PRIMARY LYMPHOSARCOMA OF THE OVARY

REPORT OF A CASE

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Lymphoblastoma involving the ovaries, either primarily or secondarily, appears to be a very unusual condition. Less than a dozen instances of metastatic lymphoblastoma have been described. In a review of lymphosarcoma of the female genitalia, published in 1934, Walther records only two primary ovarian lymphosarcomas, one from the literature and one from his own material. Since that time no cases reported by name have appeared. The disease, however, is probably not quite so rare as is suggested by such a survey of the literature. Scattered in text-books, usually under the name of small round-cell sarcoma, can be found a few descriptions and illustrations of tumors which are at least consistent with a diagnosis of lymphosarcoma. However, there does not now seem to be anything to be gained from an attempt to trace and reclassify such obscure cases.

REPORT OF CASE

The patient, a white female aged twenty-three, mother of three healthy children, entered the Mary Fletcher Hospital complaining of rapid enlargement of the abdomen, gradual loss of strength for the past three months, and gas pains for the past four days.

The family history and the patient's own past history were irrelevant. She had last menstruated five and a half months before admission. She knew herself to be pregnant, and for the past three months and a half had been able to feel in the left side of her abdomen a growing mass which she observed to be increasing in size more rapidly than in her previous pregnancies. During this period she had noticeably lost strength.

Two months before admission a small, soft, painless mass appeared at the introitus. Two weeks later, following a bump, the patient observed a small non-tender mass in the upper outer quadrant of the right breast. Simultaneously she noticed that her gums bled readily after she brushed her teeth, and discovered a small pedunculated mass attached to the gum near the left upper canine tooth. These tangible lesions and the abdominal mass continued to grow, and two weeks before admission the patient first noticed several nodules in the left breast.

On admission to the hospital, the patient appeared as a rather pale but fairly well developed and nourished woman in no obvious discomfort. Her abdomen was markedly distended, and on palpation presented two distinct, firm, ovoid masses. The larger, on the left side, appeared to arise from the pelvis and extended to the costal border. It did not move with respiration. On the right, a similar smaller mass rose to the level of the umbilicus. Fetal heart sounds could be heard in this mass.

On pelvic examination, the vaginal mucosa was found studded with many sessile, moderately firm nodules 1 to 2 cm. in diameter. All were covered with smooth mucous membrane, but the centers of the larger nodules were hemorrhagic. From the anterior vaginal wall a mass 3 by 2 cm. projected through the introitus. The cervix seemed to be continuous

with the right abdominal tumor, and the left tumor was believed to arise from the corresponding ovary.

Both breasts contained multiple, moderately firm, movable masses 1 to 4 cm. in diameter. Several small sessile nodules, similar to those in the vagina, were found along the gum margins. A few barely palpable lymph nodes were present in the axillae and along the sternomastoid muscles. Otherwise the physical examination was essentially negative.

Laboratory examinations showed a trace of albumin and occasional leukocytes in the urine. A blood count showed: hemoglobin 70 per cent; red cells 2,980,000; white cells 5,800—neutrophils 71 per cent, lymphocytes 20 per cent, large monocytes 7 per cent, eosinophils 1 per cent, basophils 1 per cent. No abnormal or immature cells were seen. The blood Wassermann reaction was negative. X-ray examination revealed pregnancy of about five months' duration, and a homogeneous mass, soft tissue or fluid, in the left side and lower abdomen. A plate of the chest and included trunk skeleton showed no evidence of metastases.

The clinical diagnosis was pregnancy and left ovarian malignancy with metastases to gums, breasts, and vagina.

Two days after admission, biopsy of one of the vaginal nodules revealed a malignant lymphoblastoma.

The patient's condition became steadily and rapidly worse. On the eleventh hospital day she gave birth to a grossly normal female fetus of approximately five months gestation, which lived only a short time. Following delivery the patient's temperature rose moderately and she died the next morning, twelve days after admission and approximately three and a half months after the onset of symptoms.

Pathological Observations: Autopsy was performed three hours post mortem. The abdomen was much distended and contained about 2 liters of clear straw-colored fluid. A large, smooth, oval mass 30 by 20 cm. replaced the left ovary and nearly filled the left side of the abdomen. There were no adhesions. The right ovary was replaced by a smaller mass, 20 by 12 cm., and this was lightly adherent to the right pelvic wall. Both tubes were grossly normal. The uterus extended 12 cm. above the pubis. The cervix was patulous. The uterine cavity was lined with smooth decidua and blood clots. No gross or microscopic tumor deposits were present. The vaginal mucosa was thickly studded with flat, sessile tumor nodules. The gross appearance of the urogenital organs is shown in Fig. 1.
The ovarian masses were soft, pinkish gray and edematous, with large areas of hemorrhage and yellowish patches of partial necrosis. The tumors contained numerous large, thin-walled blood vessels, many of which were thrombosed.

