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Rare case of ovarian and breast cancer as secondary manifestation of Non-Hodgkin lymphoma

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Abstract. Introduction The involvement of the ovary and breast of secondary lymphomas is very rare. Diagnosing Non-Hodgkin lymphoma can be possible either by primary or secondary manifestation, which usually presents with abdominal or pelvic complaints. Ovarian lymphoma is 1,5% of all ovarian cancers cited in the literature and less than 1% first manifestation of a non-Hodgkin lymphoma. **Case presentation:** We present a case of secondary involvement of the ovary with metastasis in the breast, considered stage 4 non-Hodgkin disease and discuss the histogenesis of ovarian lymphomas, treatment and general manifestation. A gynecological consultation and breast examination were performed and the upper and lower abdomen consultation revealed a tumor of 30/20 and breast palpation revealed a 4 cm mass, solid with suspect ecographic findings. **Conclusions:** Staging and treating disseminated limphoma can be very difficult and hard on the patient, family support being crucial in this process.

Keywords: OVARY, BREAST, LYMPHOMA, SURGERY.

INTRODUCTION

Ovarian metastasis from primary non-Hodgkin lymphoma is rare, but it is considered a common spread to the genital tract, by hematogenic pathway. This can be conflicting, because ovaries do not contain any lymphatic cells.

The main age for appearance is considered above 40 years old, an found during a routine abdominal or transvaginal echography. Women that accuse gastrointestinal problems, important weight loss, night sweats and a palpable mass should present as soon as possible to the doctor. (1) Disease evaluation is mandatory with CT involving the thorax, abdomen and pelvis. In case there is spreading to the lymph nodes, the disease can still be considered primary if the extension to the other organs is not present. Immunohistochemistry is used nowadays routinely for correct diagnosis and treatment. (3)

CASE PRESENTATION

Clinical findings

We present a 60-year-old female patient that was complaining at presentation to the hospital for abdominal and pelvic pain and the appearance of a mass on the right breast. A gynecological consultation and breast examination were performed and the upper and lower abdomen identified a solid mass measuring 30/20 cm extending to the

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diafragm and liver al clinical palpation and breast palpation identified a hard, solid mass measuring digitally and ecographically 4 cm.

Initial abdominal surgery was performed through a median laparotomy and a solid ovarian formation, with adherences to the Douglas and the uterus was found, total measurement of the structure was 30 cm and macroscopical aspects were compound of tumor necrosis, severe debridement and hemorrhagic aspects at the level of the uterus and bladder peritoneum (Fig. 1,2).

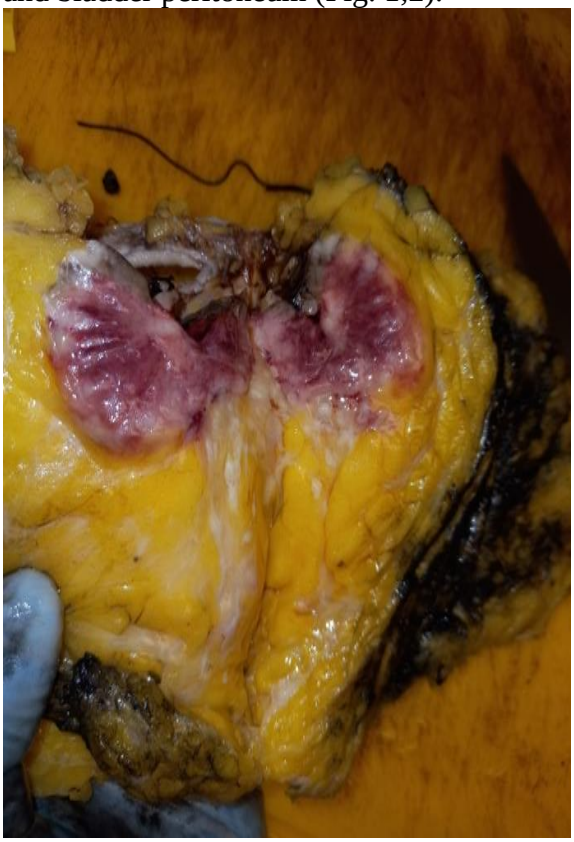

Figure 1a. Macroscopic aspects of the pelvic tumors

An extemporaneous examination of the ovary was performed concluding malignant tumors with extensive area of tumor necrosis, subject to paraffin of the final anatomopathological type. Total hysterectomy with bilateral adnexectomy, peritoneal lavage, biopsy of suspicious bladder formations, pelvic lymphadenectomy, iliac and obturator nodes were performed.

