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ACUTE GASTRIC ULCERS INDUCED BY RADIATION

by

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Gastric lesions as complications in high voltage radiotherapy have become of interest in recent years, particularly in the treatment of malignant tumours of the testis. This communication is concerned with four cases of acute gastric ulceration observed following postoperative irradiation of the lumbar lymph nodes in malignant testicular tumours.

Various forms of gastric lesions following external irradiation have been reported, especially from the Walter Reed General Hospital, Washington, by BRICK (1955), HAMILTON (1947), FRIEDMANN (ref. 9), PALMER (1948), and WARREN (1942). FRIEDMANN described four types of gastric damage in a series of about 250 malignant testicular tumours: (1) dyspepsia, (2) gastritis, (3) late chronic ulcer, and (4) acute ulcer, with or without perforation.

1. Radiation-induced dyspepsia — to be distinguished from the common roentgen 'kater' occurring during the treatment — arises 6 months to 4 years later as vague gastric symptoms without clinical or radiologic signs.

2. Radiation-induced gastritis sets in earlier than the dyspepsia, as a rule 1 to 12 months after the completion of radiotherapy, and is accompanied by radiologic evidence of spasm or stenosis of the antrum. Gastroscopy reveals smoothened mucosal folds and mucosal atrophy. The pathologic basis is fibrosis of the submucous tissue.

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3. Radiation-induced ulceration has its onset from 1 month to 6 years with an average of 5 months after radiotherapy. The usual ulcer symptoms are present, but food and antacids usually afford no relief. The ulcer is radiologically indistinguishable from an ordinary ulcer; it may heal spontaneously, but submucous fibrosis generally produces antral stenosis. FRIEDMANN recommended partial gastrectomy.

4. Unlike these late, chronic gastric sequelae, the acute, radiation-induced ulcer appears as an early complication, usually manifesting itself a month or two after the radiotherapy has been completed. This ulcer is deep and penetrates the layers of the stomach, but perforation into the peritoneal cavity is usually prevented by the omentum, the intestine, or the abdominal wall. The symptoms are severe and consist of severe epigastric pain and often gastric bleeding. Surgery is advisable before serious complications arise.

The severity and frequency of the gastric lesions depend upon the size of the dosage received by the stomach. When this exceeds 4 500 R, the incidence of gastric ulcer is 25 to 30 %. The higher the dose the more serious the gastric damage leading to penetration and haemorrhage.

FRIEDMANN (ref. 9) has also mentioned the radiation damage sustained by other structures involved in the radiation, such as the skin, subcutaneous tissue, muscles, small and large intestine, kidneys, spinal cord, and bony tissue. Although the tolerance seems to be somewhat higher in the small and large intestine than in the stomach, ulceration as well as annular stenosis due to submucous fibrosis may arise.

Only a few other authors have described gastric complications after the treatment of the retroperitoneal lymph nodes. SEJOURNE (1952) reported a case of atrophic gastritis without symptoms, which had occurred after repeated irradiation of the upper lumbar lymph nodes. MOSIMANN (1959) described a case of ulcer of the body of the stomach arising immediately after the completion of radiation to the lumbar lymph nodes through an abdominal field. The depth dose was not stated. Conservative treatment was tried but haemorrhage and penetration necessitated operation. PIET (1960) reported 4 cases of slight, late gastric lesions in a series of 89 irradiated testicular tumours. There is no exact statement of the depth dose, but the skin dose ranged from 2 200 to 3 000 R, delivered through 2 lumbar, convergent fields with 200 kV, 1 mm Cu + 2 mm Al, FSD 50 cm, field size 150 to 200 cm^2. Duodenal ulcer was observed in two cases within one year of the completion of radiotherapy, while deformation of the antrum accompanied by mild dyspepsia was present in two cases. These cases were diagnosed 4 years and 6 years, respectively, after the treatment. WOOD et coll. (1963) reported a fatal case of necrotic ulceration of the stomach and intestine after a central dose of 3 000 R, administered in two sittings at an interval of 8 days.

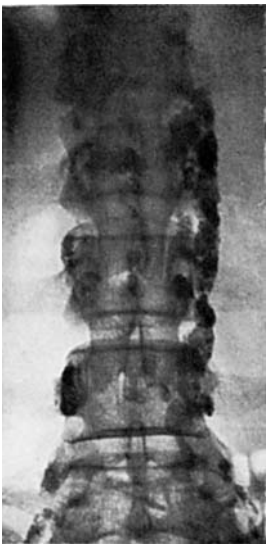

Fig. 1. Control radiography of the field limits. Contrast-filled lymph nodes are visible in the field.

The gastroscopic appearances are said to be characteristic (PALMER 1948). The irradiated area, as a rule the antrum, is transformed into an almost stiff tube, with reduced or absent peristalsis, the remainder of the gastric wall being oedematous. Where an ulcer is present, it is said to be typically deep and sharp-edged; if it heals, it does so slowly and may leave no scar.

