A 14-year-old female with Turner syndrome (karyotype 45,X) had a history of abdominal pain with distention, constipation, and fever. She was first operated on for the suspicion of appendicitis, failed to improve, and was later hospitalized for further investigation and treatment. Studies demonstrated an obstructing tumor of the transverse colon, and an emergency laparotomy was performed. The final diagnosis was a signet-ring cell carcinoma of the colon with diffuse peritoneal dissemination and metastasis to paracolic lymph nodes. On the basis of this case, we report the association of Turner syndrome with malignancies and also some aspects of colon cancer in childhood. [Key words: Colon cancer; Turner syndrome; Adolescence; MLH1; Polymorphism]


TURNER SYNDROME

Turner syndrome was classically described as the result of the absence of a second sex chromosome (X chromosome monosomy with haploinsufficiency; karyotype 45,X). However, partial sex monosomy may also be responsible for the syndrome and represented by a structurally abnormal second sex chromosome (X or Y), a sex chromosome mosaicism involving a 45,X cell line, or both. There are five cardinal features associated with Turner syndrome: female phenotype, short stature, sexual infantilism secondary to rudimentary gonads, somatic abnormalities, and embryonic lethality.1

Patients with Turner syndrome may be at higher risk of developing neoplastic diseases, including colon cancer.2 However, because colon cancer in children is rare, the low index of suspicion for such a tumor in Turner syndrome may lead to a delay in the diagnosis. We report here a case of the association of Turner syndrome with transverse colon cancer in a 14-year-old female.

REPORT OF A CASE

A 14-year-old female with previous diagnosis of Turner syndrome (karyotype 45,X; Fig. 1) had a history of abdominal pain that began in early November 2000. Her first medical consultation for this matter was on the twenty-eighth of the same month, when she also presented with constipation, abdominal distention, and fever. Because she failed to improve, she was hospitalized on December 6, 2000, and was operated on because acute appendicitis could not be excluded. The appendix showed no inflammatory signs. At medical consultation two weeks later, she presented with constipation, abdominal distention, and fever in addition to her abdominal pain. On physical examination, her general condition was fair. She was pale and had a distended abdomen with no palpable tumors. Laboratory data revealed anemia.

Figure 1. The patient’s karyotype study reveals the absence of a second sex chromosome, characteristic of Turner syndrome (karyotype 45,X).
(hemoglobin of 8.8 g/dl and hematocrit of 27.5 percent) and normal white blood cell count. Hypoproteinemia was noticed (total protein of 5.2 g/dl and albumin of 3.1 g/dl) and a reduction of the plasma sodium (Na\textsuperscript{+} of 131 mEq/l) and chloride (Cl\textsuperscript{−} of 97 mEq/l). The levels of tumor markers including carcinoembryonic antigen (0–5 ng/ml; normal range), CA19-9 (0–37 U/ml), and CA72-4 (0–4 U/ml) were 4.4 ng/ml, 5.2 U/ml, and 88 U/ml, respectively. The abdominal plain x-ray revealed dilated intestinal loops, and on CT scan, a tumor involving the colonic wall was identified. Barium enema and colonoscopy confirmed the diagnosis of a circumferential tumor of the transverse colon. On December 31, 2000, she underwent an emergency laparotomy for obstruction, when tumorous invasion of the serosa of the transverse colon and diffuse peritoneal dissemination were observed. Right hemicolectomy was performed, and the histopathologic study revealed a signet-ring cell carcinoma of the colon, with severe lymphatic and venous invasion and metastasis to paracolic lymph nodes (Fig. 2). The patient had no familial history of colon cancer or hereditary nonpolyposis colon cancer–associated tumors. The germline test on peripheral blood revealed no mutations in the familial adenomatous polyposis gene (APC on 5q). The same test for the hereditary nonpolyposis colon cancer genes revealed no mutations in MSH2 on 2p but showed intragenic polymorphism in MLH1 on 3p.

**DISCUSSION**

The manifestation of Turner syndrome may be related to the absence of a functional copy of a gene located on the long arm of the X chromosome that escapes inactivation or of its nonidentical homolog on the short arm of the Y chromosome (RPS4X and RPS4Y, respectively).\textsuperscript{3} It is expected that 1 in 2,500 to 1 in 6,000 live-born females have Turner syndrome,\textsuperscript{4} but the number of nondiagnosed cases may be high, because some of them may lack the typical stigmata, especially those with mosaicism.

Our case was of great difficulty, with delay in diagnosing colon cancer, because the patient was too young. The clinical presentation first led to the misdiagnosis of acute appendicitis, something that had already been reported in the literature.\textsuperscript{5} Turner syndrome is also thought to be involved with an increased incidence of chronic inflammatory bowel diseases.\textsuperscript{6} Given this fact and in an attempt to match the signs and symptoms with the age of the patient, Crohn’s disease would have been a suitable hypothesis. However, we realize that colonoscopy should have been performed earlier as part of the investigation for abdominal pain, as suggested by Khan et al.\textsuperscript{7}

A possible relationship between Turner syndrome and a higher susceptibility for developing malignancies has been published previously.\textsuperscript{2,8–10} Taking into account the risk of extragonadal tumors in Turner syndrome, Wertelecki et al.\textsuperscript{10} concluded that there was a preponderance of neurogenic tumors among children and young adults. Moreover, Hasle et al.\textsuperscript{2} showed a statistically significant increase in the risk of adenocarcinoma of the colon in patients with Turner syndrome (relative risk, 6.9). In a review of the literature using MEDLINE as the surveillance method, we found a total of 12 patients with such association whose ages at diagnosis varied from 38 to 90.