New treatment trends in small cell carcinoma of the urinary bladder

Dear Editor,

Small cell carcinomas (SCCs) are usually seen in the lung (SCLC) and represent approximately 15% of all lung cancers. Small cell carcinoma of the urinary bladder (SCCB) is a rare tumor accounting for <1% of all bladder tumors and represents 0.1-0.4% of all SCCs. SCCBs usually have an aggressive clinical course, often presenting with metastases at the time of diagnosis, quite similar to SCLC in clinical behavior. At least half of the cases in most series are mixed with non-small cell components (urothelial and adenocarcinoma elements). Up until today, a wide variety of management strategies has been employed. Although most clinicians believe that optimal treatment for SCCB is a combination of surgical resection and adjuvant chemotherapy, surgical resection is not curative, with adjuvant chemotherapy extending patient survival. Thus, treatment strategies require a multidisciplinary approach including surgery and chemotherapy, with associated radiotherapy after transurethral resection of the bladder tumor (TUR-BT).

Due to the rarity of SCCB, no randomized clinical trial was carried out on which to base definitive recommendations for the management of patients with this condition. SCCBs present with metastasis in up to 25% of the cases, and approximately 75% develop recurrence or distant metastasis. Although there is no standard treatment approach, a wide variety of management strategies have been employed.

Patients with SCCB have poor prognosis, even when the disease appears to be localized. For localized disease, a retrospective review of the M.D. Anderson Cancer Center (MDACC), analysed 46 patients; 5-year survival rate was 78% for patients treated with cystectomy and neoadjuvant chemotherapy, whereas it was 36% for patients undergoing cystectomy alone. This study also showed that the survival of patients treated with initial cystectomy and adjuvant postoperative chemotherapy was no better compared with those treated with cystectomy alone. Also, the pathological stage was higher in patients treated with cystectomy firstly [1]. In a Mayo clinic study, Choong et al. reported that adjuvant chemotherapy rather than surgery alone had numerically higher cure rates in patients with stages II and III disease. This study showed that adjuvant treatment is not indicated for stage II patients after radical cystectomy, but should be considered for patients with stage III disease [2]. In another large series from the University of Southern California patients receiving postoperative adjuvant chemotherapy had significantly better overall and recurrence-free survival than those treated with cystectomy alone. Alternative to cystectomy, radiation therapy has been used by some Centers. In a British Columbia Cancer Agency Center study, when chemotherapy was combined with local radiotherapy, 2- and 5-year overall survival were 70% and 44%, respectively. In another study Bex et al. reported that, in 17 patients with localized SCCB, the overall survival was 32.5 months with sequential chemotherapy and radiotherapy after TUR-BT [3]. Prophylactic cranial irradiation (PCI) is a standard treatment of limited-stage SCLC to reduce the rate of brain metastases, but there is no clear data on the use of PCI in the treatment of localized SCCB to prevent such metastases. In a recent retrospective review from MDACC, a total of 533 patients was analysed; a bladder-sparing approach involving TUR-BT combined with chemotherapy and radiation yielded no significant difference in overall survival compared with patients undergoing radical cystectomy with over 90% of them receiving adjuvant chemotherapy [4]. In another recent retrospective trial, Schreiber et al. reported that for patients presenting without distant metastatic disease, treatment with either cystectomy or radiation appeared to improve survival [5].

For metastatic SCCB cisplatin-based chemotherapy is the standard treatment [1]. Both mixed type and pure SCCBs should be treated as SCLC. Median overall survival is generally < 12 months [2]. A prospective phase II trial from MDACC included 12 patients who presented with stage IV disease; the patients were treated with ifosfamide plus doxorubicin alternating with etoposide plus cisplatin. Chemotherapy continued with 2 cycles beyond maximal response. The median overall survival was 13.3 months. Although second-line chemotherapy has been used for SCCB, no responses were reported.

In conclusion, primary SCCB is a very rare and aggressive
tumor, commonly diagnosed in advanced stage and in the elderly. For localized disease a wide variety of management strategies can be used. Despite the large series of recent retrospective analyses the main question of which treatment modality is best remains unknown.

References


Electrolyte abnormalities due to irinotecan administration in metastatic HER-2 positive breast cancer patients

Dear Editor,

Irinotecan is a topoisomerase-1 inhibitor, used widely in colon cancer and other malignancies. Among the most commonly reported side effects are diarrhea and immunosuppression [1]. However, the physician should also be aware of the less common side effects. Herein we present a case with resistant hypokalemia and hypocalcemia associated with the use of irinotecan in a patient with chemotherapy-resistant breast cancer.

A 57-year-old postmenopausal female patient was diagnosed with infiltrative ductal carcinoma of the left breast (T2N0M0) in January 2007. She received 6 cycles of adjuvant cyclophosphamide-adriamycin-5-fluorouracil. In January 2008 a HER-2 positive cancer developed in the contralateral breast for which neoadjuvant paclitaxel-trastuzumab regimen was initiated. Right mastectomy in July 2008 revealed infiltrative ductal carcinoma and the patient was administered adjuvant trastuzumab for about 9 months. During her follow-up metastatic lesions developed on the chest wall and she received multiple lines of chemotherapy including capecitabine, lapatinib, vinorelbine, carboplatin, docetaxel and trastuzumab due to ever occurring progressive disease. She also received palliative irradiation to the chest wall. Her treatment was switched to irinotecan 60 mg/m² every 2 weeks and trastuzumab 2 mg/kg on days 1, 8, 15, 22) in January 2012.

On the 6th week of treatment diarrhea and neutropenic fever necessitated administration of sulbactam-ampicillin and ciprofloxacin. Consistent with acute prerenal kidney injury her creatinine was 3.5 mg/dL at the time of hospital admission. Since stool testing showed no positive results the diarrhea was attributed to irinotecan, and loperamide with hydration were recommended. Upon normalization of creatinine levels, the patient developed hypokalemia (2.5-3.0 mEq/L) and hypocalcemia (5.5-6.5 mg/dL) which did not resolve despite replacement. Serum magnesium was as low as 0.52 mg/dL and urinary excretion of magnesium was 116 mg over 24 h (reference 6.1-20.7 mg/day). After appropriate intravenous replacement of calcium and magnesium, the patient was discharged with oral maintenance. On her polyclinics visit one month later, no electrolyte abnormality was present.

Several chemotherapeutic agents are associated with electrolyte disturbances. Nausea and vomiting-common chemotherapeutic side effects—may also contribute to these problems. As reported by some studies resistant hypokalemia and hypocalcemia are not frequent after irinotecan administration [1]. Puduvalli et al. reported grade I or II hypokalemia and hypomagnesemia with irinotecan and thalidomide in patients with glioblastoma multiforme. In another phase II study by Bathe et al. irinotecan caused hypokalemia in just one out of 35 patients with colorectal cancer [2].

The prementioned electrolyte disturbances might have life-threatening consequences in patients under chemotherapy. Thus, we recommend close monitoring of electrolytes in patients receiving an irinotecan-containing chemotherapy regimen.

References


2. Bathe OF, Ernst S, Sutherland FR et al. A phase II experience with neoadjuvant irinotecan (CPT-11), 5-fluorouracil (5-FU) and leucovorin (LV) for colorectal liver metastases. BMC Cancer 2009; 9: 156.