Histologic investigations have not disclosed any changes that could distinguish radiation-induced ulcers from simple ulcers. However, it has been emphasized (WOOD et coll. 1963) that irradiation produces particularly marked mucous and submucous oedema, as well as vascular changes involving proliferation of endothelial cells and thickening of the vessel walls. The submucous fibrosis and the endarteritic changes are also marked, without being specific, in late lesions following irradiation.

Animal experiments performed inter alios by ENGELSTAD (1938) have revealed lesions following irradiation of the stomach similar to those in man.

Present material. All testicular tumours referred during the period March 1962 to December 1964 have been treated postoperatively with telecobalt to the para-aortic and homolateral iliac lymph nodes. A total of 38 patients were treated, distributed histologically in 18 pure seminomas and 20 non-seminomatous carcinomas. Prior to radiotherapy, all the patients had been subjected to hemicastration, but not to therapeutic or prophylactic lymphadenectomy of the lumbar nodes.

The radiation technique using telecobalt, initiated 2 to 3 weeks after the operation, comprised en bloc irradiation of the para-aortic lymph nodes through two opposed fields, one ventral and one dorsal, of 200 to 240 cm^2 at 80 cm FSD. The fields extended from the middle of the body of the D11 to S1, the field width being about 10 cm, determined from the lymphographic and urographic findings. Irradiation of the major parts of the kidney was avoided as far as it was possbile (Fig. 1). Only in patients with definite or probable signs of nodal invasion in relation to one kidney, was this organ included in the field. After the irradiation of the lumbar lymph nodes, the patients received irradiation through a supplementary field to the iliac nodes on the operated side.

Fig. 2. Case 2. Large prepyloric ulcer of the stomach. Para-aortic lymph nodes filled with contrast medium.

The irradiation was administered through one field daily, with a week central dose of about 1 000 R and a maximum dose of about 1 100 R. A far as the seminomas are concerned, the central dose ranged from 3 500 R, weeks to 4 500 R/5 weeks, but with the non-seminomatuous carcinomas tl average dose was higher, the central dose being about 4 500 to 5 000 R i 4 1/2 to 5 weeks, the maximum dosage about 10 to 15 % higher.

This irradiation technique always involves parts of the stomach, transver colon, and small intestine, apart from the spinal cord. The material was ana lysed with a view to the acute radiation effects upon the stomach, while a yet the late complications cannot be assessed owing to the short follow-u time (from 5 to 25 months) for the majority of the patients treated.

Three of the 38 treated patients exhibited manifest penetrating gastri ulcers, all of which required surgical treatment, in close relation to the comple tion of radiotherapy.

Case reports

Case 1. Clerk, aged 35, who for 10 to 15 years had had periodical dyspepsia without radic logically demonstrable ulcer; otherwise in good health. In April 1963, the patient had le hemicastration, and microscopy revealed malignant testicular teratoma.

Postoperatively 4 000 R was administered centrally (maximum dosage 4 300 R) in 35 day to the lumbar and left iliac lymph nodes. This was well tolerated without any major dyspepsia but about 2 weeks after its completion the patient developed severe, constant pain in th epigastrium similar to that previously experienced. The symptoms subsided under treatmen

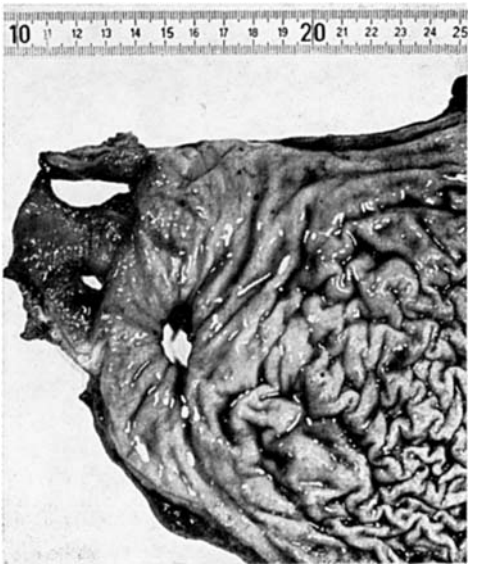

Fig. 3. Case 2. Operation specimen obtained 2 months later; the stomach has been cut along the greater curvature. In addition to the ulcer evident in fig. 2, two ulcers are present in the first part of the duodenum.

with sedatives, but recurred in 2 to 3 months; they were then severe and included vomiting and weight loss.

Urography and *lymphography* failed to reveal signs of metastases in the lumbar lymph nodes. *Roentgen examination* of the stomach disclosed an ulcer in the middle of the lesser curvature. Owing to the persistence and severity of the symptoms, Polya resection was carried out in December 1963 and revealed adhesions between the organs in the upper abdomen and increased thickness of the gastric wall. An ulcer, 2 mm deep and 15 mm in diameter, was evident on the lesser curvature.

