

Diagnostic and Treatment of Synchronous Colorectal Cancer, a Concern of Diagnosis and Treatment, Review and Case Report

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Abstract: One of the most frequent digestive tract cancers in the world today is Colorectal cancer (CRC). In the terms of incidence CRC ranks third and the second in the terms of mortality.

Synchronous colorectal cancer (SCRC) refers to more than 1 primary colorectal cancer detected in a single patient simultaneously or within 6 months of the initial diagnosis.

Case presentation: We report a Caucasian male, 74 years old, with intermittent abdominal pain and discomfort, constipation, anemia, sometimes nausea, and intestinal subocclusion symptoms. Surgical treatment consisted in extended left hemicolectomy after intraoperative recognition of two different colon cancers. The postoperative course was uneventful, HP revealed Synchronous colorectal cancer (SCRC) with free resection margins. Through our case we review literature.

Conclusions: Careful palpation of the entire colon during the operation for CRC may reduce the risk of maltreatment of SCRC.

Key words: Colorectal cancer, Synchronous colorectal cancer, diagnostic, surgical treatment

1. Introduction

The GLOBOCAN 2018 estimates cancer incidence and mortality produced by the International Agency for Research on Cancer, with a focus on geographic variability across 20 world regions, an 18.1 million new cancer cases (17.0 million excluding nonmelanoma skin cancer) and 9.6 million cancer deaths (9.5 million excluding nonmelanoma skin cancer) in 2018.

Colorectal cancer ranks third in terms of incidence but second in terms of mortality.¹

Colorectal cancer incidence rates are about 3-fold higher in transitioned versus transitioning countries; however, with average case fatality higher in lower HDI (Human Development Index) settings, there is less variation in the mortality rates.¹

The revised World Cancer Research Fund/American Institute for Cancer Research report notes convincing evidence that processed meat, alcohol drinks, and body fatness increase risk, whereas physical activity is protective (colon only). A diet high in the consumption of red or processed meats has been associated with an increased risk of colon cancer, but not rectal cancer.¹

Synchronous colorectal cancer (SCRC) refers to more than 1 primary colorectal cancer detected in a single patient simultaneously or within 6 months of the initial diagnosis.^{2,3}

Synchronous colorectal cancer (SCRC) are caused by common genetic and environmental factors.²

Case presentation

During five years, (2014-2019) retrospectively, were 375 patients who underwent different colonic resections for colorectal cancer at the Department of General and Abdominal Surgery at the University Clinical Center of Kosova.

In the same period of observation group with CRC, surgically treatment indicated electively or in emergency, were diagnosed intraoperatively four patients with synchronous colorectal cancers (SCRCs), 2 males and 2 females, the prevalence of SCRCs was 1.07%. One of them was previously treated for Ulcerative Colitis. Three of them had comorbidity with hypertension, one with Diabetes Mellitus. The mean age was 61.5 years, (37-71 years old). We are presenting a Caucasian male with intermittent abdominal pain and discomfort, constipation, anemia, sometimes nausea, and intestinal subocclusion symptoms. He was previously treated conservatively for Hypertrophica prostatae from Urologist and for anemia from Hematologist. Physical examination revealed a soft tenderness in the lower left quadrant of the abdomen without any palpable mass. Patient had family history of prostatic cancer without hereditary intestinal cancers. Barium enema failed because of annular carcinoma located in recto-sigmoidal junction and inadequate bowel preparation in upper part of colon. After laboratory examinations and clinical evaluation he was surgically treated in general endo tracheal anesthesia.



Fig.1. Photo of the case (small black arrow-first tumor; small and big black arrow-second tumor; diamonds-polyps).

During intraoperative procedures, with careful palpation of entire colon we have recognized synchronous colorectal cancers, two colon tumors in different locations, the first tumor in recto-sigmoidal colon and the second tumor located in transverse colon.

It was performed left extended hemicolectomy, and end to side anastomosis with rounded stapler. Postoperative period went well, with recuperation in general and local status. HP: they identify two ulcero-infiltrative tumors, adenocarcinomas, the first one located in transversum part of colon, around 3,5 x 3,5 cm and the second one in recto sigmoidal junction with 3,2 x 3.2 cm. The grade was G2, TNM classification was pT3,pN1 (V1)(R0), 3/18 lymph nodes were positive with tumor. The founded seven polyps with low-grade glandular dysplasia.

After a month recovery, he received adjuvant therapy, eight cycles.

Follow-up: He was followed-up every 6 month in the initial 6 month for three year, than once in 12 month. The clinical evaluations include a complete blood count, liver and kidney function test, serum carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 levels, physical examination (conducted at each visit), CT scan of the abdomen and colonoscopy (every 12 months). The four years follow-up, revealed free cancer disease.

