

# Critical analysis of cases of endometrial carcinoma of the uterine corpus incidentally diagnosed after incomplete surgery for other indications. Three case reports and a review of the literature

Małgorzata Gajewska, Mirosław Wielgoś, Grzegorz Panek

First Department of Obstetrics and Gynaecology, Medical University of Warsaw, Poland

## Abstract

Incidental diagnosis of endometrial carcinoma after the operation for presumed benign disease is rare. At present, there are no recognized guidelines on optimal management of uterine malignancy diagnosed after incomplete surgery for other indications and the reported experience is limited. Although the risk of histological diagnosis of endometrial carcinoma in the uterus removed for pre-operatively diagnosed benign disease is very low, one should always bear in mind that it may indeed occur. Omission of certain diagnostic procedures prior to hysterectomy may result in incidental finding of a malignancy at or after surgery, even when preoperative imaging studies reveal benign disease. Many centres develop their own strategies, although in most cases the adnexa and cervix are removed and thorough exploration of the abdominal cavity is performed. Also, in view of the technical difficulties involved in removing the uterus and adnexa via the vagina and a potential high risk of cancer either developing in the cervical stump or disseminated from inadvertently morcellated uterine fragments, one should carefully consider the potential benefits and risks of supracervical hysterectomy. We present three patients with endometrial carcinoma diagnosed after hysterectomy, who subsequently underwent completion surgery. A review of the literature follows, which presents opinions from international centres.

**Key words:** endometrial carcinoma, incomplete surgery, management.

## Introduction

Total hysterectomy is the most common treatment in patients with fibroids who present with pelvic pain or abnormal uterine bleeding and in women with atypical endometrial hyperplasia [1]. Endometrial hyperplasia is usually found in older, postmenopausal women and in cases of atypia, radical hysterectomy is the most appropriate management [2]. In cases of uterine fibroids, however, the extent of planned surgery depends on many factors. Often surgeons (and their patients) wish to retain the uterus or cervix or there are no apparent indications for removal of the adnexa at planned surgery for presumed benign disease. When unexpected malignancies are found at operation in the removed uterus, the uterine corpus or fibroids, the clinician has to decide what further management to choose. Uterine malignancies diagnosed at the time of surgery for benign disease are rare and there are no generally recognized guidelines on further treatment. We report on three patients with endometrial carcinoma diagnosed by final pathology of hysterectomy for other indications. The literature review is followed by the discussion of further treatment options for endometrial carcinoma

incidentally diagnosed in the removed uterus. We provide arguments against hysterectomy without adnexa in women with atypical endometrial hyperplasia, when the preoperative risk of endometrial cancer is high.

## Case description

### Case 1

A 51-year-old patient was admitted to the Department of Operative Gynaecology in August 2013 for completion surgery. Past obstetric and/gynaecological history: gravida 2, para 1; cyclic hormone replacement therapy for the past 4 years. No relevant medical history. In July 2013, at initial surgery, the uterine corpus and Fallopian tubes were removed via laparotomy and the indications for surgery included pelvic pain and abdominal distension due to fibroids. The operation was performed without previous dilatation and curettage (D&C) despite metrorrhagia. A G1 endometrial adenocarcinoma of the uterine corpus was revealed by histological examination. The lesion was exophytic with minimal myometrial invasion. Fibroids – 4 cm in diame-

Corresponding author:

Małgorzata Gajewska, PhD, First Department of Obstetrics and Gynaecology, Medical University of Warsaw, 1/3 Pl. Starynkiewicza, 02-015 Warsaw, phone: +48 22 502 14 30, e-mail: ma.gajewska@gmail.com

Submitted: 22.06.2014

Accepted: 13.10.2014

ter. The margins along the paracervical and parametrial incision lines were free from malignancy.

On admission in August 2013, the incision wound of the abdominal wall was healed. On speculum examination, the vaginal part of the cervix was clear and the cervix was cylindrical in shape. There were no pelvic masses and the ovaries were nonpalpable. Laboratory investigations and ECG were all normal. Chest X-ray – normally aerated lung parenchyma without signs of consolidation. The patient qualified for an open procedure. At laparotomy: status post amputation of the uterine corpus; the bowel was adhered to the cervical stump; no abnormalities were detected in both ovaries, omentum, abdominal organs and abdominal and pelvic peritoneum. The cervix, ovaries, omentum and external iliac obturator lymph nodes were excised. There were no intra- and post-operative complications and on the 5<sup>th</sup> post-operative day the patient was discharged home in good general condition. Histology reports of the cervix, ovaries, omentum and lymph nodes were benign. The patient has been on regular follow-up.