Comments. After the operation, the patient suffered from mild dumping symptoms, but has otherwise been in good general health. There have been no signs of recurrence. Roentgen examination of the large and small intestine 18 months after the treatment demonstrated no signs of stenosing lesions or ulceration and the function of the gastroenterostomy was satisfactory.

Case 2. A farmer, aged 48, underwent left hemicastration for a testicular seminoma in May 1964. Telecobalt therapy following the operation consisted in a central dose of 4 400 R/35 days (maximum dose 4 900 R/35 days) to the lumbar and right iliac lymph nodes. Ten days before the treatment was completed the patient developed pain in the epigastrium, accompanied by nausea and vomiting.

Roentgen examination disclosed a large prepyloric ulcer crater (Fig. 2). Despite medical treatment the symptoms as well as the radiologic signs became more marked and two months later a Polya resection had to be carried out because of melaena. This revealed three large ulcers, all of which were penetrating neighbouring structures: (1) an ulcer, 3 × 4 cm in size, of the anterior wall of the antrum penetrated the anterior abdominal wall, (2) two 'kissing ulcers' were evident in the duodenal cap: one on the anterior wall, about 0.5 to 1 cm in size, penetrated to the gallbladder while the other, on the posterior wall, 2.5 × 3.5 cm in size, was

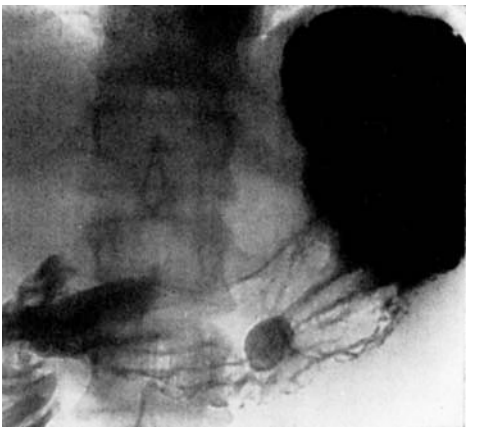

Fig. 4. Case 4. Stomach about 2 months after completion of radiotherapy; large ulcer situated close to the greater curvature.

firmly adherent to the pancreas (Fig. 3). The other abdominal organs were normal. Uneventful recovery.

Case 3. A mechanic, aged 42, previously in good health, in November 1964 was subjected to right hemicastration for a testicular seminoma. The para-aortic and right iliac lymph nodes were irradiated after the operation and received a central dose of 4 500 R/37 days (max. dose 4 900 R/37 days).

Towards the end of the treatment the patient developed constant epigastric pain which yielded to food and responded well to antacids. Roentgen examination of the stomach revealed an ulcer of the body, and gastroscopy confirmed the presence of a sharp-edged ulcer, 3 × 4 cm in size, on the posterior wall of the body. After three weeks of conservative treatment the patient had frank melaena and haematemesis, which necessitated an immediate Polya resection. An ulcer was found on the posterior wall of the body of the stomach, penetrating into the transverse mesocolon.

Case 4. Moulder, aged 21, previously in good health, in March 1959 underwent left hemicastration for a malignant teratoma followed by conventional roentgen irradiation to the lumbar nodes: 1 600 R in 54 days. No dyspeptic symptoms during or immediately after this treatment.

One year later the patient was re-admitted with constant pain in the left flank and a palpable swelling to the left of the spine.

Urography revealed lateral displacement of the left kidney and ureter, and the presumed lymph node metastases were irradiated, a maximum dose of 4 800 R being administered in 24 days by an arc technique with conventional roentgen rays.

Two weeks after the completion of this treatment the patient developed periodical epigastric pain. The pain persisted, and two months later he was admitted with haematemesis.

Roentgen examination of the stomach revealed an ulcer crater in the posterior wall of the stomach close to the greater curvature (Fig. 4). The ulcer healed under conservative treatment.

Six months later the paitent died with widespred metastases. Post-mortem revealed a scar 3 mm large, with a flat floor and convergent stellate folds of the mucosa at the site of the treated ulcer; the bottom of the ulcer scar was made up of omental tissue which at this site was fibrosed and contained a large vessel.

In the first 3 cases now reported upon, there were large ulcers that required surgery, in two because of haemorrhage and in one because of the severity of the symptoms.

Arc therapy with conventional roentgen irradiation may also lead to such a high central dose that an acute gastric ulcer results. This is exemplified by Case 4 in which the ulcer healed with scar formation during expectant treatment.

Histologic examination was carried out in all four cases, but no changes that could distinguish the radiation-induced ulcers from simple ulcers were evident.

