

## The case of advanced primary squamous carcinoma of vagina in a woman previously treated surgically for cervical dysplasia

**Przypadek zaawansowanego pierwotnego płaskonabłonkowego raka pochwy u pacjentki leczonej w przeszłości operacyjnie z powodu dysplazji szyjki macicy**

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### Streszczenie

Pierwotny rak pochwy jest rzadkim nowotworem żeńskich narządów płciowych. Wśród czynników ryzyka rozwoju płaskonabłonkowego raka pochwy najczęściej wymienia się infekcję wirusem brodawczaka ludzkiego (HPV). Zapewne z tego powodu prawdopodobieństwo rozwoju pierwotnego raka pochwy jest większe u osób z wywiadem w kierunku nowotworów okolicy anogenitalnej, w tym raka szyjki macicy, oraz ich zmian prekursorowych, jak dysplazja szyjki macicy (CIN).

Niniejsza praca prezentuje przypadek pacjentki poddanej histerektomii z przydatkami z powodu nawrotowej dysplazji szyjki macicy. Pooperacyjne badanie histopatologiczne potwierdziło doszczętność zabiegu. U pacjentki po upływie ponad trzech i pół roku od operacji rozpoznano pierwotnego raka pochwy w stadium IVA wg FIGO. Pacjentkę poddano radykalnej operacji usunięcia 2/3 pochwy z fragmentem pęcherza moczowego oraz obustronnej systemowej limfadenektomii węzłów chłonnych biodrowych, zastonowych i pachwinowych, a następnie skierowano ją na radioterapię.

**Słowa kluczowe:** pierwotny rak pochwy, dysplazja szyjki macicy.

### Summary

The primary cancer of the vagina is a rare neoplasm of the female genital tract. Among all the risk factors for a squamous cell carcinoma of vagina, the human papillomavirus (HPV) infection is mentioned most frequently. Probably for this reason, the likelihood of development of primary cancer of the vagina is higher in women with the history of cervical dysplasia (CIN) and cancer.

The article presents the case of a woman who had a hysterectomy with bilateral salpingo-oophorectomy for recurrent CIN. The postoperative pathological investigation confirmed the completeness of the excision. Almost 3.5 years after surgery, the primary cancer of vagina (at the IVA stage according to FIGO) was detected. After ineffective chemotherapy (8 courses) the patient underwent the surgical removal of the upper 2/3 of the vagina, partial resection of the bladder with left ureteric orifice and ureter transplantation, and bilateral systemic pelvic and inguinal lymphadenectomy. Subsequently, the woman was referred for the external beam radiotherapy.

**Key words:** primary cancer of the vagina, cervical dysplasia.

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## Introduction

The primary cancer of the vagina is a rare neoplasm of the female genital tract. In the USA, approximately 1100 new cases are diagnosed every year, which accounts for about 0.3% of all cancers in women and about 1-2% of all gynecological malignancies [1]. In Poland in 2008, 84 new cases of this cancer were detected (0.13% of all cancers in women) [2]. Compared to patients with cervical cancer, the highest incidence of vaginal cancer is observed at a later age. The median age at the time of diagnosis is 48 for cervical cancer (3) and 68 for vaginal cancer [1, 3].

Among all risk factors for squamous cell carcinoma of vagina, the human papillomavirus (HPV) infection is mentioned most frequently. Probably for this reason, the likelihood of development of primary cancer of the vagina is higher in women with the history of anogenital malignancies [4]. Women with at least 2-month survival after the diagnosis of cervical cancer are at 16 times higher risk of primary vaginal carcinoma [5]. Other factors predisposing to this cancer include a large number of sexual partners, early sexual initiation, smoking [4], chronic vaginitis, endometriosis, hysterectomy for benign diseases and cervical irradiation [6]. Historically, intrauterine exposure to diethylstilbestrol was related with the extended risk of the adenocarcinoma of the vagina in young women [6].

The article presents the case of a woman who had hysterectomy with bilateral salpingo-oophorectomy (BSO) for recurrent dysplasia of the cervix, in whom almost 3.5 years after surgery, the primary cancer of vagina (at IVA stage according to FIGO) was detected.

## Case report

In June 1999, a 51-year-old woman was admitted to the Department of Gynecology and Menopausal Diseases of the Polish Mother's Memorial Hospital – Research Institute in Lodz due to the abnormal Pap smear (Pap III) suggesting cervical dysplasia. During pelvic examination, the presence of ectopia on the cervix was found. The transvaginal ultrasound scan showed no other abnormalities of internal genital organs. Cervix samples were taken and the curettage of both the cervical canal and the uterine cavity was performed. The pathological analysis revealed the presence of medium-grade cervical dysplasia (CIN2) restricted to the surface of the cervix. "Cold-knife" surgical conization was advised to the patient, which was performed in September 1999.

