Int J Clin Oncol (2006) 11:329–331
DOI 10.1007/s10147-006-0571-8

CASE REPORT

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Squamous cell carcinoma of the bladder: a patient treated successfully with a new combined chemotherapy regimen, intraarterial nedaplatin and pirarubicin plus intravenous methotrexate and vincristine

Received: December 12, 2005 / Accepted: February 23, 2006

Abstract We report a case of squamous cell carcinoma (SCC) of the bladder treated successfully with intraarterial chemotherapy using nedaplatin. A 75-year-old woman was admitted to our hospital in March 2004 with gross hematuria. Cystoscopic examination showed tumors on the anterior bladder wall. Computed tomography (CT) scans and magnetic resonance imaging (MRI) revealed extravesical invasion of the tumors, and a clinical diagnosis of T3bN0M0 was made. Transurethral biopsy was performed, and histopathological examination revealed SCC, grade 2–3, invasive. The patient received a new combined chemotherapy, intraarterial nedaplatin and pirarubicin plus intravenous methotrexate and vincristine. After two courses of the chemotherapy, CT scans and MRI demonstrated no tumor in the bladder. Transurethral bladder-wall biopsy was performed in November 2004, and histopathological examination of the specimen revealed no definite tumors. The patient is alive without evidence of disease more than 1 year after the chemotherapy.

Key words Squamous cell carcinoma of the bladder · Nedaplatin · Intraarterial chemotherapy

Introduction

Squamous cell carcinoma (SCC) of the bladder is a rare disease. The prognosis is thought to be poor because of its aggressive growth, and, as yet, no standard treatment regimen has been established. Although surgical treatment is recommended for bladder SCC, recurrent disease is extremely common, even after surgical treatment. The effects of other treatments remain unclear. Here, we report a case of bladder SCC in which pathological complete remission (CR) was obtained with a new combined primary chemotherapy regimen, intraarterial nedaplatin (*cis*-diammine glycolato platinum; CDGP) plus pirarubicin and intravenous methotrexate and vincristine. This is the first report of a patient with bladder SCC treated successfully with CDGP.

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Case report

A 75-year old woman was admitted to our hospital on March 24, 2004, because of macroscopic hematuria. Cystoscopic examination showed thumb- and walnut-sized sessile tumors with mucosal edema on the anterior bladder wall. Urine cytology revealed class II disease. Computed tomography (CT) and magnetic resonance imaging (MRI) revealed extravesical invasion of the tumors (Figs. 1 and 2), and a clinical diagnosis of T3bN0M0 was made. Transurethral cold-cup biopsy was performed on April 21, 2004. Complete resection of the tumors could not be performed because, based on the cystoscopic findings, they were thought to be invasive high-grade tumors. Histopathological examination revealed SCC, grade 2–3, nonpapillary, invasive.

We planned our regimen according to the intraarterial MVAC regimen schedule, i.e., intraarterial cisplatin and doxorubicin plus intravenous methotrexate and vincristine, reported by Naito et al.,[1] but cisplatin and doxorubicin were replaced by CDGP and pirarubicin. The patient received chemotherapy consisting of CDGP (70 mg/m^2 on day 2) and pirarubicin hydrochloride (30 mg/m^2 on day 2), given intraarterially, plus methotrexate (30 mg/m^2 on days 1, 15, and 22) and vincristine sulfate (1 mg on days 2, 15, and 22), given intravenously. The patient provided her informed consent to receive the new chemotherapy regimen. Solutions of CDGP and pirarubicin were administered intraarterially via the bilateral internal iliac arteries on the peripheral side from the bifurcation of the superior gluteal arteries. The patient did not have severe side effects from the therapy,