### Case 2

A 67-year-old patient was admitted to the Department of Operative Gynaecology in January 2014 for completion surgery. Past obstetric and/gynaecological history: gravida 2, para 2; LMP, age 52. Treated for arterial hypertension and hypothyroidism. In August 2013, the patient underwent diagnostic D&C for uterine bleeding and histological examination revealed complex endometrial hyperplasia with high-degree atypia. Due to obesity (body mass index [BMI] of 35 kg/m<sup>2</sup>) and a potential high risk of incision wound dehiscence, a vaginal hysterectomy with adnexectomy was chosen and performed in October 2013. Due to considerable intraoperative blood loss, normal appearance of the adnexa in high position, adhesions and difficulty of adhesiolysis, the adnexa were not removed. The patient was discharged home on the 3<sup>rd</sup> postoperative day. A G2 endometrioid adenocarcinoma of the endometrium was diagnosed by histology. Invasion to less than half of the myometrium, but no cervical or parametrial involvement. After consultation at an oncology centre, the patient was referred for a repeat laparotomy after prior brachytherapy. At intervals of one week, she received three fractions of brachytherapy of 7.5 Gy each to the upper vaginal vault. The course of brachytherapy was uneventful and one week after its completion the patient was admitted to the Department of Operative Gynaecology. On pelvic examination on admission, the upper vaginal vault was healed without any palpable masses. Laboratory investigations, chest X-ray and ECG were all within normal limits. At laparotomy: status post-hysterectomy, pelvic and intra-abdominal peritoneum was smooth and the abdominal organs

were grossly unremarkable. The adnexa and external iliac obturator lymph nodes were removed bilaterally. There were no intra- and post-operative complications and the patient was discharged home on the 3<sup>rd</sup> post-operative day. On the 7<sup>th</sup> post-operative day the patient presented at the emergency department of the hospital with inflammatory infiltration of the incision wound and its partial disruption at the lower end for which antibiotic treatment was instituted. Histological examination did not reveal any cancer cells in the removed tissues. The patient has been on regular follow-up.

### Case 3

A 54-year-old patient was admitted to the Department of Operative Gynaecology in July 2013 for completion surgery. Past obstetric and/gynaecological history: gravida 2, para 2; LMP, age 50. Treated for arterial hypertension and type 2 diabetes. One month later, in August 2013, the patient underwent vaginal hysterectomy without adnexectomy for symptomatic uterine fibroids. The surgery was not preceded by D&C as there was no history of abnormal uterine bleeding. The uterus, due to its size, was morcellated during the procedure. Histological examination revealed a leiomyoma and a well-differentiated endometrial adenocarcinoma. Invasion of the myometrium was not reliably assessed.

On pelvic examination on admission, the upper vaginal vault was healed and there were no palpable masses in the pelvis. Laboratory investigations, chest X-ray and ECG were all within normal limits. The patient was referred for a laparotomy which revealed status post-hysterectomy; a 2-cm fibroid at the upper vaginal vault; the adnexa were grossly unremarkable; pelvic and intra-abdominal peritoneum was smooth; omentum and abdominal organs were grossly unremarkable. Bilateral adnexectomy and lymphadenectomy (external iliac obturator lymph nodes) were performed. Omentum and the fibroid were excised. There were no intra- and post-operative complications and on the 4<sup>th</sup> post-operative day the patient was discharged home in good general condition. Histological examination did not reveal any malignant invasion of the excised tissue. The patient was referred for adjuvant brachytherapy (three fractions of 7.5 Gy each to the upper vaginal vault).

### Discussion

In this paper we present three cases of suboptimal surgery for benign disease where final histological examination revealed endometrial carcinoma. This type of cancer was found after three different procedures: amputation of the uterine corpus, vaginal hysterectomy and vaginal hysterectomy with uterine morcellation.

Endometrial carcinoma is the most common gynaecological malignancy in Poland and affects mostly peri-

and post-menopausal women. The incidence of endometrial carcinoma has been dramatically increasing for the past 30 years, but the mortality rates do not change [3]. Uterine malignancies are diagnosed in 0.2-0.5% of women undergoing hysterectomy for presumed benign disease [4].

