Colonic cancer in adolescents. A report of three cases

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Abstract

Colorectal cancer is a common malignant neoplasm in adults, with a peak incidence of 60-79 years. About 1 million cases of the disease and half a million deaths associated with it are reported world-wide each year. Colorectal cancer, however, is very uncommon in children and adolescents. This is a presentation of 3 cases of colon cancer in Nigerians aged 17 and 19 years. Two of them were adenocarcinoma and the other leiomyosarcoma. The pathogenesis and aspects of management are discussed.

Introduction

Colon cancers are the second most common cancer in both men and women in America.[1,2] World-wide they are the third major cause of cancer for men and the fourth most common cause of cancer for women.[2,3] They are the second most common causes of cancer-related deaths in developed countries and the most common gastro-intestinal carcinoma.[4-6] The incidence is highest in the westernized countries of North America, Northern Europe, Australia, and New Zealand. Intermediate rates are found in Southern Europe, and low rates in Africa.[2,4] Reports have shown that close to 1 million new cases of colo-rectal cancer and nearly half a million deaths associated with colorectal cancer are reported world-wide each year.[4,7] About 98% of them are primary adenocarcinomas.[4,8,9] The remaining 2% are made up of carcinoid, mesenchymal and lymphoid tumors. These figures have decreased in the West due to increased rate of screening and polyp removal.[10]

The peak incidence for colorectal carcinoma is put at between ages 60 and 79 years, with fewer than 20% occurring before the age of 50 years.[8] According to another author, 90% of patients are older than 50 years; with highest incidence rates in individuals aged 70 to 85 years.[4] Very occasionally, it may affect much younger adults from the age of 20 years.[6]

The risk factors for development of colo-rectal cancer include age, a diet rich in fat and cholesterol, inflammatory bowel disease, and genetic predisposition, including hereditary polyposis and non-polyposis syndromes.[4,7,11]

Three cases of colonic cancer amongst Nigerian adolescents aged 17 and 19 years are presented. These are uncommon findings, and hence should be of interest to clinicians to increase their index of suspicion as early cases are potentially curable.

Case #1

OS, a 19-year old male student presented to the surgical out-patient (SOP) department of the Irrua Specialist Teaching Hospital (ISTH) with complaints of passage of bloody and watery stools, abdominal pain, lower abdominal distension and vomiting of between one week and three months duration. The abdominal pain was intermittent and colicky. He reported mild weight loss. There was no family history of similar illness. Physical examination showed a mildly dehydrated young man with tense and distended abdomen, visible peristaltic waves, and hyperactive bowel sounds. He was admitted, and after one week the abdominal distension worsened and he developed constipation. Digital rectal examination and proctoscopy showed an empty rectum with a circumferential and fungating irregular, firm mass about 5 cm from the anal verge.

An impression of intestinal obstruction secondary to rectal tumor was made, and incisional biopsy taken for histology. The histopathology diagnosis was adenocarcinoma. The patient was offered a dysfunctioning (loop) sigmoid colostomy after decompression of the dilated sigmoid colon. He was commenced on 5-flurouracil (5FU) and adriamycin following confirmation of mesenteric lymph node involvement in the colostomy biopsy specimen. He received 5 courses of chemotherapy and was referred to another center for radiotherapy. The patients has responded well to this.

Case #2

EB was a 17-year old student. She presented to the SOP of ISTH, six weeks after appendicectomy in a private hospital, with colicky abdominal pain, vomiting, weakness, and discharge from the appendicectomy scar of about two weeks duration. Family and social history was not significant. Physical examination revealed a fixed and firm, non-fluctuant mass of about 10x11 cm in the right iliac fossa region of the abdomen. Abdominal ultrasound found a large intra-abdominal mass, and suggested retained foreign body, to rule out infected appendix stump. At exploratory laparotomy, an infected appendicectomy wound and a firm to hard cecal pole mass were observed. The mass measured about 15x12 cm and was associated with about 20 mls of abscess. Right hemi-colectomy was done and histopathology examination requested. The request was never received by the laboratory. The patient recovered and was discharged home. Two months post-operation, she developed a nodule on the anterior abdominal wall over the laparotomy scar. This was thought to be a pyogenic granuloma. A repeat abdominal ultrasound reported an anterior abdominal wall mass and enlarged inguinal lymph nodes, and made an impression of rhabdomyosarcoma. The lump was excised and sent for histopathology examination, together with the hemi-colectomy specimen. Both of them showed similar histologic features composed of malignant glands and cells within fibro-cellular stroma. A diagnosis of colonic adenocarcinoma with metastasis to the anterior abdominal wall was made. The patient was commenced on 5-FU and referred for radiotherapy, after receiving 5 courses of chemotherapy. She died about two and a half years after diagnosis

