

## COMPLICATIONS FROM IRRADIATION OF CARCINOMA OF THE UTERINE CERVIX

J. ALERT, J. JIMENEZ, L. BELDARRAÍN, J. MONTALVO and C. ROCA

Cervical carcinoma is the second most frequent malignant neoplasm in Cuban women, with an annual average of about 650 new patients and a crude incidence rate of 16.1 per 100 000 and year (Registro Nacional del Cáncer 1975). Irradiation is the principal method used, with a combination of intracavitary and external irradiation. Its use implies a certain risk of complications from organs situated within the irradiated volume, the intestine and bladder being the organs most often affected.

The types and the frequency of complications in a group of patients treated by irradiation alone are now reported.

### Material and Methods

The material consisted of 2 248 patients with carcinoma of the uterine cervix who were irradiated between 1966 and 1972 at three oncologic centers: 1 280 (56.9%) at Instituto de Oncología (Havana City), 803 (35.8%) at Hospital Oncológico Docente (Santiago de Cuba) and 165 (7.3%) at Hospital Oncológico (Camagüey). The method of treatment and the results have been reported previously (JIMENEZ et coll. 1979).

Complications were classified as early, when the symptoms and signs appeared during the irradiation series or within 6 months from its completion, and as late, when they appeared 6 months or later after the end of irradiation. Cases where malignant tissue was found in the walls of fistulas were excluded.

### Results

Complications were recorded in 458 patients (20.4%). The total number was 523 as some patients had more than one complication (Table). Of these, 305 (58.3%) were classified as early and 218 (41.7%) as late.

Proctitis was the most frequent complication and occurred in 15.5 per cent of the total number of patients. The degree of proctitis varied from only tenesmus and edema of the rectal wall to ulceration and bleeding. During or at the end of irradiation, some patients developed acute symptoms such as tenesmus, painful defecation and diarrhea, which were classified as early proctitis. Late proctitis usually appeared between six months and one year from the end of irradiation. In 176 patients late proctitis occurred, and in all but 10 this was preceded by early proctitis.

More severe complications, as fistulas, ureteral stenosis with hydronephrosis, enterocolitis, sigmoiditis, intestinal obstruction and skin necrosis occurred in 81 patients (3.6%); fistulas developed only in 36 patients (1.6%).

Colostomy was performed in 11 patients (0.5%) for the following reasons: severe proctitis with ulceration of the rectal wall and uncontrollable bleeding (3 patients), fistulas (3 patients), and intestinal obstruction (5 patients).

A similar incidence of complications occurred af-

**Table***Type and frequency of complications following irradiation*

Type of complication	Number	Per cent
Proctitis	348	66.5
Cystitis	74	14.1
Recto-vaginal fistula	28	5.3
Ureteral stenosis with hydronephrosis	24	4.6
Panniculitis	17	3.3
Intestinal obstruction	13	2.5
Vesico-vaginal fistula	8	1.5
Sigmoiditis	4	0.8
Edema of legs	3	0.6
Skin necrosis	2	0.4
Enterocolitis	1	0.2
Fistula between sigmoid and jejunum	1	0.2

ter the two principal techniques used: external irradiation followed by intracavitary radium applications or intracavitary radium applications followed by external irradiation.

### Discussion

Radiation therapy, similar to surgery or cytostatic therapy, implies certain risks of complication. The literature reporting and discussing the incidence and types of complications is extensive (GRAY & KOTTMEIER 1957, FLETCHER et coll. 1958, CHAU et coll. 1962, CASTRO et coll. 1970, STROCKBINE et coll. 1970, BORONOW & RUTLEDGE 1971, FLETCHER 1971, JOELSSON et coll. 1971, SLATER & FLETCHER 1971, MICKAL et coll. 1972, ROSWIT et coll. 1972, VILLASANTA 1972, FRIBERG & JOHNSON 1974, MARUYAMA et coll. 1974, CHISM et coll. 1975, EINHORN 1975, JOHNSON 1976, MARCIAL 1977, PEREZ et coll. 1977, ALERT 1978, ALERT et coll. 1978). The complications are caused by the radiation dose to different parts of the small pelvis and the lower part of the abdomen, which causes interstitial edema, necrosis and local fibrosis. Individual variations in sensitivity and the pretreatment condition (general condition, local inflammatory diseases) certainly also play a role.

In practice, the distribution of the dose can deviate considerably from the calculated ideal dosimetry due to different clinical factors distorting the geometry of the small pelvis (SCHWARZ 1969). The determination of the doses at points in the paracervical region with regard to the intracavitary

radium arrangement can be a dangerous practice. Both with inverted T and the linear arrangement of the radiation sources a decrease in the dose may appear from the surface of the applicators to the periphery of the small pelvis. This decrease is influenced by different factors such as the distance between the vaginal sources, the length of the linear arrangement, etc. (FLETCHER, ALERT). Vaginal applicators situated preferentially in the posterior vault increase the dose in the rectovaginal wall and increase the risk of proctitis.

Although 348 patients had proctitis, colostomy was needed only in 3. Rectovaginal fistulas occurred in 28 patients, an incidence of 1.2 per cent.

External irradiation before radium application causes high doses to large parts of the intestine. By the external irradiation the thickness of the uterine wall may also be reduced, which may cause a higher intestinal dose from the intracavitary irradiation. It seems likely that both these factors contribute to the intestinal complications found (EINHORN).

Sigmoiditis has been reported as a specific complication of whole-pelvis irradiation, especially after external irradiation alone (FLETCHER). The patient with a fistula between the sigmoid and jejunum in the present series had received external and intracavitary irradiation. Probably the uterine fundus was situated close to the sigmoid, with a resulting high local dose.

