Colonic adenocarcinoma as a secondary malignancy after treatment of embryonal rhabdomyosarcoma

Moustafa Hamchou, Hilal Matta, Gabriel Ionescu, Adnan Swid, Ahmed H. Al-Salem
AbuDhabi, United Arab Emirates

Case report

Background: **Survivors of childhood malignancies are known to be at an increased risk for developing a variety of secondary cancers. Primary adenocarcinoma of the colon is very rare in children and adenocarcinoma of the colon occurring as a secondary malignancy in children is much rarer.**

Methods: **A boy with a history of successfully treated embryonal rhabdomyosarcoma developed adenocarcinoma of the colon as a secondary cancer.**

Results: **The boy presented with a solid mass of the left cheek at 3 years of age. The mass was excised and histological examination showed embryonal rhabdomyosarcoma. He was treated with multi-agent chemotherapy and local radiotherapy, which resulted in complete remission. Four years later, he presented with recurrent colicky abdominal pain and bleeding per rectum and was found to have intussusceptions. Colonoscopy revealed a tumor in the transverse colon, which was biopsied and proved to be an adenocarcinoma. The boy underwent excision followed by chemotherapy using an adult colon cancer regimen. He is currently off chemotherapy for 2 years with no evidence of the disease.**

Conclusions: **We report a rare case of colon cancer after treatment of rhabdomyosarcoma. Colorectal adenocarcinoma must be kept in mind as a secondary neoplasm following treatment for early childhood malignancies although it is extremely rare.**

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Key words: **colonic adenocarcinoma; rhabdomyosarcoma; secondary neoplasm**

Author Affiliations: Division of Pediatric Surgery, Department of Surgery, Tawam Hospital, Al-Ain, AbuDhabi, United Arab Emirates (Hamchou M, Matta H, Ionescu G, Swid A, Al-Salem AH)

Corresponding Author: Dr. Ahmed H. Al-Sslem, P.O. Box 61015, Qatif 31911, Saudi Arabia (Tel: 966505818009; Fax: 966 3 8630009; Email: ahsalsalem@hotmail.com)

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Introduction

Secondary neoplasms following treatment for an early childhood malignancy are not rare. As the survival of the patients with such malignancy after treatment improves, the risk of developing a secondary malignant tumor in children, adolescence and adulthood will increase.[1-7] A variety of second malignant neoplasms have been described and the risk increases in those who are young at first treatment and those who have undergone high-dose chemotherapy, radiotherapy and autologous hematopoietic stem cell transplantation.[1-7] Adenocarcinoma of the colon on the other hand is very rare in children.[8-20] This report describes a young patient who developed an invasive adenocarcinoma of the transverse colon after treatment of an embryonal rhabdomyosarcoma of the cheek.

Case report

A boy presented with a swelling in the left cheek close to the left nostril at 3 years of age. He had CT scan of the head and neck, showing a 1.7 cm × 2 cm solid mass in the left cheek. The mass was excised and histological examination revealed an embryonal rhabdomyosarcoma. Four months later, he was referred to our hospital for chemotherapy. Clinically, he had multiple café-au-lait spots without any other stigmata of neurofibromatosis. He had a strong family history of different malignancies. His grandfather, one uncle and two cousins died of different malignancies, but none of them had cutaneous changes suggestive of neurofibromatosis and types of the malignancies were unknown. The patient was treated with ifosfamide, vincristine and actinomycin-D. Nine months after excision and chemotherapy, MRI showed nothing abnormal and the patient was considered in complete remission. Eight months later, he developed local recurrence in the nasolabial fold, about 1.4 cm in diameter involving the upper gingival sulcus and floor of the nose. There was no evidence of distant metastasis as his abdominal and pelvic CT, bone marrow, brain MRI, cerebrospinal fluid cytology and bone scan were normal. The local recurrent tumor was

excised incompletely and the patient was treated with chemotherapy and radiotherapy (45 Gy in 25 fractions). He responded well and again he was in complete remission. Four years later, he had recurrent abdominal pain and bleeding per rectum for 3 weeks. Clinically he had a palpable abdominal mass in the left iliac fossa. Abdominal ultrasound showed intussusception which was reduced radiologically. Eleven days later he presented with recurrent intussusceptions which was also reduced radiologically (Fig. 1), but there was a mass in the transverse colon. Colonoscopy confirmed the presence of a tumor at that site but neither other abnormalities nor evidence of adenomatosis (Fig. 2). Biopsy of the tumor was performed to show an adenocarcinoma. The tumor was resected, followed by an end to end anastomosis. Histologically, the resected tumor showed an invasive but moderately differentiated adenocarcinoma involving the colonic wall and the pericolic adipose tissue (Fig. 3). The resection margins were free and there were 12 mesenteric lymph nodes showing reactive follicular hyperplasia. The tumor was staged as T3 N0 M0 and received adjuvant chemotherapy with FOLFOX (oxaliplatin + leucovorin + 5-FU). The patient was tolerable to this regimen but his physician decided to stop the treatment after 4 cycles. Subsequently the patient was subjected to two colonoscopies with normal results. He has been followed up for 2 years after chemotherapy, with no evidence of tumor recurrence.

