European Journal of Gynaecological Oncology

IMR Press

Case Report

Port site implantation of clear cell carcinoma after laparoscopic ovarian cystectomy

Joseph J. Noh[1], Kyue-Hee Choi[2], Hyun-Soo Kim[2], Jeong-Won Lee[1,*]

[1] *Department of Obstetrics and Gynecology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 06351 Seoul, South Korea*

[2] *Department of Pathology and Translational Genomics, Samsung Medical Center, Sungkyunkwan University School of Medicine, 06351 Seoul, South Korea*

*Correspondence: garden.lee@samsung.com (Jeong-Won Lee)

DOI:10.31083/j.ejgo.2021.01.2209

Submitted: August 03, 2020 Revised: October 18, 2020 Accepted: October 20, 2020 Published: February 15, 2021

Despite the fact that laparoscopic surgery has clearly shown benefits in patients with benign ovarian tumor, concerns remain regarding port site metastasis especially when final pathology reveals malignancy. Port site metastasis has been reported in early stages of malignant diseases. However, to our knowledge, there are no reports of port site implantation of malignant cells after laparoscopic surgery for benign disease. We present a 39-year-old woman who had undergone laparoscopic ovarian cystectomy for benign disease, and developed clear cell carcinoma at the site of trocar insertion 11 months after the initial operation. It is possible that the cancer was missed at the time of the initial surgery. Numerous factors have been suggested in the development of port site metastasis including aerosolization of tumor cells, lack of local immune response by the host and unskilled surgical techniques. A careful preoperative evaluation and meticulous laparoscopic maneuvers are the best way to prevent such occurrence.

Keywords

Laparoscopy; Port site metastasis; Clear cell carcinoma; Ovarian cancer

1. Introduction

Laparoscopic surgery has been used for treatment for the past 30 years in gynecology. Despite the undebatable advantages of laparoscopic surgery, surgeons expressed concerns regarding peritoneal dissemination of tumor cells and port site metastasis especially when this surgical technique was first implemented. Many researchers have suggested surgical manipulation techniques to minimize poor outcomes associated with laparoscopic surgery in cancer patients [1, 2]. In the present study, we report a case of woman who had received laparoscopic benign ovarian cystectomy, but later developed port site implantation of clear cell carcinoma. We also reviewed the pertinent literature and summarized surgical techniques to reduce such outcomes.

2. Case report

A 39-year-old unmarried nulliparous woman visited our institution for evaluation of a palpable mass on the left lower quadrant (LLQ) of her abdomen. She had no significant past medical history except for a laparoscopic bilateral ovarian cystectomy 11 months ago at a local gynecologic clinic. The resected cysts were reviewed by an expert pathologist with specialty in gynecologic diseases, and it reported a right benign serous cystadenoma and a left hemorrhagic corpus luteal cyst. The operation had been performed with three trocars - one 10-mm umbilical port and two 5-mm ports at the suprapubic area and the counter-McBurney site. The cyst was removed from ovarian parenchyma without rupture and kept in an endo-bag without any gross spillage until the complete removal from the abdominal cavity. No other abnormal findings were seen in the abdominal or pelvic cavity during the initial operation according to the operation records. The post-operative period was uneventful according to the patient. She had undergone a gynecologic ultrasound examination 5 months after the operation and it did not reveal any abnormalities in the pelvic organs. However, a small mass started to be palpated at the LLQ port site 7 months after the initial operation and it increased in size to about 8 cm in 4 months. Computed tomography (CT) of abdomen and pelvis taken 11 months after the operation revealed a 7.4 $\times$ 5.5 cm heterogeneously enhancing soft-tissue mass adjacent to the left rectus abdominis muscle (Fig. 1A). It also showed a 4.2 $\times$ 2.5 cm mass near the left external iliac artery with similar radiologic characteristics. Both ovaries did not show any abnormal findings (Fig. 1B). Pelvic magnetic resonance imaging (MRI) showed the LLQ mass at about 8.4 cm as well as a 4.6 cm mass in the left external iliac chain (Fig. 1C). No significant abnormalities were seen in the left ovary, but the right ovary was indistinguishable from adjacent adnexal structures. No other peritoneal seeding or lymph node metastasis were observed. The initial impression could not exclude the possibility of malignancy such as sarcoma with left external iliac lymph node metastasis. Therefore, she underwent a biopsy of the abdominal mass by using the 1 cm ACECUT needle (TSK Laboratory Europe B.V., Oisterwijk, Netherlands) (Fig. 1D). The pathology examination revealed poorly differentiated carcinoma. The immunohistochemistry of the biopsy showed positivity in PAX8, cytokeratin (AE1/AE3) and CK7 while negativity in CK20 was seen. The results of the immunohisto-

