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A rare case of metastatic extramammary Paget disease of the spine and review of the literature

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Abstract

Extramammary Paget disease is an intraepithelial neoplasm affecting cells rich in apocrine glands—often located in the vulvar, scrotal, or perianal region. It typically affects older patients, between the ages of 50 and 80 years old, and is most often limited to the epidermis. A 47-year-old Asian male first presented with enlargement of the right inguinal lymph node. A subsequent biopsy revealed extramammary Paget disease of the scrotum. The patient eventually developed significant worsening back pain with bilateral lower extremity numbness and weakness three months later. Imaging demonstrated a pathologic compression fracture of the L4 vertebral body with metastatic epidural spinal cord compression. The patient underwent surgical decompression of the spine with bilateral L4 laminectomy, resection of epidural tumor, and pedicle screw fixation from L2 to S1. Surgical pathology demonstrated metastatic adenocarcinoma consistent with extramammary Paget disease. Although two other case reports have described spinal metastases from extramammary Paget disease, to the author's knowledge, this represents the first report of surgical decompression and fusion for extramammary Paget disease of the spine.

Keywords

Metastasis; Extramammary; Paget disease; Surgery; Hemolytic anemia; Spine

1. Introduction

Extramammary Paget disease is an intraepithelial neoplasm affecting cells rich in apocrine glands—often located in the vulvar, scrotal, or perianal region. It typically affects older patients, between the ages of 50 and 80 years old, and is most often limited to the epidermis [1]. As a rare, slow-growing malignancy with low metastatic potential, the incidence of

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Conflicts of interest/disclosures

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metastases is estimated to be 0.11 per 100,000 person-years [2]. Herein, we present a rare case of a patient with metastatic extramammary Paget disease of the spinal column.

2. Case report

A 47-year-old Asian male with a previous history of E-antigen-negative hepatitis B was treated for fungal infections of the scrotum for several years. However, he noticed enlargement of the right inguinal lymph node. A subsequent biopsy revealed extramammary Paget disease of the scrotum. Histologic sections showed an infiltration of large histiocytic cells with prominent nucleoli, amphophilic cytoplasm, and occasional intracytoplasmic vacuoles (Fig. 1A–B). By immunohistochemistry, these cells were: strongly and diffusely positive for cytokeratin 7 (Fig. 1D), epithelial membrane antigen (EMA, Fig. 1F), and gross cystic disease fluid protein 15 (GCDFP-15, Fig. 1G); focally positive for monoclonal carcinoembryonic antigen (CEA, Fig. 1C) and NKX3.1 (Fig. 1H); and negative for cytokeratin 20 (Fig. 1E), PAX-8 (Fig. 1I), and HER2/neu (not shown). A special stain for mucicarmine highlighted the presence of rare intracytoplasmic mucin vacuoles.

The patient eventually developed significant, and progressive, worsening back pain, bilateral lower extremity numbness, and weakness three months later. Imaging demonstrated a pathologic compression fracture of the L4 vertebral body with metastatic epidural spinal cord compression (Fig. 2A–C).

The patient underwent surgical decompression of the spine with bilateral L4 laminectomy, resection of epidural tumor, and pedicle screw fixation from L2 to S1 (Fig. 2D–F). Post-operative imaging demonstrated spinal cord decompression with instrumented arthrodesis.

Surgical pathology demonstrated metastatic adenocarcinoma consistent with extramammary Paget disease (Fig. 3). Histologic sections showed sheets and nests of epithelioid cells with large pleomorphic nuclei, prominent nucleoli, and abundant eosinophilic cytoplasm with occasional intracytoplasmic blue mucin (Fig. 3).

Two months later, the patient underwent frameless stereotactic radiosurgery to L4 with an overall dose of 4545 cGy. Chemotherapy—paclitaxel and carboplatin—was initiated two months later. Four months post-operatively, the patient presented with Coombs-negative microangiopathic hemolytic anemia (MAHA), thrombocytopenia, and dyspnea—presumably driven by the underlying malignancy. The patient was able to ambulate independently at the 6 month post-operative visit, and reported stable low back pain. Seven months post-operatively, the patient succumbed to his disease.

3. Discussion

Although two other case reports have described spinal metastases from extramammary Paget disease, to the author's knowledge, this represents the first report of surgical decompression and fusion for extramammary Paget disease of the spine (Table 1). Little et al. [3] presented a case of a 57-year-old male with lytic metastases to the right ilium, right scapula, and T8 vertebral body. Of note, there were no FDG-avid metastases 13 months prior to the discovery of widespread metastatic lesions. The T8 compression fracture was treated with

vertebroplasty and the patient passed away 5 months after the discovery of spinal metastases. Beleznyay et al. [4] presented a case of a 67-year-old Asian male with extramammary Paget disease of the spine, 3 years following the diagnosis of the primary scrotal lesion. The patient presented with pancytopenia and low back pain; imaging revealed compression fractures of T5, T8, and L1. He received 5-fluorouracil chemotherapy and palliative radiation to the spine, before passing away 6.2 months following the diagnosis of spinal metastases.

