Kaohsiung Journal of Medical Sciences (2012) 28, 624–627

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: http://www.kjms-online.com

CASE REPORT

CEA-producing urothelial cell carcinoma with metastasis presenting as a rectal adenocarcinoma

Ming-Hsin Yang, Guang-Huan Sun, Dah-Shyong Yu, Sun-Yran Chang, Cheng-Ping Ma, Tai-Lung Cha*

Division of Urology, Department of Surgery, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

Received 6 April 2011; accepted 19 September 2011
Available online 23 July 2012

KEYWORDS
Bladder cancer;
CEA-production;
Chemotherapeutic pressure;
Urothelial cell carcinoma;
Rectal adenocarcinoma

Abstract This is a case study of a 61-year-old male who presented with difficult defecation for 1 month. A circumferential submucosal rectal tumor was noted on a digital rectal examination and colonoscopy. Laboratory examination revealed high serum levels of carcinoembryonic antigen (CEA; 43.75 ng/mL) and carbohydrate antigen 19-9 (CA19-9; 11,790 U/mL). In addition, tumor biopsies revealed a poorly differentiated adenocarcinoma of the rectum with intact mucosa. The patient had history of advanced stage-T2 urothelial cell carcinoma of bladder, which had been downstaged to T0 by neoadjuvant chemotherapy followed by radical cystectomy 1 year prior. After investigating the initial bladder tumor specimens, a small portion of the tumor with high CEA expression comparable to the submucosal rectal tumor was found. The size of the tumor was reduced and the levels of the tumor markers decreased after administering FOLFIRI chemotherapy targeted at the adenocarcinoma. Although neoadjuvant chemotherapy may have a selective pressure to eliminate most urothelial cell carcinoma, physicians should be aware that it can lead to rectal metastasis via CEA-producing components.

Introduction

The majority of primary carcinomas of the urinary bladder are urothelial cell carcinomas. Here, we report a patient who had a history of urothelial cell carcinoma of the bladder after neoadjuvant chemotherapy followed by radical cystectomy who subsequently developed poorly differentiated rectal adenocarcinoma with elevated plasma

* Corresponding author. Division of Urology, Department of Surgery, Tri-Service General Hospital, Number 325, Cheng-Kung Road, Sec. 2, Taipei 114, Taiwan.
E-mail address: msy681028@yahoo.com.tw (T.-L. Cha).

1607-551X/$36
doi:10.1016/j.kjms.2012.04.030

CEA (43.75 ng/mL) and CA19-9 (11,790 unit/mL) levels. These conditions might have risen from a CEA-producing component in a previous tumor and be related to intratumoral heterogeneity. The different tumor components may have various sensitivity levels to chemotherapy, resulting in remote metastases even though the primary tumor was eliminated.

Case report

A 61-year-old man presented with 3 weeks of abdominal distension in June 2009. In April 2008, the patient was diagnosed with a urothelial cell carcinoma that was situated on the left posterior wall of the urinary bladder; this carcinoma had been treated by transurethral resection of tumor. The surgical specimen was diagnosed as a high-grade urothelial cell carcinoma of bladder (Fig. 1) with muscle invasion (T2N0M0) and was immunohistochemically positive for cytokeratin 7 and negative for cytokeratin 20 and prostate-specific antigen (PSA). Six cycles of neoadjuvant chemotherapy (paclitaxel, gemcitabine, and carboplatin) were administered. In August 2008, the patient received a radical cystectomy, but the ileal conduit showed no residual evidence of the tumor on the pathological report. Another four cycles of adjuvant chemotherapy were administered after the operation. The patient was then transferred to our outpatient department.

We administered a digital rectal examination, and an exophytic mass in the proximal anal canal was revealed. Laboratory tests yielded significant results for the following: CEA (43.75 ng/mL) and CA19-9 (11,790 unit/mL). A computed tomography (CT) scan indicated segmental wall thickening at the level of the rectum that was nearly obstructing the bowel (Fig. 2A).