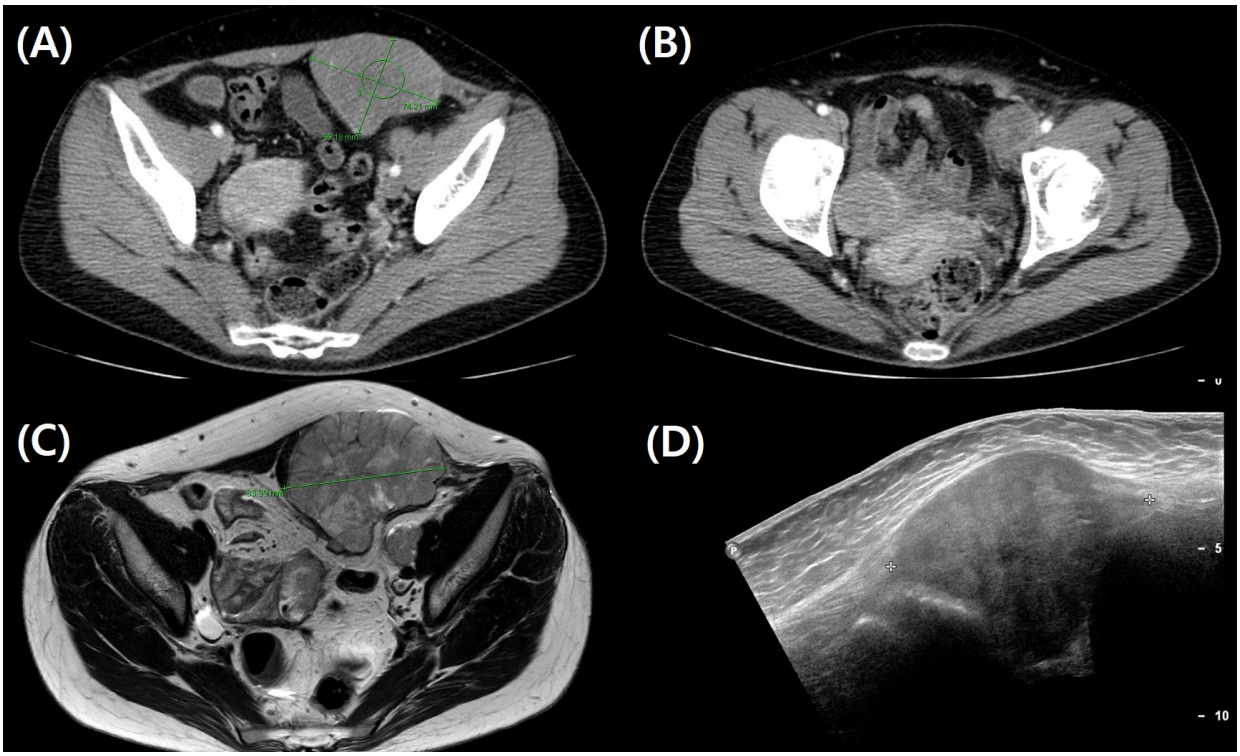

Fig. 1. (A) Abdomino-pelvic computed tomography (CT) shows a mass originating from the left lower abdominal wall that is measured 7.4 × 5.5 cm in diameter. This location corresponds to the site of trocar insertion in the previous laparoscopic surgery; **(B)** Abdomino-pelvic CT shows no specific findings in the right ovary; **(C)** Abdomino-pelvic magnetic resonance imaging (MRI) showing the mass in the abdominal wall; **(D)** Transabdominal ultrasound imaging of the mass in the abdominal wall taken during the needle biopsy.