Despite the advances in operative techniques in recent years and the increasing tendency to limit the extent of surgery for benign disease, comprehensive surgical staging remains the most important prognostic factor in the case of malignant lesions while clinical staging alone is inadequate. Surgical staging, when incomplete for any reason, may either deprive the patient of a chance of appropriate adjuvant treatment or else subject her to needless radiotherapy or chemotherapy. Comprehensive surgical staging is particularly important in the case of tumours preoperatively assessed as early stage [5]. Thus, 19% of patients with endometrial carcinoma (clinical stage I in 3 patients, stage II in one patient) were upstaged (grade IIIc) at reoperation [6]. Therefore, comprehensive surgical staging should be performed in all patients with gynaecological malignancy, with the exception of cervical cancer.

According to Ayhan *et al.* [6], complementary surgical staging in patients with endometrial cancer may reduce the percentage of patients receiving adjuvant treatment as well as increase the rates of response to postoperative radiotherapy and 5-year survival. In a group of patients with endometrial carcinoma found in simple hysterectomy, who subsequently underwent surgical staging, nine out of 21 patients (43%) were treated with radiotherapy and the recurrence rate was 4.8% compared to the group which did not undergo reoperation where 74% (14/19) of the patients were treated with radiotherapy and recurrence was diagnosed in 10.5%, although the differences were not statistically significant ( $p > 0.05$ ). Also, there were no statistically significant differences in 5-year survival rates between the groups. Still, the authors believe that with the exception of well-differentiated cancers limited to the endometrium, patients with suboptimal surgical staging would benefit from complementary surgical staging. They argue that in patients undergoing simple hysterectomy without complete surgical staging, the recurrence rates tend to be higher and 5-year survival rates lower, although the differences are not statistically significant.

Total abdominal hysterectomy with bilateral salpingo-oophorectomy is a standard procedure in endometrial carcinoma. Lymphadenectomy in early stages of endometrial carcinoma is still a matter of dispute. Most authors do not find any justification for lymphadenectomy in cases of endometrioid carcinoma, shallow invasion of the myometrium and well-differentiated tumours (G1 and G2) [7]. The same applies to surgical restaging.

Only limited benefits of adjuvant radiotherapy for early (stage 1) endometrial carcinoma were found in the randomized, multicenter PORTEC trial in 715 patients with stage 1 endometrial adenocarcinoma and a moderate risk of recurrence. After hysterectomy with salpingo-oophorectomy, patients were randomized to two groups: with and without adjuvant radiotherapy. Although local recurrence was less frequent in the radiotherapy group, 5-year survival rates were similar [8].

Einstein *et al.* [9] report on 17 patients who underwent surgery for presumed benign disease but had evidence of endometrial cancer or leiomyosarcoma on final pathology. Surgical restaging procedure was performed in 13 patients and two (15%) were upstaged due to intra-abdominal dissemination of leiomyosarcoma originally resected with morcellation at laparoscopy. None of the patients, who initially underwent laparotomy, had malignant cells in tissues excised at reoperation. Reoperation included trachelectomy, when the cervix had been retained, and thorough exploration with lymphadenectomy performed in 12 of 13 patients. In no patient there was evidence of carcinoma *in situ* of the cervical stump on final pathology. Two patients, who did not undergo restaging surgery, received whole pelvic radiation therapy, although they had clinical stage I disease. One of them was subsequently diagnosed with a new cervicovaginal carcinosarcoma, which is a potential late complication of radiation therapy. The authors emphasize the value of thorough assessment of the clinical stage of disease and add that inadvertent morcellation of malignancy is associated with a high risk of dissemination of cancer cells.

Tumour upstaging at reoperation may be attributed to many factors. The stage may be incorrectly assessed at the initial surgery, the malignancy may progress between the two operations or its histology and biology may play a role [9]. It must be remembered that even with benign disease, uterine fragments morcellated at laparoscopy and scattered in the abdominal cavity can establish blood supply and grow. Similarly, inadvertently left behind fragments of malignant lesions can become implanted, grow and metastasize [9].

In the analysis by Theben *et al.* [10] including 1584 patients after amputation of the uterine corpus for benign disease, unexpected malignancies were diagnosed on final pathology in four patients (0.25%). In patients with endometrial carcinoma and leiomyosarcoma, reoperation involved removal of the cervical stump and adnexa, and numerous biopsies. Lymphadenectomy was abandoned in a patient with a FIGO IA G1 endometrial carcinoma and a patient with leiomyosarcoma although the uterine corpus was morcellated during removal.

