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# The Lymphatic Spread of Ovarian Germinal and Stromal Tumors

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*Summary*

This paper reports the results of lymphography in germinal and stromal tumors of the ovary. The group of patients is made up of 30 cases of germ cell tumors (70 % dysgerminomas) and 29 cases of stromal tumors (62 % granulosa cell tumors). The overall incidence of metastases was 29 %; 37 % in germ cell and 21 % in stromal tumors. There was bilateral involvement in 41 % of the patients with metastases. The para-aortic region alone was involved in 23 %, the iliac alone in 18 % and both the regions were simultaneously involved in 59 %. In 17/30 operated patients (57 %) retroperitoneal node biopsies were performed and diagnostic accuracy was 9/10 in the radiographically positive and 6/7 in the negative cases.

Table 1 Total number of patients studied by lymphography.

| Histologic classification | n° cases | Positive lymphography | % |
|---|---|---|---|
| *Germinal Tumors* | | | |
| – Dysgerminoma | 21 | 9 | 43 |
| – Endodermal sinus tumor | 3 | 1 | 1/3 |
| – Malignant teratoma | 6 | 1 | 17 |
| *Stromal Tumors* | | | |
| – Granulosa cell tumor | 18 | 4 | 22 |
| – Arrhenoblastoma | 10 | 2 | 20 |
| – Gynandroblastoma | 1 | – | – |
| Totals | 59 | 17 | 29 |

In the last few years several reports stress that cancer of the ovary not only spreads by contiguity and intraperitoneal implants but also via the lymphatics to the retroperitoneal nodes (1, 4, 5, 6, 10, 11, 12). Published data are mainly devoted to epithelial cancer which accounts for about 90 % of malignant tumors of the ovary (2, 3). The problem of lymphographic detection of metastases in germ cell tumors is rarely discussed (8, 9, 13), and at present there are few comprehensive reports dealing with ovarian stromal tumors.

The aim of this study is to present our experience with lymphography in non-ephithelial ovarian tumors. The case material has been collected during a co-operative study on cancer of the ovary at the National Cancer Institute of Milan and the First Department of Obstetrics and Gynecology "Mangia galli" of the University of Milan.

## *Material and Methods*

*Patients.* From January 1973 to December 1976, 378 patients with ovarian cancer were examined by lymphography. 59 (16 %) of these patients (Table 1) had germinal (30 cases) or stromal (29 cases) tumors. The histologic classification is that suggested by W.H.O. (1973). Clinical classification is that proposed by F.I.G.O. (1975).

The mean age was 33 years; 21 for germ cell and 46 for stromal tumors. In germ cell tumors the age of the patients ranged from 2 to 49 years; 23 % were less than 15, and 57 % less than 20 years old. In stromal tumors the age of the patients ranged from 5 to 70 years. Only 10 % of the cases studied were in the pediatric age group. The majority of patients (59 %) were older than 50 years.

The case material includes 45 patients at presentation of the disease, 12 recurrences, and 2 previously treated patients who underwent restaging diagnostic procedures, including lymphangiography, in the absence of clinical evidence of disease.

*Technique of lymphography.* The technique for lymphatic cannulation was that proposed by *Kinmonth* (7). All the lymphangiograms were performed and analyzed at the Istituto Nazionale Tumori by a diagnostic radiologist (R.M.). Bilateral cannulation was successful in

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all the patients. An average of 4–6 $cm^3$ of oily contrast medium were injected for each side (1–3 $cm^3$ for the pediatric age group). No significant side effects or complications were encountered.

*Criteria for metastatic involvement.* The radiographs were interpreted as: a) normal; b) abnormal due to metastases; or c) abnormal due to benign changes (hyperplasia). No equivocal lymphographic diagnosis was made. Nodes involved with tumor nodes were usually enlarged, with rounded filling defects not traversed by lymphatic channels. The marginal sinus was often interrupted. Metastatic involvement was usually extensive but seldom did a lymphatic block occur. The presence of enlarged, granular to minimally foamy lymph nodes was considered typical for lymphographic diagnosis of hyperplasia (11–12).

## Results

*Germinal tumors.* In 11/30 patients (37 %) lymphography gave evidence of nodal metastases (Table 1). The largest subgroup was made up of patients with dysgerminoma (21/30–70 %) in whom the incidence of metastases was very high (9/21–43 %).

*Stromal tumors.* Granulosa cell tumors were the largest subgroup (18/29). Lymphography showed metastases in 4/18 patients (22 %) with granulosa cell tumors and in 2/10 patients with arrhenoblastoma.