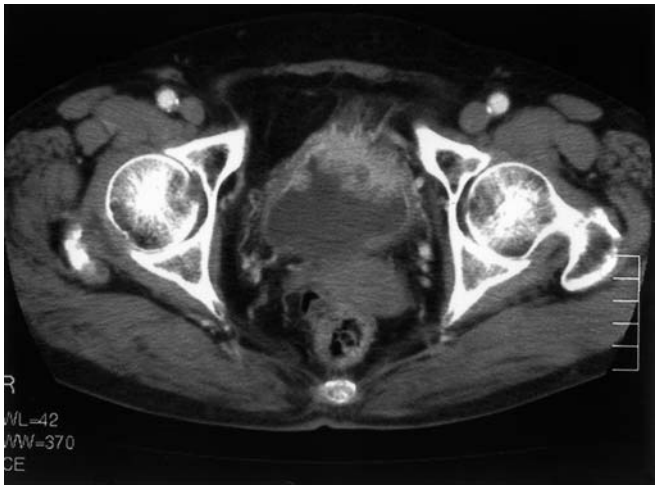

Fig. 1. Preoperative computed tomography (CT) scan suggested extravesical invasion of the tumor on the anterior wall of the bladder

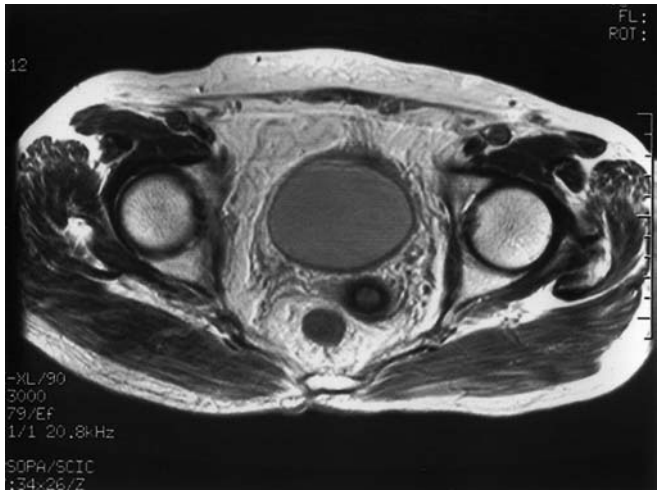

Fig. 3. MRI after two courses of chemotherapy. No tumor was detected on the anterior wall of the bladder

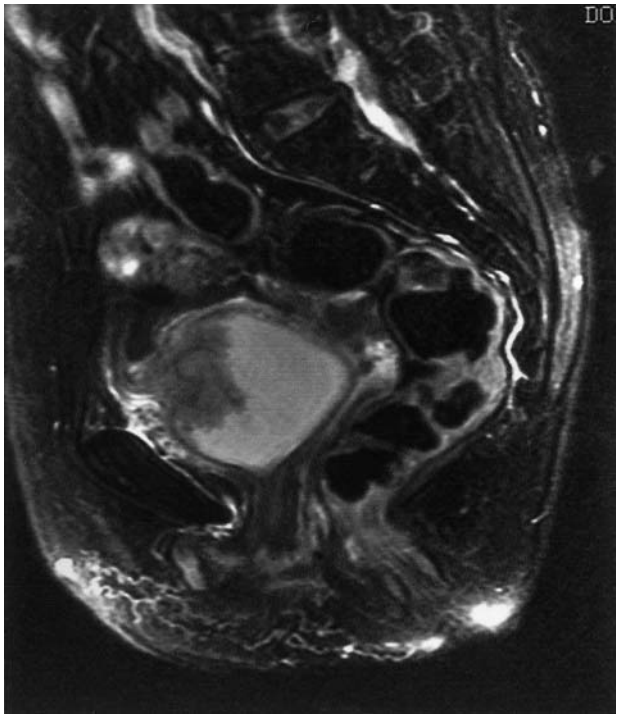

Fig. 2. Preoperative magnetic resonance imaging (MRI) also demonstrated extravesical invasion of the tumor