2. Literature review

Worldwide cancer incidence and mortality are rapidly growing. The reasons are complex but reflect both aging and growth of the population, as well as changes in the prevalence and distribution of the main risk factors for cancer, several of which are associated with socioeconomic development.¹

The rising prominence of cancer as a leading cause of death partly reflects marked declines in mortality rates of stroke and coronary heart disease, relative to cancer, in many countries.¹

GLOBOKAN estimates over 1.8 million new colorectal cancer cases to occur in 2018; around 881,000 deaths to occur in 2018.¹ In both sexes combined, lung cancer is the most commonly diagnosed cancer (11.6% of the total cases) and the leading cause of cancer death (18.4% of the total cancer deaths); colorectal cancer participate with 6.1% of the total cancer deaths for incidence and colorectal cancer (9.2%) for mortality.¹

Nosho at all. in a prospective cohort study, they compared patients with solitary colorectal cancer and synchronous colorectal cancer patients, they founded at synchronous cancer patients reduced overall survival time.²

Metachronous colorectal carcinoma is the presence of more than one primary colorectal carcinoma detected consecutively in a single person after a set time interval.⁴

The Warren and Gates established criteria to clinically diagnose SCRCs on the basis of pathological findings in CRC biopsies. These criteria include the following key elements: (a) each tumor must present a definite picture of malignancy; (b) each tumor must be distinct; (c) the probability of one being a metastasis of the other must be excluded, and (d) the synchronous lesions must be diagnosed simultaneously or within 6 months of the initial diagnosis.⁵

They are predisposing conditions at the patients with inflammatory bowel diseases (ulcerative colitis), hereditary non-polyposis colorectal cancer and familial adenomatous polyposis. They are known to have higher risk of synchronous colorectal cancer, obvious related to a multiple field of dysplasia (adenomas) that can occur in these patients.⁴

At our patient we found except two different colonic tumors, seven polyps (adenomas) in resected colon with low-grade glandular dysplasia.

Risk factors for synchronous cancer include male sex, advanced age, and hereditary colorectal neoplastic conditions, as adenoma, IBD, hereditary nonpolyposis colorectal cancer familial adenomatous polyposis.^{4,6}

The risk factors of CRC including family publication, history of colorectal cancer, smoking, excessive alcohol consumption, high consumption of red and processed meat, obesity, and diabetes, may also be associated with synchronous CRC. In the He et al. smoking history and alcohol intake may lead to a higher risk in patients with synchronous CRC as compared to those with solitary CRC.⁷

The prevalence of synchronous colorectal carcinoma ranged from 1.1% to 8.1%. In three large studies with more than 10000 colorectal cancers, the prevalence of synchronous colorectal carcinoma was 3.1%-3.9%. Lam et al. reported from the pooling data from 39 series, the overall prevalence of synchronous colorectal carcinoma was 3.5% (3667 of 105686) of colorectal cancers.⁴

In many of the series, the mean age at presentation for synchronous colorectal cancer was higher than solitary colorectal cancer. In large series from Latourniere, the age at diagnosis for solitary colorectal and synchronous colorectal carcinoma was similar.⁸ Compared to the solitary cancer patients, the synchronous cases were significantly older.²

They are reports, where the mean age at presentation of synchronous colorectal carcinoma ranged from 47 to 79 years.^{4,7}

Gender distribution of patients with SCRCs in the major studies is around 64-70% at male and 30%-36% at female.^{8,9,10,11}

There are several hypotheses that speculate for possible reasons for the high mortality, morbidity and poor outcomes at cases with synchronous tumors: the first is build on under staging of cancer which may contribute, where cancer staging is based on limited information, which stand on limited sampling of tissues (primary cancers and lymph nodes) from the entire specimen for pathologic assessment, and tissue sections represent only a two dimensional profile of tumor or lymph node. Thus, a possibility of not detecting a metastatic or more advanced focus exists, and the presence of two separate cancers in a single individual may increase the likelihood of under staging; the second one is build up in the presence of more than one cancer focus increases the likelihood of progressive disease (recurrence or metastasis), due to a larger cancer burden or due to recurrence by field effect; the third hypothesis that patients with synchronous cancers may have more chances of postoperative complications than those with solitary cancers; the fourth one is based on underlying molecular features of synchronous colorectal cancers may cause poor outcome.²

Compared to solitary cancer patients, Noshio et al. experienced significantly higher overall mortality in synchronous cancer patients.²

van Leersum et al. reported association of Synchronous colorectal carcinoma with a higher risk of severe postoperative complications and re interventions compared with solitary colorectal carcinoma but not with higher 30-day mortality, they are most likely because of extensive surgery.^{11,14}

Common sites of synchronous colorectal cancer defers from the authors, some they noted in different segments of the large intestine, some in the same segment of the large intestine or close to each other. This stresses the importance of thorough preoperative examination of synchronous colorectal cancer. More SCRCs are noted in the proximal portion of the colon.⁴