chemistry were able to exclude a malignancy of gastrointestinal origin. No significant elevation of tumor markers including alpha-fetoprotein (AFP, 5.6 ng/mL), carcinoembryonic antigen (CEA, 0.5 ng/mL) or cancer antigen (CA) 19-9 (1.2 U/mL) were seen but CA 125 was mildly elevated to 78.8 U/mL. She underwent positron emission tomography (PET), which revealed a hypermetabolic uptake in the LLQ mass and left external iliac chain. Given the rapid growth of the lesion, she underwent an exploratory laparotomy under the presumed diagnosis of gynecologic malignancy. At surgery, a ruptured 9 cm whitish and friable mass was adhered to the peritoneal wall of the left rectus abdominis muscle inside the peritoneal cavity, which was excised with muscular fascia left intact. Despite the fact that the pre-operative imaging showed no abnormal findings of both ovaries, the right ovary was found 4.0 × 4.0 cm in size with capsular rupture by lesion suggestive of malignancy. It was sent for frozen section, which revealed poorly differentiated carcinoma. The left ovary contained a 1 cm endometriotic cyst but otherwise seemed normal. Prior to the operation, the patient requested for saving fertility and not to perform staging laparotomy, therefore complete staging operation was not performed. Instead, she underwent left abdominal wall mass excision, right salpingo-oophorectomy, left ovarian cystectomy, left pelvic lymph node dissection, left external iliac chain mass removal, and infracolic omentectomy. The left pelvic lymph node dissection was performed because we could not exclude the possibility of left pelvic lymph node metastasis of malignancy considering the anatomic proximity of the enlarged pelvic mass. We performed infracolic omentectomy because partial omentectomy did not carry significant increase in surgical complications or clinical consequences while it could sufficiently eliminate potential remaining malignant lesion when considering the surgical findings of the patient that did not show peritoneal seedings or involvement of lesions other than the pelvic cavity and the trocar site abdominal wall. On gross examination, the right ovary measured 4.0 × 4.0 cm with capsular invasion. The final pathology report revealed clear cell carcinoma of the right ovary with surface involvement and capsular rupture. The right fallopian tumor did not show any involvement of tumor. The left pelvic mass that was seen near the external iliac artery measured 7.0 × 6.0 cm. The mass showed involvement with cancer cells along with endometriosis and inflamed granulation tissue on the final pathologic examination. The abdominal mass measured 10.0 × 10.0 cm with the involvement of clear cell carcinoma (Fig. 2A). The omentum, peritoneal biopsies taken from several anatomic locations, and washing cytology all revealed no evidence of malignancy. Because the patient did not undergo complete surgical staging, the final FIGO (Fédération Internationale de Gynécologie et d'Obstétrique) stage remained incomplete. However, based on the surgical and pathologic