Scattered flat nodules of tumor tissue appeared on the parietal peritoneum, most numerous in the pelvis.

In the gastric mucosa were many flat tumor deposits 1 to 3 cm. in diameter. These had the form of shallow craters with elevated edges, and in the larger ones the centers were ulcerated. None appeared to penetrate through the muscularis. Thick disc-like masses of tumor were liberally scattered in the mucosa of the small intestine. One such mass in the mid-portion of the ileum formed the head of an agonal intussusception. Only rare deposits were seen in the colon. Along the mesenteric attachment of the small bowel were many spherical tumors averaging 1 cm. in diameter. Possibly these represented enlarged lymph nodules. The mesenteric lymph nodes were soft and hemorrhagic, but only slightly enlarged.

The liver and spleen were of average size, and contained no gross or microscopic tumor.

![Fig. 2. Typical Field from Primary Tumor (Low Power)](image)

The pancreas was extensively infiltrated with tumor, the limits of which were not clearly discernible grossly. Microscopically large portions of the gland had almost completely disappeared in tumor, and there was moderate extension into adjacent fat. Curiously a few small lymph nodules and an accessory spleen in the immediate vicinity contained no tumor.

Both kidneys were symmetrically enlarged to over twice normal size, and the cortex was nearly completely replaced by large streaks and patches of tumor tissue. The ureters and bladder were negative.

The adrenals appeared grossly to be free of tumor, though the adjacent fat was grayish and hemorrhagic. Microscopic examination, however, revealed several large tumor deposits extending outward from the adrenal medulla.

Save for the heart, the thoracic viscera were nearly free of tumor. The thymus was not recognizable. The hilum nodes were small, intensely anthracotic, and apparently contained no tumor. The right lung presented only marked hyostatic congestion. The left exhibited, in addition, a few thin, flat, subpleural tumor deposits about 1 cm. in diameter. A small disc of tumor 2 cm. in diameter was also seen beneath the parietal pleura in the 7th interspace on the left. Incidentally this mass showed microscopically a few old, heavily encysted trichinae, freed by the destruction of intercostal muscle, and still surviving in the midst of tumor.

The heart was of normal size, but presented a most remarkable appearance. The epicardium was thickly studded with tumor nodules which became confluent and almost completely sheathed the coronary branches. There were no deposits in the parietal pericardium. Between the auricles posteriorly was a large, solid mass of tumor 2 cm. in
diameter. On opening the heart, the columnae carneae and papillary muscles of both ventricles were found diffusely thickened and pale from extensive tumor infiltration, giving them somewhat the appearance of having been covered with a very thick coat of heavy cream-colored paint. On section the tumor deposits seemed grossly confined to the epicardial and subendocardial surfaces. The ventricular surfaces were smooth with no evidence of mural thrombosis. The valves were negative throughout.

Both breasts were moderately hyperplastic, and contained multiple ill-defined masses of tumor 1 to 6 cm. in diameter, the larger ones being very hemorrhagic. There was no invasion of skin or pectoral muscles, and no axillary nodes were palpable.

The vertebral marrow was uniformly light brownish red in color, and contained no visible tumor.

The head and neck were not dissected.

Tissue for microscopic examination was fixed in Zenker’s fluid, and paraffin sections were stained with hematoxylin and eosin, Wolbach’s modification of the Giemsa stain, and Foot’s modification of the method of Del Rio-Hortega for reticulum. Frozen sections of formalin-fixed tissue were stained by the method of Sato for oxidase granules.

Sections of both ovaries were identical in appearance. The masses were composed purely of tumor, with no trace of ovarian tissue. Areas of closely packed small round cells alternated with looser patches, giving the whole section an irregularly mottled appearance. Fairly numerous thin-walled vessels were scattered throughout the tumor (Fig. 2). The stroma was so delicate as to be nearly invisible with ordinary stains, but silver impregnation (Fig. 3) demonstrated an abundant, regular, close meshed network of argyrophile reticulum fibers. There was no suggestion of lobulation or alveolar arrangement.

In well preserved areas the tumor cells were very uniform. The nuclei were 8 to 10 μ in diameter, and round, or occasionally slightly indented or folded. The nuclear membrane was heavy and sharp, and within it were scattered up to a dozen large rough lumps of chromatin, one or more of which were so large as to resemble nucleoli. The cytoplasm appeared as a narrow eccentric rim, homogeneous and neutrophilic in Giemsa preparations when well preserved. More often it was partly reticular and somewhat frayed. It was non-granular and oxidase-negative by the method of Sato. Mitoses were fairly numerous (Fig. 4).

