

## Bilateral Mammary Metastasis of Alveolar Soft Part Sarcoma – A Case Report –

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An alveolar soft part sarcoma (ASPS) is a rare malignant soft tissue tumor, which metastasizes to the lung, bone and brain. Recently, we encountered an unusual case of a metastatic ASPS to the bilateral breasts in a 27-year-old woman. She had undergone surgery for an ASPS in her right thigh two years ago, which metastasized to the breast on three occasions, 15 months, 20 months and two years after surgery.

**Key Words :** Sarcoma, Alveolar soft part-Neoplasm metastasis-Breast-Immunohistochemistry

An alveolar soft part sarcoma (ASPS) is a rare malignancy, accounting for 0.5-1.0% of malignant soft tissue tumors. It is characterized by an indolent but fatal course, and metastases tend to occur early in the course of the disease. The principal metastatic sites are the lungs, followed by the bone and brain. A metastasis to the lymph nodes occurs infrequently,<sup>1</sup> and a metastasis to the breast is extremely rare; only two other cases of a metastatic ASPS to the breast have been reported in the English medical literature.<sup>2,3</sup> This paper describes a case of a metastatic ASPS to the bilateral breasts.

### CASE REPORT

A 25-year-old woman presented in February 2000 with a thigh mass that had been slowly growing for three years. She underwent

an excisional biopsy of the thigh mass, which proved to be an ASPS. The tumor size was 5 × 4 cm. One month later, she underwent a wide excision of the thigh at another hospital; the resection margins were reported to be clear. The patient then underwent four courses of chemotherapy with ifosfamide, adriamycin and dacarbazine. In June 2001, she was found to have a right breast mass. An excisional biopsy revealed a metastatic ASPS, measuring 1.3 cm in diameter. During the follow up, in October 2001, bilateral breast masses were detected, two in the right breast and one in the left. The two masses in the right breast measured 1 cm and 0.6 cm in diameter, while that in the left breast was 2 cm in diameter. These were also diagnosed as metastatic ASPS. In December 2001, multiple lung nodules were found on a chest CT, and in May 2002, multiple bilateral breast masses were detected. She underwent a bilateral subcutaneous mastectomy in June 2002.

A gross examination showed three masses in the right breast, and eight in the left. The mass sizes varied from 3 mm to 1.0 cm in diameter. They were fairly well circumscribed from the surrounding parenchyma but were not encapsulated. They were yellowish-tan, soft, and bulged at the cut surface (Fig. 1).

Microscopically, the tumor cells exhibited solid growth with a focal pseudoalveolar pattern. The tumor was composed of large

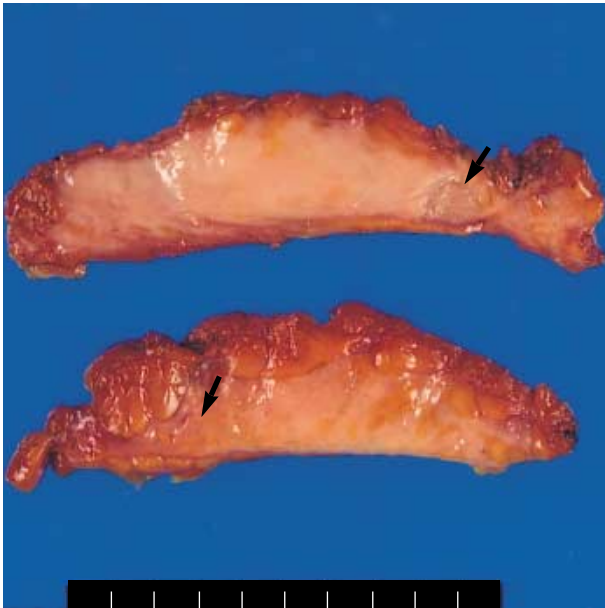


Fig. 1. Representative sections show two well circumscribed, yellowish tan masses (arrows).