In February 2005, the patient was referred again to the Department because of subsequent abnormal cytology (HSIL according to the Bethesda system). Pathological examination showed the presence of high-grade dysplasia of the cervix (CIN3). Due to the age (57) and

recurrent dysplasia, the patient was qualified to hysterectomy with BSO. The analysis of the postoperative specimen confirmed the accuracy of initial diagnosis and the completeness of the excision of dysplasia. The presence of other pathology within the removed organs was ruled out. Except the routine control 1 month after the surgery, the patient did not attend on subsequent visits until November 2009, when she reported to the family doctor because of bilaterally enlarged inguinal lymph nodes. The node samples were taken for pathological investigation, which revealed the metastatic squamous cell carcinoma. The following gynecological examination showed the presence of papillomatous lesion of the vaginal vault, and the obtained samples confirmed grade G2 partly keratinized squamous cell carcinoma. The computed tomography (CT) scan allowed for visualization of a contrast-enhanced pathological mass (37 x 27 x 42 mm) localized in the vagina, as well as enlarged inguinal lymph nodes and a single probably metastatic left-side iliac node.

Despite the primary recognition of CIN, the lesion was treated as a recurrence of cervical cancer. From December 2009 to June 2010 at the Department of Gynecologic Radiotherapy and Brachytherapy of the Regional Centre of Oncology, Lodz, the patient underwent 8 courses of chemotherapy according to the PF protocol, based on 5-fluorouracil 1.3 g + Cisplatin 122.9 mg. A subsequent abdominal CT scan, which was performed in October 2010, indicated that satisfactory results of chemotherapy were not achieved. A previously described lesion had similar dimensions (55 x 36 x 31.3 mm) and was infiltrating the posterior wall of the urinary bladder. The patient was referred for the gynecological consultation. As a result, she was admitted to the Department of Gynecological Surgery of the Polish Mother's Memorial Hospital – Research Institute in November 2010. Pelvic examination revealed the presence of a bleeding papillomatous lesion on the left side of the vagina and the ipsilateral inguinal lymphadenopathy. Considering the clinical picture as well as re-analyzing the pathological specimens after hysterectomy with BSO of 2005, the diagnosis of recurrent cervical cancer was revised and the primary cancer of the vagina was diagnosed.

The patient was qualified for laparotomy, which revealed the presence of tumor infiltrating the vaginal vault and posterior wall of the bladder near the orifice of the left ureter, which was dilated. After the bilateral preparation of the ureters from the parametria on their course from the common iliac vessels to the vesical orifices, the resection of the upper 2/3 of the vagina together with the surrounding para-vaginal tissues was conducted. Then, the bladder was opened and a significant portion of its posterior wall along with tumor, left ureteral orifice and about 3 cm of ureteral distal end were resected within healthy tissues. The ureter was

catheterized with a double-J catheter and transplanted into the left part of the bladder fundus. The bilateral systemic iliac and obturator, followed by bilateral inguinal lymphadenectomy was performed as well. The pathological examination of the postoperative specimen confirmed the presence of a squamous cell carcinoma in the fragment of the vagina and in the wall of the urinary bladder. No cancer metastases have been detected in any of the 29 resected lymph nodes. In the enlarged left-side inguinal nodes, the lymphonodulitis was present. A month later, at the postoperative control examination, the patient presented with bilateral lymphatic cysts (lymphocele) in both groins. The woman was re-admitted to the hospital, where the surgical closure of the lymphatic vessels was successfully performed. After next 2 weeks, the double-J catheter was removed.

The patient was referred to the Department of Gynecologic Radiotherapy and Brachytherapy of the Regional Centre of Oncology, where she underwent an external beam radiotherapy (to the summary dose of 44.0 Gy/g). The treatment was well tolerated, and the control tests did not indicate the presence of an early recurrence or a residual tumor. The patient was subject to constant monitoring.

## Discussion

In the opinion of some authors, the diagnosis of primary cancer of the vagina in patients who had been treated previously for invasive cervical cancer should be applied only to those, in whom lesions of the vagina were detected later than 5 years after the previous diagnosis [7]. Probably according to this idea, our patient was treated in the Oncologic Centre for cervical cancer recurrence. However, the pathological diagnosis revealed high-grade dysplasia CIN3 instead of an invasive cancer in her case. The occurrence of vaginal cancer in women with the history of CIN should not simply mimic the principle adopted for cancer patients. The oncogenic HPV infection is the same risk factor for both CIN and vaginal cancer. Therefore, existence of the consecutive vaginal cancer in previously operated CIN subjects could rather be a consequence of undiagnosed HPV-mediated neoplasia developing in the vaginal vault after the surgery [8]. Moreover, more than 5 years have passed since the initial diagnosis of CIN and former surgery (1999) and 4 years and 10 months have passed since the latter surgery (2005). Under these circumstances, the diagnosis of the primary vaginal cancer appears to be justified.

