CASE REPORT:

Abdominal skin metastasis in endometrial cancer

Eccita Rahestyningtyas[1], Pungky Mulawardhana[1*], Tomy Lesmana[2]
[1]Department of Obstetric and Gynecology, Faculty of Medicine, Universitas Airlangga, Dr Soetomo Hospital, Surabaya, Indonesia, [2]Department of Surgery, Faculty of Medicine, Universitas Airlangga, Dr Soetomo Hospital, Surabaya, Indonesia

ABSTRACT

Objectives: Surgical wound metastases in stage 1 endometrial cancer are possible, with a variety of different pathophysiological possibilities. Comprehensive management is needed to keep the patient on the possibility of a good prognosis.
Cases Report: During January 2015 – January 2018 at dr. Soetomo Hospital, there were 2 cases of metastatic endometrial cancer in the laparotomy wounds by which the condition is very rare. Case 1, The patient was diagnosed with endometrial carcinoma following the results of curettage. Anatomical pathology examination was done and obtained grade 2 endometrioid adenocarcinoma. In Case 2, the patient underwent Total Abdominal Hysterectomy and Bilateral Salpingo-Oophorectomy in 2013 at Mojokerto General Hospital, indicating Uterine Fibroids and Ovarian Cysts. The results of anatomical pathology examination were unknown. On April 2017, the patient complained abdominal swelling since 3 months ago.
Conclusion: In January 2015 - January 2018, 2 cases of metastatic endometrial cancer was found in a former laparotomy operation where this condition is very rare in endometrial cancer cases with low grade ,so that follow-up, monitoring and more vigilance are required in patients with low-grade endometrial Ca who have finished undergoing a surgery and chemotherapy. Rapture or mass resection, followed by external radiation, may be performed in patients with recurrence in the laparotomy wound area or in patients with high risk factors for endometrial cancer such as a history of estrogen use, tamoxifen, nullipara, obesity, diabetes mellitus, and family history of endometrial cancer. Currently, there is no fixed procedure (guideline) in RS. Dr. Soetomo to overcome recurrences especially in the scars of cancer surgery.

Keywords: endometrium carcinoma; endrometrioid; metastasis; abdomen; skin

ABSTRAK

Tujuan: Metastasis luka operasi pada kanker endometrium stadium 1 adalah hal yang mungkin terjadi, dengan berbagai kemungkinan patofisiologi yang berbeda – beda. Tatalaksana yang komprehensif diperlukan untuk tetap menjaga pasien pada kemungkinan prognosis yang baik.
Laporan Kasus: Di RS Dr Soetomo selama Januari 2015 – Januari 2018 didapatkan 2 kasus kanker Endometrium yang metastase di bekas luka operasi laparotomi dimana kondisi ini sangat jarang. Kasus 1 di diagnosa endometrium carcinoma setelah ada hasil Kuretase, kemudian dilakukan pemeriksaan PA didapatkan hasil Endometrioid Adeonocarcinoma grade II. Pada kasus 2, pasien menjalani operasi Total Abdominal Histerektomi dan Bisalphingo Oovorectomi pada tahun 2013 di RSUD Mojokerto dengan indikasi Myoma Uteri dan Kista Ovarium. Hasil PA saat itu tidak diketahui. Bulan April 2017 pasien mengeluh perut membesar sejak 3 bulan sebelumnya.
Simpulan: Dalam kurun waktu Januari 2015 - Januari 2018 didapatkan 2 kasus kanker endometrium yang metastasis di bekas operasi laparatomi dimana kondisi ini sangat jarang terjadi pada kasus kanker endometrium dengan low grade sehingga diperlukan follow up, monitoring dan kewaspadaan lebih pada pasien dengan low grade Ca endometrium yang telah selesai menjalani operasi dan kemoterapi. Pengangkatan atau reseksi massa diikuti dengan radiasi eksternal dapat dilakukan pada pasien-pasien dengan rekurensi di area laparatomi. Atau pada pasien dengan faktor resiko tinggi terjadinya kanker endometrium seperti adanya riwayat penggunaan estrogen, tamoxifen, nulipara, obesitas, diabetes mellitus, dan riwayat keluarga dengan kanker endometrium. Saat ini belum ada prosedur tetap (guideline) di RS. Dr. Soetomo untuk penanganan rekurensi terutama di bagian bekas luka operasi kanker.

