Clinical note

A case of brain and leptomeningeal metastases from urothelial carcinoma of the bladder

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ABSTRACT

Brain metastases are unusual from urothelial carcinoma of bladder and particularly the occurrence of leptomeningeal metastases is extremely rare, with few cases described in the literature. We present a case of a 45-year-old man with a rare brain metastases as the first metastatic manifestation secondary to uterine carcinoma of bladder followed by leptomeningeal metastases without any other organ involvement. Eleven months after the diagnosis of high-grade urothelial carcinoma of bladder (T2N0M0), the patient was detected having brain metastases by MRI. FDG PET/CT images for the metastatic evaluation showed no abnormal FDG uptake elsewhere in the body except the brain. Histopathology examination from brain lesion demonstrated the cerebral lesion to be a metastatic urothelial carcinoma. Two months later, the patient was diagnosed to have leptomeningeal metastases by MRI. Our patient’s condition gradually worsened, and he died 3 months after the diagnosis of leptomeningeal metastases.

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Un caso de metástasis cerebrales y leptomeningeas de un carcinoma urotelial de vejiga

RESUMEN

Las metástasis cerebrales del carcinoma urotelial de vejiga son poco habituales y, en particular, las metástasis leptomeningeas son extremadamente raras, siendo pocos los casos descritos en la literatura. Presentamos un hombre de 45 años con metástasis cerebral como primera manifestación secundaria de un carcinoma urotelial de vejiga seguido de metástasis leptomeningeas sin otra afectación sistémica. Once meses después del diagnóstico de un carcinoma urotelial de vejiga (T2N0M0), se detectaron metástasis cerebrales por RM. El estudio de estadificación con FDG PET/TC no demostró captación anormal en otra parte del cuerpo a excepción del cerebro. El examen histopatológico de una lesión cerebral demostró metástasis del carcinoma urotelial. Dos meses después, una RM descubrió metástasis leptomeningeas. La situación clínica del paciente se deterioró gradualmente, y falleció 3 meses después del diagnóstico de las metástasis leptomeningeas.

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Introduction

Urothelial carcinoma of the bladder (UCB) constitutes the majority of bladder carcinomas and usually gives metastases to lymph nodes, liver, lung, bones, adrenal gland and intestine.1 Brain metastases are relatively infrequent, but are often seen during chemotherapy in the advanced stage of bladder carcinoma, reported incidences 1–8%.2,3 However, leptomeningeal metastases are a very rare entity, reported only in case reports in bladder carcinoma. Leptomeningeal metastases occur in 1–8% of all cancer patients and inevitably have a fatal outcome.4,5

The staging of UCB is an essential step in appropriate management of disease. Currently the staging assessment of UCB is mainly based on imaging techniques such as CT and MRI, with contrast enhancement, both of which are recommended by current guidelines. These techniques are mainly based on morphological estimates such as size and shape of enlarged lymph node, and therefore are not sufficient to detect small metastases.6 As a metabolic and anatomic diagnostic tool, FDG PET/CT has the ability to overcome the limitations of conventional imaging modalities leading to changes in patient management.7–10 FDG PET/CT provides important diagnostic information on the location, extent, and metabolic characteristics of recurrent and metastatic bladder UCB lesions.7,8

Here, we have presented a case of a 45-year-old man with a rare brain metastases as the first metastatic manifestation secondary to UCB followed by leptomeningeal metastases without any other organ involvement and discussed the imaging modalities.

Clinical case

A 45-year-old man, smoker of 20 cigarettes/day during 22 year, was admitted to the hospital due to macroscopic hematuria. Urine cytology was negative. Abdominal MRI demonstrated a mass lesion on the right lateral wall of urinary bladder. Cystoscopic examination revealed thickening in the right lateral wall of the urinary...
bladder. Transurethral resection of the bladder tumor (TUR-Bt) was performed. Pathological examination of the TUR material revealed a high-grade UCB, pT2, G3, with foci of neuroendocrine carcinoma. The metastatic workup, including physical examination, laboratory and radiographic studies did not reveal any remarkable abnormalities. Body CT and bone scans demonstrated no evidence of metastases elsewhere in the body. The tumor was staged as T2N0M0. The patient received 4 cycles of neoadjuvant chemotherapy with gemcitabine-cisplatin. A check on cystoscopy 6 months after treatment showed evidence of tumor recurrence. The patient underwent a cystoprostatectomy with an orthotopic ileal neobladder and bilateral pelvic lymph node dissection. Histopathological examination indicated a high-grade UCB (T2N0M0).

Five months after cystoprostatectomy, the patient readmitted because of the dizziness, nausea and loss of balance. Brain MRI revealed a mass lesion located at right parieto-occipital region (Fig. 1). Five days later, FDG PET/CT images for the restaging showed two lesions with increased metabolic activity in the right parieto-occipital region of brain (Fig. 2). No other abnormal FDG uptake was detected elsewhere in the body. The patient underwent cranietomy and excisional biopsy. Histopathology demonstrated the cerebral lesion to be a metastatic urothelial carcinoma. On the basis of these finding, the patient was diagnosed as having brain metastases from UCB.

