Anastomotic Recurrence of Colon Cancer—is it a Local Recurrence, a Second Primary, or a Metastatic Disease (Local Manifestation of Systemic Disease)?

Sathiyavelavan Gopalan · Jagadesh Chandra Bose ·
S. Periasamy

Received: 19 December 2013 / Accepted: 3 April 2014 / Published online: 27 April 2014
© Association of Surgeons of India 2014

Abstract The aim of this study is to review the literature to find out the exact etiology of anastomotic cancers of colon post resection and differentiate them between a recurrence, second primary, and metastatic disease (local manifestation of systemic disease). Web-based literature search was done, and datas collected. We searched PubMed for papers using the keywords colon cancer recurrence, anastomotic recurrence, and recurrent colon carcinoma. We also searched for systematic review in the same topic. In addition, we used our personal reference archive. Anastomotic recurrences of colon are postulated to arise due to inadequate margins, tumor implantation by exfoliated cells, altered biological properties of bowel anastomosis, and missed synchronous lesions. Some tumors are unique with repeated recurrence after repeated resection. Duration after primary surgery plays a major role in differentiating recurrent and second primary lesions. Repeated recurrences after repeated resections have to be considered a manifestation of systemic disease or metastatic disease due to the virulence of the disease. A detailed analysis and study of patients with colonic anastomotic lesion are required to differentiate it between a recurrent, a second primary lesion, and a metastatic disease (local manifestation of a systemic disease). The nomenclature is significant to study the survival of these patients, as a second primary lesion will have different survival compared to that of recurrent lesions.

Keywords Anastomotic cancer · Anastomotic recurrence · Colon cancer · Recurrent colon cancer

S. Gopalan (✉) · J. C. Bose · S. Periasamy
Department of Surgical Oncology, Rajiv Gandhi Government
General Hospital, Chennai, Tamilnadu, India
e-mail: drgsathi@gmail.com

Introduction

The primary goal in management of colon cancer is to minimize the risk of development of local recurrence and metastatic disease. Radical surgery and adjuvant therapy in the post-operative period for selective patients help in achieving the goal. The reported incidences of single-site locoregional recurrence in colon cancer were between 5 and 19 % [1]. Most of the colon cancers fail locally next only to distal sites in the liver or lungs. Locoregional recurrence occur in the anastomotic site, remnant colon, peritoneal surface (nodal or soft tissue), or retroperitoneum. A number of factors were hypothesized as the cause of recurrence like the positive margin especially circumferential (inadequate excision), inadequate nodal dissection, implantation of exfoliated malignant cells, and altered biological properties at large bowel anastomosis. What defines a local recurrence is still an unanswerable question, because most of the local recurrences that occur after 2 years should be considered as metastatic recurrences (peritoneum or soft tissue) or as second primary lesion. Local recurrence occurring before 2 years is due to inadequate surgery or due to virulent biology of the disease.

Even a missed synchronous lesion can present as recurrent tumors at a later stage. We conducted a literature search to arrive at a conclusion for this dilemma.

Methods

Web-based literature search was done, and datas collected. We searched PubMed for papers using the keywords colon cancer recurrence, anastomotic recurrence, and recurrent colon carcinoma. We also searched for systematic review in the same topic. In addition, we used our personal reference archive.

Result

Web-based search did not provide any systematic reviews on this topic. Most of the reports were anecdotal. A few experimental studies have explored the etiology of anastomotic recurrence. Studies by Keighley et al and his postulation on recurrent colonic cancers was not challenged till date. Two cases of repeated recurrence after resection for anastomotic cancers were reported which was also observed in our archive.

Discussion

Colon cancer is three times more common than rectal cancer [2]. The colorectal cancer incidence in India is stable and low compared with the rising rates in East Asia as per the data collected from Indian cancer registry [3]. In the western world, colorectal cancer is the third most common cancer in men after lung and prostate and the second most common cancer in women after breast cancer. Local recurrences occur in colon cancer either in the remnant colon or the previous anastomotic site.

Theories on Recurrent Colon Carcinoma

Several theories have been postulated for the local recurrence of colon cancer. The major proposed are implantation of exfoliated tumor cells, positive distal or circumferential margin, altered biological properties of colonic anastomosis, postoperative intra-abdominal infection, and lymphatic dissemination.

Implantation of Exfoliated Tumor Cells

Cole and Goligher were the initial investigators who postulated that the implantation of exfoliated tumor cells upon the suture line at the time of operation as the causative factor for recurrence. This view was supported by John Beal and George Cornell in their paper in 1956 [4]. Interestingly, Rosenberg studied the patients from Golligher unit (16 patients had suture line recurrence) with suture line recurrence and found that remnant tumor is to be the reason for recurrence in all (14 patients) cases except two; one had a second primary and other genuinely occurred in suture line after curative resection the cause for which could not be explained [5]. Further, Rosenberg proved the exfoliated cells cause cancer in suture line only if they are viable with cancer cells which

happens when the tumor is cut or perforated during surgery [5].