*Clinical Stage and Lymphography.* Table 2 shows the results of lymphography according to the initial clinical stage. In germinal tumors (mainly dysgerminoma) lymphangiography detected retroperitoneal metastases in 5/15 (33 %) stage I patients. In stromal tumors, metastases were found in 1/7 stage I patients (14 %). In more advanced disease (stages III & IV) the numbers of patients with metastases were 3/11 in germ cell and 2/10 in stromal tumors. The frequency of metastases in those with recurrences was high (5/12–43 %), while lymphography was negative in both patients studied for restaging.

Table 2 Results of lymphography according to clinical stage.

| Stage | Nr. cases | Positive lymphogr. |
|---|---|---|
| *Germinal Tumors* | | |
| $I_A$ | 14 | 5 |
| $I_B$ | 1 | – |
| III | 11 | 3 |
| Recurrence | 4 | 3 |
| *Stromal Tumors* | | |
| $I_A$ | 5 | – |
| $I_B$ | 1 | 1 |
| $I_C$ | 1 | – |
| II | 2 | 1 |
| III | 8 | 1 |
| IV | 2 | 1 |
| Recurrence | 8 | 2 |
| Restaging NED | 2 | – |

*Site of metastases.* The lymphatic drainage of the ovary is summarized in fig. 1.

Lymphography was "abnormal" for metastases in 17 patients (29 %), with bilateral nodal involvement in 7 (41 %).

The para-aortic region alone was involved in 4/17 cases (23 %), the iliac region alone was metastatic in 3/17 patients (18 %), and both the regions were simultaneously involved in 10/17 (59 %).

The para-aortic nodes only or in combination with iliac nodes were involved in 82 % of the patients with metastases. The iliac region alone or with the para-aortic region was involved in 77 %.

For a more accurate evaluation of the site of metastases, the two sides of the inguino-retroperitoneal node chains were considered separately, and every chain was divided into four nodal regions (i.e., inguinal, external iliac, common iliac, and para-aortic). In this way eight possible sites of nodal involvement were considered for each patient and a total number of 40 involved regions were obtained. The graphic evaluation is reported in fig. 1.

*Radiologic/histologic correlation.* In 17/30 operated patients (57 %) retroperitoneal node biopsies were performed, and the results are shown in Table 3. Diagnostic accuracy was 9/10 in the radiographically positive and 6/7

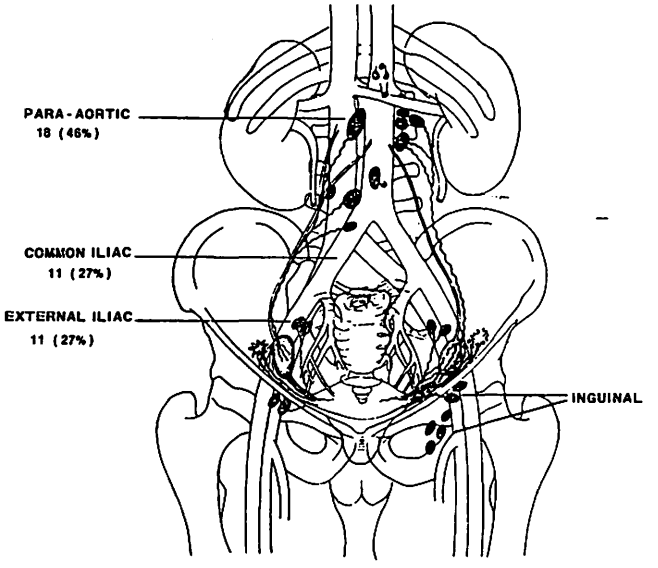


Fig. 1 Anatomic sketch of the lymphatic drainage of the ovary site distribution of metastases as determined by lymphography on the total number of involved chains.

Table 3 Radiologic/histologic correlation

| Histology | Lymph node biopsies | Lymphographic/ histologic correlation | | | |
|---|---|---|---|---|---|
| | | +/+ | +/– | –/+ | –/– |
| *Germinal Tumors* | | | | | |
| – Dysgerminoma | 8 | 6 | 1 | – | 1 |
| – Endodermal sinus tumor | 1 | | | | 1 |
| – Malignant teratoma | 2 | 1 | – | 1 | – |
| *Stromal Tumors* | | | | | |
| – Granulosa cell tumor | 3 | 1 | – | – | 2 |
| – Arrhenoblastoma | 3 | 1 | – | – | 2 |
| Totals | 17 | 9 | 1 | 1 | 6 |

in the negative cases. In the false negative case, histology showed the presence of embolic micrometastases in the marginal sinus of two common iliac nodes, ipsilateral to the primary ovarian teratoma.