During the 2nd operative time of the procedure, an open biopsy of the right breast formation was performed with an extemporaneous examination with the same type of tumor as the ovary being found, and a decision to perform a partial lumpectomy of the right breast was made for final results and chemotherapy to be considered after surgery.

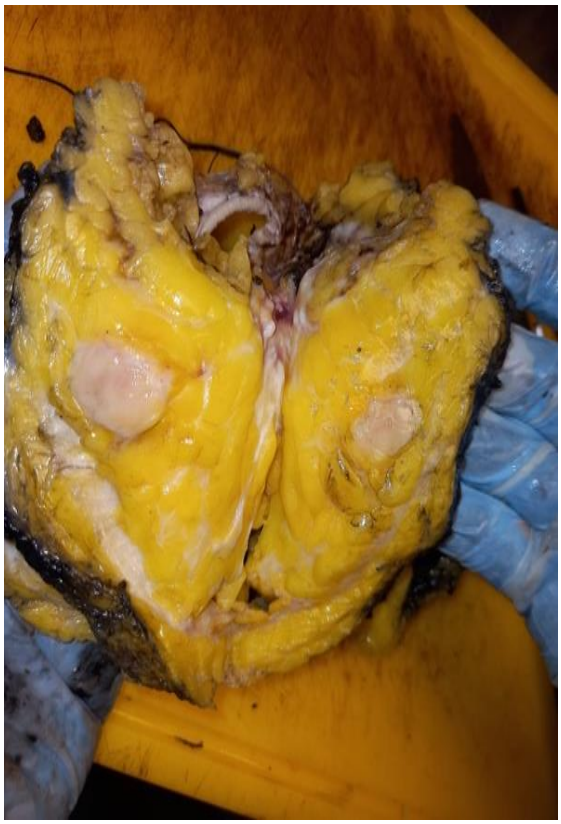

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Figure 1b. Macroscopic aspects of the pelvic tumors.

