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TOLERANCE OF CANINE PORTAL VEIN ANASTOMOSIS TO INTRAOPERATIVE X-IRRADIATION

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Abstract

Tolerance of surgical portal vein anastomosis to intraoperative radiation therapy (IORT) was studied in dogs after single doses of zero, 10, 20 and 40 Gy (290 kVp x-rays). Portal venography was performed prior to IORT and before sacrificing. The dogs were sacrificed 3 and 12 months respectively after irradiation. Portal venography revealed no radiation induced anastomotic stenosis. Autopsy disclosed macroscopic periportal fibrosis in all dogs, independent of radiation dose and observation periods. Microscopically, the three tunicas of the vein did not show any pathological changes after any dose level.

Key words: Therapeutic radiology, experimental; dogs, intraoperative x-irradiation, portal vein anastomosis, tolerance.

Intraoperative radiation therapy (IORT) is applied to selected intra-abdominal malignancies in order to exclude most of the surrounding normal viscera from the radiation field (2, 3, 5, 6). The dose for IORT is limited by the tolerance of the normal tissues or viscera still involved in the treatment volume (1).

Most pancreatic cancers are unresectable and in such cases IORT can be applied with palliative intent. When surgical resection of the gross tumor can be performed, IORT may eradicate microscopic residual tumor. Pancreatectomy is occasionally performed with the removal of the pancreatic segment of the portal vein (4). When IORT is applied to such a case, the anastomosed portal vein is to be included in the treatment volume.

The tolerance of the anastomosed portal vein to a single high dose of radiation has not yet been closely studied. Therefore the anastomosed portion is usually shielded with a lead plate or IORT is avoided because of concern for possible risks of disruption and occlusion at the anastomosis.

The aim of the present experimental investigation was to study the effect of IORT within a practical dose range on the surgically anastomosed portal vein.

Material and Methods

Experimental animals. Mongrel dogs of both sexes, ranging from 18 to 25 kg in weight, were utilized for the experiment. They were kept in separate cages and fed standard chow and water throughout the experiment.

Anesthesic and surgical procedures. Dogs were fasted for a minimum of 6 h before anesthesia. The surgical procedure was performed under general anesthesia using intravenous (i.v.) pentobarbital, 30 mg per kg body weight. They all had endotracheal intubation and ventilation regulated by a respirator with room air. I.v. drip infusion of lactated Ringer's was maintained which permitted administration of antibiotics immediately after the operation. Laparotomy was performed through a midline abdominal incision. An abdominal retractor was used to disclose the portal vein during the anastomosing manipulation and IORT.

After stripping the surrounding loose connective tissues, the portal vein was transected at about 1 cm upstream from the confluence of the splenic vein, and anastomosed end-to-end, using continuous running suture of 5-0 Ticron thread. For portal venography, a 19G polyethylene needle was inserted into a peripheral branch of the jejunal mesenteric vein. The needle was fastened to the mesenterium and filled with diluted anticoagulants.

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IORT procedure. Portal venography was performed prior to IORT which was performed with an orthovoltage machine provided for experimental use. Radiation exposure factors were 290 kVp, 10 mA, dose rate 0.60 Gy/min, SSD 35 cm and 0.5 mm Al+0.5 mmCu filter. A brass treatment cone was used having a portal size of 5×5 cm. This was coupled with a sterilized 3 mm thick lead plate with a 2.5×4 cm window which permitted localized exposure to the anastomosed portal vein. The lead plate was carefully placed so as not to hamper normal blood flow in the portal vein.

Experimental design. In order to study both early and late effects the animals were sacrificed 3 or 12 months after irradiation with zero, 10, 20 or 40 Gy. Each group contained 2 dogs and a total of 16 dogs was thus studied.

Portal venography using 20 ml of 65% Angiografin was performed prior to IORT and immediately before sacrificing. Following thorough inspection and palpation of intra-abdominal and retroperitoneal viscera and tissues, the anastomosed portal vein was resected en bloc for histopathologic examination.

