft tissue malignancies in Italian collection spanning over 110 years [3]. Recent Indian series reported 1.8% rate of ASPS [7]. The tumor is typically presented as a slowly growing painless mass of lower extremities in young females [6]. Histologically it is composed of cellular aggregates arranged into pseudoalveolar pattern due to central loss of cohesiveness and further degeneration. Less common type is made of solid sheets of cells and was mainly described in children [2]. Once it was suggested myogenic origin of ASPS based on detection of MyoD1 protein expression [8]. However subsequent studies showed that aberrant MyoD1 cytoplasmic staining is irrelevant and likely to be an artifact [9]. The most of experts agreed that myogenic theory of ASPS development is not consistent [10]. Recent microarray studies showed some neurogenic properties of the tumor [11]. So far, the histogenesis of ASPS remains obscure.

Metastases to the breast encounter 0.5% of breast tumors and in adults are mainly originated from lymphoma, followed by melanoma and carcinomas of various organs [1]. Metastases of soft tissue sarcomas into the breast are extremely rare [12].

Taking into account of quite low rates of secondary tumors of the breast and ASPS itself, one could suppose that a chance of ASPS metastasis to the breast is exceptionally uncommon. Not more than 10 reports are available in the literature [13]. Most of them were cases with known primary tumor histologically verified as ASPS which gave a rise of isolated or widespread dissemination.

The main challenge of the presented case was a “blind” diagnosing of a breast biopsy without any supportive evidence of extramammary primary lesion, which became evident only retrospectively after our diagnosis. Immunohistochemistry is particularly helpful under such instances. Tumor morphology that exhibited nested-to-solid pattern and abundant eosinophilic cytoplasm, unusual for the breast, prompted us to include the following malignancies into differential diagnosis list: apocrine cell carcinoma, paraganglioma, granular cell tumor, neuroendocrine carcinoma, alveolar soft part sarcoma and metastatic carcinoma (both hepatocellular and renal cell carcinoma).

Immunohistochemical panel was built of Pan-cytokeratin, GCDFP-15, Chromogranin, Hepat 1, S-100 and TFE3. The only positive staining was TFE3 which made the obvious diagnosis of ASPS. TFE3 nuclear staining is a highly specific marker of unique translocation der(17)t(X:17) (p11;p25), attributed to ASPS. The translocation results in fusion of alveolar soft-part sarcoma locus on 17q25 with TFE3, a transcription factor gene on Xp11, which constitutively activates nuclear expression of TFE3 protein [14]. TFE3 antibody is a well-established tool of ASPS diagnostics; however it may also detect a small subset of TFE3-positive pediatric renal cell carcinomas [15]. Further PAS staining after diastase treatment could complement ASPS diagnosis by the finding of cytoplasmic crystalline, which is not found in renal cell carcinomas.

Our case shares some classic features of ASPS such as young age at representation and female gender. The latter is explained by the presence of two X chromosomes, increasing their chances to be involved in the disease-inducing translocation [16]. Classic histopathology of ASPS is presented by pseudoalveolar pattern which provides a name of the tumor. However we dealt with less common solid type, not so morphologically unique, and therefore had more difficulties in diagnostic process. To diagnose ASPS metastasis blinded (without knowing the history of primary tumor) in small size core-needle biopsy was almost impossible without help of immunohistochemical panel. This powerful tool led by TFE3 antibody is an essential part of ASPS diagnostics, which may be optionally combined with crystalline evaluation by PAS-D staining and electron microscopy [10]. A review of the literature showed that none out of 3 previously described cases of ASPS breast metastasis without known ASPS history,
and additional 3 cases of “primary” breast ASPS could be diagnosed by biopsy or FNA [17-22]. Only surgical excision of the mass could render a diagnosis of ASPS, while FNA and biopsy reported “atypia”, “not clear” and “granular cell tumor” [17, 20-22].

Of note that none of histological and immunohistochemical features (i.e. pattern, mitotic rate) have prognostic significance. Only age, size and metastases matter in this regard [4, 6]. It was shown that 32-65% of ASPS cases are typically manifested with metastasis at presentation and 6-9% may be revealed by metastasis only [4, 5, 23]. Lungs are the most common site of dissemination, which was also revealed in our patient. However breast metastases are extremely unusual and were reported as per our knowledge only in 10 cases so far (reviewed in [13]). Four cases of ASPS with breast metastasis were previously described in Asian women by Korean, Japanese and Indian authors [19, 24-26]. We present here the case from Southeast Asia which is ethnically divergent.

The most prominent and unique feature of the case is a co-existing of ASPS with PTC, which to the best of our knowledge has not been reported. Moreover none of any malignancies has been reported with ASPS tumors. Sarcomas are well known as the second cancers after radiation therapy for childhood cancer [27]. There are some cases of second primary tumors after PTC radioiodine treatment; however in the large meta-analysis study only leukemia was found to be significantly related to radioiodine therapy [28]. Post-radiation sarcomas are defined as sarcomas arising in a previously irradiated field after a latency period of at least 2 years [29]. We do not suppose that our case represents any link between thigh ASPS and low-dose radioiodine ablation of thyroid.

According to the patient’s history, the tumor was developing after the treatment of PTC. However, it is known well that ASPS is a slowly-growing tumor. Taking into account of its metastatic spread to the breast and lung dissemination, we would propose synchronous development of both tumors prior to thyroid removal rather than ASPS preceded by PTC.

Molecular background of ASPS is highlighted by chromosomal translocations involving chromosomes 11, 17 and X [10]. It is interesting that chromosome 17q is often gained in thyroid cancer [30]. There is a possibility that the patient has particular susceptibility to chromosomal rearrangements or genetic instability in general, which may also be marked by the manifestation of both cancers in young age. However we cannot provide any substantial hints on the possible link between ASPS and PTC related to shared etiology, heredity or molecular events in the particular case.

Five-year survival rate of localized ASPS is good (more than 80%), but it dramatically dropped to 20% if metastases are found [6]. Presence of lungs dissemination gives almost 100% chances of synchronous metastases into other organs, like brain, bones, or the breast in our particular case. Overall 20 year prognosis of ASPS is fatal since no specific therapy regimens are established [4]. Surgery is a key treatment modality, which may be combined with radiotherapy [31]. Conventional chemotherapy regimens have not been found to be effective [6]. Most recent trials demonstrated potential efficacy of targeted antiangiogenic therapy [32].

In conclusion, we present the first report of ASPS diagnosed in a young patient with a history of PTC. ASPS was manifested by metastatic dissemination with the breast involvement. Diagnostic workup of metastatic breast tumors is greatly facilitated by immunohistochemistry.

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Disclosure of conflict of interest

None.

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