



Research Article

RADIATION INDUCED PROCTOCOLITIS - RISK FACTORS AND CORRELATION OF SYMPTOMS WITH COLONOSCOPY

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ABSTRACT

The prevalence of radiation colitis was investigated in 73 patients with symptoms of bleeding per rectum, six weeks after radiotherapy for Ca Cx. Investigation of blood, urine, motion, ECG, CXR, USG abdomen and colonoscopic examination retrospectively (radiation therapy injury to rectum, sigmoid- colon) were carried out. It is found that the risk factors for radiation induced damage to colonic mucosa are: age, presence of comorbid illness, low BMI, anemia, long duration of symptoms and disease factors such as stage IIIb disease, total radiation dose and brachytherapy. Also the study revealed that the risk of malignancy after radiation therapy in the affected colonic mucosa is extremely rare.

Key words:

Carcinoma cervix, Radiation procto colitis, colonoscopy.

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INTRODUCTION

Radiation induced intestinal injury was first described by David Walsh in 1897, soon after discovery of X-ray in 1895. It has an Incidence of 0.5 – 17% Following radiation to cervix uteri or urinary bladder. Rectum is commonly involved due to fixed position and proximity to the source. Injury depends on Dose Delivered, Technique Used, Sensitivity of Segment, Vascular disorders, Nutrition Status, Previous Surgery. Studies have shown test 1/5 of women with Ca Cx, after radiotherapy develop proctosigmoiditis. 75% Develop proctitis Alone 1/3 Present with Stricture, 1/4 Present with Fistula Malignancy has also been reported.

Radiation Injury: This is due to Biological effect of ionising radiation. Malignant cells are more sensitive. The nuclei vacuolate and degenerate. Gonads are very sensitive. Cell in mitotic phase are vulnerable. Anaplastic cells are more sensitive. It has been noted that fibrosis, that develop later forms beneficial restraining effect for further spread. Following radiotherapy, fast electrons are produced by Compton effect of protons or gamma rays. This ionizes molecules along its path and induce free radicals which is a charged particle, carrying an unpaired electron in the outer shell of the atom. The free radicals impair DNA replication, transcription & translation. Within 12 hours of Radio Therapy, Columnar cells flatten. Within 7 days, villi shorten and become blunt. Mucosa usually became normal in 14 days. Microscopically rectal mucosa shows leucocytic infiltration,

eosinophils gather and crypt abscess forms. Later, ulcers, necrosis, perforation, strictures, fistula occur, due to endarteritis and fibrosis formation. Radiation injury behave like ischemic bowel injury. Swelling and vacuolation of vascular endothelia occurs, telangiectasia develop. Bowels regenerate imperfectly, become thick and leathery, intestinal loops become matted, mesentery becomes short and stiff, bowel lumen narrowed and tubular, without normal haustra. Differential diagnosis should be made from Crohn's, by vasculitis and abnormal fibro blasts.

Acute Radiation Injury: Usually appear in third week of fractionated course. It can occur in few hours also. 5HT₃ has a role. It can occur in 20 – 70 %. It is severe, when concurrent chemotherapy used. Usually resolves in 2 to 6 weeks after completion of treatment. Crypt abscess occur in colon. Increased intestinal motility occurs.

Mal absorption occurs if terminal ileum involved. Usually self-limiting, but prognosis is poor when associated with bloody diarrhea.

Sub Acute Radiation Injury: Manifest 1-3 weeks after acute radiation exposures. This is due to cytotoxic events. Irradiation arrests the production of new epithelial cells from crypts of Lieberkuhn. There is depletion of mature intestinal surface epithelial cells. There is a breakdown of barrier to luminal contents and toxic substance enters systemic circulation. There is decreased absorption of fluids, electrolytes, & nutrients. Tight junction interruption is seen. Bloat, ileus, cramps, tenesmus, diarrhea, bloody stools can

occur. Using Foleys catheter putting patients in trendelenburg position can reduce injury. **Chronic Radiation Injury:** Occur in 1-15% of individuals. Old age, post op patients, collagen disorder, poor technique, high dose are risk factors. Intestine become thick with telangiectasia. Stricture formation leads to bacterial over growth due to proximal dilatation can occur from 6 months to 24 years. Fibrotic loops can wall off abscess, masking peritonitis. Vascular sclerosis leads to neo vascularisation. Fibrotic areas of serosa and muscular propria was found to be progressive with diffuse collagen deposition. C.T. Enterocolitis is considered as investigation of choice of small intestine radiation injury. Carcinoma cervix is a common malignancy. Ecto cervix is five times commonly involved. It usually present as ulcerated or fungating squamous cell carcinoma. Both intra cavitory by after load technique and external beam Radiotherapy given. Inverted pear shaped radiation field is used. Point A is 2 cm lateral to midline and 2 cm above vaginal fornix. It can tolerate 7000-8000 cGy. Point B is 5.0 cm away in pelvic side wall. It can tolerate 5000 – 6000 cGy. In Manchester Method, intra uterine tube 50mg, colpostat 30-50 mg dose used for 24 hours, for two sittings. Cesium 137, which has $t_{1/2}$ 37 days, is used in our hospital. EBRT given by fractionised method, 25 sittings in 2 months

Aim of the study

1. Identification of risk factors in severe radiation induced proctocolitis in patients treated for advanced Ca cervix by radiotherapy
2. To correlate the identified risk factors with that of endoscopic severity.