Discussion

The dose to the gastric mucosa ranged from 4 000 to 5 000 R/5 weeks in the first three cases of definite ulcers arising in close relation to radiotherapy. In the fourth case, treated by conventional roentgen rays, the dose in the first course of treatment was 1 600 R/54 days and in the second (last) course of treatment it was 4 800 R/24 days. These doses are of the same magnitude as those which others have reported in cases of radiation-induced ulcers. According to FRIEDMANN the tolerance dose in the stomach is about 4 000 R during 5 to 9 weeks, a tolerance dose being taken to be the upper limit which does not entail demonstrable damage, acute or chronic.

The tolerance limit doubtless varies widely from subject to subject. Twenty-seven of the 38 patients of the present series received a central dose exceeding 4 000 R/4 to 5 weeks but only three of the group experienced acute symptoms. Five patients even received a central dose exceeding 5 000 R and had no symptoms of dyspepsia to demand further investigation. It must however be pointed out that the short follow-up periods of not more than two years, do not warrant any assessment of the total number of gastric complications.

The irradiation includes the stomach in the external irradiation of the regional lymph nodes in malignant testicular tumours. The radiosensitivity of the lymph node metastases is extremely varied, but the histologic type affords some guidance. In the case of a pure seminoma, FRIEDMANN has given the fatal tumour dose as being between 1 500 R/14 days and 3 500 R/4 weeks, but large tumours would necessitate an increase in this dose. It is also advisable to use a minimum of 3 500 to 4 000 R/4 weeks in those instances of seminomas with considerable cellular atypia or with any suggestion of transition into non-seminomatous carcinoma. As far as the seminomas are concerned the doses would appear to be within the limit of normal gastric tolerance.

The dosage problems are on the whole unsolved in the case of non-seminomatous carcinomas. However, the fatal tumour dose appears to be considerably

higher than for the seminomas, presumably in the range 4 500 to 5 000 R/35 to 40 days (NOTTER & RANUDD 1964). The risk of radiation damage to the stomach and intestine with this sort of dosage is quite high, and the danger should be borne in mind in weighing radiotherapy against lymphadenectomy, or possibly in combining the two in treating non-seminomatous carcinomas (MÜLLER 1962). No random treatment series to afford a consistent answer to these problems has as yet been published.

Owing to the close relation of the retroperitoneal lymph nodes to the stomach and other radiosensitive organs, such as the spinal cord and in particular the kidneys, nothing is gained by altering the field technique, e.g. the multiple field or the arc therapy technique.

It is impossible to say whether interstitial irradiation (SEITZMAN et coll. 1963), using β-emitting isotopes in Lipiodol Ultrafluid (e.g. ^{124}I, ^{131}I) administered through the lymphatics of the spermatic cord by the usual lymphographic technique, may be useful in the prophylactic treatment of the lumbar and iliac lymph nodes. The dose will be insufficient in lymph nodes replaced by tumour tissue, as the latter does not take up the contrast medium. Interstitial radiotherapy can therefore be considered only for prophylactic purposes or in the presence of micrometastases.

The treatment of the acute radiation-induced ulcers should presumably be surgical owing to the risk of haemorrhage and perforation. This accords with the course in three of the present cases. Major palpable swelling in the epigastrium a short time after radiotherapy, possibly accompanied by dyspepsia, should not be interpreted, without further investigation, as nodal metastases, as it may represent a penetrating gastric ulcer with reactive changes in the neighbouring tissues e. g. the omentum.

SUMMARY

Previously reported gastric lesions produced by radiotherapy are briefly reviewed and to these the authors add four cases of gastric ulceration following the irradiation of lumbar lymph nodes associated with malignant testicular tumours. The tolerance limit of the normal gastric mucosa was found to be about 4 000 R during 5 to 9 weeks, in keeping with the experience of other authors.

ZUSAMMENFASSUNG

Die Literatur über Magenschäden nach Röntgenbestrahlung wird beschrieben. Vier Fälle von Magengeschwüren wurden vom Verfasser gesehen, die Ursache der Geschwüre war eine Tiefenbestrahlung von lumbalen Lymphknotenmetastasen bei malignen Hodentumoren. Die Toleranzgrenze der normalen Magenschleimhaut liegt bei 4 000 R/5 bis 9 Wochen, wie das auch von anderen Autoren festgestellt werden konnte.

RÉSUMÉ

Les auteurs passent rapidement en revue les cas déjà publiés de lésions gastriques causées par la radiothérapie et y ajoutent 4 cas d'ulcération gastrique après irradiation de ganglions lymphatiques lombaires dans des tumeurs malignes du testicule. Ils ont constaté que la limite de tolérance de la muqueuse gastrique normale est d'environ 4 000 R en 5 à 9 semaines, ce qui est en accord avec l'expérience d'autres auteurs.

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