

## Iatrogenic Tumor Implantation

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**ABSTRACT** Iatrogenic tumor implantation is a condition that results from various medical procedures used during diagnosis or treatment of a malignancy. It involves desquamation and dissemination of tumor cells that develop into a local recurrence or distant metastasis from the tumor under treatment. The main clinical feature of the condition is nodules at the operation's porous channel or incision, which is easily diagnosed in accordance with the case history. Final diagnosis can be made based on pathological examination. Tumor implantation may occur in various puncturing porous channels, including a laparoscopic port, abdominal wall incision, and perineal incision, etc. Besides a malignant tumor, implantation potential exists with diseases, such as a borderline tumor and endometriosis etc. Once a tumor implantation is diagnosed, or suspected, surgical resection is usually conducted.

During the diagnosis and treatment of diseases, avoiding and reducing iatrogenic implantation and dissemination has been regarded as an important principle for surgical treatment of tumors. In a clinical practice setting, if possible, excisional biopsy should be employed, if a biopsy is needed. Repeated puncturing should be avoided during a paracentesis. In a laparoscopic procedure, the tissue is first put into a sample bag and then is taken out from the point of incision. After a laparoscopic procedure, the peritoneum, abdominal muscular fasciae, and skin should be carefully closed, and/or the punctured porous channel be excised. In addition, the sample/tissue should be rinsed with distilled water before surgical closure of the abdominal cavity, allowing the exfoliated tumor cells to swell and rupture in the hypo-osmolar solution. Then surgical closure can be conducted following a change of gloves and equipment. The extent of hysteromyomectomy should as far as possible be away from the uterine cavity. The purpose of this study is to make clinicians aware of the possibility of tumor implantation and to give special attention to avoid, or reduce iatrogenic implantation during a surgical procedure.

**KEY WORDS:** iatrogenic tumor implantation, iatrogenic implantation, complication, prevention.

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### Introduction

An iatrogenic tumor refers to the implantation of malignancy, or cell exfoliation, or dissemination which can occur from various medical procedures during diagnosis, or treatment. It can cause the formation of a metastasis resulting in a local relapse, or distant metastasis of the tumor.

The major clinical feature of tumor implantation is a nodule of the neoplasm at the port-site, or incision, usually with a minor nodus as a first and inconspicuous symptom. It might be solitary or multiple, and

can grow rapidly, forming a hard, irregular, and painful, or painless nodus. It can be easily diagnosed based on the case history and final diagnosis can be made by pathological examination. A specific analysis of tumor implantation caused by common surgery was conducted as follows.

### Tumor implantation after various biopsies and paracenteses

Biopsy of a neoplasm includes the transfixion, incisional, and excisional biopsy techniques. An incisional biopsy needs dissection of the tumor capsule, which may cause tumor cell dissemination. Excisional biopsy is a biopsy with complete resection of the tumor, without an inward incision. The latter method may bring about the least tumor dissemination. So an excisional biopsy should be performed if the situation is appropriate.

In the case of a malignant tumor confirmed by pathological examination, if the surgery is performed as soon as possible after biopsy, the chance for tumor implantation is diminished. With a frozen biopsy which is available from the pathology laboratory of many hospitals, a diagnosis can be made within 30 min. The ideal way to treat the tumor, is to do the biopsy, diagnosis, and treatment within a short time span. Attention should be given to synchronous resection of the biopsy incision as the radical surgery is conducted.

The variety of paracenteses includes piercing biopsy, thoracic, abdominal, and cystic paracenteses etc. The purpose of the procedure is to obtain a diagnosis, or to reduce pressure and relieve symptoms. Qin et al.<sup>[1]</sup> reviewed a total of 29 cases from 15 articles in relation to the malignant tumor needle-track implantation in China, during the period from 1979 to 2006. The interval between the paracentesis and discovery of the tumor implantation ranged from 20 days to 780 days, with a median of 120 days. The diameter of the implanted tumor ranged from 0.5 cm to 10 cm. The ratio of liver and lung punctures ranked the first in the records of total puncturing sites, which were respectively 63% and 20%. The implantation sites included subcutaneous fatty tissue, thoracic muscular tissue, diaphragmatic muscle, costal bones, hepatic surface and peritoneum etc.

