

Port-site metastases in the laparoscopic surgery for colorectal cancer - still a real concern? Case report and review of the literature

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Rezumat

Metastazele de trocar în chirurgia laparoscopică a cancerului colorectal – sunt încă un motiv real de îngrijorare?

Prezentare de caz și recenzie a literaturii de specialitate

Introducere: Recent publicatele rezultate oncologice la distanță ale marilor trialuri multicentrice randomizate și prospective, cum ar fi COST, COLOR și UK MRC CLASICC, au redus odată în plus scepticismul inițial de la mijlocul anilor '90, referitor la oportunitatea utilizării abordului laparoscopic în chirurgia cancerului colorectal. Incidența reală a metastazelor de trocar se situează în jurul a 1 %, fiind similară statistic cu cea a metastazelor din chirurgia deschisă. Am urmărit un lot de 122 rezecții colorectale asistate-laparoscopic pentru adenocarcinom colorectal, 49 pentru adenocarcinom de rect și 73 pentru adenocarcinom de colon. Operațiile au fost efectuate în cadrul Centrului de Boli Digestive și Transplant Hepatic - Institutul Clinic Fundeni, între 1 ianuarie 2002 și 31 decembrie 2008. În această serie urmărită s-a înregistrat un singur caz de metastază de trocar (0,81 %).

Prezentare de caz: Prezentăm cazul acestui bărbat de 83 de

ani, cu o metastază de trocar apărută la nivelul mini-laparatomiei de extracție a piesei de rezecție, 4 luni post-operator după o hemicolectomie asistată-laparoscopic pentru un cancer de cec slab diferențiat G3, stadiul Dukes C.

Discuții: Am trecut în revistă articolele relevante pe acest subiect referitoare atât la incidența metastazelor de trocar din chirurgia laparoscopică a cancerului colorectal și la etiologia multifactorială a acestora, cât și la măsurile de protecție ce trebuie luate pentru prevenirea diseminării tumorale parietale la nivelul minilaparotomiilor de extracție și a orificiilor de trocar. **Concluzie:** Metastazele de trocar în chirurgia laparoscopică a cancerului colorectal nu mai reprezintă astăzi un motiv real de îngrijorare încât să contraindica beneficiile acestui tip de chirurgie. Totuși, acestea reprezintă o realitate ce trebuie luată în considerare de către orice chirurg laparoscopist. Există diverse metode de prevenire care sunt recomandate de a fi aplicate pentru reducerea incidenței acestor posibile complicații.

Cuvinte cheie: metastaze de trocar, cancer colorectal

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Abstract

Background: The recently published long-term oncological results of the large multicentric randomized prospective trials, such as COST, COLOR, and UK MRC CLASICC, have diminished once more the initial skepticism from the mid '90s, regarding the safety of laparoscopic approach for colorectal cancer surgery. The actual incidence of port-site metastases (PMSs) in the laparoscopic surgery for colorectal cancer is just around 1 %, being statistically similar to the wound metas-

tases after open colorectal surgery. We followed up a series of 122 laparoscopic-assisted resections for colorectal adenocarcinoma, 49 for rectal cancer and 73 for colon cancer. The operations were performed at the Center of Digestive Diseases and Liver Transplantation, Fundeni Clinical Institute, Bucharest, Romania, between 1st January 2002 and 31st december 2008. There was only one case of PMS (0.81%).

Case-Report: A 83-year old man developed a recurrent parietal tumor on the site of extraction minilaparotomy, 4 months after laparoscopic-assisted right hemicolectomy for a Dukes C, poorly differentiated (G3) adenocarcinoma of the cecum.

Discussions: We have reviewed the scientific relevant literature regarding the incidence and multi-factor etiology of PMSs in the laparoscopic surgery for colorectal cancer as well as the methods suggested for prevention of parietal tumour dissemination to the trocar or wound sites.

Conclusion: PMSs consecutive to laparoscopic surgery for colorectal cancer are no longer a big concern enough to contraindicate this beneficial surgery for oncological reasons. However, PMSs continue to represent a reality which must be taken into consideration by any laparoscopic surgeon. There are different prevention measures that should be applied for reducing the occurrence of this possible complication.

Key words: port-site metastases, colorectal cancer

Introduction

An unacceptable high incidence up to 21% of PSMs in laparoscopic surgery for colorectal cancer was reported in the first published series of patients during the early '90s and led to a skepticism inside the international surgical community regarding the oncological feasibility of laparoscopic surgery for colorectal malignancies, which persisted long since until recently. However, in the latest years, the oncological long-term results of the large multicentric randomised prospective controlled trials [e.g. COST (1,2), COLOR (3) and UK MRC CLASICC (4,5)] have been reported. The actual incidence of PSMs was found to be around 1%, statistically comparable to the wound-site metastases from open colorectal surgery.

Very few articles have been published about the PSMs in laparoscopic colorectal surgery for cancer in Romanian surgical journals (6-9). A review of all the papers published in *Chirurgia* journal on the topic of laparoscopy has been already done elsewhere (10), so we consider appropriate to bring it back into attention using this opportunity to present our experience and review the relevant scientific literature.

Throughout the present article we adopt the term of port-site metastases (PSMs) who is naturalized in medical language, especially Romanian one, although the term is disputed by some authors.