Takamizawa *et al.* [4] found malignancy in 4 (0.4%) out of 923 patients undergoing simple abdominal hysterectomy for presumed benign disease. None under-

went reoperation. A patient with a FIGOIB G1 endometrial carcinoma received radiation therapy and she died 9 years later from sarcoma of the bladder. Two patients with a sarcoma were treated with chemotherapy.

According to Zanagnolo *et al.* [11], simple trachelectomy, staging and adjuvant radiation therapy or radical trachelectomy and staging are the optimal management for unexpected endometrial cancer in the uterine body removed for preoperatively diagnosed benign disease. Whole pelvic radiation therapy alone is not recommended when the extent of residual disease is not well documented.

The sensitivity of preoperative D&C of the uterine cavity is another important issue as a proportion of endometrial carcinomas remains undetected. According to Bansal *et al.* [12], approximately 10% of endometrial carcinomas and 36% of uterine sarcomas are undetected by preoperative endometrial sampling. Still, despite these statistics, when conservative surgery is planned, accurate pre-operative assessment must be performed, especially D&C of the cervical canal and uterine cavity.

Another important question is the validity of subtotal hysterectomy. The incidence of cervical cancer diagnosed in the cervical stump is 0.5-1%. With three normal cytologic smears, the risk decreases to 0.05% [13]. Total hysterectomy is preferred by some authors because it decreases the risk of dysplasia or cancer which could develop in the cervical stump, persistent bleeding or recurrent pelvic pain [14, 15].

Okaro *et al.* [16] analysed the outcome of 70 laparoscopic supracervical hysterectomies. Seventeen patients (24.3%) reported symptoms related to the cervical stump, mostly pelvic pain, dyspareunia and vaginal bleeding. The latter occurs in 2.4% to 31.4% of women with the retained cervix. Interestingly, of the 17 women who reported cervical stump symptoms, 14 had been treated for endometriosis in the past and in some of them there were endometriotic deposits affecting the cervical stump. The authors suggest that a history of endometriosis may be a contraindication for supracervical hysterectomy.

Women often want a procedure that retains the cervix because they believe it will preserve the sexual function. A questionnaire-based survey conducted in Poland showed that the opinions of women who had hysterectomy were related to the indications for the procedure [17]. Some studies show that total hysterectomy does not affect sexual satisfaction and libido [16, 18, 19]. According to Helström *et al.* [20], 21% of women who had amputation of the uterine corpus report deterioration in sexual function. The authors believe that the patient's sexual activity prior to hysterectomy is a strong predictor of sexual activity after the procedure. Advocates of supracervical hysterectomy claim that it is associated with fewer intraoperative complications and urinary problems and better preserved sexual function [21], but

these arguments have not been confirmed by clinical practice [22]. According to the opinion released by the American Congress of Obstetricians and Gynecologists (ACOG) in 2007, supracervical hysterectomy does not have clear benefits over total hysterectomy and should not be recommended as a superior technique [22]. Research shows that 24% of patients who underwent amputation of the uterine body required additional surgery for removal of the cervical stump [16]. Leaving the cervix intact should not be employed as a prophylactic measure to preserve urinary and sexual function [23].

## Conclusions

To sum up, although the risk of histological diagnosis of endometrial carcinoma in the uterus removed for pre-operatively diagnosed benign disease is very low, one should always bear in mind that it may indeed occur. Omission of certain diagnostic procedures prior to hysterectomy may result in incidental finding of a malignancy at or after surgery, even when preoperative imaging studies reveal benign disease. There is no recognised standard management of such patients and many centres develop their own strategies, although in most cases, the adnexa and cervix are removed and thorough exploration of the abdominal cavity is performed. Also, in view of the technical difficulties involved in removing the uterus and adnexa via the vagina and a potential high risk of cancer either developing in the cervical stump or disseminated from inadvertently morcellated uterine fragments, one should carefully consider the potential benefits and risks of supracervical hysterectomy.

## Disclosure

Authors report no conflicts of interest.