In the literature, the patients suffering from a tumor implantation caused by using a fine needle aspiration of less than 1.0 mm accounted for 50%, and 60% of the patients showed that they had a clear history of multiple punctures. Reports of Lv et al.<sup>[2]</sup> and Cheng et al.<sup>[3]</sup> indicated that the rate of needle track implantation ranged from 0.08% to 2.33% in the rate of total tumor implantations. The piercing frequency should be reduced for diagnostic punctures and the transfixion pin should be changed if repeated puncturing is done. After the point of the needle was withdrawn from the tumor, the removal of negative pressure did not decrease needle track

implantation, but favored it. However, it allowed some samples to be left in the injection unit which resulted in a difficulty in removal of a sample by suction and frequent failure in obtaining a sample. This gave a high, false positive diagnosis while avoiding a false negative.

Mechanisms which produce needle-track implantation, following pleural fluid and ascites punctures, include the following: *i*) transfixion pin causing damage to the tissues near the needle track and blood capillary, and the regional host-immuno-suppressive action and growth factor released from the regenerated tissue promotes the growth of tumor cells; *ii*) when the transfixion pin is withdrawn, the tumor cells are released into the needle track; *iii*) a large amount of pleural fluid and ascites is produced, which increases the intracavitary pressure and retards healing of the needle track.

Du et al.<sup>[4]</sup> reported 13 cases with needle track implantation after cancerous ascites puncture. These implantations occurred at a period from day 3 to 75 following a multiple bodkin needle puncture, with an average of 14 days. On clinical observation and evaluation it was found that 84.6% of the cases experienced puncture-site pain and nodi occurred in 100% of the cases.

Repeated piercing should be avoided during puncturation, thus preventing needle track implantation. For remedial piercing in the case of liver cancer, it is recommended that absolute ethanol be injected when withdrawing the needle in order to seal the needle track, and to coagulate and destroy the malignant tumor cells introduced into the needle track.

### Penetration point implantation following a laparoscopic operation

With improvement of the laparoscope and its technology, laparoscopic surgery has been used on some benign and malignant tumors. Han et al.<sup>[5]</sup> have set up an animal model using the aeroperitoneum to compare the laparoscopic procedure and laparotomy. This comparison showed that there is no significant difference in the tumor-cell implantation and organ-metastatic rate between the two surgical methods. However, a big difference still remained between the simulated and real laparoscopic procedure, and it was reported in the literature<sup>[6-9]</sup> that various laparoscopic procedures could bring about tumor implantation in the abdominal-wall puncturing track. The mechanisms for an easy implantation at the point of the laparoscopic surgery are as follows: *i*) the laparoscope increases the opportunity of tumor cell exfoliation; *ii*) repeated contact between the medical instrument contaminated with tumor cells, and the piercing point, and *iii*) exfoliation of the malignant cells while taking out the excised tissue at the point of puncturation.

Meta-analysis was done by Ramirez et al.<sup>[6]</sup> comparing 58 patients in 31 English articles where there was

implantation at the penetration point following laparoscopic surgery of malignant gynecologic tumors. See Table 1 for the penetration point implantation following laparoscopic surgery of various gynecological tumors. Among the cases in Table 1, 40 underwent surgery for ovarian cancer (7 junctional and 33 malignant tumors), of which 83% were in an advanced stage and 71% had ascites. Multiple foci were found in 97% of the cases, and single implantation in 71%. For the other cases in the Table 1, 12 were uterine-cervix cancer cases, of which 80% were squamous cancer, and 4 corpus carcinoma, 1 carcinoma of the fallopian tube and 1 vaginal carcinoma. The analysts pointed out that after laparoscopic surgery the penetration point implantation was a potential complication in early cases.

Fan et al.<sup>[7]</sup> reported 3 metastatic tumors resulting front penetration point implantation in laparoscopic cholecystectomy of carcinoma of the gallbladder. In our patients 5 months after laparoscopic cholecystectomy, a regional metastasis in the right subdiaphragmatic peritoneum was found resulting in the death of the patients 19 months later. In another case of a gallbladder cholecystic polypus with accompanying carcinoma, a 31-month survival was achieved following laparotomy. Therefore, laparotomy is preferred over laparoscopic cholecystectomy if carcinoma of the gallbladder is suspected.

Based on the literature<sup>[9,10]</sup>, the incidence of penetrating point implantation of carcinoma from laparoscopic surgery was very high. However it should not affect the prognosis for a suitable treatment. Vergote et al.<sup>[9]</sup> reported that after undergoing an open laparoscopic operation, 71 of the 173 patients with FIGO Stage III-IV ovarian cancer received a total puncturing port-site resection during the cytoreductive surgery. The puncture point implantation was found in 30 of the total 173 cases, of which 8 were found by clinical diagnosis and 22 by final pathological diagnosis. These analyses showed that the clinical indices included the priority for surgery, or chemotherapy group, ascites, etc. There was no correlation between the FIGO Stage IV and the puncture point implantation and its median time. All the puncture point implantations disappeared after the resection, and no recurrence occurred. The prognosis was similar to cases without puncture point implantation.