Preparation of tissues. The resected portal vein was cut along the lumen. After fixation in a 10% phosphate buffered formaldehyde, longitudinal blocks through the anastomotic portion were embedded in paraffin. The sections were stained with hematoxylin and eosin, Masson's trichrome and van Gieson.

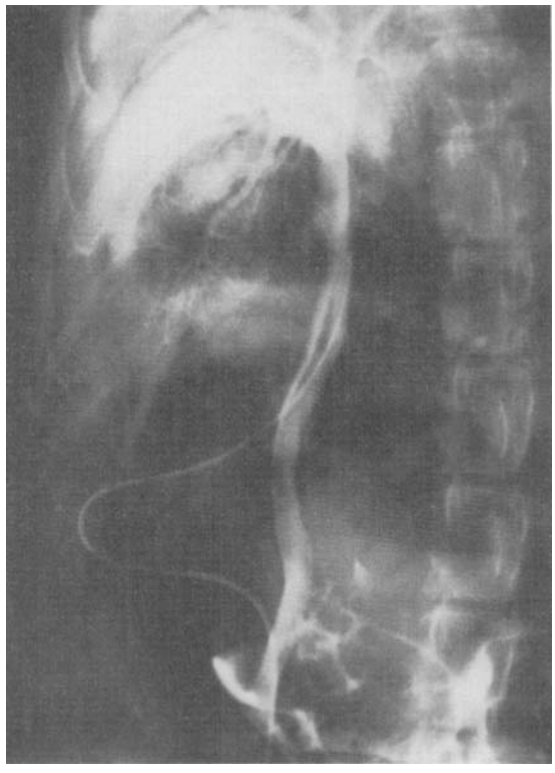


Fig. 1. Portal venogram prior to sacrificing 12 months after 40 Gy of IOR.

Results

In the anastomosing procedure, the cross clamping time of the portal vein was less than 15 min for all 16 dogs. The congestion within the jejunal loops abated within 5 min after the release of the clamps.

As all dogs survived until autopsy, no disruption of anastomosis was encountered. Portal venography before IORT revealed no remarkable stenosis at the anastomosing portion attributable to the surgical technique. The second venography did not show stenosis or occlusion of the portal vein in any of the dogs (Fig. 1).

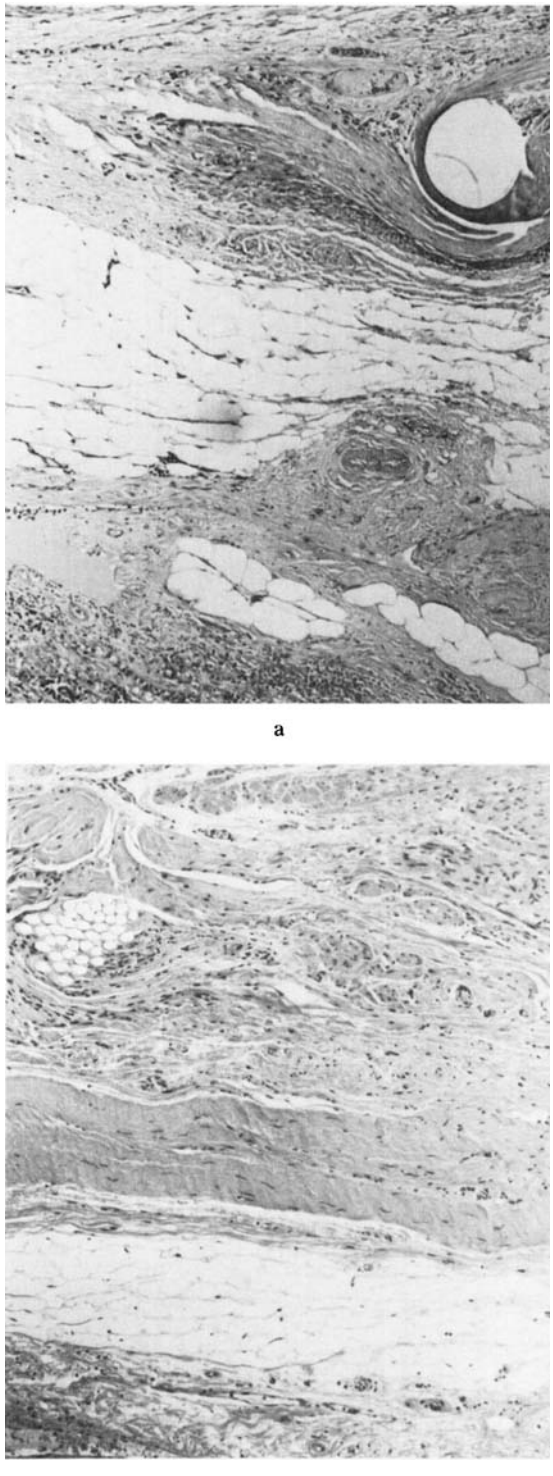
At autopsy the dogs showed various degree and extent of fibrosis and adhesions around the portal vein. The duodenum, jejunum, pancreas and part of the liver often adhered toward the portal vein regardless of radiation dose. There was no manifest difference in the degree of fibrosis between the acute and the late study groups. The portal vein was removed only together with adjacent areolar tissues in the lightly to moderately fibrosed cases. However, it was resected en bloc with the surrounding viscera in severely fibrosed cases.

