IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 9 Ser.5 (September. 2020), PP 23-25
www.iosrjournals.org

Colorectal cancer in young Adults: Experience from a tertiary cancer center in India.

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Abstract: *The Young colorectal cancer patients account for 5-15% of total colorectal cancer patients. The disease in these patients is aggressive with poor clinical response and outcome.There is a recent trend in increased incidence of rectal cancers in young adults.This is a retrospective analysis of colorectal cancer in young adults (age below 40 years of age) in a single instituition comprising of seventeen patients over a period of two years. Results showed that most of these cases were detected in late stages and are associated with an aggressive course, poor response and unfavorable outcomes .*

Keywords: *Rectum in young, rectal cancer, cancer outcomes.*

Date of Submission: 04-09-2020 Date of Acceptance: 19-09-2020

I. Introduction

Colorectal cancer is rare in young patient group with an incidence of 1.3 – 2 cases per million population.[1]Young colorectal cancer patients account for 5-15% of total colorectal cancer patients. The disease in these patients is aggressive with poor clinical response and outcome. The reasons for poor prognosis being advanced stage of presentation, mucinous histology and inoperability of most of the cases. There is a recent trend in increased incidence of rectal cancers in young adults. This is a retrospective analysis of colorectal cancer in young adults (age below 40 years of age) in a single instituition.

II. Materials and methods

We conducted a retrospective analysis of young adults (age ≤ 40 years) with rectal cancers treated at our institute from January 2017 to January 2019. Information regarding stage, histology, treatment and outcomes were collected from patient records. Patients/family members were contacted for information regarding demographic, socioeconomic, dietary habits and occupational parameters. All patients had a baseline Computed tomography scan of abdomen, Chest Radiograph, colonoscopy and biopsy as apart of staging workup. After appropriate staging and assesment of operability of non metastatic cancer patients, patients undergo neoadjuvant chemoradiotherapy to total dose of 50 Gy in 5 weeks 2Gy per fraction. Surgery is done after an interval of 4-6 weeks after radiation therapy. Based on post operative histopathology report adjuvan chemotherapy is planned in some cases. Disease free and overall survival was analyzed by Kaplan Meier estimates using the SPSS version 22.

III. Results

In this retrospective study, over a period of 2 years, we reviewed 17 cases of colorectal cancers in individuals aged less than 40 years. In this same period, the total number of colorectal carcinomas registered at our centre was 53. The mean age of presentation in our study was 34 years. The median age at presentation was 31 years. About 75% of our patients presented in the age group of 31–39 years, while another 25% cases were in the adolescent age group (less than 30 years) . Fourteen cases (82%) presented with duration of disease less than or equal to one year, while only 3 cases (18%) presented with symptoms of more than one year duration. The average duration of presenting complaints was 7 months. The male to female distribution showed a male preponderence, 12 male patients and 5 female patients.

More than four fifth of the cases presented with locally advanced disease,(stage III – 82%, stage IV – 18%). There were no stage I and stage II cases in our study population. Nodal involvement was seen in 14 (82%) cases and metastatic disease in another 3 (18%) cases. There was no associated family history, dietary history or past history of inflammatory bowel disease in any case. The rectum was the most commonly involved site, seen in 82% cases, followed by the sigmoid colon in 18% cases. Anal canal was also involved in 18% cases. The sites of metastases were peritoneum, liver and lungs. A majority of the patients presented with altered bowel habits, pain and bleeding per rectum The most common derangement in bowel habit was an increased frequency of passing stools.

The most common type of histopathological subtype was was the mucin secreting adenocarcinoma, accounting for 58% of cases. Alongwith signet cell carcinoma; both together accounted for fourteen (82%) of the total number of cases. Poorly differentiated carcinomas totaled 3cases. Perirectal spread and serosal involvement was seen in 82% of cases indicating advanced disease presentation in a majority of cases. Sixteen cases underwent surgery, of which radical surgery was performed in 12 cases and palliative colostomies in 4 cases. In all cases of palliative surgery, the outcome was very poor with none of the patients responding or completing treatment. Radical surgery performed included radical colectomies (sigmoid, hemicolectomy) in 2 cases; abdominoperineal resection (APR) in 9 cases and low anterior resection (LAR) in 1 case. Radiotherapy was used in 15 patients inout of which the intent in 3 cases was palliative, in the rest radiotherapy was used either pre-operatively (10 cases), post-operatively (2 cases) . Dose given preoperatively was 50 Gy in 25 fractions followed by surgery after 4 to 6 weeks. Post operative radiation dose was 45 Gy in 5 weeks followed by maintenance chemotherapy. Concurrent chemotherapy given involved oral capecitabine chemotherapy. Adjuvant chemotherapy was used in twelve cases and palliative chemotherapy in five cases. Chemotherapy regimen given was either FOLFOX regimen or Capecitabine plus Oxaliplatin regimen.

Response evaluation of the patients was done at completion of treatment, and further evaluation was undertaken at one year after completion of their treatment. WHO criteria were used for evaluation of response. Of the cases undergoing preop radiation followed by radical surgery and adjuvant chemotherapy, six cases had complete remission after 1 year of completion of treatment and six cases showed progression of disease.One out of the three patients with metastatic disease at presentation succumbed to disease after 6 months and two were lost to follow up.