3. To find out the occurrence of adenocarcinoma of rectum and distal large bowel in patients who has radiation proctocolitis.

MATERIAL AND METHODS

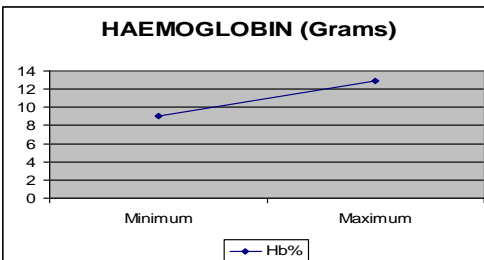
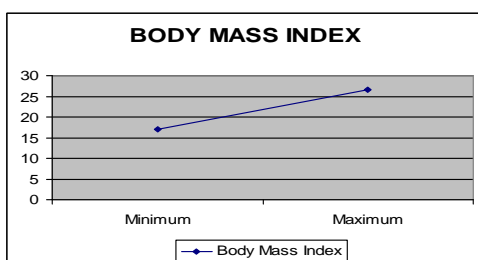
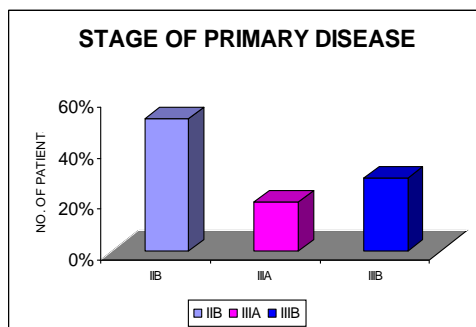
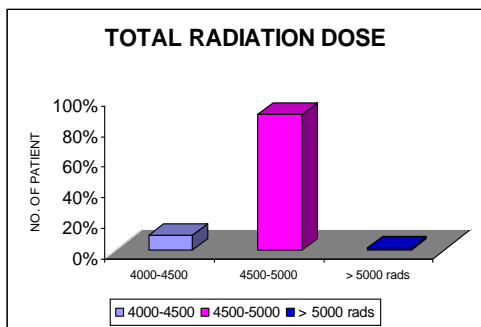
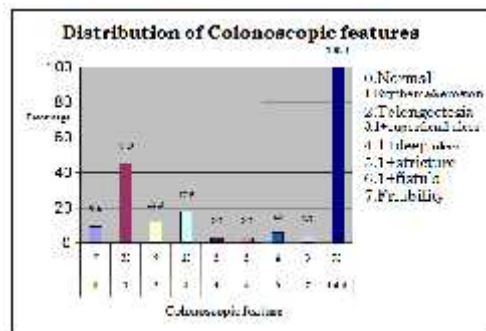
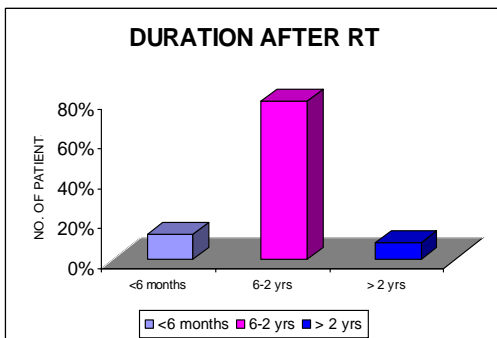
We retrospectively analysed 73 patients who presented with rectal bleeding along with other symptoms at least six weeks after radiotherapy for Ca Cervix.

Study type: Retrospective analytical study **Study period:** June 2003 to July 2005 (25 months)

Venue: Government General Hospital, Chennai

Protocol: Inclusion criteria: Patients with Ca cervix who had radiotherapy (external, Internal or both) presenting after 6 weeks with following symptoms: Rectal bleed, Mucous diarrhea, Tenesmus, Lower abdominal pain, Constipation.

Exclusion criteria: Patients presenting less than 6 weeks with above symptoms. Infectious diarrhea (as ruled out by stool examination and culture). Intrinsic diseases of ano-rectum and sigmoid colon including hemorrhoids, fissure in ano, solitary rectal ulcer, IBD and malignancy (by colonoscopy and HPE). All the patients were admitted. Complete history including co morbid illness and thorough physical examination were done in all patients Routine blood, urine, motion examination, ECG, CXR, USG abdomen were done. Once stabilized elective colonoscopy was done in all. Colonoscopy was done with Pentax fibro optic colonoscope.



