A Prospective Study of Radiation Induced Damage of Pancreatic Ducts

V SANTHI SWAROOP, K M MOHANDAS, KETAYUN A DINSHAW, DEVENDRA C DESAI, VINAY DHIR, AABHA NAGRAL, P JAGANNATH, L J DESOUZA

Departments of Medical Gastroenterology, Radiation Therapy and Surgical Gastroenterology, Tata Memorial Hospital, Parsi, Bombay 400 012

Abstract
To study radiation-induced pancreatic duct damage, endoscopic retrograde pancreateograms of 11 patients with primary gastric lymphoma who had completed chemotherapy and moderate dose external radiotherapy were compared with those of 22 normal subjects. No significant alteration was seen in the length and caliber of the main pancreatic duct and number of side branches. Clubbing of one or two side branches was observed in four patients who had received radiation (p = ns). We conclude that significant structural changes do not develop in the pancreas following moderate dose upper abdominal radiation. (Indian J Gastroenterol 1992; 11: 124-126).

Introduction
Early and late effects of external beam radiotherapy (EBRT), on the gastrointestinal organs are well established.\(^1\) The first report of radiation effect on the human pancreas was published in 1924 by Case and Warthin.\(^2\) Very few reports have been published thereafter regarding the adverse effect of EBRT on the structure and function of the human pancreas. It has long been supposed that the pancreas is radiation resistant.\(^3\) This prospective study was undertaken to ascertain the structural changes in the pancreatic ductal system following EBRT.

Material and Methods
The study group included 11 patients with primary gastric lymphoma (PGL) who had previously received moderate dose EBRT to the stomach bed (including pancreas). Five patients had undergone distal gastrectomy. All the 11 patients had received 3 cycles of CHOP chemotherapy (cyclophosphamide 650 mg/M\(^2\), adriamycin 40 mg/M\(^2\), vincristine 1.4 mg/M\(^2\), prednisolone 40 mg/M\(^2\)) at 4 week intervals. This was followed by moderate dose EBRT (3500 to 5000 cGy) to the stomach and stomach bed. The radiation field was determined from the stomach as outlined on a barium study. After completion of EBRT, 3 more cycles of CHOP were given. Informed consent for the procedure was obtained from all these subjects.

The control group included 22 patients matched as closely as possible in respect to age and sex with normal endoscopic retrograde pancreateograms (ERP).

All the PGL patients were disease free and on regular follow up at the time of ERP. The records of the PGL group were reviewed for any abnormalities of the pancreas on pretreatment ultrasound and/or computed tomography scans. ERP was performed using an Olympus JF-IT10 duodeoscope. Pancreateograms were obtained in antero-posterior (prone) and oblique positions. The main pancreatic duct (MPD) was filled up to the tail and first and second order side branches were delineated but without acinar filling. At ERP, the pancreas from genu up to tail was seen to lie behind the stomach and therefore within the radiation field. Additional efforts to obtain a cholangiogram (prolonged cannulation attempts and precutting) in the PGL group were avoided to minimize complications.

All the ERP were studied independently by two observers who were not aware of source of ERP. The parameters studied were the length and width of the MPD, number of side branches and abnormalities of the MPD, accessory ducts and their side branches. Magnification correction was applied using the magnification of the endoscope diameter.

The findings at ERP in the two groups were compared using Student's t-test for unpaired data and \(\chi^2\) test with Yates' correction.

Results
The study group comprised 11 patients with PGL (7 men, 4 women; aged 30 to 65 yr, mean 43.2 yr) who were disease free at the time of ERP. The indications for ERP in the control group (14 men, 8 women; aged 24 to 60 yr, mean 45.5 yr) were undiagnosed abdominal pain in 18 patients and obstructive jaundice in four.

