Proceedings of UCLA Healthcare
-VOLUME 18 (2014)-

CLINICAL VIGNETTE

Alveolar Rhabdomyosarcoma Cutaneous Metastases in a Zosteriform Distribution

Lily Adelzadeh B.S.[1], Andrew Breithaupt M.D. [1], Noah Federman M.D. [2,3], Julie Jackson M.D. [4], Lorraine Young M.D. [1]

[1]Department of Dermatology, David Geffen School of Medicine at UCLA, Los Angeles, CA
[2]UCLA's Jonsson Comprehensive Cancer Center, Los Angeles, CA
[3]Department of Pediatrics, Division of Hematology/Oncology, UCLA's Mattel Children's Hospital, David Geffen School of Medicine, Los Angeles, CA
[4]Department of Pathology, David Geffen School of Medicine at UCLA, Los Angeles, CA

Introduction

Cutaneous metastases of primary internal malignancy are relatively uncommon, with an overall incidence ranging from 0.7 to 10.4%. The most common presentations of cutaneous metastatic disease are papules and nodules, either solitary or widespread, and sometimes ulcerated. Zosteriform lesions represent a rare pattern of cutaneous metastases[1].
We report a patient with alveolar rhabdomyosarcoma (ARMS) who presents with cutaneous metastases in a zosteriform distribution.

Report of a Case

A 26-year-old woman presented with a vesicular plaque on her left upper chest and axilla in the T1, T2 and T3 dermatomes (Figure 1). She had a two-year history of refractory, recurrent and metastatic alveolar rhabdomyosarcoma originating from a left upper extremity soft tissue mass surrounding the humerus, with spread to the left axilla, left breast, and thoracic spine. The rash appeared suddenly two weeks prior to presentation with no associated pain or pruritus and did not cross the midline. No other skin lesions were present. She was receiving concurrent treatment with chemotherapy, which included vinorelbine, cyclophosphamide and bevacizumab.

Although the patient had a lack of symptoms, the lesion was initially attributed to herpes zoster based on the zosteriform distribution, and was started on acyclovir. However, two weeks after the initial presentation, the lesion continued to progress.

Varicella-zoster virus PCR scraping and chest lesion culture from the left lateral chest wall were negative. A biopsy from the left lateral chest wall demonstrated a malignant small blue cell neoplasm, characterized by sheets and columns of tumor cells dispersed in an infiltrative growth pattern in the dermis and subcutis. Tumor cells had pleomorphic and hyperchromatic nuclei and minimal to small amounts of eosinophilic cytoplasm. Several foci demonstrated an “alveolar” growth pattern (Figure 2). Immunohistochemical stains showed strong positive staining of tumor cells with antibodies to desmin, S-100 protein, and myogenin. Histological features and immunohistochemical staining were consistent with metastatic ARMS.

Despite ongoing chemotherapy, the patient succumbed to her disease two months after the initial skin presentation.

Comment

The underlying molecular pathogenesis of zosteriform metastases is not completely understood, but proposed theories include direct invasion of neoplastic cells from underlying tissue, tumoral invasion via fenestrated vessels of the dorsal root nerves with peripheral extension, perineural lymphatic invasion of the intercostal nerves, accidental surgical implantation of neoplastic cells, Koebner’s isomorphic response and Wolf’s isotopic response.[1] Wolf’s isotopic response describes a phenomena of a new, unrelated disease appearing at the site of a previously injured site of healed disease, whereas Koebner’s isomorphic response is the appearance of a second skin disease related to an existing one, but occurring at a different anatomical location of diminished resistance[2].

While cutaneous metastases are exceedingly rare in sarcomas, skin metastases appear to be slightly more prevalent in rhabdomyosarcoma versus other sarcoma diagnoses[3]. Of the rhabdomyosarcoma histologic variants, the alveolar subtype has a more aggressive

phenotype and a greater potential for metastatic disease compared to the more common embryonal subtype.

In ARMS, chromosomal translocations t(2;13)(q35;q14) and t(1;13)(p36;q14) and subsequent chimeric gene fusion products involving PAX and FOX(FKHR) family members are characteristic of these tumors. Moreover, these PAX-FKHR fusions appear to play a direct role in the oncogenesis and metastatic pathways of ARMS[4]. This patient had a documented FOXO1A(FKHR) rearrangement present in the tumor at initial diagnosis increasing its metastatic potential, and perhaps resulting in the unusual cutaneous spread of disease. Furthermore, it has been suggested in ovarian cancer that treatment with anti-vascular endothelial growth factor inhibitors such as bevacizumab, as in the treatment our patient received, is associated with cutaneous metastatic spread[5].