RESULTS

Total number of patients 73 females. Age group of 31 to 40 yrs were 11 patients. 41 to 50 yrs were 27 patients, 51 to 60 yrs were 30 patients and more than 60 yrs were 5 patients.

Presentation after radiotherapy with bleed: Duration more than 6 months after radiotherapy were 19 patients, less than 2 yrs after radiotherapy were 50 patients and more than 2 yrs were 4 patients.

Extent of confluent lesion in colonoscopy: Extent less than 6 cm seen in 22 cases. Extent upto 12 cms seen in 24 cases. Extent more than 13 cms seen in 23 cases. Normal mucosal appearance seen in 4 cases.

Age distribution: 39.7% of cases belonged to age group of more than 50 years while 13% were between 31 – 40 years.

Symptoms; It is noted that the predominant symptom was bleeding per rectum (100%), tenesmus (1.4%) mucus diarrhea (2%), constipation (4.1%), pain abdomen (13.5%) were also seen in increasing frequency.

Comorbid illness: Various co morbid illness were noted in these patients who had radiotherapy. The break up was as follows. Diabetes was seen in 10 cases, atherosclerotic disease in 2 cases, obesity in 2 cases.

Radiation dose: Most patients who received radiation come in middle radiation dosage (4500 rads to 5000 rads) (89%). Only one patient exceeded dose of 5000 rads (1 case)

Most common lesion identified was erythema and erosion which comprised of 45.2% (41). Other findings included telengectasia 12.5% (13), superficial ulcers 17.8% (06), deep ulcers 2.7% (03), stricture in 4(5.5%) cases, fistula in 2 cases and Normal appearance in 4 cases

Biopsy and histopathology: Biopsy was done in all cases. The entire specimen had significant findings. The common findings in HPE are as follows. Mucosal ulceration- 45%, submucosal fibrosis -23%, Cellular infiltration 45% Obliteration of vessels in submucosa- 25%

Malignancy After careful histopathology examination of the samples no dysplasia or malignant changes were noted (0%).

DISCUSSION

We analysed 73 patients with radiation induced mucosal damage and tried to identify the risk factors in the causation. Age correlated significantly with the severity of symptoms. Patients in the third group more than 50 years have high incidence of severe symptoms. But it did not have significant implication on the extent of lesion or the colonoscopic severity. Duration of symptoms is also an important factor identified. Those patients who are symptomatic for more than 2 years have severe lesions on colonoscopy. This finding may be attributed to spontaneous healing within 6 months in milder forms of injury as described by various authors. Gehrig J *et al* has shown that mean duration of illness and age strongly predicted severe damage. Williams HRT *et al* has also shown similar results but presence and severity of rectal bleeding was the best predictor. Total radiation dose when exceeded 5000 rads caused severe disease. It has good correlation with the extent of lesion, severity of lesion by colonoscopy. Clark BG, Souhami L *et al* has shown that the total radiation dose and

the reference point from rectal reference point (arbitrary point which receives maximum radiation exposure) influences the patient outcomes. Similar study by Dinakaran *et al* also confided with the same findings.

Intracavity radiation (brachytherapy) correlates well with extent of lesion. More proximity to sigmoid and less protection to the mucosa may be implicated as the causative factor. Yalman D *et al* has described that intracavity radiation accounted for more extensive disease and more morbidity. Low BMI when combined with atherosclerotic disease causes severe and more extensive lesions. Diabetes and low Hb% in the setting of brachytherapy cause extensive damage and fistulization. This finding confides with various authors but Gehrig J, Hacki WH did not find any correlation with co-morbid illness like diabetes and hypertension. BMI was however influential in determining the extent of illness. Stage of the disease is also linked to severe disease probably because increased usage of brachytherapy was seen in this subset. Patients having III b disease when having diabetes and atherosclerotic disease with brachytherapy have long duration of symptoms, fistulizing disease, strictures, and more than 12 cm lesion. In our study of 73 patients biopsy was taken in 20 when the lesions have increased friability, nodularity and fistulization. None of the biopsy had any dysplasia or malignant cancer. Probably long term follow may be necessary for identification of dysplasia and malignancy. Risio M, Coverlizza S *et al* have postulated that Late cytokinetic abnormalities in irradiated mucosa is a strong predictor of future carcinogenesis though the exact incidence of malignancy occurring in irradiated mucosa appears to be extremely low. Definitive indication favoring surveillance programs post radiotherapy cannot be advised at this stage.

CONCLUSION

After the completion of the study the following facts were conceded.

1. The incidence and severity of radiation induced damage to colonic mucosa was influenced by patient factors: age, presence of co-morbidities, low BMI, anemia, long duration of symptoms, disease factors: stage III b disease, treatment factors: total radiation dose, brachytherapy.
2. The clinical assessment of patients with the above risk factors is strong predictor of severe lesions at colonoscopy
3. The risk of malignancy after radiation therapy in the affected colonic mucosa in extremely rare and routine surveillance for the detection of the same is not required.

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