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Colorectal Adenocarcinoma as a Second Malignant Neoplasm Following Rhabdomyosarcoma of the Urinary Bladder : A Case Report

Following improvements in therapy for childhood malignancies, the striking increase in survival rate over the past 30 years has led to the increase risk of developing second malignant neoplasms (SMNs). We report a case of colorectal carcinoma as a SMN, following treatment for rhabdomyosarcoma. The patient was diagnosed with rhabdomyosarcoma of the urinary bladder at his age of three years, and developed adenocarcinoma in the colon 13 years later. Histologic examination of the surgical specimen revealed adenocarcinoma involving the rectosigmoid area with radiation colitis in its background. The tumor cells showed strong immunoreactivity for p53 protein, suggesting the role of irradiation and p53 mutation in carcinogenesis. This case emphasizes the need for close observation in survivors of early childhood malignancies treated with radiation and multiagent chemotherapy.

Key Words: *Neoplasms, Second Primary; Colorectal Neoplasms; Child; Rhabdomyosarcoma*

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INTRODUCTION

Second malignant neoplasms (SMNs) have been reported with increasing frequency over the past 30 years as a late effect of childhood malignancy treatments (1-14). The intensive adjuvant therapy given to improve survival also contributes generally to the late side effects, and SMN in particular. The most common SMNs are bone and soft tissue sarcomas and hematologic malignancies, but there are sporadic cases of unusual childhood tumors. Colorectal adenocarcinoma is extremely rare in childhood and adenocarinoma as a second malignant neoplasm after childhood malignancy is also rare (9-14). We report a case of colorectal adenocarcinoma as a SMN following multiagent chemotherapy and irradiation for rhabdomyosarcoma of the urinary bladder with a latency of 13 years.

CASE REPORT

A 16 year-old- male with hematochesia visited Seoul National University Children's Hospital on January of 1999.

In 1986, at the age of three, he complained of voiding difficulty and gross hematuria. He was diagnosed as rhabdomyosarcoma, botryoid type in the urinary bladder after the biopsy. He received multiagent chemotherapy (vincristine, adriamycin, and cyclophosphamide) and irradiation (total dosage unknown) without surgery.

Until 1991, there was no evidence of other malignancies but we lost follow-up since then. The patient has no special family history of a familial cancer syndrome, especially the Li-Fraumeni syndrome and familial adenomatous polyposis.

Diagnostic work-up demonstrated a pelvic mass encircling the rectosigmoid colon. Colonoscopic biopsy from rectum revealed adenocarcinoma. The tumor was partially excised and colostomy was performed.

The resected rectal specimen was 9 cm in length, containing an ulceroinfiltrative mass encircling the entire lumen, very close to the distal resection margin, measuring 3×2 cm in maximum diameter (Fig. 1). Histologically, a nonmucinous, moderately differentiated adenocarcinoma extended into the pericolic adipose tissue without perineural, lymphatic and vascular invasions (Fig. 2A). There was also no evidence of lymph node metastasis. Chronic radiation change such as moderate sub-

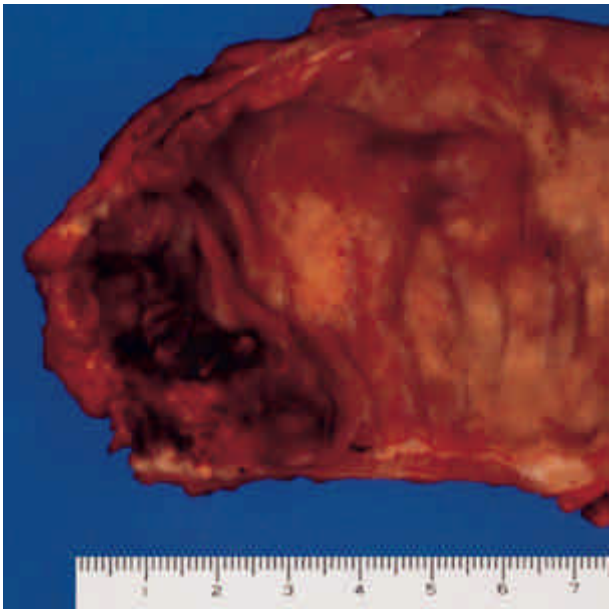

Fig. 1. Gross specimen of the rectum. Examination reveals a ulceroinfiltrative mass encircling the entire lumen, very close to the resection margin, measuring 3×2 cm in diameter.

mucosal fibrosis and medial and intimal vascular thickening were noted in the background.

Immunohistochemical staining for p53 protein showed strong nuclear immunoreactivity in a majority of adenocarcinoma cells but not in the surrounding normal mucosa (Fig. 2B).

DISCUSSION

The development of SMNs after treatment of childhood cancer has been an area of increasing concern, due to the improvement of survival rate with intensive therapy. Early reports of SMNs after childhood cancer included patients with all types of primary malignancies and covered a span of acquisitions that extended over decades of time (1-14). Smith et al. reported 162 cases of SMNs, the most common SMN was osteosarcoma followed by soft tissue sarcomas, breast cancer, thyroid cancer, leukemia, CNS tumor, and others (6).