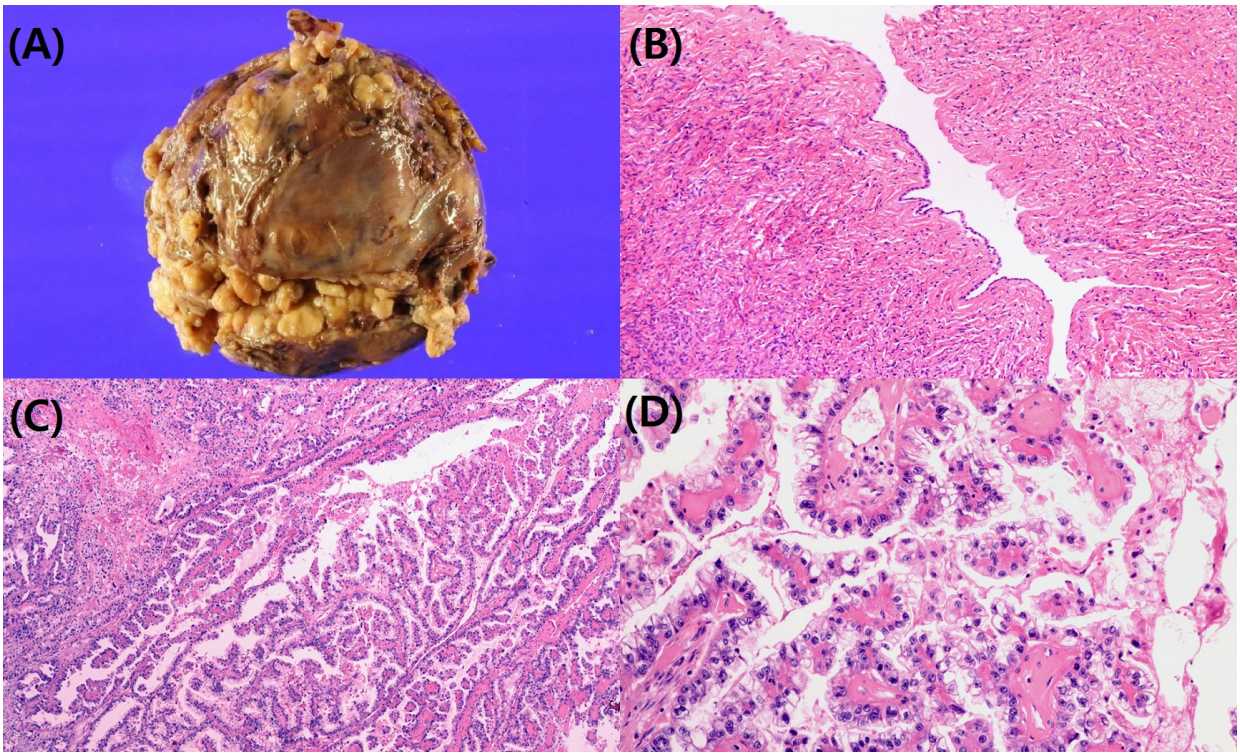

Fig. 2. (A) The mass removed from the left lower abdominal wall that is measured at 10 cm in diameter. Whitish and friable mass was excised with muscular fascia left intact; **(B)** Representative photomicrograph showing serous cystadenoma from the previous operation (100×); **(C)** Representative photomicrograph showing clear cell carcinoma (40×); **(D)** Representative photomicrograph showing clear cell carcinoma (200×).

findings obtained, it was supposed that she had clear cell carcinoma of right ovary with FIGO stage IIIC. After the final diagnosis of clear cell carcinoma, the tissues obtained from the previous ovarian cystectomy were re-reviewed along with the tissues obtained from the present operation. (Fig. 2B-D). It confirmed the diagnosis of benign serous cystadenoma of the past operation. The post-operative days were uneventful and she was recommended to undergo adjuvant chemotherapy with paclitaxel and carboplatin but the patient refused further treatment. Therefore, she was scheduled to be followed up in the outpatient clinic with CT evaluation. The last CT and serum tumor marker (CA 125) taken 12 months after our operation showed no evidence of recurrence.

3. Discussion

In the present study, we reported a case of the implantation of malignant cells at the trocar site from previous surgery, in which the pathology evaluation had revealed a benign disease. There are two possible explanations for this occurrence. One explanation for this occurrence is that the clear cell carcinoma was present at the time of the first operation, co-existing with the serous cystadenoma, and it was not removed. There is an association between clear cell carcinoma and endometriosis, which this patient also had. Therefore, it is unlikely that this is malignant transformation of benign serous cells that implanted at the port site. It is more likely that the malignancy was present at the initial surgery and was missed. We usually do not perform deep serial sectioning on all specimens unless they demonstrate any possibilities of malignancy. Therefore, the occult lesion might have been missed on the initial pathology. Another possibility is that the implantation of ovarian tissue at the port site during the initial surgery might have undergone malignant transformation, although it is less likely. The lesson from this report is that all ovarian masses should be managed as if they carry malignant potential.

The laparoscopic approach is now considered the standard surgical care for many benign gynecologic diseases [3, 4]. Indications for laparoscopic surgery have even extended to various gynecologic malignancies [5–8]. However, there have been concerns about port site metastasis, risk of spillage, effects on patient outcome, and the possibility of incomplete tumor staging. The true incidence of port site metastasis is unclear. Long-term follow-up results are lacking, and the clinical significance remain controversial. Literature reports an incidence around 2% for port site metastasis in gynecologic cancer, but numbers vary depending on patient selection and the definition of port site metastasis [1, 9, 10].

Numerous factors have been implicated in the development of port site metastasis including aerosolization of tumor cells, tumor implantation at the port site by direct contamination, lack of local immune response and surgical techniques performed by those who do not have enough experience in laparoscopy. High concentrations of angiogenesis and growth

factors at the port site due to the healing process can promote the implantation and proliferation of malignant cells with high metastatic potential [11]. In addition, failure of activation of the immune system at the port sites encourages tumor growth [12]. Preclinical data suggest that the effect of laparoscopic surgery on the antitumor immune response differs from that of open surgery. Carbon dioxide (CO_2) pneumoperitoneum inhibits macrophage and neutrophil function and reduces tumor necrosis factor (TNF) production [12].