The results of the colonoscopy indicated a submucosal rectal mass just above the dentate line (Fig. 2B). Multiple biopsies were obtained from the mass during the colonoscopy. The pathological examination indicated poorly differentiated adenocarcinoma (Fig. 1). The microscopic findings revealed pleomorphic tumor cells arranged in glandular and solid nest patterns at the submucosa layer. The immunohistochemical study demonstrated the expression of CEA, positivity for cytokeratin 7 and cytokeratin 20, and negativity for PSA and synaptophysin. A diagnosis of metastatic poorly differentiated adenocarcinoma was rendered. The aforementioned results led us to investigate the initial bladder tumor specimens, which was confounded by a small portion of the tumor that demonstrated high CEA expression that was compatible with a diagnosis of a submucosal rectal tumor. The patient was subsequently administered FOLFIRI chemotherapy (folinic acid, fluorouracil, and irinotecan).

Three months later, after six cycles of chemotherapy, repeated CT scans of the abdomen confirmed shrinkage of the tumor. The results of the treatment were supported by the laboratory data: 5.05 ng/mL CEA and 84.89 units/mL CA19-9.

Discussion

Tumor heterogeneity can be characterized by differences in histopathology and functional properties such as anchorage-independent growth, proliferative capacities, and apoptotic responses to therapies [1]. Several studies have suggested that such intraneoplastic heterogeneity arises from genetic or epigenetic differences in tumor cells via selective pressure that is exerted during tumor evolution. The identification of multiple components with different histological patterns within a single malignant tumor is a common finding in pathology. These variable components are thought to result from tumor cell dedifferentiation or transformation with the subsequent evolution of different subpopulations of tumor cells, a concept that is illustrated by the coexistence of different carcinomas in the bladder. Several studies had reported that the different components of urinary bladder carcinomas can produce CEA or CA 19-9, as was true in our case [2—4].

CEA was first described by Gold and Freedman in 1965 [5] as a complex glycoprotein on the cell surface that is primarily produced during fetal development. It is overexpressed in several kinds of adenocarcinomas, including those found in the colon, rectum, ovaries, and lung, and has been widely used as a tool in diagnosis and disease follow-up. CA 19-9 was discovered in patients with colon and-pancreatic cancerin 1981 by Koprowski et al. [6]. It is a tumor-associated antigen that is found in the cell membrane, which has also been reported in association with gastrointestinal carcinomas, thyroid papillary carcinomas, and endometrial adenocarcinomas. In general, CEA and CA19-9 are well known tumor markers for a variety of cancers of the digestive system. Although rare, they are sometimes produced by urinary tract carcinomas [2—4]. In our present case, high serum levels of CEA and CA19-9 initially led us to the diagnosis of newly developed rectal tumor. Contiguous spread or metastasis from elsewhere should always be clinically excluded, especially when the patient has history of urothelial cell carcinoma. Diagnosing poorly differentiated adenocarcinoma may be difficult or impossible to distinguish from involvement by a primary colon adenocarcinoma via histology [7]. The expression of cytokeratin 7 has been reported in urothelial adenocarcinoma, whereas the colonic epithelium and the majority of colonic adenocarcinomas lack cytokeratin 7 immunoreactivity [8]. In the present case, the rectal tumor was positive for cytokeratin 7 and, therefore, considered to be a metastatic tumor. Furthermore, on the colonoscopy findings, the presence of a submucosal lesion also indicated that the tumor came from the recurrent carcinoma. Our findings show that the pelvic adenocarcinoma was immunohistochemically similar to conventional urothelial cell carcinoma.

It is widely accepted that heterogeneous cancers result from the accumulation of mutations in the genes that directly control cell birth and/or cell death. Such genetic instabilities in tumor cells are partly induced by the tumor environment, including cell-cell interactions, aberrant cell substratum, and drug influence [9]. Usually gemcitabine and cisplatin or MVAC (methotrexate, vinblastine, doxorubicin, and cisplatin) serve as the first-line choice for chemotherapy to treat urothelial cell carcinoma, whether for neoadjuvant, adjuvant, or metastatic treatment. In this case, paclitaxel, gemcitabine, and carboplatin were the initial chemotherapeutic agents. After neoadjuvant therapy, the tumor was downstaged to stage T0 following