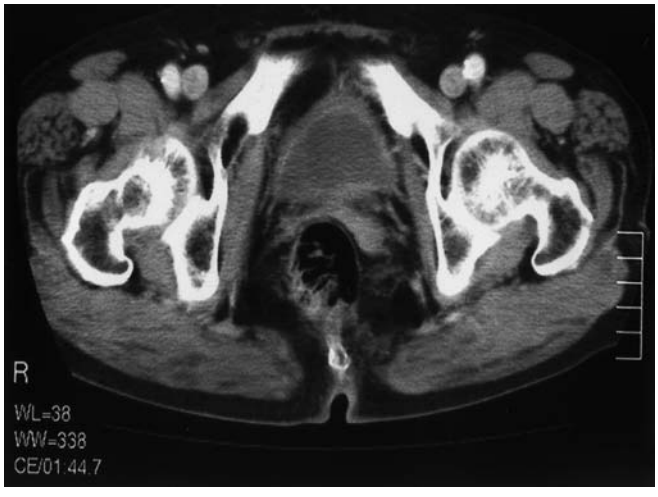

Fig. 4. CT scan 16 months after chemotherapy

and two courses of chemotherapy were performed with no adverse events. After two courses of chemotherapy, CT and MRI showed no solid tumors in the bladder (Fig. 3). Cystoscopic examination showed small edematous changes in the mucosa on the anterior bladder wall. The patient rejected further examinations (bladder-wall biopsy) and has been followed-up carefully by radiological and cystoscopic examination on an outpatient basis.

Three months after the chemotherapy, the edematous changes in the bladder mucosa had almost disappeared, and small white moss-like changes were observed on cystoscopic examination. Transurethral resection (TUR-biopsy) was performed on November 18, 2004. The bladder-wall biopsy specimens contained part of the muscle layer, and histopathological examination revealed no definite cancer cells. The patient is currently well without disease 16 months after the chemotherapy (see Fig. 4, in which the CT scan shows no tumor in the bladder).

Discussion

SCC of the bladder occurs in approximately 4% of bladder tumors. Many patients present with advanced-stage disease at the initial diagnosis because of the aggressive local invasive tendency of the tumor.[2] It was reported previously that 90% of patients present with higher than clinical stage T2.[3] Chemotherapy and radiotherapy, unlike their effects on

transitional cell carcinoma, are of limited benefit in bladder SCC. Even for patients who underwent chemoradiotherapy combined with total cystectomy, the 5-year survival rate was reported to be 24%.[2–4] Therefore, effective adjuvant therapies are required.

MVAC chemotherapy as adjuvant therapy has not been effective against bladder SCC. Recently, there have been some reports that intraarterial chemotherapy, using cisplatin combined with radiotherapy, is effective against bladder SCC and that it is expected to allow bladder preservation. Hayakawa et al.[5] reported a CR in a patient treated with intraarterial cisplatin injection combined with irradiation of the bladder. Manabe et al.[6] reported a patient showing long-term survival following total cystectomy after intraarterial cisplatin injection and the application of radiation therapy to the pelvis. In addition, Sugiura et al.[7] reported a patient who received total cystectomy after intraarterial chemotherapy (using cisplatin and pirarubicin hydrochloride) combined with radiation therapy to the bladder, in whom the resected bladder specimens revealed no tumor cells (pathological CR).

CDGP is a second-generation platinum complex synthesized to produce less nephrotoxicity and gastrointestinal toxicity as compared with cisplatin, and it has shown a spectrum of antitumor activity equivalent to that of cisplatin.[8] CDGP is effective against pathological SCC in head and neck cancers,[9] esophageal cancer,[10] and cervical cancer.[11] It was reported that the concentration of CDGP in the local tissue could be increased with intraarterial infusion as compared with intravenous administration.[12] Although there have been no reports of chemotherapy using CDGP against bladder SCC, we employed a new combined primary regimen, using CDGP instead of cisplatin, in an intraarterial MVAC regimen. Doxorubicin in the MVAC regimen was replaced by pirarubicin, which causes fewer gastrointestinal and cardiovascular complications. We achieved pathological CR, with bladder preservation, without severe side effects. Our results indicate that CDGP may be effective for SCC, regardless of the organ in which the lesion occurs.

There have been reports indicating a complete lack of cross-resistance between cisplatin and CDGP.[8,13] We feel that CDGP should be evaluated not only as chemotherapy for bladder SCC but also as second-line chemotherapy[14] for patients who have received prior cisplatin-based chemotherapy.

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