Moreover, lymph node invasion is not common in males with extramammary Paget disease and, when present, may progress to distant metastasis. In one of the largest published series, Kang et al. [5] described 246 Chinese male patients with extramammary Paget disease. Notably, lymph node invasion was only confirmed in 19 of 246 patients (7.7%).

The rare Coombs negative paraneoplastic syndrome, cancer-related microangiopathic hemolytic anemia (CR-MAHA), has been previously described in a case series of 168 patients [6] but has yet to be described in the setting of extramammary Paget disease. Underlying malignancy may be considered as the driver for microangiopathic hemolytic anemia when other sources such as thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), atypical HUS (aHUS), disseminated intravascular coagulopathy (DIC), and vasculitis have been ruled out. The phenomenon of CR-MAHA may be more common in metastatic extra-mammary Paget disease, compared to other metastatic tumors, but there is a lack of published literature in this area [6,7].

Distant metastases from extramammary Paget disease are rare. However, any suspicion for metastatic spine disease should be carefully evaluated and may necessitate surgical intervention to preserve neurologic function, reduce pain, and improve quality of life.

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Fig. 1.

Immunohistochemistry of right inguinal lymph node metastasis. A-B. Histologic sections showed an infiltration of large histiocytic cells with prominent nucleoli, amphophilic cytoplasm, and occasional intracytoplasmic vacuoles. By immunohistochemistry, these cells were: strongly and diffusely positive for cytokeratin 7 (D), epithelial membrane antigen (EMA, F), and gross cystic disease fluid protein 15 (GCDFP-15, G); focally positive for monoclonal carcinoembryonic antigen (CEA, C) and NKX3.1 (H); and negative for cytokeratin 20 (E), PAX-8 (I), and HER2/neu (not shown). A special stain for mucicarmine highlighted the presence of rare intracytoplasmic mucin vacuoles.

Fig. 2.

Pre-operative and post-operative imaging. Pre-operative sagittal (A) and axial (B) T2-weighted MRI demonstrate a pathologic compression fracture of the L4 vertebral body. Sagittal CT (C) shows a lytic lesion at L4. Surgical decompression with bilateral L4 laminectomy, resection of epidural tumor, and pedicle screw fixation from L2 to S1 is demonstrated by sagittal T2-weighted MRI (D), coronal topogram (E), and sagittal CT (F).

Fig. 3.

Surgical pathology of epidural spine metastasis. A-B. Histologic sections showed sheets and nests of epithelioid cells with large pleomorphic nuclei, prominent nucleoli, and abundant eosinophilic cytoplasm with occasional intracytoplasmic blue mucin. By immunohistochemistry, these cells were: diffusely positive for cytokeratin AE1/AE3 (C), epithelial membrane antigen (EMA, D), GATA-3 (E), and gross cystic disease fluid protein 15 (GCDFP-15, F); and negative for S-100 protein (not shown), thyroid transcription factor-1 (TTF-1, not shown), and PAX-8 (not shown).

Table 1

Literature Review of Metastatic Extramammary Paget Disease of the Spine.

Author	Number of Patients	Age	Presentation and Spine Level	Medical Management	Management of Spine Disease	Survival From Spinal Metastasis
Little et al. [3]	1	57	Initially presented with scrotal rash, presumed to be dermatitis. Two years later, the lesion was biopsied and diagnosed as EMPD. 13 months following initial diagnosis, patient presented with severe back pain due to T8 pathologic fracture	Mohs surgery of the perineum. Systemic chemotherapy with paclitaxel	T8 vertebroplasty for pathologic fracture. Palliative radiation to the spine	5 months
Beleznay et al. [4]	1	67	Presented with fatigue and back pain three years following initial diagnosis of EMPD of the scrotum. Physical exam revealed left sided pyramidal tract deficits. Imaging demonstrated compression fractures at T5, T8, and L1	Patient declined Mohs surgery. He was treated with Imiquimod for 1 year following diagnosis. Three cycles of 5-fluorouracil and leucovorin were administered	Palliative radiation to the spine	6 months
Present Case	1	47	Initially presented with inguinal node enlargement. Three months later, imaging demonstrated a pathologic compression fracture of L4	Paclitaxel and carboplatin. The patient declined Mohs surgery	Bilateral L4 laminectomy, resection of epidural tumor, and pedicle screw fixation from L2 to S1	7 months