Preventive measures that have been proposed include minimizing tissue trauma at the transfer of instruments, rinsing the trocars and the instrument tips in povidone-iodine, topical treatment of port sites with cytotoxic agents (i.e., 5-FU (Fluorouracil)), removing all intra-abdominal fluid before trocar removal, and closure of peritoneal trocar sites of 10 mm or more [1, 13]. Avoidance of the rupture of removing tissue and spillage has also been emphasized. Among various endeavors by surgeons to minimize the risk of trocar site implantation of malignancy, the finer control of tissue removal without rupture or spillage has been proposed as the most crucial consideration. Previous studies reported a wide range of spillage rates during laparoscopic management of adnexal masses from 12% to 25% [11, 14]. Although the rupture and spillage of the contents of benign mass such as cystadenoma or endometrioma would not result in significant clinical consequences, there always is the possibility of the presence of occult malignant cells with potential to transform if it is spilled in the peritoneal cavity, such as the present case. Therefore, it is important to avoid the spillage of adnexal mass even if it is suspected to be benign. Placing all the specimens in plastic endo-bags and removing them intact could decrease the possibility of spillage of tumor cells at the port sites because the effects of CO_2 pneumoperitoneum and its continuous flux in the abdomen could enable the spread of neoplastic cells freed by spillage [2, 15, 16]. A lower CO_2 pneumoperitoneum pressure and avoidance of subcutaneous emphysema could further decrease the risk of dissemination and implantation of tumor cells in the subcutaneous tissue. Slow and controlled release of the pneumoperitoneum with the trocars in place or lowering intra-abdominal pressure of CO_2 gas by suction before removing trocars could limit the contamination of the laparoscopic incisions with tumor cells. Finally, limiting the number of the port sites could also be considered.

Advanced disease with ascites and peritoneal seeding conveys a higher risk [12, 15] whereas early stage diseases seem to have low risk of port site metastasis [17]. However, port site metastasis has been reported in early stages of gynecologic malignancy such as FIGO stage IA of endometrial adenocarcinoma and node-negative IB1 cervical adenocarcinoma [18–21]. Moreover, as shown by the present case, it is possible to have port site implantation of malignant cells after laparoscopic removal of benign adnexal mass. Therefore, the current policy of many institutions including ours suggest to avoid the laparoscopic approach for adnexal surgery suspicious of malignancy. Laparotomy also carries the risk of implantation of malignancy at the incision site, but the incidence is lower and it better allows surgeons to perform maneuvers with control [22].

A careful preoperative evaluation and meticulous laparoscopic maneuvers are the best way to prevent such incidence. In addition, more studies are warranted to identify modifiable risk factors and develop methods for prevention and optimal management of port site metastasis.

Author contributions

The present study was designed, directed and coordinated by JL, as the principal investigator. JL provided conceptual and technical guidance for all aspects of the project. The pathology examinations were performed by KHC and HSK. The manuscript was written by JN and commented on by all authors. The authors meet the recommendations for the conduct, reporting, editing, and publication of scholarly work in medical journals provided by the International Committee of Medical Journal Editors.

Ethics approval and consent to participate

The need for ethics approval for the present study was waived by the Institutional Review Board of Samsung Medical Center. The consent for publication from the patient described in the present study has been obtained.

Acknowledgment

We would like to express my gratitude to all those who helped me during the writing of this manuscript.

Conflict of interest

The authors declare no competing interests.

References

[1] Ramirez PT, Frumovitz M, Wolf JK, Levenback C. Laparoscopic port-site metastases in patients with gynecological malignancies. International Journal of Gynecological Cancer. 2005; 14: 1070-1077.

[2] Wittich P, Marquet RL, Kazemier G, Bonjer HJ. Port-site metastases after CO_2 laparoscopy. Surgical Endoscopy. 2000; 14: 189-192.

[3] Mais V, Ajossa S, Guerriero S, Mascia M, Solla E, Melis GB. Laparoscopic versus abdominal myomectomy: a prospective, randomized trial to evaluate benefits in early outcome. American Journal of Obstetrics and Gynecology. 1996; 174: 654-658.