According to the current FIGO classification, the presented case belongs to the IVA stage. The treatment of choice for vaginal cancer of this kind of advancement is combined brachy- and external beam teleradiotherapy. For less advanced cases (I – IIA FIGO), radical resection of the vagina alongside with adjuvant radiotherapy is

recommended [9]. The clinical picture and inefficient chemotherapy have forced us to use surgical treatment, even though the FIGO staging was higher. Such clinical approach is justified in individual cases [9]. The prognosis in vaginal cancer, as in many other cancers, depends on its clinical stage. The 5-year survival rate varies between 17% and 23%, depending on age. It is lower for lesions localized in the distal parts of the vagina [10, 11].

There are still no uniform rules for vaginal cancer prevention in women, who have undergone prior hysterectomy due to dysplasia or invasive cervical cancer. The simple and less controversial method is cytological investigation of the vaginal vault. Guidelines for the gynecologists in the UK leave the monitoring of women after cervical cancer treatment, including Pap smear and/or colposcopic examination, for individual consideration of the clinician [12]. In the USA, there is a recommendation to continue Pap smear screening after cervical cancer treatment as long as a general state of health allows the patient to benefit from the early diagnosis and treatment of vaginal cancer [13]. It is emphasized that the importance of vaginal cytology for early detection of recurrent cervical cancer is limited, and that vaginal Pap smear is aimed strictly to detect vaginal premalignant lesions and early cancer. Consequently, the screening should be performed no more frequently than once a year [14]. In women who were previously treated for cervical cancer the Polish Gynecological Society recommends vaginal Pap smear control every 12 months [15].

In women who have undergone hysterectomy for cervical dysplasia (CIN), especially for high-grade cases, the vast majority of vaginal dysplasia (VAIN) are recognized in the first 2 years after the surgery [16, 17]. Therefore, some authors advise that the vaginal Pap smear should be carried out once or twice a year for the first 2 years after the surgery. When the results indicate no pathology, the return to screening in a 3-year interval is recommended [16, 17]. In the UK, vaginal cytology is performed at 6 and 18 months after hysterectomy if the dysplasia has been removed completely. In the cases of incomplete resection or suspected tissue margins it is advised to screen the CIN2/CIN3 patient at 6 and 12 months after hysterectomy, and then annually for 9 consecutive years. In the cases of CIN1, the screening procedure should be repeated after 6, 12 and 24 months respectively [12]. In the USA, the follow-up for patients with CIN2/CIN3 is conducted at least for 10 years after the surgery [13]. The Polish Gynecological Society recommends that patients treated surgically for CIN ought to be investigated using Pap smear every 12 months [15].

Performing a routine Pap smear of the vaginal vault in women, who have undergone the hysterectomy for reasons other than malignant or premalignant cervical lesions, is much more questionable. Although many gy-

necologists are used to attributing a significant role to detection of precancerous changes for this procedure, there is an increasing number of reports about lack of its efficacy [19, 20]. In both the UK and the USA, it is not recommended to perform a routine Pap smear in this group of women [12, 13]. The Polish Gynecological Society's recommendations allow to abandon the annual cytological controls in this group of patients [15].

Due to the large surface and folding of vaginal walls, colposcopic evaluation of the vagina is a very tedious and time-consuming procedure. Therefore, it is often omitted in the daily practice, although in the opinion of some practitioners, it should be an integral part of everyday colposcopy [21]. Lesions in the vagina present similarly to those on the cervix. However, colposcopically they seem to be more advanced than cervical lesions of the same pathological degree of dysplasia [22]. The dysplasia and invasive cancer of the vagina occur most frequently in the upper one-third of the vagina [18]. Every abnormal Pap test result in women who have undergone hysterectomy for cervical dysplasia or invasive cervical cancer is an indication for colposcopic evaluation of vaginal walls and sampling.

The presented case clearly points out to the necessity to inform the patients treated surgically due to cervical dysplasia about the need of a routine gynecological control and vaginal vault cytology following surgery. Awareness of the risk of HPV infection for origin of premalignant lesions and squamous cell carcinoma of the vagina and vulva is important in the prevention of these cancers.

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