

Clinical Presentation and Management of Rectal Cancer in Pregnancy: A Multimodality Approach

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Abstract

Introduction

Colorectal cancer in pregnancy is associated with diagnostic and therapeutic challenges which mostly lead to late diagnosis in advanced stages and poor prognosis.

Objectives

To study the various presentations and the clinical outcome of pregnant women with rectal cancer and to sensitize the concerned doctors about this rare possibility in pregnancy.

Methodology

A retrospective analysis of 4 cases of rectal cancer in pregnancy during a 7 year period (March 2006 – March 2013) was done. These cases were managed with a multidisciplinary approach at S. S. Institute of Medical Sciences and Research Centre, Davangere.

Result

Mean age at presentation was 29 years, bleeding per rectum was their common symptom, two of them being below 20 weeks of gestation. Flexible sigmoidoscopy showed the lesion details and aided biopsy for confirmation. Abdominopelvic ultrasonography helped to detect peritoneal metastasis, serum CEA levels were in the range of 40-60 ng/dl. Two of them were in stage III, one in stage II and another in stage IV. Only one patient had an emergency caesarean at 32 weeks, while the remaining had medical termination of pregnancy.

Surgery in the form of anterior resection with end to end anastomosis followed by chemotherapy was the standard mode of management in three patients while, one patient needed additional radiotherapy for distant metastasis. One patient with stage IV disease had a Transverse loop diversion colostomy with palliative chemotherapy and palliative pain relief. One patient died within 6 months of diagnosis due to advanced disease, others still on follow up.

Conclusion

Colorectal cancer in pregnancy is rare, often presents in an advanced stage, a multidisciplinary approach with recommended guidelines will optimize the outcome in pregnancy. More randomized trials are required to standardize management protocols.

Keywords: Colorectal carcinoma in pregnancy; CEA in pregnancy.

Introduction

In women of childbearing age, cancer represents one of the major causes of death. The incidence rate of cancer in pregnancy reported in the literature ranges from 0.07-0.1%. [1]

The most common malignancies in

pregnancy include lymphoma, leukemia, melanoma, breast cancer, cervical, ovarian, thyroid and colorectal cancers.[2]

Rectum is the last six inches of the large intestine. The incidence rate of colorectal cancer in pregnancy is 0.002%.[3] A mean age of 31 years was reported in the literature.[4] Most patients present in late pregnancy, usually localized to the rectum (upto 85% of cases). 55% of large bowel cancers occur in the rectum, 80% of them are sporadic and 20% have genetic predisposition.[5]

Predisposing factors for colon cancer include hereditary nonpolyposis colorectal cancer (Lynch Syndrome), familial adenomatous polyposis, Gardner's Syndrome, ulcerative colitis, chronic irritable bowel syndrome, Peutz Jegher's syndrome.[5]

Rectal cancer is most commonly as ulcerative type of adenocarcinoma, commonly spreads through pararectal nodes to the mesenteric nodes. Veins of the colonic wall are involved in blood spread to the liver (10-15%), lungs (5%), ovary (25%), kidneys, adrenals, brain, bone and exfoliation into the peritoneal cavity happens through the transperitoneal route.[6]

Many of the presenting symptoms of rectal cancer are frequently confused with the usual complications of pregnancy. Delay in diagnosis leads to cancer presenting in advanced stages and may contribute to the poor prognosis associated with this disease. Common presenting signs and symptoms of rectal cancer include abdominal pain, anemia, nausea, vomiting, constipation, rectal bleeding, poor weight gain and rarely abdominal mass.

The carcinogenesis of colorectal cancer in pregnancy is not fully understood. Studies have demonstrated the presence of estrogen receptor (ER) and progesterone receptor (PR) on the tumour cells. So increased levels of these hormones in pregnant women could stimulate the growth of colorectal cancers.[7] Role of P53 gene and cox-2 enzymes has also been studied. [7]

A detailed general physical and rectal examination by an oncosurgeon would be appropriate followed by routine investigations,

including complete blood count, liver and kidney function tests, blood sugars, universal screening, blood group, electrocardiography, echocardiography and x-ray chest. Apart from these the diagnostic evaluation of a patient with colorectal cancer involves these major components, endoscopy with biopsy, serum carcinogenic embryonic assay (CEA) and abdominopelvic imaging.

Colonoscopy is contraindicated in pregnancy due to its maternal and fetal risks, instead a flexible sigmoidoscopy can be performed.