At microscopic examination, special attention was paid to the changes in the three tunicas of the portal vein, that is, the intima, media and adventitia. However, no pathological changes were observed after 3 or 12 months in any of the dose groups (Fig. 2). The endothelium covered the luminal surface smoothly and no thrombus formation was encountered, nor was infiltration of inflammatory cells observed. The vasa vasorum were patent. At the portion of anastomosis, the muscle bundles were disrupted and in its place fibrous connective tissues proliferated.

Discussion

The majority of patients with pancreatic cancer have advanced disease at the time of diagnosis and only a small proportion of them are candidates for surgical resection (8). Even after resection, the tumor often recurs because of local tumor remnants (7). The authors have applied IORT with high energy electrons in locally advanced pancreatic cancer (9, 10). Most of these cases were unresectable and the intent of IORT was a palliative one, largely because of involvement of the blood vessels, especially the portal vein. Some of these cases actually had localized tumor. For such potentially curable cases, extensive resection including resection of the involved portal vein followed by IORT might be indicated.

The dose range adopted in IORT is derived from the tolerance of normal tissues or viscera. However, after extensive surgical resection of the tumor, the anastomotic portion often became included in the treatment field, which might restrict the dose delivered. Only a few stud-



a

b

Fig. 2. Microphotograms of the anastomosed portion of the portal vein (HE stain, 40×). a) 12 months after 0 Gy (control). b) 12 months after 40 Gy.

ies have been reported concerning radiation tolerance of different types of surgical anastomoses to a single dose (11, 13). We could find no study concerning the tolerance of portal vein anastomosis in the literature.

As to tolerance of the intact portal vein, TODOROKI (14) studied late effects on the rabbit liver hilum irradiated with electrons in a single fraction. He observed thickening of the intima, break down of elastic fibers of the media, fibrous thickening of the adventitia and occlusion of the portal vein branch 3 months after 50 Gy of IORT. However, no prominent pathological change was observed after 30 Gy at either 3 or 10 months. SINDELAR et coll. (12) also reported the changes of portal vein in their study of tolerance of the canine bile duct to IORT and could not find any pathologic change up to 45 Gy of electrons.

The present study revealed that portal vein anastomosis in dogs could tolerate IORT up to 40 Gy (290 kVp x-rays). RBE of high energy electrons is approximately equivalent to or somewhat lower than that of orthovoltage x-rays and our findings should therefore also be valid for electron therapy. The irradiated area, 2.5×4 cm=10 cm^2, corresponds to about 20 cm^2 for an adult human when corrected for body weight and it is well known that the biological effect of a given dose will increase when a larger volume is irradiated. The treatment cones clinically used in IORT are often so large that they include also some other normal tissues and viscera surgically manipulated during pancreatectomy and the radiation injury might be aggravated by the surgical trauma. For these reasons we are preparing cautious clinical application of IORT starting with doses around 20 Gy or less. More comprehensive experimental studies should also be performed in order to clearly establish the tolerance dose level.

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