[4] Olsson J, Ellstrom M, Hahlin M. A randomised prospective trial comparing laparoscopic and abdominal hysterectomy. International Journal of Obstetrics and Gynaecology. 1996; 103: 345-350.

[5] Querleu D, Leblanc E, Castelain B. Laparoscopic pelvic lymphadenectomy in the staging of early carcinoma of the cervix. American Journal of Obstetrics and Gynecology. 1991; 164: 579-581.

[6] Childers JM, Brzechffa PR, Hatch KD, Surwit EA. Laparoscopically assisted surgical staging (LASS) of endometrial cancer. Gynecologic Oncology. 1993; 51: 33-38.

[7] Lee CL, Huang KG, Wang CW, Huang HY, Lai YM, Lai CH, *et al.* New approaches in laparoscopically assisted radical vaginal hysterectomy. International Surgery. 1998; 82: 266-268.

[8] Paolucci V, Schaeff B, Schneider M, Gutt C. Tumor seeding following laparoscopy: international survey. World Journal of Surgery. 1999; 23: 989-995.
[9] Nagarsheth NP, Rahaman J, Cohen CJ, Gretz H, Nezhat F. The incidence of port-site metastases in gynecologic cancers. Journal of the Society of Laparoendoscopic Surgeons. 2004; 8: 133-139.
[10] Zivanovic O, Sonoda Y, Diaz JP, Levine DA, Brown CL, Chi DS, *et al.* The rate of port-site metastases after 2251 laparoscopic procedures in women with underlying malignant disease. Gynecologic Oncology. 2008; 111: 431-437.
[11] Canis M, Rabischong B, Botchorishvili R, Tamburro S, Wattiez A, Mage G, *et al.* Risk of spread of ovarian cancer after laparoscopic surgery. Current Opinion in Obstetrics and Gynecology. 2001; 13: 9-14.
[12] Ramirez PT, Wolf JK, Levenback C. Laparoscopic port-site metastases: etiology and prevention. Gynecologic Oncology. 2003; 91: 179-189.
[13] Wang PH, Yuan CC, Lin G, Ng HT, Chao HT. Risk factors contributing to early occurrence of port site metastases of laparoscopic surgery for malignancy. Gynecologic Oncology. 1999; 72: 38-44.
[14] Havrilesky LJ, Peterson BL, Dryden DK, Soper JT, Clarke-Pearson DL, Berchuck A. Predictors of clinical outcomes in the laparoscopic management of adnexal masses. Obstetrics & Gynecology. 2003; 102: 243-251.
[15] Hopkins MP, Dulai RM, Occhino A, Holda S. The effects of carbon dioxide pneumoperitoneum on seeding of tumor in port sites in a rat model. American Journal of Obstetrics and Gynecology. 1999; 181: 1329-1334.
[16] Hewett PJ, Texler ML, Anderson D, King G, Chatterton BE. In vivo real-time analysis of intraperitoneal radiolabeled tumor cell movement during laparoscopy. Diseases of the Colon and Rectum. 1999; 42: 868-866.
[17] Lu Q, Qu H, Liu C, Wang S, Zhang Z, Zhang Z. Comparison of laparoscopy and laparotomy in surgical staging of apparent early ovarian cancer: 13-year experience. Medicine. 2016; 9: e3655.
[18] Grabosch S, Xynos F. Isolated port-site metastasis after robotic hysterectomy for stage IA endometrial adenocarcinoma. Obstetrics & Gynecology. 2013; 122: 437-439.
[19] Mautone D, Dall'asta A, Monica M, Galli L, Capozzi VA, Marchesi F, *et al.* Isolated port-site metastasis after surgical staging for low-risk endometrioid endometrial cancer: a case report. Oncology Letters. 2016; 12: 281-284.
[20] Muntz HG, Goff BA, Madsen BL, Yon JL. Port-site recurrence after laparoscopic surgery for endometrial carcinoma. Obstetrics & Gynecology. 1999; 93: 807-809.
[21] Deshmukh U, McAdow M, Black J, Hui P, Azodi M. Isolated port site recurrence of node-negative clinical stage IB1 cervical adenocarcinoma. Gynecologic Oncology Reports. 2017; 20: 54-57.
[22] Bogani G, Dowdy SC, Cliby WA, Gostout BS, Kumar S, Ghezzi F, *et al.* Incisional recurrences after endometrial cancer surgery. Anticancer Research. 2016; 35: 6097-6104.