Serum CEA levels are normal or marginally elevated in normal pregnancy. (normal levels being <3.4 ng/ml).[8] CEA levels cannot be used as a screening test for colorectal cancer because of its lower sensitivity and specificity indices. However CEA levels obtained prior to surgery provide a baseline to monitor the response to treatment. Very high levels prior to surgery are associated with disseminated disease and increased recurrence rates.

Abdominal computed tomography remains contraindicated in pregnancy due to its radiation teratogenicity, particularly in the first trimester. An abdominopelvic ultrasound is an alternative in evaluating the presence of hepatic, ovarian metastasis, ascites and local spread, with a sensitivity of 75%.[9]

Staging of cancer rectum in pregnancy follows the TNM staging as per the American College of Surgeons.[6]

Stage 0 belongs to T_{is}, N_0, M_0 ,

Stage I T_1, N_0, M_0 or T_2, N_0, M_0 or T_3, N_0, M_0 ,

Stage II T_3, N_0, M_0 or T_4, N_0, M_0 ,

Stage III Any T, N_1, M_0 or Any T, N_2, M_0 ,

Stage IV Any $T, Any N, M_1$.

Once the diagnosis is made during pregnancy, multidisciplinary involvement of obstetrician, neonatologist, oncosurgeon, radiation and medical oncologists is essential. The gestational age and tumour stage are two important factors which will influence the treatment modality. If the diagnosis occurs in the first half of pregnancy (< 20 weeks) termination of pregnancy is recommended and

if the diagnosis is made in the second half of pregnancy (> 20 weeks) surgical resection could be delayed until the fetus has attained lung maturity (probably 32 weeks). Management of colorectal cancer in pregnancy raises major ethical and medicolegal issues, involving the conflicting interests of the mother and fetus.

The mode of delivery is not affected by cancer, with the exception of caesarean section owing to distal tumour obstructing the birth canal or anterior rectal carcinoma. The adequacy of pelvis should be carefully examined as metastasis is common to the adjacent structures.[10]

The primary treatment for stage I,II and III is surgery, followed by chemotherapy and or radiotherapy. The goal of surgery being removal of the tumour with an adequate margin of at least 5 cm, as well as the draining lymph nodes which will stage the disease and reduce the risk of recurrence and spread.

Lesions on the upper and middle third of the rectum can be approached with a low anterior resection with restoration of intestinal continuity and preservation of a continent sphincter apparatus. A temporary colostomy is maintained for atleast six weeks period.[11]

Lesion in the distal third of the rectum or those within 5 cms of the anal verge, an abdominoperineal resection with permanent colostomy is the standard treatment for these patients.

In the treatment of cancer rectum,use of chemotherapy serves three purposes,as an adjuvant after surgery, to enhance the effect of radiation for locoregional malignant disease and to treat advanced metastatic disease. Usually started 2- 3 weeks following surgery,5 Flurouracil 450 mg/m² intravenous bolus day1-5,once in 3 weeks for 4-6 weeks along with Leucovorin 425mg/m².After each cycle complete blood count, liver function and renal function tests are repeated. Newer chemotherapeutic drugs like Gemcitabine and Oxaliplatin are also tried. Gastrointestinal disturbances, bone marrow suppression and alopecia are expected side effects of 5

Flurouracil.[12]

In locally advanced disease, radiotherapy in the form of teletherapy or brachytherapy, has been used as an adjuvant to treat positive lymph nodes and reduce local recurrences.

The prognosis of colorectal cancer is related to the degree of penetration of the tumour through the bowel wall and the presence or absence of nodal involvement. Bowel obstruction and bowel perforation are indicators of poor prognosis.[6] Pregnant women with colorectal cancer generally have a poor prognosis. Most women died within one year of diagnosis and the median survival is usually less than 5 months.[13] Overall 5 year survival rates are Stage I 80-95%,Stage II 65-75%,Stage III A,B 42-55%,Stage III C 0-7%.[14]

On follow up, related symptoms are noted with complete blood count, renal and liver function tests done once in 3 months for the first three years. CEA levels, abdominopelvic sonography, chest x ray done once in six months along with colonoscopy once in an year and if CEA is elevated or scan is suspicious then a Positron emission scan is advised.

Aim and Objective

To study the various presentations and the outcome of pregnant women with colorectal cancer and to sensitize the concerned doctors about this rare possibility in pregnancy.