The patient was started whole brain radiotherapy. Two months later, in the last week of radiotherapy, the patient complained of weakness in the bilaterally upper and lower extremity, urinary and fecal incontinence. On neurological examination revealed paresis

![Fig. 1. Postcontrast axial T1-weighted MRI of the brain showing a hyperintense lesion with surrounding edema (arrow) in the right parieto-occipital region.](image1)

![Fig. 2. Maximum intensity projection (MIP) (A), sagittal MIP (B), transaxial PET (C, D) and coronal PET (E, F) images showed two lesions with increased metabolic activity in the right parieto-occipital region of brain (arrows). Physiologic accumulation of excreted FDG in the orthotopic ileal neobladder was confirmed by postvoid MIP images of pelvis (G) (arrow). Focal FDG uptake in the right iliac region was considered to be due to metallic material placed after surgery. However, no other abnormal FDG uptake was observed elsewhere in the body.](image2)
in the bilaterally upper and lower extremity. MRI with contrast administration showed diffuse leptomeningeal enhancement consistent with metastatic leptomeningeal disease (Fig. 3). A lumbar puncture was performed and with pathological analysis of the cerebrospinal fluid was negative for tumor cells, with increased protein concentration, and decreased glucose concentration. Leptomeningeal metastases were diagnosed with positive imaging, strict neurological symptoms and signs, although cytology was negative.

Systemic chemotherapy as well as palliative radiotherapy of the brain and spinal cord was begun despite a poor prognosis. However, our patient’s condition gradually worsened, and he died 3 months after the diagnosis of leptomeningeal metastases.

Discussion

In recent years, the improved radiological techniques and multi-therapeutic approaches to bladder cancer have prolonged the survival period but at the same time increased the risk for developing uncommon metastatic lesions, such as brain and leptomeningeal metastases. Usually, the development of brain and leptomeningeal metastases is a late event in the course of bladder carcinoma, occurs most often in patients with extensive systemic disease and have a bad prognosis despite aggressive therapy. Brain or leptomeningeal metastases as the first metastatic manifestation of UCB without evidence of recurrent or disseminated disease is extremely rare, with few cases reported in the literature.2–5 Noninvasive imaging plays a pivotal role in the staging and restaging of bladder cancer. Currently, staging of patients with UCB depends on CT or MRI to detect metastatic disease; however, these have limited accuracy, and thus imaging methods with improved accuracy are clearly needed.5 In recent years, PET/CT has been proposed as a noninvasive imaging modality based on functional molecular or metabolic, rather than morphologic, criteria that may help to overcome some of the problems of CT and MRI imaging.7–10 Often the metabolic changes detectable by PET precede morphologic changes detectable by anatomic imaging methods, leading to greater sensitivity of PET. PET/CT is specific for urothelial carcinoma metastases, is more sensitive than standard CT, and is allowing for complete tumor staging in single examination.7,8 In the present case, two lesions in the brain were detected by FDG PET/CT while only one lesion was revealed by MRI. Reason for the failure to identify the second lesion by MRI is that lesion may be metabolically activated, but not be developed anatomically yet. Different intensity FDG uptake of two metastatic lesions can be explained by different differentiation degree. As no evidence of metastases was detected elsewhere in the body except in the brain, treatment was planned as only whole brain radiotherapy.

FDG PET/CT has been used with limited success in primary diagnosis and locoregional staging of urinary bladder cancer, mainly due to the presence of excreted FDG in the urinary tract, which often masks the urinary bladder lesion and probably the adjacent lymph nodes.7 To overcome these limitations, some investigators have attempted to achieve washing out the excreted FDG by using postvoid delayed imaging, diuresis, fluid loading or bladder catheterization.9 Recent efforts with PET/CT have focused on alternate PET tracer in bladder cancer staging, such as 11C-acetate, 11C-choline and 11C-methionine.9 Whether tracer other than FDG can have a role in the imaging evaluation of patients with UCB requires additional experience. For this reason, FDG PET/CT has not been useful in local staging but have a role in detection of nodal and distant metastases.10

Diagnosis of leptomeningeal metastases is based on contrast-enhancement MRI and the detection of carcinomatous cells by the cytological examination of the cerebrospinal fluid. However, in the initial lumbar puncture a positive cytology is found in only 50% of patients with neoplastic meningitis. Although cytology was negative in our patient, diagnosis of leptomeningeal metastases was certain because of typical symptoms, neurological signs and apparent MRI findings.

Surgical excision followed by brain radiotherapy has been considered the mainstay treatment for brain metastases. However, the overall survival is very poor, being between 2 and 7 months.1,2 In the last week of radiotherapy, the patient developed leptomeningeal metastases. The specific treatment of leptomeningeal metastases is aimed toward palliation, preventing further neurological deterioration, and improving survival. However, the median survival is 38 days (range, 6–270 days).4,5 Our patient died 3 months after the diagnosis of leptomeningeal metastases, consistent with the data reported in the literature.

References