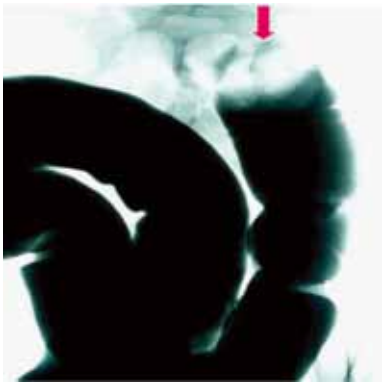

Fig. 1. Barium enema showing intussusception being reduced radiologically.

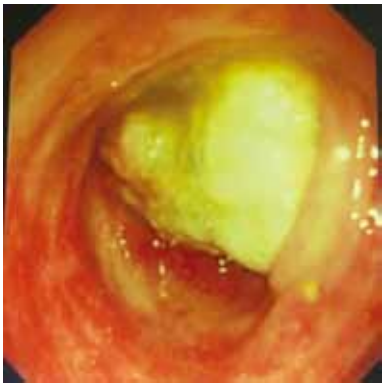

Fig. 2. Colonoscopic pictures showing a tumor in the transverse colon.

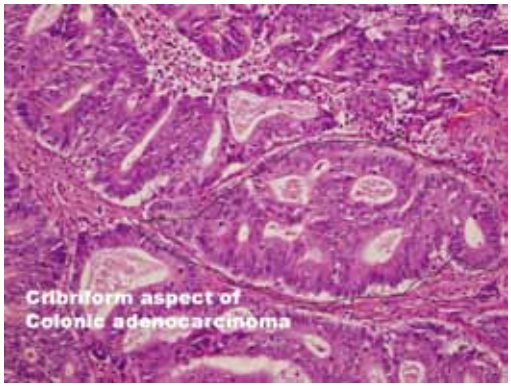

Fig. 3. A histological picture showing an invasive, moderately differentiated adenocarcinoma of the colon.

Discussion

Survivors of childhood malignancies are known to be at an increased risk of developing a variety of secondary cancers relative to the general population. The magnitude of this risk and the specific types of secondary cancers are dependent widely on the types of first cancers and the treatment received. Inskip and Curtis[3] in a population-based study of 25 965 survivors of childhood cancers found that there is a 6-fold risk of developing a new cancer relative to the general population. The risk of a solid secondary neoplasm was more common in the irradiated tissues, and the risk of secondary solid cancers was higher in patients who had been initially treated by radiotherapy.[4] Cohen et al[7] found a 6-fold risk of developing a secondary cancer in survivors of soft tissue sarcomas in children as compared to the general population and the risk of developing subsequent malignancy was increased among children with rhabdomyosarcomas. In 4367 patients enrolled in five consecutive IRS studies (I, II, IV-Pilot, IV; 1972-1997), 67 developed a secondary malignancy at a mean of 5.5 years (range: 11 weeks to 16.7 years) after the diagnosis of rhabdomyosarcoma. At a follow-up of 9.5 years, the estimated cumulative incidence of secondary malignancy for all IRSG I-IV patients was 3.5% at 20 years.[21]

Primary adenocarcinoma of the colon is an unusual and rare disease in children. Because of its rarity, most of the cases of primary adenocarcinoma are in an advanced stage and had a poor outcome. There is no consensus on the best treatment modality of the tumor. Literature retrieval showed only sporadic case reports of colonic adenocarcinoma in children.[8,9,11,12] The largest series

Table. Summary of children with colorectal cancer as a secondary malignancy

Authors	No. of patients	Age at initial diagnosis	Primary diagnosis	Therapy	Duration to development of colonic cancer
Densmore et al[13]	2	(1) 9 mon	Wilms' tumor	Radiation, surgery	42 y
		(2) 1 y	Retroperitoneal rhabdomyosarcoma	Radiation, surgery, chemotherapy	10 y
Kalteis et al[14]	1	-	Rhabdomyosarcoma	Chemotherapy, radiation	9 y
Prabakaran et al[15]	1	-	Acute lymphoplastic leukemia	Chemotherapy	
Brugha et al[16]	1	6 y	Cerebellar medulloblastoma	Radiotherapy	10 y
Park et al[17]	1	3 y	Rhabdomyosarcoma of the urinary bladder	Radiotherapy, chemotherapy	13 y
Present case	1	3 y	Rhabdomyosarcoma	Surgery, chemotherapy, radiotherapy	4 y