Positive Distal/Circumferential Margin

Later, it was Keighley who on his work on anastomotic recurrence of colon has stated positive distal margin, implantation of exfoliated tumor cells, and altered biological properties of colonic anastomosis as the three major causes of local recurrence in the colon [6]. But, Kighley et al study quotes the anastomotic recurrences as a rare event which is contrary to a present study from St. James University who have observed recurrences at colon anastomosis to be around 21 % [7]. There are even anecdotal case reports of repeated anastomotic recurrences in the same patient [8, 9].

Postoperative Infection

Experimental studies have been conducted in mice to know the reasons for recurrences. One such study from Spain has shown that the postoperative intra-abdominal infection increases angiogenesis and tumor recurrence after surgical excision of tumor in mice [10]. Apart from this, anastomotic break down in the postoperative period either clinically or radiologically is considered to be a risk factor for recurrence. A case control study from Cleveland clinic has shown that colon cancer was not associated with recurrence due to anastomotic break down, but rectal cancers do [11].

Lymphatic Dissemination

Lymphatic emboli can cause satellite lesion which result in recurrence. This was proposed in the work by Gricouroff lymphatic way hypothesis [12, 13].

Is it a Local Recurrence?

A tumor recurring within 2-year lag period from previous surgery is considered to be a locally recurrent tumor. The high risk individuals are those with a positive margin, perforated tumors, and lymph nodal relapse in node positive (inadequate lymphadenectomy) tumors. Although most of the studies talk about colorectal recurrences, not a single study was exclusively directed towards colon cancer. This has to be further more studied as they behave differently compared to rectal cancers in their recurrence pattern and some even had repeated recurrences. In our series, a patient, who underwent left hemicolectomy (clear margin

Fig. 1 Selected axial section of CT abdomen in venous phase with oral contrast showing moderately enhancing irregular circumferential growth involving previous anastomotic site (ileo colic) (*bold arrow*)

and node negative) for a descending colon tumor 1 year before, with a recurrent colonic anastomotic lesion was operated. Such patients with tumors recurring within 24 months of resection of primary tumors are considered as recurrent tumors.

Is it a Metastatic Disease (Local Manifestation of Systemic Disease)?

Can these anastomotic recurrences be considered a local manifestation of a metastatic disease? This question arises due to the fact that some tumors are more virulent with repeated recurrence and recurring within a short span of time (less than 6 months). They also show no response to adjuvant treatment. These factors are observed in patients who are ruled out of having a synchronous tumor by colonoscopy pre-operatively. We experienced a case in our series where patient had a colon cancer, resected, recurred at the anastomotic site within

6 months, re-operated, and recurred again at the anastomotic site for the second time. In literature search, there are anecdotal case reports of similar nature [8, 9]. The repeated recurrences may be a part of systemic manifestation of the disease similar to a metastatic lesion that needs further detailed study.

Is it a Second Primary?

Patients who had a primary colorectal cancer are diagnosed with second primary cancer in 15 % of cases [14]. What defines a second primary is the topic of debate. A cutoff period of 24 months is considered as lesions occurring after 24 months are considered as second primary tumors. Ideally, a median time to presentation of second malignancy is between 32 and 38 months which is observed in several studies [15, 16]. A large-population-based study from California Cancer Registry (CCR) has shown the median time from the diagnosis of

Fig. 2 Intra-operative picture showing the tumor at anastomotic site (*bold arrow*)

Fig. 3 Specimen cut open confirms tumor at previous anastomosis (*bold arrow*)

primary colon cancer to the development of a second primary colon cancer was 32 months with almost 50 % of tumors occurring after 2.5 years [15]. These factors were observed in our series with most of the patients having a tumor presentation after 3 years. They occur either due to field cancerisation or altered biological properties at the anastomotic site. In our series, we operated on a 35-year-old patient who had a previous right radical hemicolectomy in 2004, now presented with a lesion at the anastomotic site in 2013 without distant metastasis [Figs. 1, 2, and 3]. This has to be clearly classified under second primary than an anastomotic recurrence as the time interval between the first and second tumor is 9 years with no systemic metastasis. He underwent a radical resection of remnant colon with an ileal pouch rectal anastomosis. Another interesting observation in these second primary tumors is the increased risk of second cancer occurring more pronounced in patients with a previous colon cancer located in the transverse to descending colon [14]. It is difficult to ascertain the cause of development of a second primary at the previous anastomotic site. The one possible explanation is the altered biological properties at the anastomotic site as described by Keighley et al. It is fine with the proximal resections where the anastomosis is between the small bowel and large bowel, but does it hold good for a distal resections with a colocolic anastomosis is debatable.