To our best knowledge, there have been no other documented cases of zosteriform cutaneous ARMS metastases.

Financial Disclosure: Dr. Noah Federman is supported by the St. Baldrick's Foundation Career Development Award

REFERENCES

1. **De Giorgi V, Grazzini M, Alfaioli B, Savarese I, Corciova SA, Guerriero G, Lotti T.** Cutaneous manifestations of breast carcinoma. Dermatol Ther. 2010 Nov-Dec;23(6):581-9. doi: 10.1111/j.1529-8019.2010.01365.x. *Review*. PubMed PMID: 21054704.
2. **Zalaudek I, Leinweber B, Richtig E, Smolle J, Hofmann-Wellenhof R**. Cutaneous zosteriform melanoma metastases arising after herpes zoster infection: a case report and review of the literature. *Melanoma Res.* 2003 Dec;13(6):635-9. PubMed PMID: 14646630.
3. **Wesche WA, Khare VK, Chesney TM, Jenkins JJ**. Non-hematopoietic cutaneous metastases in children and adolescents: thirty years experience at St. Jude Children's Research Hospital. *J Cutan Pathol*. 2000 Nov;27(10):485-92. PubMed PMID: 11100807.
4. **Mercado GE, Barr FG**. Fusions involving PAX and FOX genes in the molecular pathogenesis of alveolar rhabdomyosarcoma: recent advances. *Curr Mol Med*. 2007 Feb;7(1):47-61. Review. PubMed PMID: 17311532.
5. **Robinson WR, Beyer J, Griffin S, Kanjanavaikoon P**. Extraperitoneal metastases from recurrent ovarian cancer. *Int J Gynecol Cancer*. 2012 Jan;22(1):43-6. doi: 10.1097/IGC.0b013e31823532ce. PubMed PMID: 22193642.

Submitted on January 22, 2014

FIGURE LEGEND

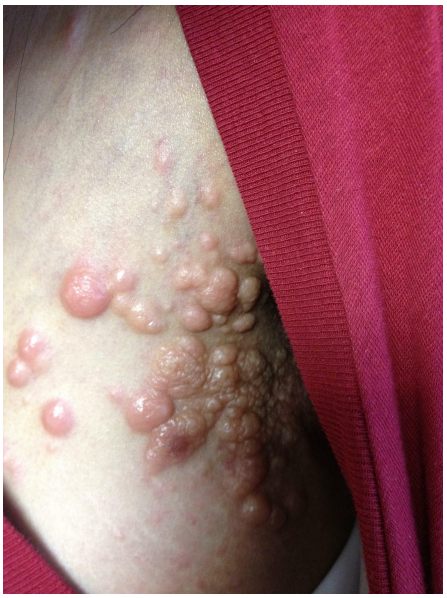

Figure 1: Alveolar rhabdomyosarcoma (ARMS) metastases. The metastases present as a vesicular plaque at the left axilla and lateral left chest, T1, T2 and T3 dermatomes.

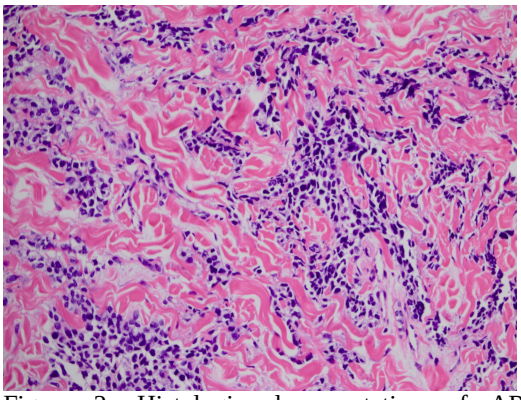

Figure 2: Histologic documentation of ARMS metastases. Hematoxylin-eosin stain, 20x, demonstrates sheets and columns of tumor cells dispersed in an infiltrative growth pattern in the dermis and subcutis. Tumor cells had pleomorphic and hyperchromatic nuclei and minimal to small amounts of eosinophilic cytoplasm. Numerous mitoses were identified. Several foci demonstrated an “alveolar” growth pattern.