

Sporadic colonic polyposis and adenocarcinoma associated with lymphoblastic and large B-cell lymphoma in a young male patient: A case report

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Abstract. We herein report a case of colonic polyposis, colorectal carcinoma and large B-cell lymphoma in a 22-year-old male patient with a previous history of childhood lymphoblastic lymphoma. Eight years after lymphoblastic lymphoma, which presented as mediastinal mass and superior vena cava syndrome, the patient complained of abdominal pain, lower gastrointestinal bleeding and an abdominal mass. The surgical exploration revealed numerous mucosal polyps throughout the large intestine, and multifocal masses in the ascending and transverse colon and the rectosigmoid region. A retroperitoneal mass was also found. The pathological examination revealed >100 tubular adenomatous polyps and a multifocal, well-differentiated adenocarcinoma, with lymph node involvement and pericolic invasion. Interestingly, the immunohistochemical studies confirmed the malignant undifferentiated retroperitoneal mass as large B-cell lymphoma. Over a period of ~10 years, the patient had suffered from three different malignancies. To the best of our knowledge, such a combination of sporadic adenomatous colonic polyposis, colorectal carcinoma and two extra-intestinal non-Hodgkin lymphomas has not been reported to date. It should be considered that each malignancy increases the risk for other neoplastic diseases and a close follow-up is crucial for early detection of second malignancies and neoplastic syndromes.

Introduction

Colonic polyposis includes different types of polyps, such as adenomatous, hamartomatous and hyperplastic (1,2). Familial adenomatous polyposis (FAP), Gardner's syndrome, MUTYH-associated polyposis (MAP), familial juvenile polyposis and Peutz-Jeghers syndrome, are colonic polyposis syndromes with different genetic backgrounds and associated symptoms (1,2).

Over several years, the disorders associated with colonic polyposis syndromes were gradually identified (1,2). The extracolonic disorders associated with these syndromes are mainly benign. However, several associated malignancies have also been reported (1-3).

Hematological malignancies have not been described in the original polyposis syndromes (1,2); however, an increasing number of studies highlighted the association between colonic polyposis and hematological malignancies, of either lymphomatous or myeloid origins (4-6).

We herein describe the case of a young male patient with a history of childhood lymphoblastic lymphoma who, 8 years after the initial malignancy, was diagnosed with colonic polyposis, colorectal adenocarcinoma and synchronous retroperitoneal large-B cell lymphoma.

Case presentation

Our patient was a 22-year-old man from Zahak, located in southeast Iran. In June, 2002, when the patient was 9 years old, he was admitted to the Emergency Department with dyspnea, facial edema, intermittent low-grade fever and productive cough that had appeared 8 days prior to admission. The detailed family history was negative for malignancies, colonic polyposis and other familial syndromes.

On physical examination, the patient was febrile, with respiratory distress and periorbital and facial edema extending to the submandibular area, neck and anterior chest wall. There was

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no cervical lymphadenopathy, but a lymph node sized 2x2 cm was found in the left axilla. The other physical findings were normal, apart from bilateral hydrocele. The clinical findings were compatible with superior vena cava syndrome.

The laboratory findings were as follows: White blood cell count, $7.8 \times 10^6/\text{ml}$; hemoglobin concentration, 8.9 g/dl; platelet count, $406 \times 10^6/\text{ml}$; erythrocyte sedimentation rate (ESR), 55; and lactate dehydrogenase (LDH) level, 587 U/l. A chest X-ray revealed mediastinal widening. The abdominal ultrasonography was negative for para-aortic lymphadenopathy and hepatosplenomegaly. A contrast-enhanced chest computed tomography (CT)-scan revealed an anterior mediastinal mass. The abdominopelvic CT-scan was normal. Following a trans-thoracic incisional biopsy, the mediastinal mass was diagnosed as lymphoblastic lymphoma. The bone marrow aspiration and cerebrospinal fluid analysis were negative.

After 8 days of hospitalization and initial treatment with dexamethasone, vincristine and cyclophosphamide, the patient was discharged with an improved general condition. For 24 months the patient was treated with the Berlin-Frankfurt-Munich non-Hodgkin lymphoma (BFM-NHL) protocol. In February, 2003, maintenance therapy was initiated at week 34 of the protocol, with daily 6-mercaptopurine and weekly oral methotrexate. After 15 months of maintenance therapy, the BFM-NHL protocol was completed in June, 2004. The complete blood count, abdominal and testicular ultrasonography and chest CT scan were normal at the end of the maintenance therapy. Prophylactic cranial irradiation was performed, with 1,800 cGy in 10 sessions over 2 weeks in July, 2003.

In March, 2010, ~8 years after the first presentation and when the patient was aged 18 years, he was referred to the Adult Hematology and Medical Oncology service with a history of vague sustained periumbilical abdominal pain and lower gastrointestinal bleeding. The physical examination revealed a soft abdominal mass in the periumbilical area; the other findings were not significant. Given the prolonged interval from the previous lymphoblastic lymphoma diagnosis, a second malignancy was suspected. A contrast-enhanced abdominopelvic CT scan revealed solid masses in the retroperitoneal and intra-abdominal areas.

