

Intralymphatic isotope therapy with P32 in the treatment of female genital cancer

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A great obstacle to the treatment of female genital cancer is the frequent spread to the lymphatics, because the traditional therapies fail to be really radical and effective on the lumbopelvic lymphatic centres.

New methods are being studied to give real control of those lymphatic centres most affected by metastasis and these will be of value both in abdominal surgical operations and, with greater justification, in vaginal operations as well as in traditional radiotherapy. We have studied endolymphatic isotope-therapy; oily radio-opaque media can be the vehicles for isotopes of sufficient radioactivity and appropriate biophysical characteristics.

« Radiant lymphography » has both diagnostic and therapeutic value. In our experience, the oily radio-opaque and radioactive vehicle (Lipiodol U.F. ^{131}I or ^{32}P) infused by a suitable technique (¹) becomes localized in the pelvic lymph nodes most affected by metastasis of female genital cancer (88.95%): the inguinal, external iliac, internal iliac, obturator and lumbo-aortic lymph nodes. The parametrial, pararectal and presacral lymph nodes escape this control but are rarely the site of metastatization. In our view, the method is effective especially against those micrometastases and small tumour foci which, because of their small size, are not revealed by lymphography.

This reduces the necessity for lymphographic diagnosis, which was particularly open to doubt in the case of such small lymph node metastases.

At first, following other clinical trials (²) we used ^{131}I which has beta radioactivity (90%) and gamma radioactivity (10% of its energy); the range of these radiations is limited (2.3 - 3 mm of tissue with a minimum of 0.5 - 1 mm) and could therefore be inadequate against metastasis of a certain volume.

Subsequently, we used ^{32}P which only emits beta rays with radiations three times as powerful as ^{131}I (^{6, 7}). The maximum range is one cm of tissue. With the help of the Istituto di Chimica Generale of the University of Padua and the National Centre for the Chemistry of Radiations and Radio-elements of the National Research Centre we synthesized the tri-n-ottilic ester of radioactive phosphoric acid (³). This is liquid at room temperature with a specific weight of 0.95 at 25 °C, it cannot be distilled and is soluble in organic solvents but insoluble in water.

The ethylic ester was chosen because: 1) it is liposoluble; 2) it is completely insoluble in water; 3) it is a liquid which permits the preparation of low viscosity solutions; 4) it is a substance with no clinically appreciable anticholinesterase activity at the doses used (⁴).

LD₅₀ and LD₁₀₀ toxicity tests enabled us to establish that a dose of 5 ml per

kg of body weight is well tolerated and without side effects in both animals and man ⁽⁴⁾.

By slowly (one hour each limb with a pressure of two atmospheres) injecting 1 - 1.5 mC of ³²P in 4 - 5 ml of Lipiodol U.F. per side, high therapeutic radioactive levels are achieved in the endolymph nodes (mean levels 36,000 rads per centre of infection) ⁽³⁾.

The histological picture of the lymph nodes and lymph node metastasis after endolymphatic isotope therapy is characteristic: the lymph node tissue assumes a « gruyere-like » appearance and quickly proceeds to necrosis and hyalinosis; the neoplastic tissues are rapidly damaged and show all the regressive phenomena following radiotherapy. After some time there is complete disappearance of the lymphatic structures which are substituted by hyalinosis and sclerosis; in this way real radiological lymphadenectomy is obtained.

Autoradiography and histoautoradiography show that the topicospatial distribution of the radioactivity is homogenous and accurate; the progressive reduction of the lymph nodes brings about concentration of the radionuclide so as to reduce the chance of any eventual areas of overdosage.

Up to the present ⁽⁵⁾ time we have used radiation lymphography in hundreds of cases of genital tumours using ¹³¹I and ³²P.

Systematic application of this method to all cases of genital and mammary neoplasia enables us to draw favourable conclusions regarding the method and its valuable therapeutic associations.

In our experience endolymphatic isotope therapy has been absolutely free from side effects; it has been associated with traditional radiotherapy from external and internal sources and with radical abdominal and vaginal surgery, and has been included in complex therapeutical associations (radio-chemo-surgical).

We recommend endolymphatic isotope therapy before radical surgery (abdominal or vaginal) and during or after radiotherapy, particularly when internal.

The « radiological lymphadenectomy » achieved by this method is regarded only as a complementary therapy aimed at extending the area of treatment of malignant genital neoplasias. It should therefore be included in traditional therapeutic programmes and be adapted to them in such a way as to increase the prospects of success.

SUMMARY

The major difficulties in the treatment of gynaecological cancer are connected with lymphatic metastases.

The endolymphatic infusion of radionuclides, especially of ³²P, would ensure a biologically sufficient dose of radiant activity.

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