## References

- Polak G, Kotarski J. Rozród u kobiet z mięśniakami macicy. In: Kotarski J (ed.). Mięśniaki macicy (zeszyt edukacyjny). Ginekologia po Dyplomie 2006; 37-42.
- Malinowski A, Sobczuk A, Wilczyński J. Leczenie stanów przedrakowych błony śluzowej trzonu macicy. In: Markowska J, Mądry R (eds.). Zarys ginekologii onkologicznej. Tom II. Wydawnictwo Medyczne Termedia, Poznań 2012; 75-94.
- Wojciechowska U, Didkowska J, Zatoński W. Nowotwory złośliwe w Polsce w 2008 roku. Centrum Onkologii – Instytut im. M. Skłodowskiej-Curie, Warszawa 2010
- Takamizawa S, Minakami H, Usui R, et al. Risk of complications and uterine malignancies in women undergoing hysterectomy for presumed benign leiomyomas. *Gynecol Obstet Invest* 1999; 48: 193-196.
- Ayhan A, Celik H, Coskun F, et al. Restaging in gynaecological cancers. *Eur J Gynaecol Oncol* 2005; 26: 25-30.
- Ayhan A, Kart C, Guven S, et al. The role of reoperation in the management of endometrial carcinoma found in simple hysterectomy. *J Surg Oncol* 2006; 93: 373-378.
- Bieńkiewicz A, Wójcik-Krowiranda K. Leczenie operacyjne raka endometrium. In: Markowska J, Mądry R (eds.). Zarys ginekologii onkologicznej. Tom II. Wydawnictwo Medyczne Termedia, Poznań 2012; 95-105.

8. Scholten A, van Putten W, Beerman H, et al. Postoperative radiotherapy for Stage 1 endometrial carcinoma: long term outcome of the randomized PORTEC trial with central pathology review. *Int J Radiat Oncol Biol Phys* 2005; 63: 834-838.
9. Einstein M, Barakat R, Chi D, et al. Management of uterine malignancy found incidentally after supracervical hysterectomy or uterine morcellation for presumed benign disease. *Int J Gynecol Cancer* 2008; 18: 1065-1070.
10. Theben J, Schellong A, Altgassen C, et al. Unexpected malignancies after laparoscopic-assisted supracervical hysterectomies (LASH): an analysis of 1,584 LASH cases. *Arch Gynecol Obstet* 2013; 287: 455-462.
11. Zanagnolo V, Magrina J. Robotic radical trachelectomy after supracervical hysterectomy for cut-through endometrial adenocarcinoma stage IIB: a case report. *J Minim Invasive Gynecol* 2009; 16: 655-657.
12. Bansal N, Herzog T, Burke W, et al. The utility of preoperative endometrial sampling for the detection of uterine sarcomas. *Gynecol Oncol* 2008; 110: 43-48.
13. Scott J, Sharp H, Dodson M, et al. Subtotal hysterectomy in modern gynaecology: a decision analysis. *Am J Obstet Gynecol* 1997; 176: 1186-1192.
14. Gimbel H. Total or subtotal hysterectomy for benign uterine disease? A meta-analysis. *Acta Obstet Gynecol Scand* 2007; 86: 133-144.
15. Mettler L, Ahmed-Ebbiary N, Schollmeyer T. Laparoscopic hysterectomy: challenges and limitations. *Minim Invasive Ther Allied Technol* 2005; 14: 145-159.
16. Okaro E, Jones K, Sutton C. Long term outcome following laparoscopic supracervical hysterectomy. *BJOG* 2001; 108: 1017-1020.
17. Stadnicka G, Iwanowicz-Palus G, Mazurek A, Pięta B. Poczucie satysfakcji z życia u pacjentek po histerektomii. *Ginekol Pol* 2012; 83: 347-352.
18. Nathorst-Böös J, Fuchs T, von Schoultz B. Consume's attitude to hysterectomy: the experience of 678 women. *Acta Obstet Gynecol Scand* 1992; 71: 230-234.
19. Kilkku P, Grönroos M, Hirvonen T, Rauramo L. Supravaginal uterine amputation vs. hysterectomy. Effects on libido and orgasm. *Acta Obstet Gynecol Scand* 1983; 62: 147-152.
20. Helström L, Lundberg PO, Sörbom D, Bäckström T. Sexuality after hysterectomy: a factor analysis of women's sexual lives before and after subtotal hysterectomy. *Obstet Gynecol* 1984; 81: 357-362.
21. Lyons T. Laparoscopic supracervical hysterectomy. *Baillieres Clin Obstet Gynaecol* 1997; 11: 167-179.
22. Kill L, Kapetanakis V, McCullough A, Magrina J. Progression of pelvic implants to complex atypical endometrial hyperplasia after uterine morcellation. *Obstet Gynecol* 2011; 117: 447-449.
23. Kives S, Lefebvre G, Wolfman W, et al. Supracervical hysterectomy. *J Obstet Gynaecol Can* 2010; 32: 62-68.