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Case Report

Skull metastasis in urothelial cell carcinoma of the bladder

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ABSTRACT

Urothelial cell carcinoma of the urinary bladder with metastasis to the skull is extremely rare. We present a case of occipital bone metastasis arising from a previously verified bladder urothelial carcinoma. An 81-year-old woman presented with a painless, nonpulsatile mass in the left occipital region of the scalp that had progressively increased for 1 year. Skull radiography demonstrated a large osteolytic lesion in the left occipital bone. Computed tomography of the head showed a 6.5 cm × 6.0 cm skull defect from the midline to the left occipital bone, overlying the posterior superior sagittal sinus. The patient underwent a wide craniectomy with en bloc removal of the mass. Because of widespread disease, the patient died 3 months after surgery.

1. Introduction

Tumor metastasis to the skull occurs in various malignancies, most often from the lung, breast, prostate, and thyroid. Urothelial carcinoma of the urinary bladder (UCB) usually disseminates to the liver, lung, and bone marrow. Skull metastasis from UCB is uncommon, and occurs in less than 1.0% of patients harboring this pathology.

UCB is the fourth most common cancer in white men, with a male to female ratio of 8:1 in those older than 50 years [1]. Women and black people are most likely to present with advanced disease [2,3]. When distant metastasis is present, the disease becomes invasive with a poor outcome. A solid mass causing lytic lesions in the skull is suggestive of metastasis and can present with various radiological findings. Skull metastasis can cause many clinical manifestations including cosmetic problems, pain, local swelling, skin ulcerations, bleeding, neurological deficit, dural sinus compression, and sinus thrombosis.

Bone metastasis noticeably worsens the prognosis of cancer patients because of organ infiltration or progression of the original cancer. If cranial metastases overlie or invade the dural venous sinus, surgical resection may provide effective palliation of symptomatic skull metastasis. Focal palliative radiotherapy might also be helpful in relieving symptoms or preventing recurrence [4,5].

2. Case report

An 81-year-old woman presented to the Department of Neurosurgery, Chung Shan Medical University Hospital, Taichung, Taiwan, with painless, progressively increasing swelling in the left occipital region close to the midline of the scalp (Fig. 1A). High grade, lamina propria infiltrative UCB following transurethral resection (pT1N0M0, grade 1) had been diagnosed in this patient 1 year previously. After admission, skull radiography and contrast-enhanced computed tomography (CT) demonstrated a 6 cm × 6 cm × 6.5 cm lytic lesion in the left occipital bone destroying the outer and inner tables, and extending extradurally under the scalp (Fig. 1B and C). A total tumor resection via a left occipital craniectomy was performed. Grossly, the tumor was elastic and immobile with a thickened capsule and central necrosis, expanding intracranially and overlying the posterior superior sagittal sinus (Fig. 2). The entire tumor along with the involved bone was removed, and the portion overlying the sinus was gently

Conflicts of interest: none.

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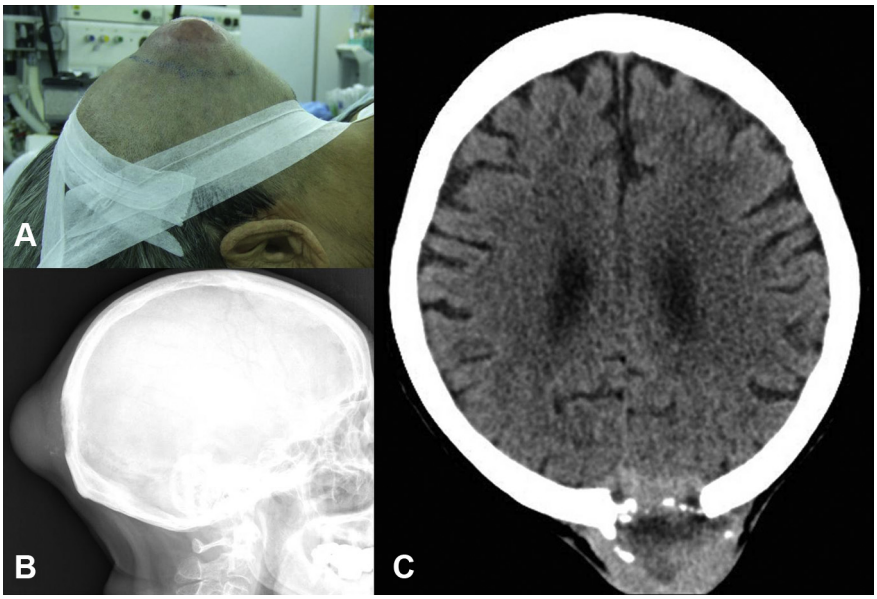

Fig. 1. (A) Lateral view of the head demonstrates a scalp mass. (B) Plain radiography of the skull depicts an osteolytic defect in the occipital bone. (C) Computed tomography reveals a defect in the left occipital bone and a soft mass compressed the superior sagittal sinus.