Case #3

A 19-year old male, PO, presented to the emergency room of Joe Alufohai Medical Center, Sabongida-Ora on 26/10/07 with a two-week history of abdominal pain and vomiting. On examination he was found to be in painful distress and to have moderate rebound tenderness and guarding. This was worse over the right lower quadrant of the abdomen. A diagnosis of acute appendicitis was made and the patient taken in for emergency appendicectomy.

Findings at surgery included a dilated, longish and coiled appendix; dilated terminal ileum; and an atrophic cecum with a localized firm mass. In view of these findings, an additional intra-operative impression of congenital hypertrophy of the ileo-cecal valve was considered and a limited right hemi-colectomy performed. The specimen was sent for histology. The patient did well and was discharged to the out-patient clinic two weeks after surgery.

The histopathology diagnosis was leiomyosarcoma, together with acute appendicitis. The patient has yet to honor his out-patient appointment, six months after discharge.

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Discussion

Almost all bowel cancers arise in the colorectum, since the small intestine is strikingly free from cancer risk.[6] Colon cancer is a silent killer, often causing no recognizable symptoms until it is too late.[3] Most of them occur sporadically in the absence of well-defined familial syndromes. Regardless of the inciting event, a well-described set of genetic alterations occurs that ultimately leads to colorectal malignancy.[8] Fitzgibbons *et al.* described a genetic factor found in young patients belonging to Scandinavian families with the Lynch syndrome.[12]

The vast majority of colorectal cancers are adenocarcinomas, which arise from pre-existing adenomatous polyps.[6] This adenoma-carcinoma sequence is a well-characterized clinical and histopathologic series of events with which discrete molecular genetic alterations have been associated.[7] However, about 30% of colorectal carcinomas arise from flat lesions without evidence of adenomatous precursors.[6] These suggest that some dysplastic lesions can degenerate into malignancy without passing through a polypoid stage.[8] This particularly occurs with cancers of the proximal colon and rectum.[6] Two of the cases being reported were in the proximal colon; the third was in the rectum. Sebbag *et al.* did not consider heredity to be involved in the pathogenesis of colon cancer.[13] More recently though a known genetic link was described in first degree biological family members of persons with colon cancer.[3] They have 3 times greater risk of developing colon cancer than the general population. However, 80% of colon cancers strike people without genetic connection to the disease.[3] No family history of similar illness was obtained from any of the index patients. Vogelstein and colleagues identified a number of very important genetic alterations that contribute, through their multiplicity over the years, to the eventual development of colorectal cancer.[14,15] These are grouped into two pathogenetically distinct pathways that are believed to be responsible for the development of colon cancer.[16] Both pathways involve the stepwise accumulation of multiple mutations. The first pathway (*APC/β-caterin pathway*) is characterized by chromosomal instability that results in accumulation of mutations in a series of oncogenes and tumor suppressor genes. These include mutations of the adenomatous polyposis coli (*APC*) gene and *K-RAS* gene, and loss of *SMAD4* (formerly called *DPC4* – deleted in pancreatic cancer – gene) and *p53* genes.[7,8] The morphologic evolution of the lesion is through a localized colon epithelial proliferation to formation of small adenoma that progressively enlarge, become more dysplastic, and ultimately develop into invasive cancer (the adenoma-carcinoma sequence). The second pathway (*microsatellite instability pathway*) is characterized by inheritance of a mutation in one of several genes involved in DNA mismatch repair, which are *MSH2, MLH1, MSH6, PMS1* and *PMS2*. It is involved in 10-15% of sporadic cases of colon cancer and in the hereditary non-polyposis colonic cancer (HNPCC or Lynch) syndrome.[6-8] Inheritance in this type of cancer is autosomal dominant. Affected patients also carry an increased risk of cancers of the stomach, ovaries, breast and uterus. The colon cancers in this syndrome tend to develop as flat lesions rather than as polyps. Cancers arising through this pathway occur at a younger age, usually before 45 years.[6] Unlike in the adenoma-carcinoma sequence, this pathway does not produce identifiable morphologic correlates.