If altered biological properties of anastomosis are considered as a cause, then it confirms the formation of a new process of tumor development rather than occurring due to recurrence from previous tumor remnant. The other fact to consider is the time period taken by the tumor to reappear. In our observation, most of them occurred after a minimum period of 3 years, which arise the question of considering them as recurrent lesion because they fall into the category of a second primary lesion unless the previous surgical specimen had positive margins, which is very unlikely in colon cancer resections. This is due to the fact that the radical margins given during colonic resections are wide. We never had a perforated tumor in our series which rules out the implantation of tumor cells causing recurrence.

In spite of these confusions in the nomenclature for the anastomotic lesions of colon, the primary treatment of choice is surgery followed by adjuvant chemotherapy, as patients with only a locoregional disease without distant metastasis do well with repeated resections [17]. Except for the patient with repeated recurrence, all other patients are doing well and are under follow-up.

Conclusion

A detailed analysis and study of patients with colonic anastomotic lesion is required to differentiate it between a locally

recurrent, a second primary lesion, or a metastatic (local manifestation of a systemic) disease. The lag period of onset of local recurrence is the most important factor to determine if it is a locally recurrent, a second primary, or a metastatic (local manifestation of systemic) disease. Any anastomotic tumor recurring within 2 years of primary surgery is considered as locally recurrent tumor, after 2–3 years is a second primary, and that recurring within 1 year is a local manifestation of systemic disease. The nomenclature is significant to study the survival of these patients, as a second primary lesion will have different survival compared to that of recurrent lesions.

Acknowledgments None

References

1. Galandiuck S, Wieand HS, Moertel CG et al (1992) Pattern of recurrence after curative resection of carcinoma of the colon and rectum. *Surg Gynecol Obstet* 174:27–32
2. Weiser MR, Posner MC, Saltz LB (2007) Adenocarcinoma of the colon and rectum. In: Yeo CJ, Dempsey DT, Klein AS (eds) *Shackelford's surgery of the alimentary tract sixth edition*, vol 2, Ch 156, p 2183
3. Pathy S, Lambert R, Sauvaget C, Sankaranarayanan R (2012) The incidence and survival rates of colorectal cancer in India remain low compared with rising rates in East Asia. *Dis Colon Rectum* 55(8): 900–906
4. Beal JM, Cornell GN (1956) A study of the problem of recurrence of carcinoma at the anastomotic site following resection of the colon for carcinoma. *Ann Surg* 143(1):1–7
5. Rosenberg IL (1979) Lecturer in surgery, St James's University Hospital, Leeds. The aetiology of colonic suture-line recurrence. *Ann R Coll Surg Engl* 61:251–257
6. Keighley MR, Hall C (1987) Anastomotic recurrence of colorectal cancer—a biological phenomenon or an avoidable calamity? *Gut* 28 (7):786–791
7. Harji DP, Sagar PM, Evans M et al (2013) Surgical resection of recurrent colonic cancer. The John Goligher Department of Colorectal Surgery, St James's University Hospital, Leeds, LS7 9TF, UK. *Br J Surg* 100(7):950–958
8. Roncoroni L, Costi R, Bordi C et al (2004) Second anastomotic recurrence after radical left hemicolectomy: report of a case. *Dis Colon Rectum* 47(9):1547–1549
9. Funahashi K, Saito N, Shiokawa H et al (2007) A rare case of repeated anastomotic recurrence due to tumor implantation after curative surgery for sigmoid colon cancer. *World J Surg Oncol* 5:91
10. Bohle B, Alonso S, Salvado M et al (2010) Postoperative intra-abdominal infection increases angiogenesis and tumor recurrence after surgical excision of colon cancer in mice. *Surgery* 147(1): 120–126
11. Eberhardt JM, Kiran RP, Lavery IC (2009) The impact of anastomotic leak and intra-abdominal abscess on cancer-related outcomes after resection for colorectal cancer: a case control study. *Dis Colon Rectum* 52(3):380–386
12. Gricouff G (1966) *Bull Cancer* 53:409

13. Gricoureff G (1967) *Cancer* 20(5):673–676
14. Phipps AI, Chan AT, Ogino S (2013) Anatomic subsite of primary colorectal cancer and subsequent risk and distribution of second cancers. *Cancer* 119(17):3140–3147
15. Raj KP, Taylor TH, Wray C et al (2011) Risk of second primary colorectal cancer among colorectal cancer cases: a population based analysis. *J Carcinog* 10:6
16. Artac M, Demiral AN, Sarper A et al (2005) Different clinical features of primary and secondary tumors in patients with multiple malignancies. *Tumori* 91(4):317–320
17. Bowne WB, Lee B, Wong WD et al (2005) Operative salvage for loco regional recurrent colon cancer after curative resection: an analysis of 100 cases. *Dis Colon Rectum* 48(5):897–909