CASE REPORT

Metastatic urachal cancer responding to FOLFOX chemotherapy

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Metastatic urachal cancer is a rare disease and subsequently, does not have a defined systemic treatment. Although urachal cancer is most commonly adenocarcinoma and histologically similar to colon cancer, treatment selection is usually based upon location (the proximity of the urachus to the bladder) with bladder cancer regimens the most commonly prescribed. We report a case of metastatic urachal cancer where the immunohistochemical profile's similarities to colon cancer led to treatment with colon cancer specific chemotherapy. Our case is the first to report urachal cancer treated with and responding to modified FOLFOX6. In the age of targeted therapy, where molecular biology drives treatment selection, our case highlights that in rare tumors, when evidence is often lacking, a common sense approach can often prevail.

Key Words: urachal cancer, bladder adenocarcinoma, chemotherapy

Case report

In April 2008, a previously well 60-year-old male presented with macroscopic hematuria. Urinary cytology revealed atypical degenerate cells suspicious for malignancy and a bladder ultrasound demonstrated a mass at the bladder dome. Computed tomography (CT) scanning of the abdomen confirmed a 3 cm bladder mass contiguous with an urachal remnant and a 1.2 cm left lower lobe lung mass.

A rigid cystoscopy demonstrated a 3 cm papillary/sessile tumor and the patient went on to have a transurethral resection of the bladder tumor (TURBT).

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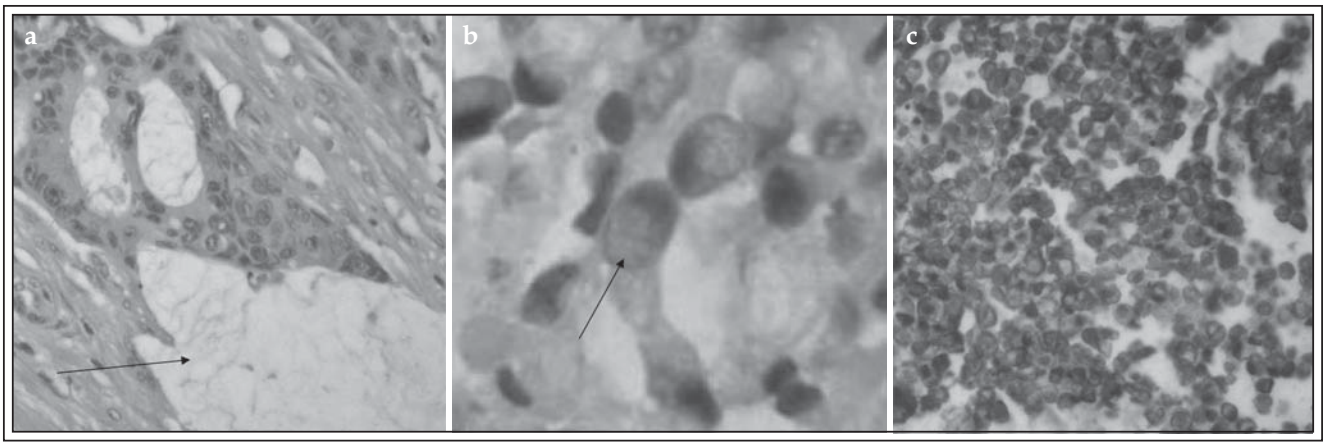

Figure 1. a) Poorly formed glands with abundant mucin. b) Signet ring cells. c) Cytokeratin 20 positive immunohistochemistry.

Pathology revealed bladder mucosa infiltrated by moderate-to-poorly differentiated adenocarcinoma. Poorly formed glands contained abundant mucin, Figure 1a and were lined by pleomorphic columnar epithelium. Some signet-ring cells were also seen, Figure 1b. The tumor invaded smooth muscle and the surrounding urothelium showed reactive change without intestinal metaplasia. On immunohistochemistry, the tumor was cytokeratin-20 positive, Figure 1c, and cytokeratin-7 negative. Serum levels of carcinogen embryonic antigen (CEA) were also elevated. Given this profile is characteristic of colorectal cancer, a colonoscopy was performed and excluded the diagnosis of primary colorectal cancer invading the bladder.

The patient was diagnosed with metastatic urachal cancer and went on to have a partial cystectomy with en bloc resection of the urachus and umbilicus as a palliative measure for hematuria. Postoperatively, the patient was referred to medical oncology, but did not attend until he developed a 5 cm thyroid nodule in September 2008. Biopsy of this nodule was consistent with the original urachal histology. A restaging CT of his chest, abdomen and pelvis revealed widespread metastatic disease involving his thyroid gland and lungs.

Using the immunohistochemistry profile as guidance, the patient was treated with colorectal cancer specific chemotherapy, modified FOLFOX6. A partial response was demonstrated on CT after six cycles; the largest lung mass reduced from 2.2 cm to 1.6 cm in diameter, Figure 2a, and the thyroid mass reduced from 4.3 cm to 2.5 cm in diameter, Figure 2b. There was also a parallel decrease in CEA from 570 µg/L to 8.2 µg/L. During the following six cycles, the patient's CEA level remained between 6 µg/L - 8 µg/L. Following his 12th cycle, the patient's CEA increased to 27.3 µg/L and a restaging CT confirmed disease progression. The patient was asymptomatic and opted for a treatment holiday with plans to start second line FOLFIRI chemotherapy at clinical progression.