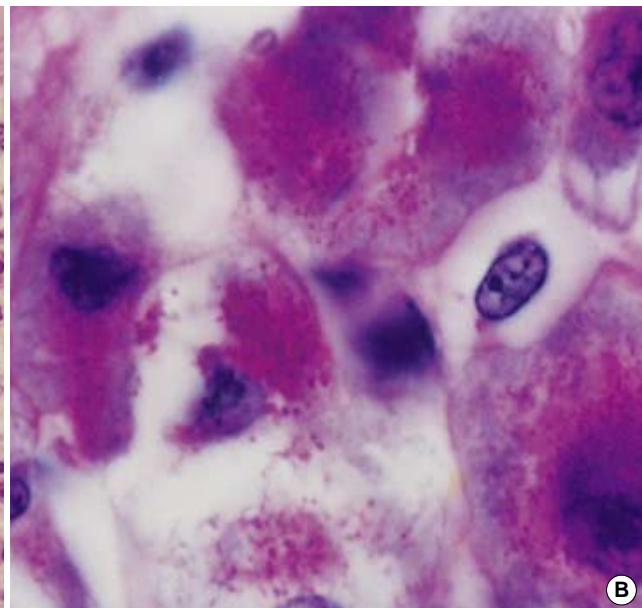
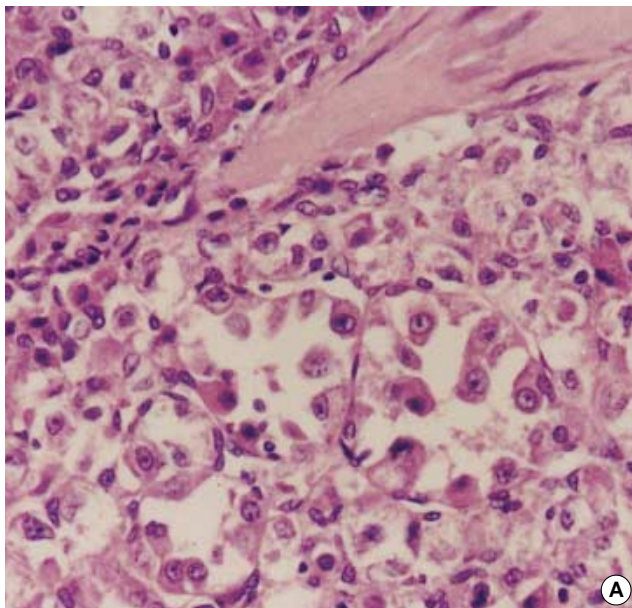


Fig. 2. (A) The tumor cells show mainly a solid growth pattern with focal pseudoalveolar pattern. (B) Periodic acid-Schiff (PAS) positive, diastase-resistant intracytoplasmic crystalline materials are illustrated.

round to polygonal cells with abundant eosinophilic granular, often vacuolated, cytoplasm. The cells had large vesicular nuclei with prominent nucleoli (Fig. 2A), and the cytoplasm contained PAS-positive diastase resistant granules and rod shaped crystals (Fig. 2B).

The tumor cells showed immunoreactivity for desmin (D33, 1:150, Dako, Glostrup, Denmark) focally and were all negative for S-100 protein (1:1,200, Dako, Glostrup, Denmark), vimentin (V9(1), 1:150, Dako, Glostrup, Denmark), CD56 (123C3, 1:200, Zymed, San Francisco, CA, USA), CD68 (PG-M1(3), 1:70, Dako, Glostrup, Denmark), HMB45 (HMB45<sup>1</sup>, 1:150, Dako, Carpinteria, CA, USA), cytokeratin (MNF116, 1:600, Dako, Glostrup, Denmark), epithelial membrane antigen (E29(3), 1:200, Dako, Glostrup, Denmark), estrogen receptor (1D5(1), 1:80, Dako, Glostrup, Denmark), progesterone receptor (1A6, 1:80, Dako, Carpinteria, CA, USA), c-kit (1:250, Dako Japan Co., Shimogyoku, Japan), synaptophysin (1:200, Dako, Glostrup, Denmark), carcinoembryonic antigen (11-7(7), 1:100, Dako, Glostrup, Denmark), and myoglobin (1:500, Dako, Glostrup, Denmark). Vimentin was strongly expressed in the surrounding vessel walls and fibroblasts, but tumor cells showed no vimentin expression. Smooth muscle actin (1A4(1), 1:150, Dako, Glostrup, Denmark) and CD34 (QBEND10, 1:400, Immunotech, Marseille, France) were negative in the tumor cells but showed an obvious sinusoidal vascular channel revealing a nest pattern. Electron microscopy showed a well developed Golgi apparatus, and diffusely scattered glycogen particles. The membrane bound crystals have been

reported to be specific for ASPS, but they were not observed in this case.