Kata kunci: kanker endometrium; endometrioid; metastase; abdomen, kulit

***Correspondence:** Pungky Mulawardhana, Department of Obstetric and Gynecology, Faculty of Medicine, Universitas Airlangga, Dr Soetomo Hospital, Surabaya, Indonesia. Email: pungkym@yahoo.co.uk

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INTRODUCTION

Endometrial cancer is the most gynecological malignancy in developed countries and the second highest in developing countries. With endometrioid as the most common histological subtype, endometrial cancer actually has a good prognosis and is often diagnosed at an early stage due to complaints of abnormal uterine bleeding which is then curetted to obtain endometrial material which is then examined for Anatomical Pathology. While other histological subtypes (serous, clear cell, etc.) have a poor prognosis. About 54 thousand more new cases of endometrial cancer have been diagnosed in the United States in 2015 (3.3% of all new cancer cases), and of these cases, around 10 thousand will die of endometrial cancer (1.7% of the total death from cancer). [1]

The management of endometrial cancer in the early stages is mainly operative with the aim being the removal of the uterus and lymph nodes that may be involved, which is adjusted according to the subtype and histopathological degree. Surgery for early-stage endometrial cancer, although generally not as difficult as surgery for other gynecologic malignancies, certainly has risks, both before, during and after surgery. At present malignancy in early-stage endometrium is more often done by laparoscopic procedures with consideration of lower postoperative short-term complications compared to laparotomy and long-term complications that are not significantly different. [2] However, laparotomy is still performed in some cases, especially in cases where there is no suspicion of prior endometrial malignancy and endometrial cancer diagnosis is established after histopathological results are complete. Some operators also still perform laparotomy procedures in gynecological cases due to limited advice and infrastructure at the Hospital where the operation was performed.

The prognosis in endometrial cancer is determined by the stage of the disease and the type and degree of histopathology. Most women with endometrial cancer have a good prognosis because often endometrial cancer is found at an early stage and the most common type of histopathology is endometrioid. [1]

Metastasis in endometrial cancer has an incidence of approximately 30% of total cases with endometrial cancer, of which 21% metastases to the local lymph nodes and 9% distant metastases. [3] Metastases in post-laparotomy and laparoscopic surgical wounds have the same definition and pathophysiological basis. [4] Metastases in surgical wounds in endometrial cancer cases are still a rare occurrence. In this paper we will discuss two case reports regarding surgical wound metastasis in endometrial cancer planned for tumor resection by Digestive Surgery but due to the patient's condition it is not possible to operate so that these two patients are treated with External Radiation 25 times at Dr. Soetomo Hospital, Surabaya, Indonesia.

It is hoped that this paper can open the discourse that surgical wound metastasis in stage 1 endometrial cancer is possible, with a variety of different pathophysiological possibilities. Comprehensive management is needed to keep the patient on the possibility of a good prognosis.

CASE REPORT

Case 1 (Mrs. MA/43 years) was diagnosed with endometrial carcinoma after the results of curettage, then a PA examination showed grade II endometrioid adeonocarcinoma, then the patient was referred to the one-stop oncology clinic at Dr. Soetomo Hospital. The patient underwent Radical Hysterectomy, Bisalphingo Oovorectomy and Selective Lymphadenectomy on January 14, 2016 at GBPT.

PA results obtained endometrioid carcinoma endometrium grade III, tumors grow to> 1/2 myometrium thickness and are <1 mm away from the nearest serous sero (FIGO stage 1B). on 21-January-2016 control patients with complaints of wet surgery, it was decided to EBRT + Vaginal Brachytherapy with chemotherapy Paclitaxel - Carboplatin 6x (3 weeks). The patient underwent wound care using honey at POSA. July to August 2016 underwent ER 25x and AFL 3x. The patient complains of swollen feet and an enlarged abdomen. Pelvic MRI results showed suprapubic mass in the abdominal wall to cutaneous - subcutaneous size of 10x5.5x6.7 cm, performed FNAB abdominal wall mass obtained Adenocarcinoma results. In November 2017 the Mass Excision was planned by joint surgery with the Digestive Surgery division, but due to the inoperable mass the patient was treated with External Radiation. The patient underwent palliative radiation 25 times, but after that the patient never controlled anywhere. On April 3, 2018 the patient was declared dead at Soewandhie Hospital with the cause of death suspecting an advanced stage of malignancy.

Case 2 (Mrs. MM/52 yrs) patient underwent Total Abdominal Hysterectomy and Bisalphingo Oovorectomy in 2013 at Mojokerto Regional Hospital with indications of Myoma Uteria and Ovarian Cysts. PA results at that time were unknown. In April 2017 the patient complained of an enlarged abdomen since 3 months ago. Control patients to Sp.OG are advised for Paclitaxel-Carboplatin chemotherapy and FNAB has

been performed on the abdominal mass to obtain the results of Metastase Adenocarcinoma.