Methodology

A retrospective analysis of 4 cases of rectal cancer in pregnancy during a 7 year period (March 2006 – March 2013) was done. All the 4 cases were managed with a multidisciplinary approach at S. S. Institute of Medical Sciences and Research Centre, Davangere. The team involved an Obstetrician, Neonatologist, Oncosurgeon, Medical Oncologist, Radiation Oncologist, palliative care physician and social workers.

Results

Taking the following parameters the results were tabulated as below.

Age incidence was in the 25-33 years age group, bleed per rectum being the commonest presentation and urinary retention was an uncommon presentation in the first case, significant risk factor was seen in the third case, probably hereditary origin.

Sigmoidoscopy was possible in three cases, serum CEA was elevated in all the cases. Ultrasound evaluation gave a good insight of the tumour spread. Liver, peritoneal cavity, ovary, uterus, pararectal nodes, paraaortic nodal spread were commonly seen though on patient had spread to the supraclavicular node too.

Three patients underwent termination of pregnancy as they did not wish to continue pregnancy with chemotherapy. Depending on the pararectal extension, adjuvant 5 Fluorouracil based chemotherapy was given in two patients and palliative chemotherapy in one patient.

Apart from the symptomatology and routine investigations like complete blood count, liver and renal function tests, blood sugar levels, urine routine and ECG, chest X-ray PA view, patients were followed up every six months with serum CEA levels and ultrasound abdomen and pelvis and colonoscopy once in a year. PET scan was done once a year or if any of the investigations were suspicious. Presently two patients are on follow up, the third case died within six months of diagnosis, interestingly the second case conceived during her follow up almost two years later and was advised termination of pregnancy at 7 weeks gestation as the recurrences are highest during the first five years following treatment, she refused to take our advice and so she was lost for follow up.

Limitations of the Study

The ER,PR status of the tumour could not be done at our institute and oocyte banking

was not possible for these patients prior to chemotherapy and we have managed these cases with the limited resources available at our institute.

Discussion

Available literature on rectal carcinoma in pregnancy is very scarce with small clinical series that are retrospective and uncontrolled. [15]

Prevailing life style changes, like faulty dietary habits may predispose women towards the rare possibility of large bowel disease, as symptoms are nonspecific, can be confused as those of normal pregnancy. However persistent anemia should be an alert sign in pregnancy.[4]

In pregnancy, sensitive counseling towards the risk benefit ratio is to be carefully planned, which demands deep ethical and religious considerations. Reported literature points out the late presentation of the disease during pregnancy with the age incidence of around 33 years[4] and the follow up reported is 41 months[4] and the prognosis and pregnancy outcome does not differ much as compared to non pregnant women.

Khodaverdi[16] in their study point out that colorectal cancer mostly involves the elderly women and so there could be additional risk factors which can make women susceptible during pregnancy.

Management involves a multidisciplinary team and the choice of treatment depends on the operability of the tumour and period of gestation.[17,18] Mode of delivery is not affected by cancer unless obstruction to the birth canal by the large anterior rectal wall tumours. One case in our study needed an emergency cesarean section at 32 weeks of gestation.

Chemotherapy is safer during the second and third trimester of pregnancy although there is an increase in the incidence of intrauterine growth retardation and prematurity.[17] Adjuvant chemotherapy is

suggested for stage III tumours and two patients in our study needed chemotherapy following surgery and one patient needed palliative chemotherapy as she was already in stage IV disease.

Adjuvant radiotherapy is another form of treatment used in the management of rectal cancer, in case of metastasis, radiotherapy should be definitely following pregnancy management.

Liver being the most common site for metastasis[19] which was noted in two patients included in the study and another patient in addition had metastasis to the uterus, ovary and the para arotic nodes too. Metastasis to the ovaries is seen in 25% of cases with rectal carcinoma as reported by Chang *et al.*[20]

The median survival in a series reported by Khodaveri,[16] was less than 5 months. In the present study we have two patients still on regular follow up for the past two years and one was lost for followup.

The present study is aimed at learning more about cancers in pregnancy with a goal of giving reliable information to obstetricians who manage patients with cancer.

Conclusion

Colorectal cancer in pregnancy is rare and carries a poor prognosis. Delay in diagnosis leads to cancer presenting in advanced stages, so a high degree of suspicion can seek an early referral to the general surgeon to rule out the rare possibility of rectal carcinoma. Hallmark symptoms include a change in bowel habits and blood in the stool. It would be reasonable that in cases with persisting bowel symptoms during pregnancy warrant an early referral to a general surgeon for an opinion.

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