peeled away. Because there was no dural sinus involvement, en bloc resection of the tumor was accomplished with minimal blood loss. An acrylic plate was used for the bony defect. Histopathologic examination showed a papillary arrangement of cancer cells with central necrosis (Fig. 3A and B). The individual cancer cells showed pleomorphic nuclei and prominent nucleoli with frequent mitoses. The skull was infiltrated by cancer cells without involvement of the overlying dermis (Fig. 3C). Immunohistochemical stains with p63, CK20, and CK7 were all positive, thus confirming the diagnosis of metastatic urothelial cell carcinoma (Fig. 3D–F).

Three weeks after surgery, technetium-99m methylene diphosphonate (^{99m}Tc-MDP) bone scintigraphy showed abnormal ring-shaped uptake in the occipital skull related to postcraniectomy changes, but no other abnormal bone or vertebral uptake (Fig. 4). The occipital skull was the site of the initial distal metastasis originating from UCB. The patient had an uneventful recovery, and completed whole brain radiotherapy with 5040 Gy in 28 fractions. Because of refractory gastrointestinal bleeding and uremia, the patient died 3 months after the initial diagnosis of skull metastasis.

3. Discussion

The incidence of skull metastasis from malignant tumors is increasing, most commonly from breast cancer, pulmonary cancer, and prostate cancer. Breast cancer accounts for 55% of metastatic skull lesions, the highest rate of these cancers [6]. This report shows a rare case of skull metastatic urothelial cell carcinoma producing destruction of the left occipital bone. It also emphasizes an atypical appearance of urothelial cell carcinoma.

Skull metastasis from UCB is uncommon. Babaian et al [7] reported 107 cases of metastatic urothelial cell carcinoma; the most common site for metastases was the lymph nodes (78%), followed by the liver (38%), lung (36%), bone (27%), and adrenal glands (21%), with rare involvement (1–8%) of the heart, brain, kidney, spleen, pancreas, meninges, uterus, ovaries, prostate, and testes. Skull metastasis was found in only one case (1/107), accounting for less than 1% [7].

Skull metastases are classically osteolytic and hypervascular with an expansile palpable scalp mass, as in our case. In 2003, Stark

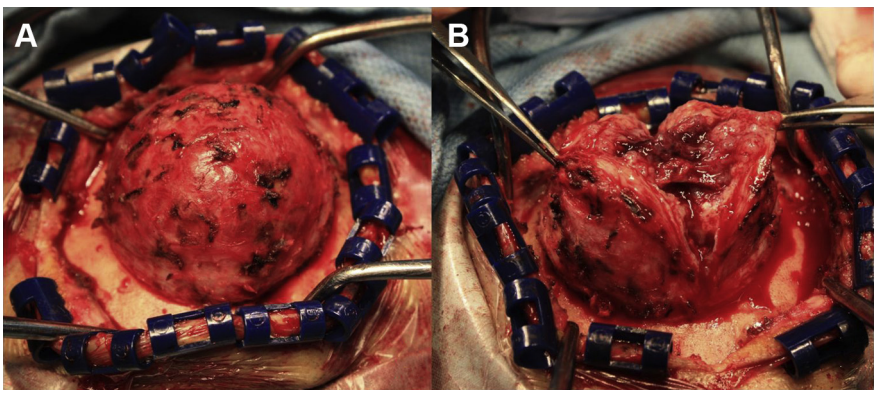

Fig. 2. Intraoperative photographs. (A) An elastic, immobile, occipital mass on the left side of the skull is seen. (B) The tumor capsule is thickened with central necrosis.