The overall diagnostic accuracy was 88 % (15/17), the sensitivity was 90 % (9/10) and specificity 88 % (6/7)

*Hyperplasia.* Impressing was the high frequency of nodes with hyperplastic changes, 42 % in our series. Hyperplasia was more often encountered in the positive (8/17–47 %) than in the negative cases (17/42–40 %). In patients with epithelial cancer (11) hyperplasia was found in 18 %, particularly in the negative lymphograms (22 %). Hyperplastic nodes were found independently of prior abdominal surgery, and this could perhaps be due to immunologic disorders.

## *Discussion*

There have been few reports concerning the results of lymphography in special histological types of ovarian tumors (mainly in dysgerminoma) (8–9–13). *Markovits* et al. (9) documented 31 patients with dysgerminoma of whom 33 % had demonstrated metastases. Another important contribution is by *Sarrazin* et al. (13) who described 25 patients with dysgerminoma (23 stage I and 2 recurrences), 36 % of whom had pathologic lymphograms. Unfortunately, only a few of the published cases had retroperitoneal node biopsies taken for radiologic-histologic correlation.

In this study the number of positive lymphangiograms (33 %) in stage I dysgerminomas is exactly the same as that found by *Markovits* et al. in 31 stage I patients (9). This is more than four times the value of 8 % found in ovarian epithelial cancer (11). The value

for stromal tumors (14 %) is similar to the value disclosed in epithelial cancer.

Our experience suggests a double mode of spread in germ cell tumors: in the first, tumor confined to the ovary metastasises to retroperitoneal nodes; in the second, it progresses within the pelvis to give locally advanced stages with a lesser degree of retroperitoneal invasion. By contrast, in cancer of epithelial origin, the rate of retroperitoneal involvement increases in direct relationship to the clinical stage (11). The pattern of metastases in recurrent epithelial cancer is very similar (46 %).

Lymphography changes the initial staging diagnosis in 33 % of germ cell and in 22 % of stromal tumors. This percentage is higher than the values of 8 % at stage I and 0 % at stage II observed for tumors of epithelial origin (11).

Such a finding might be anticipated in dysgerminoma, in which a high degree of lymphotrophism is well known, but it seems even more interesting in stromal tumors, in which the capacity for lymphatic permeation is almost unknown.

One might surmise that as major lymphatic drainage of the ovary follows gonadal vessels, the para-aortic nodes would be at the highest risk for lymph node metastases, either alone or with concomitant iliac lymph node involvement. Our series of stage I and II patients shows involvement of para-aortic nodes alone or para-aortic plus iliac nodes in 86 %. Iliac nodes or iliac plus para-aortic nodes are involved in 57 %. These findings are similar to those of *Markovits* et al. (9) and *Sarrazin* et al. (13) who demonstrated 100 % involvement of para-aortic nodes and 40 and 55 % involvement in iliac nodes respectively, in patients with stage I or II disease. Iliac node disease was always accompanied by involvement of para-aortic nodes.

In comparison ovarian epithelial cancers were found to involve para-aortic region alone or para-aortic plus iliac nodes in 45 % and iliac nodes alone or with para-aortic nodes in 82 % (10, 11). In the four stage I patients with epithelial cancer and lymphographic evidence of metastases, the para-aortic region alone was compromised in two patients just as the iliac chains. These findings suggest that in ovarian special tumors the upper draining trunk has slight predominance for metastatic dissemination, and in epithelial cancer the two lymphatic trunks have the same importance, with some preference for the iliac one.

Radiographic appearance of involved nodes from special tumors of the ovary are non-specific, as in the case in solid tumors. The second finding of diagnostic importance is the high frequency of hyperplasia, found independently from prior abdominal surgery.

In the group of patients who underwent retroperitoneal node biopsies, the degree of confidence in lymphography is good. The data of the radiologic-histologic correlation are equivalent to those obtained in ovarian cancer of epithelial origin (11).

The results of this study encourage the routine use of lymphography in patients with ovarian germinal and stromal tumors, both in the initial diagnostic work-up and in the follow-up. These tumors, which are highly radiosensitive, need external radiotherapy for a completion of treatment. The radiation therapy plan is obviously dependent upon the results of the lymphogram. (In practice, even a normal lymphogram must be followed by prophylactic irradiation to the lymphatic area most at risk for microscopic involvement). A positive lymphogram indicates that therapeutic irradiation of the involved and adjacent areas is necessary and in dysgerminoma prophylactic irradiation above the diaphragm is required. Germinal and stromal tumors are relatively unaffected by chemotherapy.

Abdominal surveillance films and eventually repeat lymphography permit careful evaluation of treatment and the discovery of recurrences. It is not the aim of this paper to give the survival in these patients, but we agree with *Markovits* et al. (9) who state that lymph node involvement as determined by lymphography has a less ominous prognostic significance than does intra-abdominal extension of tumor or hematogenous dissemination.

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