Oncology

Urothelial carcinoma with sarcomatous variant of the bladder following radiotherapy for cervical cancer: A case report

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1. Introduction

Development of second malignant neoplasms (SMNs) induced after radiation treatment for several adult-onset cancers are rare in clinical practice.1 In particular, there are few reports of radiation induced SMNs in the bladder.2 Along with the aging society, radiotherapy for cancers developed in perivesical organs such as uterine cancer and prostate cancer has been generalized and an increase in SMNs of urinary bladder is concerned in the future. We experienced a case of developing urothelial carcinosarcoma of the bladder about 40 years after irradiation to the pelvic region for uterine cancer.

2. A case report

A 72-year old female underwent hysterectomy and radiation treatment for cervical cancer at the age of 33. She had been suffering from urinary urgency and urge incontinence for a long time and was prescribed anticholinergic medicine. On January 2017, she visited a nearby doctor complaining of watery stool and abdominal pain. Bilateral hydronephroses and urinary retention were pointed out by abdominal ultrasonography when referral to our hospital. Blood examination did not reveal abnormal levels except for elevation of CRP (2.29 mg/dL). Cystoscopy showed ulcerative lesions with calcification on the left side of the bladder. CT and MRI revealed a well-defined tumor 4 cm in diameter in the bladder infiltrating sigmoid colon, ileum, and the left pelvic wall with bilateral mild hydroureterophoreses (Fig. 1). Abdominal wall scarring hernia and gallstone were also shown. No lymph node and distant metastasis were detected at the time. Malignant tissue with carcinosarcomatous variant expressing cytokeratin (CAM 5.2) and vimentin was revealed by histopathologic examination in the tumor biopsy specimen. She was diagnosed with bladder carcinosarcoma infiltrated to sigmoid colon, ileum, and pelvic wall. She underwent radical cystectomy with sigmoidectomy and ileectomy, and ileal conduit diversion and colostomy on April 2017. The tumor was infiltrated to ileum, sigmoid colon, and pelvic wall. Because of severe adhesions of abdominal wall scarring hernia, first of all removal of adhesions between muscular layer and intestinal canal of the abdominal wall hernia was needed.

Postoperative course was uneventful. She discharged from the hospital on the 18th postoperative day. Unfortunately, she had been suffering from cancer recurrence and died of the disease on September 2017.

Pathologic findings revealed urothelial carcinoma with sarcomatous variant, pT4b, INFb, ly1, v1 (Fig. 2). The specimen showed urothelial carcinosarcoma with a transition from the epithelial component to the sarcomatoid and spindle cell component. Immunohistochemically, GATA3, as a transcription factor important in the differentiation of urothelium, and cytokeratin 7 (CK7) were observed in both urothelial carcinoma and carcinosarcoma. CK5/6 was detected in urothelial carcinoma but not detected carcinosarcoma. Vimentin was detected in carcinosarcoma but not detected in urothelial carcinoma. With these results the diagnosis was urothelial carcinoma with sarcomatous variant. Elastofibrosis was conspicuous in the colon subserosal tissue, which was thought to be an influence of radiotherapy.

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**Fig. 1.** CT and MRI findings. a: CT findings of the tumor show a well-defined tumor 4 cm in diameter in the bladder. Enhancement effect at the border of the tumor was suspected invasion of the extra-vesical region. b: MRI T1 weighted image findings of the tumor show invasion of the small intestine and the rectum.

**Fig. 2.** The pathological finding on hematoxylin and eosin (HE) shows urothelial carcinosarcoma with a transition from the epithelial component to the sarcomatoid and spindle cell component (a, b). Immunohistochemically, CK7 and GATA3 are both positive for urothelial carcinoma and carcinosarcoma (c, d). CK5/6 is positive for urothelial carcinoma but negative for carcinosarcoma (e). Vimentin is positive for carcinosarcoma but negative for urothelial carcinoma (f). HE staining. (a: left ×10, b: right ×5), Sar: Carcinosarcoma, UC: Urothelial carcinoma. Immunostainings. (×20, c: CK7, d: GATA3, e: CK5/6, f: vimentin).
3. Discussion

Radiotherapy has been performed as treatment of various solid tumors with curative intent. However, radiation has the potential to induce cancer decades after the treatment. Radiation induced SMNs are reported to develop in about 0.45% of all cancers.1 A sizable amount of SMNs data has accrued for several adult-onset cancers in which radiotherapy has played pivotal roles, including cancers of cervix.2 Cervical cancer patients treated with radiotherapy were at increased risk of SMNs at sites in close proximity to the cervix beyond 40 years of follow-up. It is difficult to distinguish the radiation-induced SMNs from the late recurrences. Hallmarks of radiotherapy-associated cancers include a long latency period of at least 5–10 years and a tendency to arise within or at the edges of prior treatment fields.3 In the present case elastofibrosis was conspicuous in the colon subserosal tissue, which was thought to be an influence of radiotherapy. Radiotherapy for cervical cancer was associated with statistically significantly increased risks of several SMNs including bladder cancer.4 Urothelial cancer in patients with previous radiation therapy was reported to be often high grade, and a majority of patients has cancer progression requiring cystectomy.5 A high incidence of urothelial carcinoma with sarcomatoid features was seen in these patients.

The mechanism of carcinogenesis by radiation has not been clearly elucidated; however, radiation is considered to induce DNA damage followed by proliferation process of cancerous cells.6 For invasive and locally advanced SMNs, complete resection with negative surgical margin is mandatory to achieve longer diseases free survival; however, unfortunately positive margin was detected in the specimen in the present case. She had been suffering from cancer recurrence and died of the disease six months following the operation.

Longer survival over than decades can be accomplished because of multi-modality treatment including radiation. Nevertheless, radiation has the potential to induce cancer and SMNs following radiotherapy might arise decades after the treatment. Therefore, long-term surveillance after radiotherapy is necessary for the cancer survivors treated with radiation even if disease free is continued. These survival advances have been offset by SMNs comprising one of the most potentially life-threatening sequelae. A higher incidence of urothelial carcinoma with sarcomatoid features is observed in patients treated with radiation in the region of pelvis such as in the present patient. It is important for both physicians and patients to know the potential risk of radiation induced SMNs after radiotherapy.

Conflicts of interest

None declared.

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