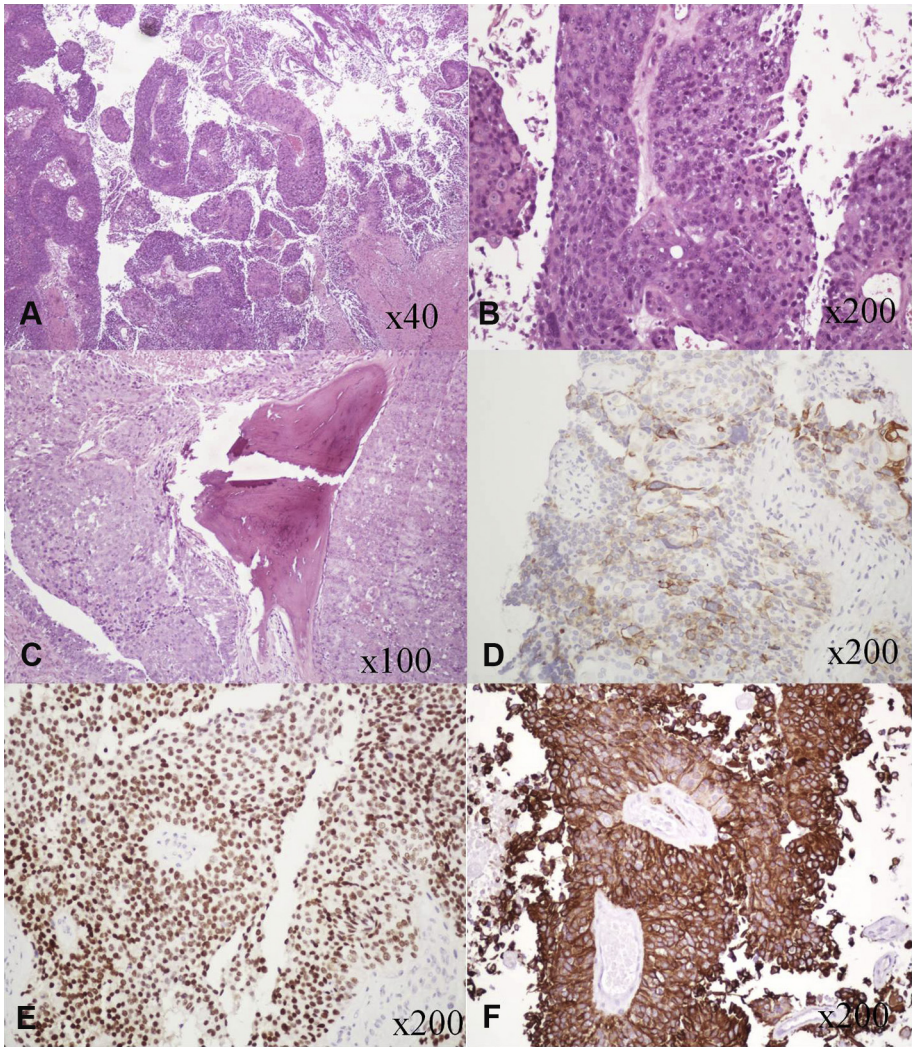

Fig. 3. Histopathology of a biopsy specimen from the skull lesion. (A) Low-power view shows the skull bone tumor has papillary fronds with frequent branching and fusion [hematoxylin and eosin (H&E) stain, ×40]. (B) High-power view shows atypical tumor cells that are pleomorphic with hyperchromatic nuclei, prominent nucleoli, and frequent mitoses (H&E, ×200). (C) The skull is infiltrated by tumor cells (H&E, ×100). (D) Immunostaining with CK20. (E) Immunostaining with p63. (F) Immunostaining with CK7.

et al [4] presented their experience with 12 cases of skull metastases from breast carcinoma, malignant melanoma, colorectal cancer, prostate cancer, parotid cancer, leiomyosarcoma, soft-tissue sarcoma, and Ewing sarcoma. The most common symptoms were painless swelling in five patients (42%), local pain and neurological deficit (facial palsy, hypoesthesia of the trigeminal nerve area) in three patients (25%), and dural invasion with compression of the dural sinuses causing increased intracranial pressure, meningeal irritation, and focal neurological signs in six patients (50%).

The mechanism of skull bone metastasis from urothelial cell carcinoma has not been completely elucidated. In general, there are five mechanisms by which a metastatic tumor spreads from a primary site to the skull bone: direct extension from an intracranial primary tumor, hematogenous spread, lymphatic spread, direct meningeal extension, and leptomeningeal seeding. The most common mechanism of urothelial cell carcinoma metastasis is local lymphatic spread. Brain or skull metastasis most likely occurs by hematogenous spread rather than other mechanisms, and is regarded as a late appearance of systemic extension. Some identified risk factors, such as radiation exposure or tobacco use, increase the incidence of brain or skull metastasis in urothelial cell carcinoma. In 2010, Ogunyemi et al [8] reported on 734 patients with genitourinary tumors, of whom 75% with brain metastases had a strong history of tobacco use.

Plain skull radiography is the most frequent initial step in patients with clinical suspicion of a bone lesion. CT and magnetic resonance imaging (MRI) enable screening for important information prior to surgery, CT can determine the degree of bony destruction, and MRI contributes to understanding of the tumor type, location, multiplicity, and relationship to the brain, dural sinus, and nerve tissue. ^{99m}Tc-MDP bone scintigraphy and ^{18}F-fluoride positron emission tomography/CT (PET/CT) are usually used to detect bony metastases [9,10]. ^{18}F-fludeoxyglucose (^{18}F-FDG) PET has been reported to be more sensitive, specific, and accurate than ^{99m}Tc-MDP bone scintigraphy in patients with skeletal metastases in urinary bladder carcinoma [11].