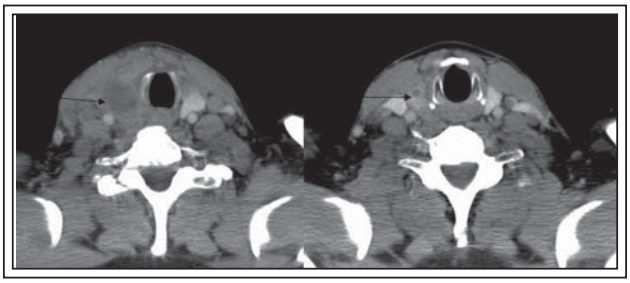

Figure 2a. Thyroid metastases before (left) and after (right) six cycles of FOLFOX6.

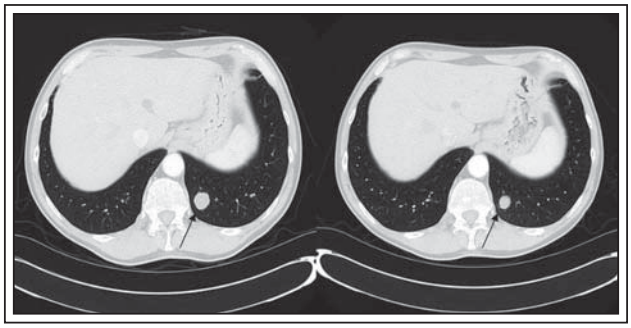

Figure 2b. Lung metastases before (left) and after (right) six cycles of FOLFOX6.

TABLE 1. **MDACC criteria for diagnosis of urachal cancer**

Location in bladder dome or elsewhere in midline of bladder
Sharp demarcation between tumor and normal surface epithelium
Supportive criteria
Enteric histology
Absence of urothelial dysplasia
Absence of cystitis cystica or cystitis glandularis transitioning to tumor
Absence of primary adenocarcinoma in another organ

Discussion

The urachus (median umbilical ligament) extends from bladder dome to umbilicus. It develops during embryogenesis from a diverticulum within the hindgut (allantois). As the cloaca divides and develops into the bladder anteriorly and the rectum posteriorly, the allantois is obliterated to form the urachus.[1] The urachus is a three layer structure consisting of an outer muscular layer, middle connective tissue layer and an inner layer lined with transitional epithelium.[2] In 30% of adults, congenital urachal anomalies, such as fistulae, cysts, sinuses and diverticulae, are present.[3] These remnants increase the risk of urachal cancer.[3]

Urachal cancer is rare, accounting for less than 1% of all bladder cancers.[4] The median age at diagnosis is 47-56 years[2] and the male-female ratio is approximately 1:1.[5] Although the urachus is lined by transitional epithelium, adenocarcinoma is the predominant histology in urachal cancer.[4] Urachal adenocarcinoma generally secretes mucin and includes mucinous, enteric and signet-ring cell subtypes.[6] Despite its resemblance to colorectal cancer, there is only one previous report of cytokeratin-20 positive immunohistochemistry in urachal cancer.[7]

Urachal cancer commonly presents with hematuria and mucinuria.[4] Given its extraperitoneal location, presentation is generally late.[8] Common metastatic sites include lung, pelvic lymph nodes and bone.[8] This case is the first report of thyroid metastasis from urachal cancer. Diagnosis of urachal cancer is best made by cystoscopy, although urinary cytology is positive in 38% of cases.[8] Ultrasound and CT are useful in assessing the extent of local and distant disease.

During diagnosis, it is important to differentiate between urachal and non-urachal bladder adenocarcinoma, as staging, prognosis and treatment differ.[9] A series of criteria have been developed to assist in this process. These include midline location and sharp demarcation between tumor and normal surface urothelium, Table 1.[2]

Tumor markers including CEA and CA19-9 have been elevated in multiple case reports. In one series, 13 of 22 patients demonstrated an elevated CEA, and five of these patients had a CEA decrease parallel to an objective response to chemotherapy.[5] Staging systems used for traditional bladder cancers cannot be applied to urachal cancer, as the pattern of growth is intrinsically different. Two major staging systems have been proposed for urachal cancer, but neither has been validated.[8]

Historically, radical cystectomy was the operation of choice for resectable urachal cancer. However, due to umbilical involvement in 7% of patients, urachal cancer surgery now consists of a partial cystectomy with en bloc resection of the umbilicus and urachal ligament. Compared to radical cystectomy, this has significantly reduced the risk of local relapse and improved quality of life.[8,10]

There is no evidence to support the use of chemotherapy in urachal cancer in either the adjuvant or metastatic setting. Multiple regimens have been trialed with varying response rates. One review reported cisplatin containing regimens resulted in stable disease or partial response in 5 of 7 patients.[4] Another review reported the same in 11 of 14 patients.[5] Although, there are no previously published reports of oxaliplatin-based chemotherapy being used in metastatic urachal cancer, two case reports have described patients responding to irinotecan-based chemotherapy, another commonly used colorectal cancer regimen.[7,11] A phase II study using gemcitabine, 5FU, leucovorin and cisplatin (GemFLP) in metastatic urachal cancer is currently accruing patients at MD Anderson Cancer Centre.

Despite the histological similarity between urachal cancer and colorectal cancer, our patient is the first reported case of metastatic urachal cancer being treated with and responding to modified FOLFOX6. In the age of personalized cancer care, where molecular biology influences treatment selection, our case report highlights that in rare tumors where evidence is limited, a common sense approach can often lead to the selection of effective treatment. □

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