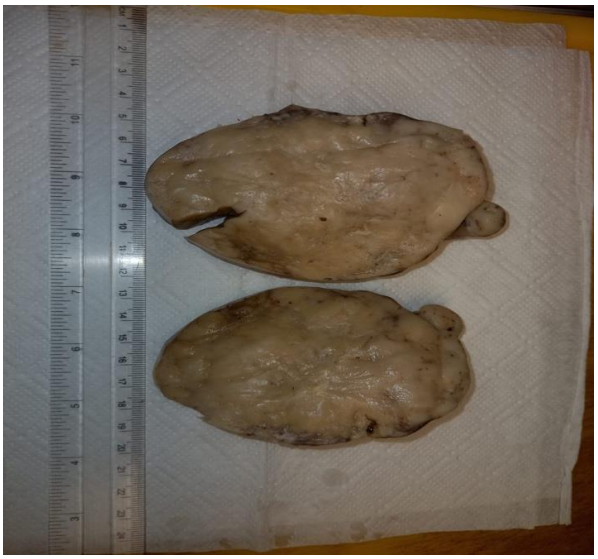
RESULTS

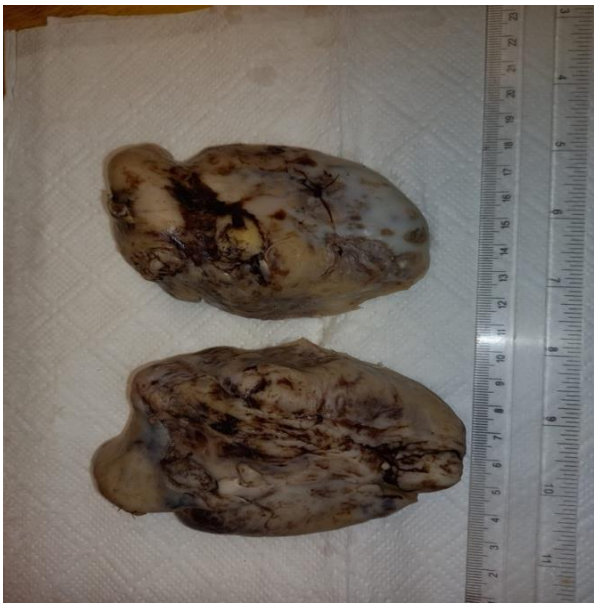
1.1.Anatomopathological

The final anatomopathological examination revealed high-grade, disseminated, non-Hodgkin's lymphoma, the patient being directed to the Oncological Institute IRO Iasi for immunohistochemical evaluation of the biopsy block, additional

investigations and specialized therapeutic conduct.

This hospital has a multidisciplinary approach for the patients with an oncological committee weekly and possibility of ambulatory or hospitalized treatment for oncological patients. The patients can be monitored for side effects during chemotherapy treatment and anesthesiology is on standby in case of adverse reactions.





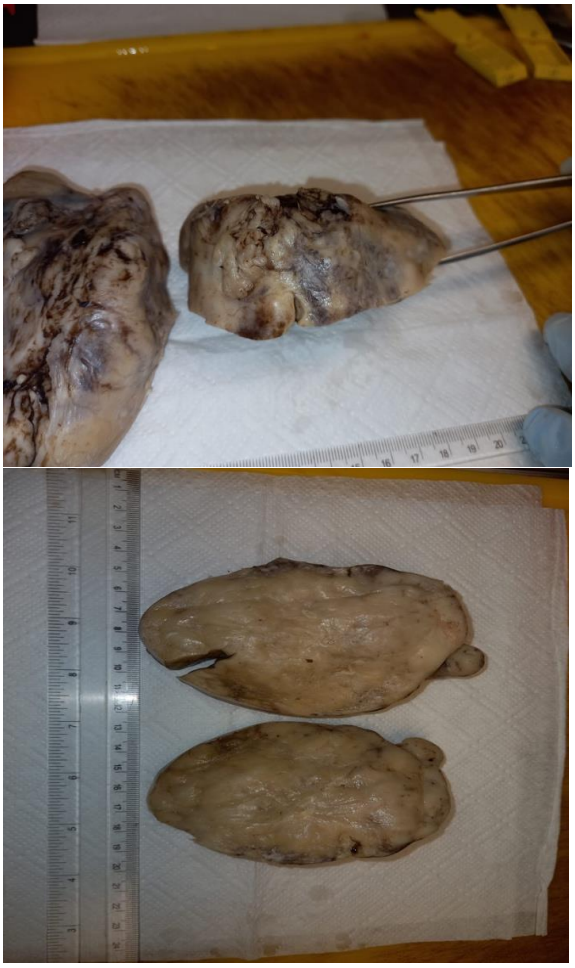


Figure 2. Macroscopic aspect of the ovaries

At the first presentation in September 2022, one month after surgery, the patient presents a slightly affected general condition, afebrile, complains of marked physical asthenia, fatigue, significant weight loss and profuse night sweats.

Clinical examination: sclero-integumentary pallor, bilateral laterocervical adenopathy, bilateral axilla of maximum 2 cm, distended abdomen.

1.2. Paraclinical parameters

Biologically, mild anemia was detected, hemoglobin 10.3 g/dl, thrombocytosis 640,000/mmc. Biochemically, the patient presents an inflammatory syndrome: ESR-25

mm/h, fibrinogen 364 mg/dl, CRP 127 mg/L, LDH 2375 U/L, hyperuricemia uric acid 9.49 mg/dl, the rest of the analyzes being within normal limits.