The exploratory laparotomy revealed numerous mucosal polyps throughout the large intestine, and multifocal masses in the ascending and transverse colon and rectosigmoid region. A retroperitoneal mass was also identified. Total colectomy with ileorectal anastomosis and retroperitoneal tumor resection and lymphadenectomy were performed.

The pathological examination revealed >100 tubular adenomatous polyps with a diameter of ≤ 2 cm, and a multifocal, polypoid, well-differentiated adenocarcinoma with a mucinous component. Lymph node involvement and pericolic invasion were detected. However, the appendix and terminal ileum were tumor-free. Furthermore, the immunohistochemical examination confirmed the malignant undifferentiated retroperitoneal mass to be large B-cell lymphoma, positive for CD45 and CD20 and negative for cytokeratin.

The patient received 6 cycles of ifosfamide, etoposide and oxaliplatin (IVOX protocol) from June to November, 2011. The gallium scan confirmed complete remission and surveillance was scheduled from February, 2011 onwards.

Although the surveillance laboratory markers, including ESR, LDH and carcinoembryonic antigen, were negative for recurrence of epithelial and/or lymphomatous malignancies, the follow-up colonoscopy in 2013 revealed an ulcerated tubulovillous adenomatous polyp with high-grade dysplasia. In addition, two tubular adenomatous polyps were found at a distance of 3 and 8 cm from the anal verge. A subsequent colonoscopy performed 6 months later detected a mass with malignant characteristics in the rectum. The pathological examination revealed an invasive adenocarcinoma in a background of a high-grade villous adenomatous polyp.

The patient underwent local surgical therapy with permanent colostomy. Subsequently, 6 cycles of adjuvant chemotherapy with the FOLFIRI protocol were administered and the patient has been receiving capecitabine and bevacizumab as maintenance therapy, without any relapses to date. The detailed family history was negative for malignancies, colonic polyposis and other familial syndromes.

Discussion

Colonic polyposis is a heterogeneous group of neoplastic disorders with different characteristics, including adenomatous and hamartomatous polyps (1,2). FAP is an inherited polyposis syndrome characterized by the presence of adenomatous polyps in the colon and rectum (1). The classic syndrome originates from a germline mutation in the adenomatous polyposis coli (APC) gene and the patients are at high risk of colon cancer if left untreated (1,7). A strong family history of colonic polyps and cancer is present (1). Different variants of this syndrome include attenuated FAP, Gardner's syndrome, and MAP (1,2). Familial juvenile polyposis, hyperplastic polyposis and Peutz-Jeghers syndrome are other examples of colonic polyposis, with different origins (1,2). Furthermore, lymphoproliferative disorders may resemble polyposis coli (8).

Different types of colonic polyposis are associated with certain neoplasms (1,2,9). These neoplasms are mainly benign, including desmoid tumors, osteomas and epidermoid cysts (1,3,9,10), but malignancies such as thyroid cancer and upper gastrointestinal adenocarcinoma have also been reported (11-16).

Clinical and genetic data suggest that hematological malignancies are not common extracolonic manifestations in FAP and other colonic polyposis syndromes (6). For example, it has been reported that the mutation of the APC gene may not be the major cause of hematological malignancies (17). However, the number of reports on the association between colonic polyposis and hematological malignancies is increasing. These malignancies are of myelogenous origin, such as acute and chronic myelogenous leukemia, as well as lymphoproliferative disorders (4-6,11).

We reported a unique combination of sporadic adenomatous colonic polyposis, colorectal carcinoma, lymphoblastic lymphoma and large B-cell lymphoma in a young male patient.

The reports of lymphoblastic lymphoma in association with colonic polyposis are limited. Kiratli *et al* (18) reported a sporadic unilateral retinoblastoma in a 3-year-old boy treated with enucleation, with no adjuvant chemoradiation. Lymphoblastic lymphoma and juvenile hamartomatous polyposis were diagnosed 5 and 6 years later,

respectively. Kaplan *et al* (19) reported siblings with hereditary von Recklinghausen's neurofibromatosis and familial lymphoblastic lymphoma. Colonic polyposis and the characteristics of Gardner's syndrome were found in one of the siblings.

Certain studies report synchronous occurrence of colorectal carcinoma and gastrointestinal NHL (20-22). However, co-occurrence of colonic polyposis and colorectal carcinoma with two extraintestinal synchronous and meta-chronous non-Hodgkin lymphomas is unusual.

Second malignancies are very important when a patient is under surveillance for a primary malignancy. Suspicion should arise when the clinical findings, such as time course, are not fully compatible with relapse of the primary malignancy. A precise schedule of surveillance and patient adherence are crucial for optimal follow-up outcomes.

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