These pathogenic pathways, which involve stepwise accumulation of mutations, explain why colorectal cancer is a disease of adults. It is rare in patients under 40 years of age, and even rarer in younger age groups.[17] Of the 1,250 cases seen by Sebbag *et al*. over a 25-year period, only 3 (0.24%) were under 19 years.[13] It is said that when colorectal cancer is found in a young person, pre-existing ulcerative colitis or one of the polyposis syndromes must be suspected.[8] None of our cases had any of these. Environmental factors, especially dietary practices, have been implicated in the observed striking geographic contrasts in incidence. People who eat high calorie, high fat (Western) diets are at higher risk than people who eat balanced low fat, high fiber (Eastern) diets.[3,18] This is partly because fiber increases the bulk and the transit time of stool. This does not allow enough time for both bacterial breakdown of bile salts into carcinogenic lithocholic and deoxycholic acids, and their contact with colonic mucosa.[2] It had been mentioned that low fecal pH had a role to play in the genesis of colon cancer. Also the role of obesity in colorectal cancer has been discussed.[20] There is a well-known link between obesity and a Western diet. Japanese and Polish families who migrated from their low risk areas to the US acquired, over the course of 20 years, the rate prevailing in their new environment.[6] They had adopted the dietary practices of their hosts.[8] Dietary factors account for 90% of the risks for bowel cancer.[21] A Western-type dieting has become very common with us in Africa, even without migrating. This may account for why the incidence in black Africans is increasing, especially in the major urban cities.[2] Its introduction to our children very early in life may be an important influence when combined with other environmental/racial/social factors peculiar to us, which have not been studied. After all, black Americans are said to be more prone to developing colon cancer than their white counterparts.[22] Apart from this, a possible increased risk among lower socioeconomic groups especially in the third world has been suggested.[23,24] This is related to poor nutrition or chronic gastro-intestinal infections, such as amoebiasis and schistosomiasis, which are thought to be associated with an increased incidence of malignancy. All three cases being presented belonged to the lower socioeconomic group. None of them was immunosuppressed. Their exposure to chronic gastro-intestinal infestations was not determined.

Colon cancers progress slowly and may be asymptomatic for as many as five years or until a much later phase.[9] However, patients usually have occult blood losses from their tumor.[4] It is likely that the index tumors started while the patients were still in the pediatric age group. Most studies suggest a delay in diagnosis with an associated deleterious effect on outcome. This is because many of the clinical features are similar to those found in common childhood problems such as intussusception, appendicitis, gastro-enteritis and simple constipation.[23] Two of the presented cases were initially thought to be appendicitis. This is understandable considering the rarity of colon cancer in children/adolescents.

Treatment must be aggressive and include a combination of surgery and adjuvant chemotherapy. The surgical resection must be as radical as feasible for growth.[13] Both systemic and loco-regional chemotherapy, such as intra-hepatic, intra-arterial for liver metastasis, have a role.[7] Where technically feasible, resection of metastatic deposits in the lungs or liver is advisable.[25,26] The chemotherapeutic agents in use include 5-FU, irinotecan, leucovorin, and the more recent anti-vascular endothelial growth factor, bevacizumab.[7] Radiotherapy finds use in cases of rectal cancer to reduce the risk of local recurrence.

When tumors are detected early, 90% of patients survive at least five years after diagnosis and treatment.[27] This is not the case for adolescents where it carries an extremely poor prognosis, owing to late diagnosis and aggressive tumor biology.[23]

Conclusions

Colorectal cancer remains a leading cause of death from cancer in adults, especially in the Western world. It is a very rare disease in children and adolescents. Even so, colon cancer in the young is of great concern, especially since screening strategies are focused on older patients.[17] Progress has been made in understanding the molecular basis of its predisposition and progression. Efforts are being made on to develop better treatment and preventive approaches, and better screening strategies. Such screening strategies must incorporate

children and adolescents since they are not immune to colorectal cancers, as demonstrated by this report. As Sebbag *et al.* put it, the distribution pattern of colorectal carcinoma appears to have changed.[13] There is no point waiting until older age to check for risks.

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