In looser areas of the tumor there was much pyknosis and some fragmentation of nuclei. Here and there single cells or small groups had their cytoplasm stretched by crowding with multiple, rounded, refractile and homogeneous masses of material staining very intensely with eosin (Russell’s fuchsin bodies).

Scattered among the tumor cells could be seen rarely the pale oval nuclei of reticular
fibroblasts, a few macrophages sometimes phagocytosing tumor cells, and occasional leukocytes, often eosinophils. No plasma cells or immature forms of the hematopoietic series were seen.

Throughout its various metastases, the tumor maintained an absolute uniformity of cell type and arrangement. Brief note may be made, however, of certain anatomic peculiarities of these secondary deposits. In the heart the most extensive infiltration was in the columnae carneae and papillary muscles, and invasion of the ventricular wall took place as an extension from these foci. The interstitial tissue was flooded with great numbers of tumor cells, and the muscle fibers became attenuated, fragmented, and finally disappeared. Heavily infiltrated papillary muscles were often covered with a thick, irregular mantle of tumor cells (Fig. 5). Silver impregnation showed this mantle of tumor cells to be supported by a rather abundant, regular network of reticulum sprouting from the underlying subendocardial connective tissue. An endothelial lining could be traced over part of these tumor mantles, and was probably nearly complete, as there was no mural thrombosis.

The numerous metastases occurring along the gastro-intestinal tract appeared almost always to start in the submucosa, and to produce first elevation and then ulceration of the

![Fig. 4. Tumor Cells, One in Mitosis (High Power)](image1)

![Fig. 5. Tumor Mantle over Papillary Muscle (Low Power)](image2)
overlying mucosa. Penetration into the muscularis was usually relatively superficial, seldom extending beyond the inner circular layer. The nodules seen grossly along the mesenteric attachment consisted of masses of tumor showing no trace of lymph node architecture.

The kidneys exhibited an extremely massive infiltration. Isolated glomeruli and small groups of tubules were sparsely scattered in solid masses of tumor tissue. The tumor seemed to squeeze the capsule down upon the glomerular tuft, but no glomerulus was seen actually in the process of being invaded by tumor. The surviving tubules were moderately dilated, and contained a few hyaline casts, but no tumor cells.

The bone marrow contained no recognizable tumor cells. It was slightly hyperplastic, the increase in cellularity being due to a considerable number of stem cells in small groups, and a greater than average proportion of myelocytes in various stages of maturation.

Throughout all sections, vessel walls appeared almost invariably to resist invasion. No recognizable tumor cells were seen in the blood within vessels, and there was nowhere, either in blood studies during life, or in the post-mortem tissue sections, any suggestion of a leukemic state.

The premature fetus was dissected three days post mortem, and showed no gross abnormality. No sections were taken. Slides of the placenta and umbilical cord showed no trace of tumor.

**Discussion**

The diagnosis of lymphosarcoma in this case rests primarily on the type of tumor cell, which closely resembled the medium-sized lymphocyte. This cell type was constant in all sections of tumor examined. Strong corroboration was provided by the fine, net-like reticular stroma, which was also constant, and showed no trace of alveolar arrangement. Some further support was furnished by the occurrence in the primary tumor and in the majority of the metastases of numerous Russell's fuchsin bodies.

The tumor was believed to be primary in the left ovary chiefly because this was by far the largest mass present. The only other likely primary sites seemed to have been the breasts, the pancreas, the gut, and the kidneys. The breasts may be ruled out, as the tumors appeared definitely after the beginning of the abdominal enlargement, and nearly simultaneously with the metastases in the gums. The gut may be rejected as the masses there were too small, numerous, and uniform in size and distribution. The pancreas also seemed an unlikely source, as the gland was only partially infiltrated, with no gross enlargement. Because the kidneys were nearly identical in size and appearance, they could hardly be considered as the point of origin, unless the improbable assumption be made that the tumor arose simultaneously in both.

The starting point of an ovarian lymphoblastoma must still remain a theoretical problem. The standard works on normal histology, while occasionally admitting the existence of lymphatic vessels, are unanimous in denying the presence of lymphoid tissue in the normal ovary. Walther, in his case reports, attempted to circumvent this difficulty by supposing that lymphoid tissue might have been present as a result of previous chronic inflammation. We may presume to suggest another theoretical mechanism: viz. that our tumor arose as a massive overgrowth of the lymphoid element of a preexisting teratoma. Proof of this suggestion, however, is not now obtainable, as the ovarian mass was both uniform and very large, and a thorough microscopic search for fragments of teratoma was manifestly impracticable.
The clinical history and pathological findings of a case of primary lympho-sarcoma of the ovary have been described. The tumor appeared in the left ovary of a twenty-three-year-old female, grew with great rapidity, produced generalized metastases, and caused death in a period of approximately five months.

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