



## Meningeal Carcinomatosis in a Patient with an Upper Urinary Tract Urothelial Cell Carcinoma

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### Keywords

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### Introduction

Meningeal carcinomatosis (MC) is an infrequent complication of the solid tumors, normally in advanced stages of the disease. It has a very poor prognosis, with a median survival less than 6 month. To our knowledge, meningeal carcinomatosis from upper urinary tract urothelial cell carcinoma (UUT-UCC) has not been reported.

### Case Report

We report the case of a 79-year-old patient, former smoker, with a history of hypercholesterolemia and chronic carrier hepatitis B.

He was diagnosed in 2008 because of hematuria of a grade 2 urothelial bladder cancer (stage T1 N0 M0) and treated with a transurethral bladder resection and local mitomycin administration.

Four months later the patient began to suffer intermittent hematuria. The urine cytology was positive for transitional carcinoma, but repeated cystoscopies and bladder ultrasounds were normal.

Six months later an intravenous urography showed absence of visualization of the left kidney parenchyma and the ureter. A retrograde pyelography demonstrated a partial obstruction in the proximal third of the left ureter. He underwent ureteroscopy that showed an erythematous lesion not available for biopsy. A sample of urine from selective catheterization of the left ureter showed carcinoma consistent with urothelial carcinoma.

A computed tomography (CT) of the thorax and abdomen showed multiple adenopathies in the abdomen and metastasis in the lungs, liver and spine. A bone gammagraphy showed pathological deposits in the left shoulder, ribs, spine and the right pelvis. A biopsy of a liver lesion was positive for urothelial carcinoma.

In March 2010, the patient received radiotherapy to the right pelvis and started chemotherapy with biweekly carboplatin and gemcitabine. After ten cycles a CT scan showed partial response. Treatment was discontinued due to hemathological toxicity (neutropenia and thrombocytopenia).

One month later he referred headache and instability. A brain CT scan did not reveal any abnormality. Three weeks later he described dysphagia to solids and liquids, persistence of the headache and a decline in his performance status. He was admitted into hospital for further evaluation. An otolaryngologist's examination and an

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upper endoscopy didn't show any anomaly and a whole-body CT scan showed stable disease.

Patient's condition kept on worsening with disorientation (aphagia) and decrease of level of consciousness. A lumbar puncture performed found normal cerebrospinal fluid glucose and elevated proteins levels (68 mg/dl). Cytologic examination showed neoplastic cells compatible with metastases of the urothelial carcinoma. Due to the poor performance status, only symptomatic treatment was administered, and the patient died a few days later.

## Discussion

Meningeal carcinomatosis (MC) is a serious complication resulting from the diffuse or multifocal invasion of the subarachnoid space by neoplastic cells. Although any cancer can seed the leptomeninges, it is more common in lung, breast, melanoma, head and neck and gastrointestinal tract cancers [1]. It is seen in less than 5% of the solid cancers, but its frequency is increasing. This has been attributed to an increased survival and a better systemic control of the disease, to the difficulty of many cytotoxic agents to cross the blood-cerebrospinal fluid (CSF) barrier and to the better diagnostic techniques available.

Neoplastic cells reach the meninges through hematogenous or lymphatic spread, direct extension from the central nervous system, centripetal migration along perineural spaces or iatrogenic spread. The most frequently affected regions are the basilar cisterns, posterior fossa and cauda, where the characteristics of the CSF flow facilitate deposits of circulating cells.

MC is usually diagnosed in patients with advanced stages (> 70%) but it can also appear after a disease-free interval (20%) and even be the first manifestation of cancer (5-10%) [2].

Clinical manifestations are broad and can be divided into cerebral hemisphere symptoms (headache, mental status changes, confusion, cognitive impairment, seizures, hemiparesis...), cranial nerve symptoms (diplopia, trigeminal sensory or motor loss...) and spinal dysfunction (weakness, dermatomal sensory or motor loss, pain following radicular patterns...). These manifestations must be differentiated from those the side effects of the chemotherapy treatments and some paraneoplastic syndromes.

Response to treatment and survival are independently related to the performance status and the neurological disability. Other prognostic factors have also been related, but not universally accepted, such as high levels of glucose in CSF [3]. Due to this fact, treatment should be offered only to patients with an acceptable life expectancy and a good performance status. Anyway, prognosis

is very poor, with a median survival of 4-6 weeks without treatment and, in selected patients, 4-6 months with chemotherapy.

Imaging techniques can suggest the diagnosis (MRI with gadolinium enhancement shows dural enhancement due to irritation of the leptomeninges, although it has a false negative rate higher than 30%). The gold standard test is the lumbar puncture. Suggestive abnormalities in CSF are an increased opening pressure (> 20 cm H<sub>2</sub>O), increased leukocytes (> 5/mm<sup>3</sup>), elevated protein (> 50 mg/dl) and decreased glucose levels (< 60 mg/dl). The presence of malignant cells is diagnostic. Anyway, only 45% of the patients with a positive CSF cytology were cytologically positive on initial examination, percentage that raised up to 80% on a second puncture [4,5].

Treatment traditionally has included chemotherapy and sometimes concomitant radiation [6,7]. Radiotherapy can be used to palliate symptoms or to correct CSF flow abnormalities demonstrated by radionuclide ventriculography. Chemotherapy can be administered intrathecally or systemically. Intrathecal administration remains the preferred route [8], and the most used drugs are methotrexate, cytarabine (and its liposomal formulation) and thiotepa.

In conclusion, NM is a complication usually seen in advanced stages of the cancer with a very poor prognosis. Diagnosis shouldn't be delayed, as treatment has been shown to improve survival, but it can only be administered to patients with an acceptable quality of life.

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