Computed tomography and ultrasound examinations had revealed normal pancreas prior to therapy in all the PGL patients. Nine patients had received 4500-4600 cGy
Table: Findings in pancreatic ductal system at ERP

<table>
<thead>
<tr>
<th></th>
<th>Primary gastric lymphoma</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 11)</td>
<td>(n = 22)</td>
<td></td>
</tr>
<tr>
<td>MPD length (cm)</td>
<td>17.6 ± 2.5 (14.4-23.9)</td>
<td>18.3 ± 2.6 (13.5-23.9)</td>
</tr>
<tr>
<td>MPD diameter (mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head</td>
<td>3.8 ± 0.7 (3.2-5.4)</td>
<td>3.3 ± 0.8 (2.5-5.2)</td>
</tr>
<tr>
<td>Body</td>
<td>3.2 ± 0.6 (2.5-4.5)</td>
<td>3.0 ± 0.6 (1.8-4.5)</td>
</tr>
<tr>
<td>Tail</td>
<td>1.6 ± 0.3 (1.0-2.3)</td>
<td>2.0 ± 0.5 (1.4-2.7)</td>
</tr>
<tr>
<td>Side branches (No)</td>
<td>36 ± 8 (24-49)</td>
<td>38 ± 9 (26-60)</td>
</tr>
<tr>
<td>Abnormality of MPD (No)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Side branch clubbed</td>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>

Measurement data are expressed as mean ± SD (range). None of the findings was significantly different in the two groups. MPD = Main pancreatic duct

of EBRT, one 3500 cGy and another 5000 cGy using anterior and posterior fields. Acute radiation sickness necessitating temporary discontinuation of EBRT had occurred in two patients. None of the patients had any episode of acute abdominal pain during or after chemotherapy or EBRT. All had gained weight after completion of therapy. None had symptoms of pancreatic deficiency or diabetes. Delayed onset EBRT toxicity included persistent radiation gastritis in seven patients, radiation enteritis in one and radiation nephritis in four patients. The mean interval between completion of EBRT and the ERP was 30.7 (range 8-50) months.

The length and width of the MPD and the number of first order side branches were not significantly different in the PGL and the control groups (Table). Clubbing of the side branches was observed in 4 (36.4%) patients in the PGL group (p > 0.05). Three patients had clubbing of two side branches each while one had clubbing of a single side branch. All the 4 patients demonstrating clubbing also had associated chronic radiation damage to the stomach, intestine and kidney. Biliary tract was normal in all the five PGL patients in whom it could be visualized.

Discussion

Reports on radiation injury to the human pancreas are scarce. The present study is the first prospective study evaluating the pancreatic ductular system following EBRT to the upper abdomen.

None of our patients had clinical acute pancreatitis during the radiotherapy. Hennenqut et al. did not observe amylase elevation following pancreatic EBRT. Normal pancreatic anatomy on imaging studies before therapy excluded lymphomatous involvement of the pancreas. The extensively studied and used CHOP chemotherapy has not been reported to cause chronic pancreatic damage.

No significant difference in the length and caliber of the MPD and number of side branches was observed in the PGL and control groups. Four patients in the PGL group had clubbing of one or two side branches, which was not significantly different from that in the controls.

Occasional dilation of side branches, as seen in our patients, may be a normal variant as reported previously in endoscopic pancreatectographic and autopsy studies.

Late damage to the pancreas following EBRT is similar to that in chronic pancreatitis barring active inflammation and necrosis. Although we did not carry out specific tests for pancreatic exocrine insufficiency, none of the PGL patients had any symptoms attributable to pancreatic dysfunction (weight loss, malabsorption or diabetes).

Use of intraoperative radiotherapy for carcinomas of the pancreas has led to the accumulation of additional information on radiation damage to the pancreatic ductular system. Animal experiments and autopsy studies following a combination of intra-operative and external beam radiotherapy have revealed delayed structural and functional pancreatic alterations. These changes appeared to be radiation dose related, are mild and easily managed with enzyme replacement therapy.

We conclude that the human pancreas is resistant to a moderate dose of EBRT when used as a part of multimodality therapy.

References


RADIATION INDUCED PANCREATIC CHANGES
- SANTH SWAROOP ET AL.

INDIAN J GASTROENTEROL. JULY 1992 VOL 3 NO 3


NEWS AND NOTICES

World Congresses of Gastroenterology 'Los Angeles, California October 2-7, 1994. These mark the 40th year of the Congress and its 10th world meeting. The congress will include state-of-the-art lectures, workshops, symposia, free papers, other scientific events and exhibits of interest. Wait for further announcements in 1993. For details, contact:

MARTIN H FLOCH, MD
International Information Chairman
24, Stevens Street
Norwalk, Conn 06856
USA

(More News and Notices on page 158)