Ureteral strictures, which have been reported to occur with a very low incidence (SLATER & FLETCHER) were observed in 24 patients. The signs of obstruction varied from slight or moderate dilatation of the ureter and renal pelvis to complete lack of kidney function on the obstructed side.

The total observed incidence of severe complications was in the present series 3.6 per cent. Only in 0.5 per cent of the patients was surgical treatment of complications required.

The risk of complications in connection with radiation therapy may be reduced to some extent by careful dose planning and continuous observation of the patient during the treatment. However, it must be emphasized that a certain frequency of complications must always occur as a consequence of irradiation.

### SUMMARY

The types and frequency of complications in 2248 patients irradiated for carcinoma of the cervix using different techniques are reported. Proctitis was the most frequent

complication. Severe complications such as fistulas, ureteral stenosis with hydronephrosis, enterocolitis, sigmoiditis, intestinal obstruction and skin necrosis occurred in 81 patients (3.6%). Only 36 patients (1.6%) developed fistulas.

## REFERENCES

- ALERT J.: Las complicaciones de los tratamientos radiantes de los carcinomas cervicouterinos. Experiencias en 626 pacientes. (In Spanish.) *Rev. cuba. Méd.* 17 (1978), 303.
- JIMENEZ M. J. y RODRIGUEZ M. J.: Las complicaciones intestinales en los tratamientos por radiaciones ionizantes de los carcinomas del cuello del útero. Estudio en una serie de 1530 pacientes. (In Spanish.) *Rev. cuba. Méd.* 17 (1978), 423.
- BORONOW R. C. and RUTLEDGE F. N.: Vesicovaginal fistula, radiation and gynecologic cancer. *Amer. J. Obstet. Gynec.* 111 (1971), 85.
- CASTRO J. R., ISSA P. and FLETCHER G.: Carcinoma of the cervix treated by external irradiation alone. *Radiology* 295 (1970), 163.
- CHAU P. M., FLETCHER G. H., RUTLEDGE F. N. and DODD H.: Complications in high dose whole pelvis irradiation in female pelvic cancer. *Amer. J. Roentgenol.* 87 (1962), 22.
- CHISM S. E., KEYS H. M. and GELLIN M. T.: Carcinoma of the cervix. A time-dose analysis of control and complications. *Amer. J. Roentgenol.* 123 (1975), 84.
- EINHORN N.: Frequency of severe complications after radiation therapy for cervical carcinoma. *Acta radiol. Ther. Phys. Biol.* 14 (1975), 42.
- FLETCHER G. H.: Cancer of the uterine cervix. Janeway Lecture 1970. *Amer. J. Roentgenol.* 111 (1971), 225.
- BROWN T. C. and RUTLEDGE F. N.: Clinical significance of rectal and bladder dose measurements in radium therapy of cancer of the uterine cervix. *Amer. J. Roentgenol.* 79 (1958), 421.
- FRIBERG L. and JOHANSSON J. E.: Bladder and intestinal injuries following intracavitary irradiation of carcinoma of the uterine cervix. *Acta radiol. Ther. Phys. Biol.* 13 (1974), 288.
- GRAY M. J. and KOTTMEIER H.: Rectal and bladder injuries following radium therapy for carcinoma of the cervix at the Radiumhemmet. *Amer. J. Obstet. Gynec.* 74 (1957), 1294.
- JIMENEZ J., ALERT J., BELDARRAIN L., MONTALVO J. and ROCA C.: Carcinoma of the uterine cervix. Results of treatment in 2248 cases. *Acta radiol. Oncology* 18 (1979), 465.
- JOELSSON I., RÅF L. and SÖDERBERG G.: Stenosis of the small bowel as a complication in radiation therapy of carcinoma of the uterine cervix. *Acta radiol. Ther. Phys. Biol.* 10 (1971), 593.
- JOHANSSON J. E.: Bladder and intestinal injuries following radiation therapy of carcinoma of the uterine cervix. *Acta radiol. Ther. Phys. Biol.* 15 (1976), 541.
- MARCIAL V.: Carcinoma of the cervix. Present status and future. *Cancer* 39 (1977), 945.
- MARUYAMA Y., VAN NAZELL J. R., UTLEY J., VIDER M. and PARKER J. C.: Radiation and small bowel complications in cervical carcinoma therapy. *Radiology* 112 (1974), 699.
- MICKAL A., TORRES J. E. and SCHLOSSER J. V.: Complications of therapy for carcinoma of the cervix. *Amer. J. Obstet. Gynec.* 112 (1972), 556.
- PEREZ C. A., ZIVMESKA F., ASKIN F., CAMEL M., RAGAN D. and POWERS W. E.: Mechanisms of failure in patients with carcinoma of the uterine cervix extending into endometrium. *Int. J. radiat. Oncol. Biol. Phys.* 2 (1977), 651.
- ROSWIT B., MALSKY S. J. and REID C. B.: Severe radiation injuries of the stomach, small intestine, colon and rectum. *Amer. J. Roentgenol.* 114 (1972), 460.
- SCHWARZ G.: Evaluation of Manchester system of treatment of carcinoma of the cervix. *Amer. J. Roentgenol.* 105 (1969), 579.
- SLATER J. M. and FLETCHER G. H.: Ureteral strictures after radiation therapy for carcinoma of the uterine cervix. *Amer. J. Roentgenol.* 111 (1971), 269.
- STROCKBINE M. F., HANCOCK J. E. and FLETCHER G. H.: Complications in 831 patients with squamous cell carcinoma of the intact uterine cervix treated with 3000 rads or more whole pelvis irradiation. *Amer. J. Roentgenol.* 108 (1970), 293.
- VILLASANTA V.: Complications of radiotherapy for carcinoma of the uterine cervix. *Amer. J. Obstet. Gynec.* 114 (1972), 717.