With the diagnosis at that time Ca Endomterium post TAH - BSO + post pacli carbo II + Subcutaneous Metastases. In April - July 2017 the patient received Paclitaxel - Carboplatin chemotherapy from the 3rd to the 6th, but the patient's condition after re-evaluation was diagnosed with Stable Disease. CT scan results of the abdomen and pelvis found a solid lesion with a cystic component in it, the wall of the anterior midline abdomen inferior side of the umbilicus, leading to the appearance of malignant soft tissue mass. Results of the Tumor Board of Dr. Soetomo's Oncology Division planned for tumor resection by the digestive surgery division of Dr. Soetomo Hospital.

On 29 - November - 2018, dick patients to POSA with complaints of growing stomach accompanied by open sores on the stomach. The patient was treated in the Peacock Room. Tumor Board was repeated on 06-December-2018, the patient was said to be Inoperable, planned by Cito Radiotherapy so that the mass did not touch the intestine because of Adenocarcinoma's response to Radiotherapy. Patients underwent radiotherapy 25 times during December 2017 - January 2018, patients were routinely controlled at POSA Dr Soetomo Hospital every 2 months or if there were complaints.

DISCUSSION

In the 2 case reports presented, describing patients undergoing post-chemotherapy laparotomy for grade I endometrial Ca, which results in metastasis in the surgical incision. Our case also shows that relapse of laparotomy wound in endometrial carcinoma can occur even in patients without unfavorable prognostic factors. This case further underlines the complexity of the mechanisms involved in the occurrence. Endometrial carcinoma can spread through several routes, depending on the type of histology and local invasion. The pattern of spread includes direct spread, lymphatic and hematogenous spread, and retrograde release of neoplastic cells through the fallopian tube. The anterior abdominal wall, especially the umbilical region, has a rich arterial supply, anastomotor venous tissue, and lymphatic system that flows cranially and caudally to several lymphatic chains including the pelvic lymph nodes and para-aorta. All of these systems can be involved in the dissemination of neoplastic cells into the soft tissue of the abdominal wall. Another explanation may be related to the direct expansion of peritoneal and spread through the rest of the embryo. Recurrence of endometrial cancer is most often localized in the vagina, pelvic lymph nodes and para-aorta, peritoneum, lungs, and liver. Unusual sites include the abdominal wall and muscles (2-6%), spleen (1%), central nervous system (<1%), extra-abdominal lymph nodes (0.4-1%), and more rarely, adrenal, pancreas, and appendicitis.

In this case and by considering its location near the umbilicus, the umbilical metastasis hypothesis can also be thought of as Maria Joseph Nodules, most typically appearing as an irregular lump in the umbilicus, ranging in size from 0.5 to 2 cm, although there are reports with nodules reaching up to 10 cm. May experience ulceration and necrosis and have bloody, mucinous, serous, or purulent fluid. This can be detected before or during the diagnosis of the primary tumor or after treatment. This umbilical metastasis is found in 1-3% of patients with gastrointestinal or genitourinary malignancies, including endometrial cancer. There are more than 30 cases reported in the literature originating from endometrial cancer. The presence of these nodules generally indicates advanced cancer with widespread metastases and shows a poor prognosis.

Figure 1. Maria Joseph Nodules

Figure 2. Second patient

Metastases in the abdominal wall are also associated with surgical incisions, regardless of the surgical approach (laparotomy or laparoscopy). The exact

mechanism of this event is usually explained by hematogenous spread to the site of trauma, seeding neoplastic cells after direct contact between the tumor and the wound, the effect of pneumoperitoneum, surgical techniques, and local immune response. Management of port-site metastases and recurrence of laparotomy wounds include extensive examination to rule out other metastases. In the absence of distant disease, surgical excitation and exploratory or laparoscopic laparotomy must be achieved. In this case, the first operation is vaginal, and the patient has no history of abdominal surgery, which discards this hypothesis.