1.3. Immunohistochemistry

Pathological anatomy and immunohistochemistry containing fragments of fallopian tubes, ovary, mammary gland with diffuse infiltration of medium-large discohesive tumor cells, with large, vesicular nuclei with prominent nucleoli, immunoblastic type. Numerous mitoses, fine sclerohyaline stroma are identified. Immunohistochemistry shows CD 20 diffusely positive in the tumor cells, MUM 1 -diffusely positive with variable intensity in the tumor cells, CKc, CD10, CD3- positive in the tumor cells, positive in the associated small T lymphocytes. The aspects described correspond to a malignant non-Hodgkin lymphoma with large diffuse B cells, with a post germinal center phenotype (Fig 3).

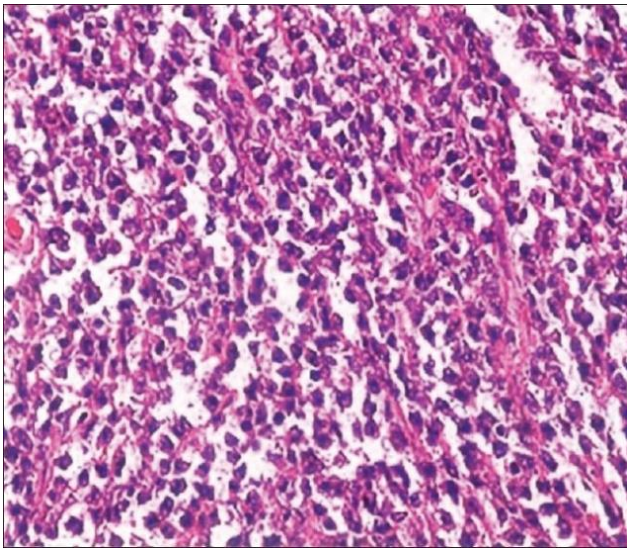


Figure 3. Large B cells associated with hyperchromatic nuclei

1.4. Staging and evolution of disease

The thoraco-abdominal-pelvic computer tomograph showed a voluminous retroperitoneal tumor formation extended to the pelvic level. Lower cervical, supraclavicular, subclavicular, axillary, mediastino-pulmonary and abdomino-pelvic adenopathies, skin thickening and skin nodules at the level of the remaining right breast.

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The patient was hospitalized on September 30, 2022, with an affected general condition, profuse sweating and a marked weight loss of 20 kg in 3 months.

Clinical examination: lung: diminished right basal vesicular murmur, abdomen: abdominal tumor mass without clear boundaries on palpation, liver and spleen at the costal edge, right laterocervical lymph nodes, 3/2 cm of bilateral dura and axillary consistency, lower limb edema, mass right breast tumor.

Biological samples: leukocytosis 21300/mmc (with neutrophilia 8860/mmc and lymphocytosis 7000/mmc), thrombocytosis (462000/mmc), increased tumor markers (CA 125 - 127 U/ml, CA 19-9 -- 60 U/ml), non-specific inflammatory syndrome CRP 116 mg/l, hyperuricemia 11.3 mg/dl, hypoglycemia 55 mg/dl, increased LDH 3885 U/L, hyponatremia 132 mmol/l, TGO 67 U/L.

The peripheral blood smear reveals 40% lymphocytes, of which 14% are of

medium/large size, oval, irregular nucleus, semi-dense chromatin, with 1-2 nucleolar outlines, moderate basophilia with small vacuoles.

