# Vaginal bleeding as a first symptom of malignant lymphoma: Case reports, diagnosis and successful treatment

**J. Sobotkowski[1], M. Błasińska-Morawiec[2], I. Dowgier-Witczak[3]**

*[1]Department of. Gynaecological Radiotherapy, [2]Department of Proliferative Diseases, [3]Department of Chemotherapy*
*Regional Oncological Center of Copernicus Memorial Hospital, Lodz (Poland)*

**Summary**

Uncommon pathologic changes of the uterine cervix are rare but not impossible. Described cases of cervical lymphoma indicate the necessity of great attention and careful diagnosis. A watchful examination, imaging procedures and detailed histopathologic findings are of crucial importance in treatment planning. Each of our three patients underwent different types of treatment. A proper choice of therapeutical methods is based on individual disease and patient performance status features. In our patients, chemotherapy, radiotherapy (brachy- and teletherapy) were considered and applied as the sole method or in combination.

*Key words:* Malignant lymphoma; Vaginal malignancy; Chemotherapy; Vaginal irradiation.

## Introduction

The vaginal wall is a rare place of primary lymphoma occurrence [1-3]. Diffuse large cell lesions, mainly of B-cell lineage, are relatively frequent in vaginal localisation. However T-cell angiocentric pleomorphic tumors have been described in the literature [4].

A basis for adequate treatment is a detailed patient examination and establishment of precise clinical stage. Use of modern imaging methods as CT or MRI are necessary [5]. Of great importance are extensive pathological examinations of surgical biopsy specimens. Experienced gynecologists and pathologists have to keep in mind that even such rare malignancies may occur in the vagina, and following microscopic examination immediate treatment is required.

## Case reports

*Case 1*

A 67-year-old woman complained of vaginal bleeding, increasing urinary retention and dysuria for at least four weeks before admission. She underwent TAH & BSO because of a large uterine myoma when she was 49. She suffered from arterial hypertension. A family history revealed breast cancer in her sister. General symptoms were absent. At presentation she was in good performance status (Zubrod 0). She had painless enlarged bilateral inguinal lymph nodes. There was no sign of respiratory or cardiovascular insufficiency. Blood pressure remained within normal limits. She had no palpable hepato- or splenomegaly. Gynaecologic bimanual examination revealed an extensiv, tough, uneven tumor of the vaginal vestibule. All distal walls of the vagina were infiltrated. The tumor was so painful and obturating vaginal light, that even under general anaesthesia the examination was impossible to perform. Immobile parametria were infiltrated bilaterally. No macroscopic changes were seen at the vaginal mucosa surface. Fine needle biopsy of the tumor mass was performed but cytological features were not characteristic of any malignancy. Surgical removal of the inguinal lymph nodes was done. Routine histopathological and immunohistochemical examination showed diffuse large B-cell non Hodgkin's lymphoma (CK-, LCA+, CD20+) according to the REAL/WHO classification. Morphology and biochemistry of peripheral blood and urine tests were within normal limits. Chest X-ray examination was normal. Computed tomography of the pelvis showed an irregular mass infiltrating the vagina, perirectal fat tissue, rectal wall and urinary bladder. Abdominal ultrasound showed no hepatosplenomegaly nor abdominal lymphadenopathy. A bone marrow biopsy did not show lymphomatous infiltration. Clinical staging according to the Ann Arbor classification was estimated as Stage II A "bulky" and the International Prognostic Index score was 2/5. Because of rapid tumor growth, polychemotherapy with a CHOP-Bleo schedule was started (cyclophosphamide, adriamycine at standard doses on day 1, bleomycine and vincristine on days 1 and 5, and 60 mg of prednisone was given orally days 1-5). The response to chemotherapy was very good. Tumor regression was confirmed ultrasonographically. After three courses a small residual infiltration of the urethra and levator anus muscle was detected. However, chemotherapy had to be withdrawn because of grade 3 cardiotoxicity. The treatment was followed by teleradiotherapy. The patient received a total dose of 30.0 Gy/t, in 15 daily fractions at 2.0 Gy, for three weeks. A-p and p-a portals (16 cm x 16 cm) were used. Photons of 12 MeV from a Neptune linear accelerator were used. Tolerance of radiotherapy was satisfactory. The patient has now been in a clinical remission for 12 months and remains under careful follow-up.