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was reported by Hill et al.[10] The series included 77 children and adolescents (aged 7 to 19 years) treated for colorectal carcinoma between 1964 and 2003. At presentation, 86% of the patients were in advanced stage of the disease and over 50% had distant metastases. Hill et al found that advanced stage and mucinous histology were significant predictors of adverse outcome. Stage-specific survival at 10 years was 67%±27% (stage 1), 38%±15% (stage 2), 28%±11% (stage 3), and 7%±4% (stage 4). Karnak et al[19] treated 20 children (7-16 years of age) with colorectal carcinoma in a period of 25 years (1972-1997). All of the children were at advanced stages of the disease (stage C, 7; stage D, 13). Delayed diagnosis, advanced stages of the disease at presentation, and, most importantly, mucinous type in histology are the major determinants of poor outcome in childhood colorectal carcinoma. Colorectal adenocarcinoma as a secondary neoplasm after treatment of early childhood malignancies is extremely rare (Table).[13-17] Our patient had an embryonal rhabdomyosarcoma of the cheek which was treated by surgery and chemotherapy. He subsequently had tumor recurrence, which was treated by surgery, chemotherapy and radiotherapy. In this patient, adenocarcinoma of the transverse colon as a secondary neoplasm developed 4 years after initial presentation of rhabdomyosarcoma in a non-irradiated area. Colonic cancer is one of the common malignancies worldwide but approximately 10% to 15% of the cases may be caused by genetic abnormalities in families.[22] There are two major types of hereditary disorders that lead to colorectal cancers, familial adenomatous polyposis and hereditary non-polyposis colorectal cancer. Hereditary non-polyposis colorectal cancer accounts for about 5% to 10% of all colorectal cancers, while familial adenomatosis polyposis cases make up about 1%. Individuals with hereditary non-polyposis colorectal cancer have an 80% lifetime risk for colon cancer. In children, colorectal cancer is sporadic, but it can also arise in those with predisposing conditions such as gastrointestinal polyposis syndromes, non-polyposis familial cancer syndromes, and inflammatory bowel disease.[23] Our patient also had café-au-lait spots but no other stigmata of neurofibromatosis. Neurofibromatosis type I is a hereditary multisystem disease inherited as an autosomal dominant. Clinically, it is characterized by the presence of café-au-lait spots, peripheral neurofibromatosis, axillary flickering, optic nerve glioma and hammartoma of the iris. Affected individuals have an increased risk of developing malignant tumors at different parts of the body and peripheral nerve sheath tumors in particular which are estimated to be 5%-15% higher than the general population.[24] Among 6678 pediatric cancer patients treated at St. Jude Children's Research Hospital over a 29-year period, 32 cases of neurofibromatosis type I were identified. A total of 35 malignant tumors have been diagnosed in these patients. Two of three patients with secondary malignant tumors had colon cancer as the primary or secondary tumor. Of particular interest were two cases in which both neurofibromatosis type I and malignant peripheral nerve sheath tumors were present in multiple successive generations.[25]

In conclusion, we report a child who developed adenocarcinoma of the transverse colon 4 years after initial presentation of rhabdomyosarcoma in a non-irradiated area. The reason for the early development of secondary neoplasm in our patient and in a non-irradiated area is obscure. In consideration of the strong family history, we suggest the possibility of familial predisposition.

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References

1 Taylor AJ, Winter DL, Pritchard-Jones K, Stiller CA, Frobisher C, Lancashire ER, et al. Second primary neoplasms in survivors of Wilms' tumour-a population-based cohort study from the