Both of these cases were stage I Figo with low risk so it was decided to do Abdominal Histerectomy and Bilateral Salphingo Oophorectomy (TAH-BSO) with selective Lifadenectomy. Radical radiation or hysterectomy and pelvic lymphadenectomy are therapeutic options for localized endocervical adenocarcinomas, radical radiation or hysterectomy and pelvic lymphadenectomy are therapeutic options for endocervical adenocarcinomas which are still localized, whereas surgical staging includes simple hysterectomy and pelvic lymphadenectomy is a therapeutic choice for endocervical adenocarcinoma which is still localized, whereas surgical staging includes simple hysterectomy and pelvic lymphadenectomy. clear the aorta is a common management of endometrial adenocarcinoma. Laparoscopic staging with the aid of laparoscopy for stage 1 endometrial cancer has been widely reported, which includes vaginal hysterectomy with the aid of laparoscopy with pelvic and para-aortic lymph nodeectomy. [5] Grade tumor before surgery can also help in prioritizing patients for lymphadenectomy.

Low grade endometrioid cancer is the majority of endometrial cancer and is the most controversial group in surgical therapy. Many studies recommend lymphadenectomy for all grades of endometrial cancer. Several observational studies have found the benefits of lymphadenectomy in low grade tumors. However, another large study, in patients with preoperative stage I endometrial cancer with and without lymphadenectomy, found no difference in free-recurrence or overall survival.

In the two cases presented, the patient underwent chemotherapy and external radiation using External beam radiotherapy (EBRT) and vaginal brachytherapy and chemotherapy with Paclitaxel (Taxol ®) and carboplatin 6 times per 3 weeks followed by ER 25 times and AFL 3 times.

The patient underwent mass resection and continued with external radiation and from all of the above cases there was a disease free with no symptoms appearing after resection that was followed for several months except in case no 1. Treatment in these patients was optimal with the therapeutic results of these two patients improving with a smaller mass size. However, follow-up is still needed to see developments in both cases.

The two patients discussed in this case report compared risk factors that can cause recurrence, including older age. The first patient did not have a risk factor for recurrence in terms of age and type and grade of disease. Whereas in the second case there are several risk factors that can trigger a recurrence, including type and grade and histological type of Ca endometrium. Where in the literature it was found that patients who experienced a recurrence had significantly older age than patients without recurrence. In addition, the prevalence of low grade endometrioid carcinoma was significantly lower in patients who recurred (64.7%) compared to patients who did not (86.3%) ($p = 0.032$). Type I prevalence was also significantly lower in patients who experienced recurrence (42.3%) compared to patients who did not (75.4%) ($p <0.001$).

Recent studies report low levels of incisional recurrences (IR) (0.11%) in large numbers of patients with endometrial Ca who undergo open abdomen, laparoscopy, and robotic-assisted surgery. In fact, analysis of data available in the literature shows that primary surgery (ie, minimally invasive vs. open surgery) does not affect IR levels or significantly affect survival.

Patients who underwent minimally invasive surgery were more likely to have extrauterine disease at the time of primary diagnosis than those who underwent open surgery ($p = 0.01$). Insignificant results on age differences, International Federation of Gynecology and Obstetrics (FIGO) classes (G1 & G2 vs G3), or histological types (type I vs. type II) were observed. Events that could be considered as potentially beneficial factors in IR development described in 4 patients who had minimal surgical-site-hernia port surgery requiring reoperation ($n = 1$), uterine perforation ($n = 2$), and difficulties in uterine extraction ($n = 1$) (15, 25, 28, 32); None of these events were reported for patients who underwent open surgery ($p = 0.13$). The median (range) of time from major surgery to IR is significantly shorter after minimally invasive surgery than open procedures [11 months vs. 24 months; $p = 0.02$]. However, the primary surgery route did not affect the proportion of patients who survived (HR = 1.23; 95% CI, = 0.30-5.05; $p = .76$).