The accurate preoperative diagnosis of SCRC remains difficult and diagnostic failures may lead to inappropriate treatment and poorer prognosis.⁵

They are a lot of preoperative study methods, such as a double contrast barium enema, Colonoscopy, Virtual colonoscopy, etc. In a double contrast barium enema they found preoperatively in 1.6%-3% SCRCs.^{12,13}

Preoperative diagnosis with barium enema may failed at the presence of annular carcinoma or inadequate bowel preparation and retained feces failure to inadequate bowel preparation and retained feces, or failure to perform completion colonoscopy at annular carcinoma, may be crucial intraoperatively to palpate the entire colon carefully before the end of the operation for CRC so that a misdiagnosis of SCRCs can be avoided.⁴ At our case barium enema fail to discover the second colon tumor because of annular carcinoma, and inadequate bowel preparation in upper colon.

Adloff et al. reported preoperative difficulties in diagnosis, being achieved in no more than 30 percent of patients. Because of the poor accuracy of barium studies, total colonoscopy is the method of choice for this evaluation. They adopted a conservative surgical policy backed by life-long follow-up.¹⁷

Spizzirri et al. emphasizes a complete pre-operative study with colonoscopy or virtual colonoscopy is always necessary to perform a diagnostic evaluation of entire colon and rectum, allowing to detect the presence of synchronous lesions. Colonoscopy is the most appropriate mean of investigation for colorectal cancer, but it cannot be performed in case of obstructive neoplastic lesions or in case of megacolon. In both cases either a double contrast barium enema, a virtual colonoscopy or an intraoperative colonoscopy can be performed. The recent employment of virtual colonoscopy has allowed an accurate study of the colonic segments upstream the stenosis.¹⁴ The findings from Heald and colleagues that since intraoperative palpation can be one of the methods which might help finding palpable intraluminal colonic tumors, 31% of them had been accidentally discovered during intraoperative bowel manipulation.¹² Intraoperative palpation can miss up to 69% of the Synchronous Neoplasia.¹⁴

Wang et al. emphasis importance to palpate the whole colon and to check pathological specimens carefully before the end of operation so that misdiagnosis of SCRC can be avoided. Even now, miss-diagnosis is still existed. The report showed that there were still 13 patients without detection of SCRC by operative palpation in the 31 preoperative undiagnosed cases.¹⁶

He et al. reported that surgery was challenging for synchronous CRC because the tumors were distantly localized.⁷

The presence of SCRC or multiple neoplasms requires operative techniques tailored to individual patients, based on the number, location, and stage of the tumors. Patients with SCRC and established predisposing conditions such as HNPCC, FAP, and ulcerative colitis require extensive surgery, usually total colectomy or proctocolectomy. In the other cases the optimal surgical strategy is still debated. Conventional hemicolectomies or extended hemicolectomies can be indicated if multiple tumours are located in adjacent segments.¹¹

Although colonoscopy can detect and effectively remove the promalignant and malignant lesions, it is not used commonly in patients with CRC or synchronous CRC.⁷ For other cases, appropriate surgical resection with colonoscopic examination of follow-up is recommended. If one of the synchronous cancers is early-stage colorectal cancer, colonoscopic resection (endoscopic mucosal resection or endoscopic submucosal resection) may be used for detecting and effectively remove the promalignant and malignant lesions.

Otherwise, dual colon resection may be needed if the synchronous cancers are in a large distance apart and at an advanced stage.⁷

He et al. in his study reported that patients with synchronous CRC underwent an extensive resection in some cases. In 60 (47.6%) patients, the tumors were localized in different sites, and 103 (81.7%) patients with synchronous CRC accepted open surgery and hospital stay after the surgery duration was longer than that for solitary CRC, which indicated that extended surgical resection is often required in synchronous CRC.⁷

The short-term outcome did not differ significantly between the two groups. The 30-day postoperative mortality was 0.8% in both groups, and no difference was noted in the hospital stay. Five (3.9%) patients with synchronous CRC and three (2.4%) patients with solitary CRC developed anastomotic leakage. Prolonged surgery was correlated with high intra- and postoperative complications and for developing anastomotic leakage. However, the long-term outcomes showed a significant difference between the two groups.⁷

However, overall perioperative results of colorectal resections for SCRC seem to be worse than those of solitary CRC with more postoperative complications and reinterventions and longer hospital stays.¹⁵

When SCRC are located in distant colonic segments, some authors suggest total or subtotal colectomy, while others suggest more conservative surgical strategies with resection of two intestinal segments, either open or laparoscopic-assisted, seemingly resulting in a higher risk of anastomotic dehiscence.^{15,16,17}

3. Conclusions

Careful palpation of the entire colon before the end of the operation for CRC may reduce the risk of maltreatment of Synchronous colorectal cancers. Intraoperative colonoscopy when they are a possibility, and have doubt must be done. This surgical policy should have backed by life-long follow-up.

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