*Case 2.*

A 77-year-old female, para 2, presented a 6-week history of vaginal, lately profuse, bleeding. Her performance status was 1-sec on Zubrod's scale. Gynecological examination showed uterine cervix ulceration about 3.0 cm diameter. No fornice infiltration was seen. Both parametria on rectal palpation were thick, with limited movement features, and suspicious of neoplasmatic infiltration (sonographically confirmed suspicion). A cervical biopsy specimen revealed the diagnosis of diffuse large

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B-cell malignant lymphoma (L 26+, LCA+, CKMNF-). On the basis of all examination outcomes Stage IA, E and JPI 2/5 was established. Considering the high dynamics of disease development, the limitation to the true pelvis, and general contraindications to chemotherapy, the patient was qualified to undergo radiation treatment. She received external irradiation with gamma rays of $^{60}$Co to a dose of 40,0 Gy/t, in 20 daily fractions at 2.0 Gy, for four weeks with four opposite ap-pa fields covering the lymph nodes of this region. As a concomitant treatment high-dose brachytherapy was used. The patient was irradiated with an $^{192}$Ir uterine/cervical tandem, five weekly fractions of 7.0 Gy to a total 35.0 Gy dose. Therapy tolerance was good. At the end of irradiation complete regression was noted. She has been under observation for 48 months with no signs of recurrence.

*Case 3.*

A 59-year-old old woman with vaginal bleeding and enlargement of the left supraclavicular lymph nodes was diagnosed in 1998. Her performance status was good – Zubrod 0 and B – and symptoms were absent. Gynecological examination showed uterine cervix infiltration and thick left parametrium. A cervical biopsy specimen proved the diagnosis of high grade malignant lymphoma. Fine needle biopsy of the left supraclavicular lymph nodes showed the presence of suspicious cells. Abdominal CT and chest CT scans were normal. Bone marrow was not involved but the serum LDH level was increased.

Because of Stage III AE of disease the patient received combination chemotherapy according to the CHOP-B regimen – cyclophosphamide, doxorubicin, vincristine, prednisone, bleomycine. Complete remission of supraclavicular lymph nodes and uterine cervix infiltration were observed and confirmed at ultrasound examination after four cycles of chemotherapy. The LDH level also normalised. The patient received eight cycles of CHOP-Bleo treatment and was then started on gynecological brachytherapy. In high-dose rate iridium afterloading treatment she received three weekly fractions of 6.0 Gy (ref. Point A), which was an isodose 1.0 cm apart from the applicator surface and typical "pear shaped" volume around the uterus. Therapeutical isodose covered two-thirds of the vagina walls with adequate margins and the whole uterus. Tolerance of treatment was good. The patient has remained in complete remission since March 1999.

## Discussion

The incidence of nonepithelial tumors like lymphomas or other malignancies are rare in gynecological sites, but it does happen in clinical practice [5-8] . Extremely rare is Bartholin's gland lymphoma [10]. In the majority of patients in the literature the vaginal mucosa surface appears noninfiltrated [11]. In our first patient fine needle biopsy was of lower significance during diagnosis and a surgical biopsy was necessary. It is obvious that optimal diagnosis requires special strategies of diagnostic procedures, i.e., bone marrow biopsy, etc. and application of adequate treatment like chemotherapy, radiotherapy or a combination according to clinical indications. For instance in case 2, the patient was treated with radiotherapy alone because of I AE stage, whereas patients 1 and 3 received combined treatment using chemo- and radiotherapy. In these uncommon cases treatment depends on diagnosis, stage of disease and clinical status. In patient 1 chemotherapy was not completed because of her cardiovascular contraindications.

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Address reprint requests to:
J. SOBOTKOWSKI, M.D.
Dep. of Gynaecological Radiotherapy
Copernicus Memorial Hospital
Regional Oncol. Center
Ul I Paderewskiego 4,93 Lodz 509
(Poland)