Over the past 30 years, SMN cases after rhabdomyosarcoma has also increased due to the remarkable improvement in survival rate of patients. In the study performed by the Intergroup Rhabdomyosarcoma Study committee in 1993, it has been reported that 22 cases of SMNs occurred among 1,770 patients who had been treated for rhabdomyosarcoma during the period of 1972 to 1984, with the cumulative incidence being 1.7% (8).

Cases of colorectal carcinoma have been reported as a SMN following irradiation for other malignancies in childhood, mainly Wilms' tumor (10-12). In the study by Scaradavou et al., one case of colonic adenocarcinoma developed among 210 patients with rhabdomyosarcoma (9). Densmore et al. reported two cases of colorectal adenocarcinoma which developed in patients treated for Wilms' tumor and rhabdomyosarcoma, respectively (10). The latter case has many similarities with our case in clinical and pathological aspects. Both cases were treated

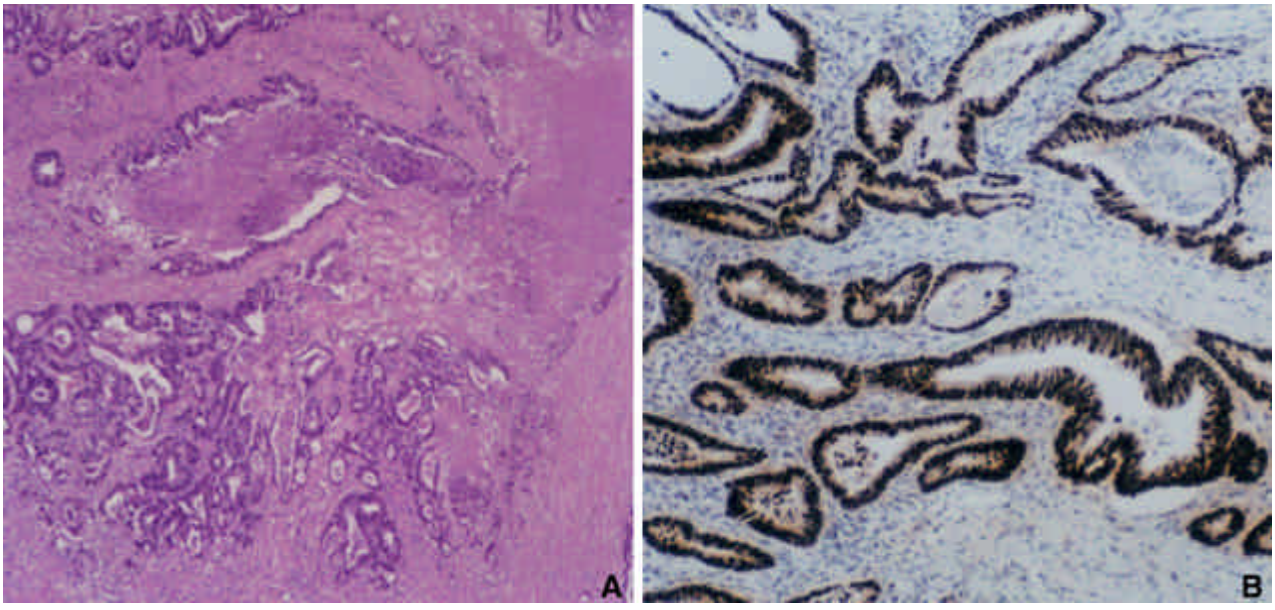

Fig. 2. Microscopic finding of the mass: the moderately differentiated adenocarcinoma of the rectum forms irregular glands with infiltrative pattern (**A**, H-E, ×40). p53 staining is demonstrated in the nuclei of the adenocarcinoma cells (**B**, immunohistochemistry for p53, ×200).

with a combination of radiation and chemotherapy, with the latency of more than 10 years in developing colonic carcinoma. Both cases also shared the same pathologic features such as radiation colitis in its background and strong p53 immunoreacticvity in the adenocarcinoma cells.

Radiotherapy is shown to contribute substantially to the development of secondary solid tumors as supported by their location, distribution and histology, and the interval between radiotherapy and occurrence of SMN (9-17). There is a significant correlation between the radiation dosage and development of SMN, with a higher than 40-fold risk associated with doses greater than 6000 cGY (13, 14). Moreover high-dose radiotherapy combined with high-dose chemotherapy, cyclophosphamide and dactinomycin in particular, was found to increase the risk of SMN (9).

The reported case meet the criteria of radiation-induced carcinoma; a relatively great exposure of radiation to the large bowel, a minimum period of 10 years between exposure to tumor development, and radiation-induced changes in the immediate vincity of the tumor (16). Unlike primary colorectal carcinoma, histologically most being poorly differentiated mucin-producing adenocarcinoma (11, 12), radiation-induced carcinomas are mostly non-mucin producing tumors with better differentiation (10-12).

The p53 overexpression in the adenocarcinoma indicates that mutation of the p53 tumor suppressor gene was involved in the malignant transformation. And there being no history of familial cancer syndrome, it is more tempting to speculate that combined radiation and chemotherapy induced a p53 mutation in this case and resulted in malignant transformation.

Multimodality therapy has improved long-term survival for children with malignant neoplasm. However, successfully treated patients are at a significantly increased risk for developing a second malignancy. Our case documents the phenomenon of early onset of adult-type tumors and also emphasizes the need for continued clinical evaluation of patients who have been treated with combined radiation and chemotherapy for childhood malignancies.

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