Table 1. Comparison of the cases

Cases	FIGO	EC therapy	Time ot metastasis	Location and characteristics	Therapies	Outcome
Saudi Med J 2017; 55 year, EC	Not explained	1.Abdominal histerectomy, 2.Adjuvant chemotherapy, 3.External radiation, 4.Vaginalvault brachytherapy	3 years	Wound infection with necrotic signs	1.Neoadjuvant chemotherapy 2.Surgical resection.	Wound size enlarged after 9-month follow-up
Oncology Letters, 2016 57 years	Stage IA grade 1	1.Total laparoskopic histerectomy (TLH) with BSO	7 months	Pain in iliac fossa near the port site, along with painful nodule	1.Skin defect treated with synthetic, nonabsorbable polypropylene mesh 2.Chemotherapy 3.External radiation	Disease free after 9 months with CA 125 examination negative
Int J Gynecol Cancer 2005 62 years	Stage IB, grade 1	1.Total histerectomy, bilateral salpingo-oophorectomy	3 years	The mass enlarged gradually at laparotomic wound site & lateral abdominal wall	1.Mass resection 2. Six-cycle chemoterapy with paclitaxel and carboplatin	Disease free after 24 months
Case reports in obstetrics and Gynecology, Hindawi 2014 66 years	Stage IB, grade 3	1.Vaginal histerectomy 2. External radiation 3. Brachytherapy	6 months	Painless nodule on anterior abdominal wall	1.Resection 2.Washing peritoneal and bilateral salpingo-oophorectomy	1 year after resection the patient became asymptomatic
Gynecol Oncol. 2003 64 years	Stage IIIA	1.Chemotherapy 2.Total abdominal histerectomy and bilateral salpingo-oophorectomy	6 years	Mass at surgical wound site sized 10-12 cm	1.Tumor removal 2. Radiotherapy	7 months post-therapy USG and CT scan showed no abnormality
Case 1 43 years	Grade II	Radical Histerectomy + Bisalphingo Oovorectomy + Limfadenektomi Selektif	19 months	Mass in umbilical area of surgical wound site + DVT	1.External radiation	Reduced mass
Case 2 52 years		TAH-BSO	4 years	Abdominal enlargement	1.External radiation	Reduced mass

Table 2. Clinicopathological characteristics

Clinicopathological characteristics	P value	Case I	Case II
Age (years)	0.042	43	52
BMI (Kg)	NS	30.46	28.75
DET	NS	-	-
Ca 125	NS	-	-
Histology Endometroid Non-endometrioid	0.006	Endometroid	endometroid
Grade Low grade High Grade	0.032	Low grade Grade 1	High grade Grade 3
Histological types Type 1 Type 2	< 0.001	Tipe 1	Tipe 2
Extrogen receptor expression Positive Negative	0.010	-	-
Progesteron receptor expression	0.007	-	-

Metastasis at the surgical site or port site in laparoscopy is a frequent complication in the field of gynecological oncology and has been reported in the literature to have an incidence of up to 16%. Factors contributing to this metastasis are divided into three categories including: 1) related to surgery, 2) related to surgical wounds and 3) related to tumors. Based on several experimental studies and case reports, many theories were put forward regarding the ability of tumor cells to spread to surgical wounds. The "tumor cell entraptment" hypothesis, which had been proposed since 1989, revealed that free cancer cells were able to attach to the surface of tissues including the damaged surface of the peritoneum. In the post-operative period these are covered by fibrin exudates which can protect tumor cells from the body's resistance mechanisms. In instrumental laparoscopic attachment directly from the side of the trocar, the presence of a pneumoperitoneum can cause a 'chimey effect' which can increase the attachment of tumor cells at the port site and the growth of malignant cells in the area of the laparascopic peritoneal perforation.

Several studies have found that the effects of carbon dioxide (CO2) pneumoperitoneum and wound closure techniques (skin taps alone compared to all layers) can affect the attachment of tumor cells. Where the number of tumor cells that stick higher in the skin closure technique only. Other studies have found that laparoscopy using less gas can reduce the attachment of tumor cells. Several articles reported that cases with metastasi that occurred at laparascopi port sites found that 71% of cases were caused by network manipulation at the port-site location. Significant reduction was found in the incidence of port site metastases in mouse models by dilution using povidine-iodine which was insulated in the peritoneal cavity. By using the murine model, it was found to prevent this metastasis by giving intraperitoneum injection using anti-adhesion molecules. Other studies have also suggested the antiproliferative effects of aspirin and indomethacin on tumor cells in vitro and in vivo and the potential of these drugs to inhibit port site metastasis and intraperitoneal metastases. However, this has not been recommended for clinical use as a confirmation of metastasis. Some researchers suggest that contraindications for laparoscopy are patients with ascites conditions for laparoscopy in patients with anxiety.

CONCLUSION

In the period of January 2015-January 2018, there were 2 cases of metastatic endometrial cancer in the former Laparatomy surgery where this condition was very rare in cases of low grade endometrial cancer so that follow-up, monitoring and more vigilance were observed in patients with low grade Ca endometrium finished undergoing surgery and chemotherapy.

Mass removal or resection followed by external radiation can be performed on patients with recurrence in the area of the laparatomy. Or in patients with high risk factors for endometrial cancer such as a history of estrogen use, tamoxifen, nulliparous, obesity, diabetes mellitus, and a family history of endometrial cancer. At present there are no fixed procedures (guidelines) in hospitals. Dr. Dr. Soetomo for handling recurrence, especially in the endometrial cancer surgery scar, it is hoped that guidelines can be made for the treatment of endometrial cancer that has recurrences in the surgical wound.

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