IV. Discussion

Colorectal cancer in the younger age group is a rare subtype, accounting for 5-15% of total colorectal cancer cases.[3] Incidence is 1.3 – 2 cases per million mostly occurring in the 2nd decade of life. [2]Patients younger than 36 years of age make only 1-2% of the total number of cases of colorectal carcinoma in most western populations.[4] However according to the Hong Kong Cancer Registry (Annual report 1995); patients younger than 36 years of age account for 3-5% cases in the east Asian population. Very few large scale studies have been undertaken in Indian patients and no studies have been performed to evaluate the genetic profile or study mutations in such patients.

Colorectal cancer in young patients has often been associated with underlying predisposing conditions like inflammatory bowel disease or hereditary polyposis syndromes.[5] These patients may also be at an increased risk of developing a second GI or extra-intestinal malignancies.[6] Gafanovich et al studied paediatric colorectal cancer patients who developed second malignancies, and reported a high frequency of micro-satellite instability and germline mismatch mutations in these tumours.[7] Another study from Hong Kong by Chan et al[8] showed that 84% of patients below 31 years of age carried a germline mutation in one of the mismatch repair genes. Bhatia et al[9] studied subjects with colorectal cancer diagnosed below 21 years of age. This study showed a six fold increase in the number of cases among relatives of patients diagnosed with colorectal cancer before 15 years of age.

This type of cancer is thought to be clinically aggressive. The prognosis of younger age patients presenting with colorectal cancer is generally poor and can be accounted for by a predominance of mucinous histopathology, lack of a high index of suspicion in cases presenting with rectal bleeding, constipation, vague pain abdomen or vomiting.[2,3,10] Lin et al[11] reported a higher incidence of Duke's D (66%) lesions in the patients with subsequent very poor five year survival rates (0%) even after aggressive treatment. Most cases are treated for amoebiasis, granulomatous infections, and worminfestations, resulting in delayed diagnosis and treatment with most cases presenting at an advanced stage. A high level of suspicion followed by a digital rectal examination and a sigmoidoscopy and / or colonoscopy, if required, can help in diagnosing cases at an early stage.

The most common histologic types associated with childhood and younger age group colorectal cancers are the poorly differentiated varieties like the mucinous type or signet ring cell type seen in a majority of cases,[3,10,13] compared to around 5% of similar cases in older age groups.[13] The signet ring tumor has a higher propensity for early bowel wall invasion and involvement of peritoneal surface, with a much lesser propensity for metastases to the liver, behaving like ovarian tumors.[14]In our study also the most common histologic type was the mucinous type (58% patients); while the combined mucinous and signet ring types accounted for almost 82% of cases.It has been noted that up to 80% of patients present with nodal or distant metastases, with the majority of tumors being inoperable.[15] The common sites of metastases include the omentum, peritoneum, liver, ovaries, lungs, brain and skeletal system.[10,14].

The Indian scenario shows very sparse literature on this subject. Two studies, one by Rao et al[2] and another by Bhatia et al[16] show a predominance of mucinous type histopathology. This correlates well with the western literature. The mucinous type of tumor is deemed an aggressive type and is associated with a poorer

prognosis. Bhatia et al[16] reviewed 7 cases over a 15 year period in western India. This study showed a predominance of left sided lesions in contrast to western literature which presents an even distribution. Six out of seven patients presented with locally advanced disease and could undergo only suboptimal resection. The median survival ranged from 2 – 13 weeks.

Unlike in the older age group, where the most common site of involvement is the lower rectum and also sigmoid colon; colorectal cancer in the younger age group according to western literature is evenly distributed in all parts of the large bowel. In a large series of 1025 patients, Dozois and Boardman17 reported that the left colon was the most common site of involvement as noted in 51% cases followed by rectum (49%); with 66% cases presenting in stages III and IV. In the series of 20 patients by Karnak et al[14] the authors reported that the rectosigmoid area was the most common site involved and mucinous type was most common histopathology. In our series also, the rectum was the most commonly involved site (82% patients) followed by the sigmoid colon (19% patients); correlating with the study by Bhatia et al[16] which showed predominant left sided disease.

This is in contrast to published western literature. The treatment of choice is curative surgical resection with wide margins with treatment guidelines remaining the same as for older age groups.[18] But this is rarely feasible because of the advanced stage at presentation and poor general condition. Pre-operative radiotherapy, chemo-radiation or the use of chemotherapy (Leucovorin / 5-FU) may be considered to increase resectability rates. Pratt et al in a phase II study showed favorable response in young patients with colorectal cancer.[19]Guidelines for radiation and chemotherapy are same as in the older age group. However, usually the poor presenting general condition of patients precludes the use of radical treatment modalities; thus translating into very poor median and overall survival rates, especially in the Indian scenario.

V. Conclusion

2-10% of colorectal cancers are reported to occur in young adults with many showing a familial association. In our series we had a higher proportion of young adults with sporadic cancers. Various occupational and environmental factors may be associated with these cancers. They are often detected in late stages and are associated with an aggressive course and unfavorable outcomes; hence early detection is of vital importance. Towards this end, identification of risk factors and screening programs need to be carried out.

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