British Childhood. Int J Cancer 2008;122:2085-2093.
2 Borgmann A, Zinn C, Hartmann R, Herold R, Kaatsch P, Escherich G. Secondary malignant neoplasms after intensive treatment of relapsed acute lymphoblastic leukemia in childhood. Eur J Cancer 2008;44:257-268.
3 Inskip PD, Curtis RE. New malignancies following childhood cancer in the United States, 1973-2002. Int J Cancer 2007;121:2233-2240.
4 Mudie NY, Swerdlow AJ, Higgins CD, Smith P, Qiao Z, Hancock BW, et al. Risk of second malignancy after non-Hodgkin's lymphoma: a British Cohort Study. J Clin Oncol 2006;24:1568-1574.
5 Broniscer A, Ke W, Fuller CE, Wu J, Gajjar A, Kun LE. Second neoplasms in pediatric patients with primary central nervous system tumors: the St. Jude Children's Research Hospital experience. Cancer 2004;100:2246-2252.
6 Aung L, Gorlick RG, Shi W, Thaler H, Shorter NA, Healey JH, et al. Second malignant neoplasms in long-term survivors of osteosarcoma: Memorial Sloan-Kettering Cancer Center Experience. Cancer 2002;95:1728-1734.
7 Cohen RJ, Curtis RE, Inskip PD, Fraumeni JF Jr. The risk of developing second cancers among survivors of childhood soft tissue sarcoma. Cancer 2005;103:2391-2396.
8 Shih HH, Lu CC, Tiao MM, Ko SF, Chuang JH. Adenocarcinoma of the colon in children presenting as abdominal pain: report of two cases. Chang Gung Med J 2002;25:349-354.
9 Chopra R, Masih K. Adenocarcinoma of the colon in children and adolescents-report of three cases. Indian J Pathol Microbiol 1992;35:370-374.
10 Hill DA, Furman WL, Billups CA, Riedley SE, Cain AM, Rao BN, et al. Colorectal carcinoma in childhood and adolescence: a clinicopathologic review. J Clin Oncol 2007;25:5808-5814.
11 Musa AA, Agboola AO, Banjo AA, Shonubi AM. Rectal carcinoma in a nine-year-old Nigerian male child: case report. East Afr Med J 2007;84:93-96.
12 Jerkic S, Rosewich H, Scharf JG, Perske C, Füzesi L, Wilichowski E, et al. Colorectal cancer in two pre-teenage siblings with familial adenomatous polyposis. Eur J Pediatr 2005;164:306-310.
13 Densmore TL, Langer JC, Molleston JP, Dehner LP, Coffin CM. Colorectal adenocarcinoma as a second malignant neoplasm following Wilms' tumor and rhabdomyosarcoma. Med Pediatr Oncol 1996;27:556-560.
14 Kalteis T, Heers G, Elsner R. Adenocarcinoma of the rectum in childhood following chemotherapy and radiotherapy for a rhabdomyosarcoma-a case report. Eur J Pediatr Surg 2005;15:210-212.
15 Prabakaran S, Senthilnathan SV, Venkatadesikalu M, Prasad N, Sridharan S. Adenocarcinoma of the colon as a second malignancy in a child. Pediatr Surg Int 2001;17:475-477.
16 Brugha RE, Sherwood W, Scarsbrook A, Mitchell C, Lakhoo K. Rectal adenocarcinoma following cranio-spinal radiotherapy for cerebellar medulloblastoma. Pediat Surg Int 2007;23:605-607.
17 Park SS, Kim BK, Kim CJ, Kim WS, Kim IO, Park KW, et al. Colorectal adenocarcinoma as a second malignant neoplasm following rabdomyosarcoma of the urinary bladder: a case report. J Korean Med Sci 2000;15:475-477.
18 Rao BN, Pratt CB, Fleming ID, Dilawari RA, Green AA, Austin BA. Colon carcinoma in children and adolescents. A review of 30 cases. Cancer 1985;55:1322-1326.
19 Karnak I, Ciftci AO, Senocak ME, Büyükpamukçu N. Colorectal carcinoma in children. J Pediatr Surg 1999;34:1499-1504.
20 Skinner MA, Plumley DA, Grosfeld JL, Rescorla FJ, West KW, Scherer LR. Gastrointestinal tumors in children: an analysis of 39 cases. Ann Surg Oncol 1994;1:283-289.
21 Spunt SL, Meza JL, Anderson JR, Donaldson SS, Qualman SJ, Robison LL, et al. Second malignant neoplasms (SMN) in children treated for rhabdomyosarcoma: a report from the Intergroup Rhabdomyosarcoma Studies I-IV. American Society of Clinical Oncology 37th Annual Meeting, May 12-15, 2001, Philadelphia, PA.
22 Al-Sukhni W, Aronson M, Gallinger S. Hereditary colorectal cancer syndrome. Surg Clin North Am 2008;88:819-844, vii.
23 Saab R, Furman WL. Epidemiology and management options for colorectal cancer in children. Paediatr Drugs 2008;10:177-179.
24 Barbaric D, Stevens M, Dalla-Pozza L. Neurofibromatosis type I and multiple primary malignancies. Med Pediatr Oncol 2003;41:568-569.
25 Shearer P, Parham D, Kovnar E, Kun L, Rao B, Lob T, et al. Neurofibromatosis type I and malignancy: review of 32 pediatric cases treated at a single institute. Med Pediatr Oncol 1994;22:78-83.

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