Surgical Treatment of Brain Metastasis of Extramammary Paget’s Disease: A Case Report

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Extramammary Paget’s disease (EMPD) is a rare form of neoplasm. Metastasis of EMPD to locations other than lymph nodes and intra-epithelial regions is rare; there are a limited number of case reports of metastases to the liver, lung, bone, and brain. We present a rare case of EMPD that metastasized to the brain and was treated with surgical resection. A 66-year-old man presented with a small palpable mass in the scrotum. After 5 years of observation, he was diagnosed with EMPD that metastasized to the lymph nodes and lung. Tumor resection and postoperative chemotherapy were performed. Six months after the last chemotherapy treatment, he presented with a right temporal lobe tumor and underwent surgical resection. Histopathological analysis revealed brain metastasis of EMPD. Three months after surgery, magnetic resonance imaging (MRI) showed local tumor recurrence, and intensity modulated radiation therapy (IMRT) (45 Gy/15 Fr) was performed. Although the metastatic brain tumor was well controlled, the primary tumor progressed. He was provided best supportive care and died 5 months after brain tumor resection. In this report, we present a rare case of brain metastasis of EMPD, treated with surgical resection, and histopathologically confirmed to be metastatic EMPD.

Keywords: extramammary Paget’s disease, metastasis

Introduction

Extramammary Paget’s disease (EMPD) is a rare form of neoplasm. EMPD originates from the apocrine sweat gland and is common in elderly men.¹,³⁰ Early diagnosis is usually difficult due to eczema-like erythema and erosion; thus, it is sometimes diagnosed as eczema, psoriasis, intertrigo, or a fungal infection.² The prognosis of EMPD depends on infiltration into the basement membrane. EMPD limited to the epidermis is curable with surgical removal, but in cases with EMPD invading below the basement membrane, the prognosis is poor and metastasis sometimes occurs. The most common metastatic sites for EMPD are the lymph nodes and intra-epithelium.⁴ Metastasis of EMPD to locations other than the lymph nodes and intra-epithelium are rare, but there are limited case reports of metastases to the liver, lung, bone, and brain.⁴ ⁰

In this report, we report a rare case of brain metastasis of EMPD that was treated with surgical resection.

Case Presentation

A 66-year-old man presented with a small palpable mass in the scrotum. After 5 years of observation, he visited our dermatology clinic and underwent a biopsy. He was diagnosed with EMPD. Tumor resection was performed. Initial systemic computed tomography (CT) showed metastasis to the lymph nodes; thus, he was considered to have stage III disease. However, metastasis to the liver was diagnosed 18 months after the initial diagnosis of EMPD and his clinical stage had progressed to Stage IV. Postoperative chemotherapy with weekly paclitaxel (PTX), docetaxel (DOC), fluorouracil (5-FU), cisplatin (CDDP), and irinotecan (CPT-11) was performed, and his clinical course was stable.

Six months after the last chemotherapy treatment, he presented with ideomotor apraxia and left upper quadrant hemianopsia. Head CT and magnetic resonance imaging (MRI) showed a tumor in the right temporal lobe with extensive peritumoral edema. Contrast-enhanced MRI showed the maximum diameter of the tumor was 34 mm, accompanied by ring enhancement and a wide range of edematous lesions throughout the right temporal lobe (Figs. 1A–1C). The tumor was attached to the dural surface of the middle cranial fossa. Metastatic brain tumor of EMPD was highly suspected, but glioblastoma and malignant meningioma were also considered differential diagnoses. Since the patient could tolerate surgical resection, tumor resection was performed. The tumor was soft and elastic, had clear boundaries, and bled easily. The boundary between the tumor and healthy brain was clear; thus, the tumor was completely removed en bloc. Histopathological analysis revealed heteromorphic cells with sheet-like and alveolar-like clumps. Immunostaining showed...
CK 7-positive and CK 20 and p40-negative cells accounted for the majority of the sample (Figs. 2A–D and 2F). The carcinoembryonic antigen (CEA) is partially positive (Fig. 2E). Primary scrotum tissue also had similar heteromorphic cells with enlarged and slightly irregularly shaped nuclei and was positive for CK7 by immunohistochemistry which was consistent with metastatic EMPD (Figs. 3A–3F).