Most metastatic skull tumors may not directly influence the survival time of patients, but are clinically significant in relation to quality of life. The prognosis of skull metastatic tumors varies based on the type of primary cancer. In one study, the median interval between treatment of the primary cancer and detection of skull metastases was 4 years (mean, 6 years; range, 0–16 years, 5 months) [6]. The mean survival time from skull metastasis was 19.5

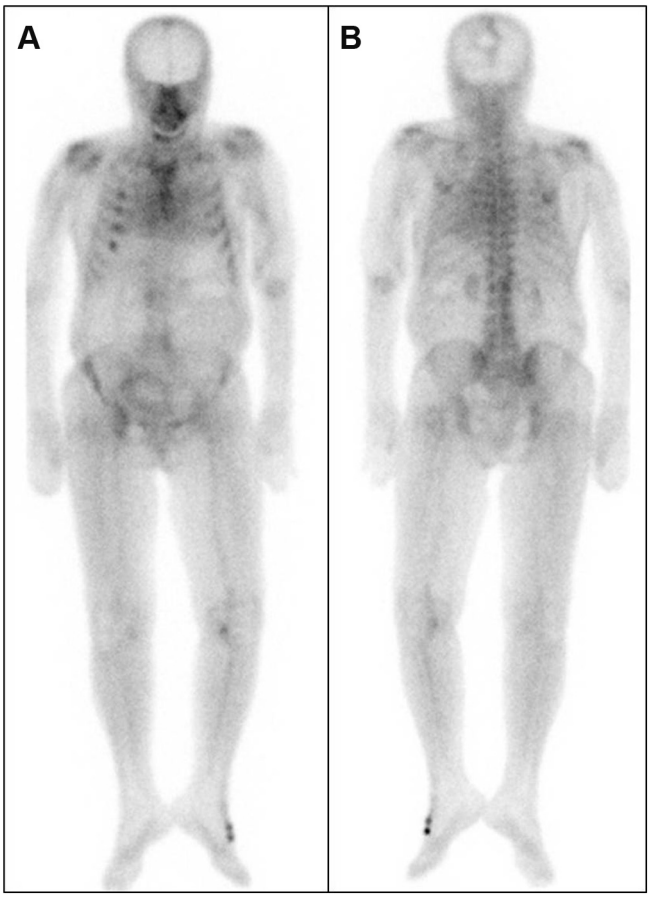

Fig. 4. (A) ^{99m}Tc-MDP bone scintigraphy shows several consecutive hot spots in the right rib cage, most likely rib fractures. (B) ^{99m}Tc-MDP bone scintigraphy shows increased ring-shaped uptake in the occipital skull, consistent with postcraniectomy changes.

months (median, 9 months; range, 3–65 months). Distant metastasis of urothelial cell carcinoma has seldom been studied. Mahmoud-Ahmed et al [12] reported the overall survival after brain metastasis in 16 patients with UCB was poor, with a median survival time of 2 months (range, 0.5–12.75 months). Babaian et al [7] reported a median survival time of 3 months (range, 1–58 months) in 107 patients with urothelial cell carcinoma with various sites of metastasis. The causes of death were sepsis (42%), carcinomatosis (28%), and uremia (15%) [7]. Our patient died because of gastrointestinal bleeding and uremia.

There are four modalities in the treatment of skull metastasis: surgical removal, irradiation, chemotherapy, and endocrinological therapy. Conventional fractionated radiation therapy remains the primary treatment for skull metastasis. However, some patients are candidates for surgical resection when skull metastases compress/infiltrate the dural venous sinus. Michael et al [5] reported 13 patients with skull metastasis involving the dural sinus, most of whom benefited from surgery and/or radiotherapy in terms of pain control or improvement of neurologic deficits. The benefits from surgical removal of skull metastasis include a rapid decompression of perifocal edema, elimination of mass effects, a decrease in dural sinus compression, and improved cognitive function.

Histologically, the metastatic tumor is often poorly differentiated, and immunohistochemical staining is needed to find its primary origin. CK20 and p63 are regularly used to differentiate between urothelial cell carcinoma and squamous cell carcinoma. Urothelial cell carcinoma frequently expresses both CK20 and p63 positivity. Gruver et al [13] showed a positive immunophenotype with strongly expressed CK7 (100%), CK20 (53%), and p63 (78%) in 37 cases of primary invasive tumors of the urinary bladder. Ogata et al [14] reported that CK20 was strongly associated with recurrence and histologic grades in cases of urothelial neoplasms.

Generally, multitherapeutic approaches to bladder cancer surgery, chemotherapy, and radiotherapy improve the patient's long-term survival. Although there is no direct relationship between the prognosis and skull metastasis, the prognosis is usually poor in patients with urothelial cell carcinoma with skull metastasis. Metastasis of urothelial cell carcinoma to the skull is attributed to the uncontrolled progression or infiltration of the original cancer. Early detection of bone metastasis is therefore important for selecting appropriate treatment as well as a better prognosis.

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