Van Dam et al.<sup>[10]</sup> reported that suturing the full-thickness of the abdominal wall could reduce the penetration point implantation. These included 83 cases with a primary advanced ovarian cancer, and 21 cases with

recurrent ovarian cancer. Puncturing point implantation occurred in a 58% of the cases (7/12) with only skin closure, and the implantation percentage only accounted for 2% of the cases (2/92) with suture of the full-thickness of abdominal wall. Analysis indicated that the prognosis of the patients with suture of the full-thickness of the abdominal wall was similar to other patients (i.e. without previous implantation). Therefore it is recommended that treatment of advanced ovarian cancer, with a laparoscopic operation, chemotherapy should be implemented after a careful closure of the peritoneum, muscular fasciae, and skin. Cytoreductive surgery should be performed within a week following the closure, with resection of the puncturing porous channel. Iatrogenic implantation and dissemination could also be decreased by putting the cancerous tissue into a sample bag and then removal through the puncture point.

### Tumor implantation at the abdominal-wall incision

Zhang et al.<sup>[11]</sup> analyzed 10 cases with abdominal-wall incision implantation and metastasis following surgery for carcinoma of the bladder, with an abdominal-wall metastasis of (1.0~6.9) cm × (1.4~11.5) cm. Seven of the cases resulted in deaths. It was concluded that there was usually a poor differentiation of the abdominal-wall incision implantation and metastatic carcinoma, or a complication with other cancers. Although surgery and adjuvant radio-chemotherapy could prolong the patient's survival, however the prognosis was poor. Exploratory surgery should be conducted on distant organs and pressure on the tumor should be avoided. Preventing or limiting an intraoperative exfoliation of the cancer cells may significantly reduce implantation and dissemination. Wang et al.<sup>[12]</sup> used a blocking glue of cancerous serosa to smear and cover the tumor surface to prevent cancer cells from exfoliation. In addition, distilled water was used to rinse the incision before the closure of the abdominal cavity. Implantation at the site of the incision caused by disruption and spreading of exfoliated tumor cells can be reduced by use of a hypomolal solution in the closure. Gloves and instruments should also be changed.

Besides a malignant tumor, borderline tumor implantation may also occur in cases with diseases such as endometriosis. Morice et al.<sup>[13]</sup> reported 3 cases with an ovarian borderline tumor, in which the puncture point

**Table 1. The penetration point-induced recurrence following laparoscopic surgery of various gynecological tumors.**

	Ovarian cancer	Uterine cervix cancer	Endometrial cancer
Cases	40	12	4
Median age, years	50 (22~79)	44 (31~74)	63 (56~72)
Purpose of operation	Diagnosis for 37% of the patients	-	Treatment for 75% of the patients
Median time of relapse	17 days (4~730 days)	5 months (1.5~19 months)	13.5 months (6~21 months)

implantation occurred following a laparoscopic procedure. Two of the 3 cases were serous tumors, which were found by surgery, and 1, a mucous tumor found by clinical examinations 11 months later. Resection of the implantation resulted in a favorable prognosis. Li et al.<sup>[14]</sup> reported 12 cases with abdominal-wall and perineal-incision endometrioses. The average time between onset of the diseases and surgery was 2.3 years (4 months to 6 years), with a poor efficacy of drug treatment. Therefore, surgical resection became the treatment of choice. Sun et al.<sup>[15]</sup> treated 10 cases of abdominal-wall perineal-incision endometriosis after parturition using an electrochemical therapy machine with a platinum-gold electrode needle. A good curative effect was obtained with rapid recovery, and no scarring. Except for parturition, implantation into the uterine cavity should be avoided as much as possible during hysteromyectomy, thereby reducing the endometrial tissue at the incision and preventing endometriotic implantation.

Resection can usually be adopted if there is a definite or even a doubtful tumor implantation. When there is extensive excision, various medical patches can be used in doing a one-time resection of the entire implanted tumor. Although biological characteristics of tumor cells and poor immunity of patients play important role in tumor implantation after surgery, the major cause is iatrogenic tumor-cell exfoliation and residuals resulting from not using a tumor-free procedure. Clinicians should pay more attention to avoiding and decreasing iatrogenic implantation and dissemination of tumors.

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