## DISCUSSION

A breast metastasis from extramammary primary tumors is rare, accounting for 0.5-2.0% of all breast malignancies.<sup>4</sup> A malignant melanoma and lymphoma are the most common source of metastases, followed by carcinomas of the lung, ovary and stomach.<sup>5</sup> A metastasis to the breast from the soft tissue sarcomas is also quite rare, although a few cases of a metastatic leiomyosarcoma, hemangiopericytoma, and malignant schwannoma have been reported.<sup>6-9</sup> In addition, some cases of a mammary metastasis of a rhabdomyosarcoma have been reported in children.<sup>10</sup> Two cases of a metastatic ASPS have been reported.<sup>2,3</sup> One case involved a unilateral breast and the other was bilateral. To our knowledge, this is the third reported case of a mammary metastasis of an ASPS. No clear predisposing factors for the development of metastases to the breast have been identified, although hormonal factors have been suggested in males with a metastatic adenocarcinoma from the prostate to the breast.<sup>4</sup>

ASPS is a rare tumor with a highly characteristic morphology and an ultrastructure. However, it has a controversial histogenesis. It occurs primarily in adolescents and young adults, and the peak age ranges from 15 and 35 years.<sup>1,11</sup> Females outnumber males, particularly among patients under 30 years of age.<sup>11,12</sup> There are two main locations of an ASPS. When it occurs in adults, it is observed mainly in the lower extremities, particularly the thigh. When it affects infants and children, it is often located in the region of the head and neck, especially the orbit and tongue.<sup>1</sup> ASPS is characterized by an indolent, but fatal course and an early dissemination. A significant number of patients (up to 65%) present with metastatic disease,<sup>11,12</sup> and ASPS shows an unusual pattern of metastatic spread. The most common sites of the metastasis are the lungs, brain and bone.<sup>1,11,12</sup> Other sites include the regional lymph nodes, the liver, and ovaries.<sup>12</sup> A metastasis to the breast is extremely rare. The long term survival of patients with localized ASPS is quite favorable. Portera *et al.*<sup>12</sup> observed disease free and overall 5-year survival rates of 71% and 88%, respectively, when compared to a 20% 5-year overall survival rate for patients with metastatic disease.

Treatment is not particularly promising. Most reviewers recommend a radical surgical excision of the primary and metastatic lesions combined with radiotherapy or chemotherapy.<sup>1</sup> A metastectomy is often considered for patients with isolated metastatic

ASPS, and it has been suggested that a metastectomy might be of value for some patients with a brain or pulmonary metastasis.<sup>11-14</sup>

Several theories concerning the origin of ASPS have been proposed. Many studies have reported immunoreactivity for vimentin, muscle-specific actin, desmin, and other myogenic markers in the tumor cells and suggested a skeletal muscle differentiation. However, others were unable to confirm these findings.<sup>1</sup> The immunopositivity for desmin observed in our case favors a skeletal muscle differentiation. Smetana and Scott<sup>15</sup> regarded ASPS to be a variant of a paraganglioma, and DeSchryver-Kecsckemeti *et al.*<sup>16</sup> regarded ASPS to be an extrarenal renin-producing tumor, and therefore proposed the name 'angioreninoma'. Recently, a chromosomal translocation, der(17)t(X;17)(p11.2;q25) that results in the fusion of the TFE3 transcription factor gene at Xp11 with a novel gene at 17q25 designated ASPL was discovered.<sup>17,18</sup> In addition, Ladanyi *et al.*<sup>19</sup> reported that the monocarboxylate transporter 1 (MCT1) and its chaperone CD147 were located in the cytoplasmic crystals of an ASPS. However, the histogenesis of an ASPS remains unclear, even though these findings might provide some indication.

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