Postoperative MRI showed complete removal of the tumor; thus, postoperative radiation therapy was postponed until local tumor recurrence (Figs. 4A–4E). Three months after the surgery, MRI showed tumor local recurrence from the dura mater and IMRT (45 Gy/15 Fr) was performed (Figs. 4F–4H).

Although the metastasis in the cranium was well controlled, tumors at the primary lesion site progressed. The patient was terminally ill, and he chose best supportive care 4 months after metastatic brain tumor surgery. He was transferred to a palliative care unit and died 5 months after the brain tumor surgery.
EMPD is a rare form of neoplasm and exact incidence is unknown. EMPD originates from the apocrine sweat gland and is common in elderly Asian men\textsuperscript{1–3)} aged 65–80 years, which is consistent with our case. In addition, secondary EPMD, which is a less common form of EPMD, develop from epidermotropic spread of malignant cells from underlying carcinoma such as in the gastrointestinal and urothelial tract.\textsuperscript{2)}

In this case study, we present a rare case of brain metastasis of EMPD treated with surgical resection. The most common metastatic sites for EMPD have been reported to be the lymph nodes and intra-epithelium.\textsuperscript{4)} Metastasis of EMPD to locations other than the lymph nodes and intra-epithelium is rare, but there are limited case reports of metastases to the liver, lung, bone, and brain.\textsuperscript{4–5)} There have been previous case reports of brain metastasis of EMPD; however, most cases died shortly after metastasis and could not undergo surgical resection. Thus, in most cases, brain metastasis of EMPD was not histopathologically confirmed and brain metastasis of EMPD was diagnosed because they presented with multiple brain lesion.\textsuperscript{5,6)}

One case report presented a patient with brain metastasis of EMPD who underwent surgical resection and postoperative whole brain radiotherapy. In this case, the patient presented with multiple cystic lesions of the cerebellum, underwent cyst puncture, and only limited tumor tissue was available. In addition, the patient died 2 months after radiotherapy.\textsuperscript{4)} Thus, our case is different from previous studies in that the patients presented with a single solid lesion, attached to dura matter, and required differential diagnosis from glioblastoma and meningioma. In addition, our patient underwent total tumor resection and the tumor was histologically confirmed to be brain metastasis of EMPD.

Histopathologically, the EPMD presented with Paget cells which have clear cytoplasm and large pleomorphic nuclei and immunohistochemical analysis showed positive staining for CK7. In addition, EPMD cells secrete CEA; thus, CEA is usually partially positive although this is not specific to EPMD.\textsuperscript{2,6)} Previous case which was histopathologically confirmed to be a metastatic EPMD to brain showed a typical histopathological and immunohistochemical profile from brain metastasis, including existence of Paget cells and immunopositivity to CK7.\textsuperscript{4)} Thus, EMPD brain metastasis and the primary lesion were histopathologically quite similar. In our case, we also observed heteromorphic Paget cells with enlarged and slightly irregularly shaped nuclei and positive Immunohistochemistry (IHC) staining for CK7; thus, our case also had similar histopathological features between primary scrotum lesion and brain metastasis. In addition, it is also essential to
distinguish primary from secondary EMPD to find whether patients have underlying malignancy. In this case, we used CK20 and p40 to distinguish primary from secondary EMPD. CK20 is positive in gastrointestinal and urothelial carcinoma and p40 is positive in squamous cell carcinoma. Based on the immunochemical findings that both CK20 and p40 are negative, we diagnosed this case as metastatic primary EMPD.

In our case, the patient died 5 months after the surgical resection of the brain metastasis. EMPD patients with brain metastasis usually die within a few months of the diagnosis of brain metastasis, thus, our patient lived relatively longer compared with past reported cases. We resected the brain metastasis because this patient had a single brain metastasis and resection is indicated the same as for brain metastasis from other types of cancer. However, the prognostic factors of brain metastasis of EMPD and the role of surgical resection in EMPD patients with brain metastasis are unknown. Future case studies are necessary to examine prognostic factors and the role of surgical resection in EMPD patients with brain metastasis.

**Conclusion**

We reported a rare case of single brain metastasis of EMPD treated with surgical resection. The prognosis of metastatic EMPD is very poor and surgical resection is not indicated for most metastatic EMPD patients. However, surgical resection can prolong survival when patients can tolerate surgical resection.
Conflicts of Interest Disclosure

No potential conflicts of interest were disclosed.

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