1.5. Chemotherapy protocol and treatment of disease

Upon admission, the patient presented the absence of transit for faecal matter and gas for 3 days, with significant abdominal pain and an enlarged abdomen, which is why she is being investigated by imaging, no pneumoperitoneum is detected, and at the coliomesenteric level she presents an adenopathic block of 74/118 mm and hepatomegaly with a diameter anteroposterior right liver lobe of 171 mm, and left liver lobe of 69 mm. On 05.10.2022-06.10.2022 the patient performs the first R-CHOP chemotherapy treatment: Rituximab 375 mg/m2 with a total dose of (DT): 648 mg) day 1, Cyclophosphamide 750 mg/m2 (DT 1297 mg), day 2: Doxorubicin 50 mg/m2 (DT 86 mg) day 2, Vincristine 1.4 mg/m2 (DT 2 mg) day 2, in association with Solumedrol and adjuvant medication with good clinical-biological tolerance.

In March 2023, after 9 months from her initial diagnosis, the patient presented with total paresis of the left oculomotor nerve as an observation of the paraneoplastic syndrome, following increased blood pressure values of 180/100 mm Hg the day before the onset of symptoms. She was admitted to the Neurology Hospital, with a blood pressure of 150/70 mm Hg, conscious, cooperative, without signs of meningeal irritation, presenting all the signs of complete oculomotor nerve paresis: complete eyelid ptosis, limitation of adduction and verticality of the eye up and down, weakly reactive mydriasis, horizontal diplopia when looking at the right side and vertical when looking up and down, without other signs of neurological focus, without motor deficits.

The dosage of anti-neuronal antibodies was recommended, given the paraneoplastic context treatment with gabaran and corticosteroids was initiated to relieve the headache, ophthalmological examination normal anterior pole, pupil with weak reflex, vessels of normal caliber. The possibility of spontaneous disappearance of this syndrome of oculomotor paresis in 3-6 months was explained.

DISCUSIONS

Literature data

Non-Hodgkin's lymphoma can have a first presentation in the ovaries and cause difficulties for gynecologists because it resembles other tumors. In the literature its incidence is considered 1.5% of all ovarian cancers and 1% of non-Hodgkin lymphomas. (2)

Moreover, the association with a breast tumor can lead to suspicions for positive BRCA 1 and BRCA 2 genes, much more common tumors. Lymphoma cells may occur in the ovary as a primary neoplasm or as a secondary manifestation as part of non-Hodgkin lymphoma. (4)

Immunohistochemistry can help diagnose large B cell lymphomas with positive CD 20.

Patient data immunohistochemistry

The patient had CD 20 positive cells, MUM 1 was diffusely positive with variable intensity in the tumor cells, CKc, CD10, CD3- positive in the tumor cells, positive in the associated small T lymphocytes. (5)

Common symptoms of malignant lymphomas involving the ovaries are abdominal or pelvic pain or mass of the ovaries presenting as advanced ovarian cancer, significant weight loss, asthenia, genital bleeding, pleural effusion, and marked elevation of CA-125, LDH or inflammatory syndrome.(6)

The Ann Arbor classification was performed in our patient and she was considered stage four with secondary ovarian

and breast involvement. The patient had a progressive disease despite chemotherapy and developed paraneoplastic ocular syndrome. The differential diagnosis with cavernous sinus aneurysm or thrombosis was made, the patient performed angio-CT with contrast substance with normal results. Another differential diagnosis left mesencephalic ischemic stroke, leptomeningeal infiltration, craniocerebral MRI with contrast substance was performed which refuted the diagnoses.(7)

CONCLUSIONS

Non-Hodgkin lymphoma as primary presentation to the ovary is rare, and multiple cell types should be investigated. Immunohistochemistry can help differentiate the subtypes like follicular lymphomas, large cell or Burkitt lymphoma. Secondary lymphoma is differentiated by primary lymphoma by disease free interval of at least 60 months for primary type. Other authors consider primary lymphoma of the ovary even though there is a spreading to the proximal tissues. The secondary manifestation to the ovary of a lymphoma can also be classified in two subtypes as a presentation of a non-detected extra-ovarian disease or as a presentation of a largely disseminated disease. Survival rates differ greatly from 80% to 30%. Patients should be treated with chemotherapy and can benefit from external radiation to the lymph nodes.

Informed Consent Statement: Informed consent was obtained from the patient involved in the study.

Conflicts of Interest: The authors declare no conflict of interest.

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