We analyzed 160 patients with colorectal adenocarcinoma laparoscopically operated in the Center of Digestive Diseases and Liver Transplantation, Fundeni Clinical Institute,

Bucharest, Romania, between 1st January 2002 and 31st December 2008. We followed up 122 patients, the others being excluded from our study. Exclusion criteria were: conversion to open surgery, colorectal tumor associated with peritoneal carcinomatosis, parietal invasion, ascites or extrahepatic metastases at the time of initial operation. Laparoscopic-assisted resections for cancer were performed on 49 patients with adenocarcinoma of the rectum and 73 patients adenocarcinoma of the colon. Among all these selected patients there was only one who developed a single PSM (0.81%) on the minilaparotomy extraction site of right hemicolectomy specimen.

This case is further presented.

Case report

A 83-year old patient, with no significant past medical history, was investigated for a two months history of abdominal right lower quadrant pain, weight loss and alternating constipation and diarrhea. He was diagnosed in the Gastroenterology and Hepatology Center - Fundeni Clinical Institute, Bucharest, Romania, with an infiltrative cecal tumor. Patient was then transferred for surgical treatment in the Center of Digestive Diseases and Liver Transplantation, on March 9th, 2007. Preoperative imaging and endoscopic investigations excluded the presence of synchronous tumors or distant metastases. Tumor markers were within normal range. Besides of mild anemia (Hb 10,2 g/dl), no other abnormality was noted on routine blood tests. With adequate preoperative preparation, under general anesthesia, a laparoscopic exploration of abdominal cavity was performed. An infiltrative-stenotic cecal tumor with serosal expression was visualized. No sign of local invasion, no peritoneal nor liver subcapsular metastases was identified. The tumor was resected by laparoscopic-assisted radical right hemicolectomy respecting the oncological surgical principles. The operative specimen was extracted through a 9-cm-long transverse minilaparotomy, 4 cm above the umbilicum. The abdominal parietal edges of the incision were protected by gauze dressing pads. Manual extracorporeal ileo-transversoanastomosis was performed through the same incision. The operation was straightforward and postoperative recovery was uneventful. Histopathological report of the specimen showed an aggressive form of poorly differentiated (G3) tubulo-papillary and trabecular adenocarcinoma of cecum, with tumor invasion through all layers of the colon to the surface of visceral peritoneum (pT4a), and 3 out of 12 lymphnodes metastases (pN1), Dukes' stage C. The patient received no adjuvant chemotherapy.

Four months later, on July 9th, 2007, the patient was readmitted in our clinic for the occurrence of a solid, round shaped, ulcerated, parietal mass grown at the site of the previous extraction minilaparotomy (Fig. 1). Routine blood tests showed no significant abnormalities. Imagistic and endoscopic check-up ruled out locoregional and distant recurrences. Under general anesthesia a wide excision within oncological limits of the parietal metastasis was performed. No other abnormality was noted by inspection of the



Figure 1. Port-site metastasis on the extraction minilaparotomy



Figure 2. Resected port-site metastasis specimen 4 months after laparoscopic-assisted right hemicolectomy

abdominal cavity through parietal incision. The resulted parietal defect of abdominal wall was closed and enforced using a 5 x 5 cm polypropylene mesh. The postoperative recovery was with no complications.

The parietal tumor (Fig. 2) proved to be a poorly differentiated (G3) tubulo-papillary and trabecular adenocarcinoma, histopathologic identical with the laparoscopically resected cecal tumor.

Unfortunately, the patient was lost from our follow-up study one month after PSM resection.

Discussions

PSMs are early tumor recurrences that develop locally in the abdominal wall, at the site of trocar or wound incision after laparoscopy for cancer. They are not associated with peritoneal carcinomatosis and must be differentiated from the cutaneous metastases that occur in advanced cancers. For this reason, Raymond M.A. et al. (11) consider the term of port-site recurrence more appropriate than port-site metastasis. Other authors consider that PSM means only the parietal recurrence without any other local or distant recurrences. (12).

In 1991, Jacobs et al. (13) reported the first series of 20 laparoscopic colon resections in the world. In Romania the first laparoscopic operation for colorectal cancer was performed by Vasilescu et al. (14) at Fundeni Clinical Institute, in 1995. In 1993, the first two cases of PSM that occurred 8 weeks after radical right laparoscopic hemicolectomy for Dukes' stage B, respectively C colon cancer, were published in Lancet (15,16). One year later, in 1994, Berends et al. (17), reported a percentage of 21% (3 patients) of PSMs in a series of 14 patients with laparoscopic colectomy for Dukes B2, C2 and D colon cancer, and thus amplified the initial concern of surgeons about the safety of laparoscopic approach in the treatment of colorectal malignancies.

Until 1995, at least 35 cases of PSMs were reported in the literature, some surgeons even suggesting that the "alarming rate" would proscribe colorectal cancer from the indications of laparoscopic surgery, which should be reserved only for

benign lesions (18). Gradually, year after year, this phenomenon has revealed its real dimension. A review of 3266 patients with colorectal cancer laparoscopically resected, revealed a PSM incidence of 0.58 % (19 cases) (18). Another review of 29 published series that totalised 5305 patients found an incidence of 0.72 % (38 cases) of PSMs (19).

During the last years, the oncological long-term outcomes at 3 and 5 years of large multicentric prospective randomized controlled trials have been reported and unequivocally proved the oncological safety of laparoscopic resection for colorectal cancer. COST trial (1;2), which studied 428 laparoscopic colectomies versus 435 open colectomies for colon cancer, reported a 5-year incidence of PSM of 0.9 % (2 cases) in the laparoscopic arm and 0.5 % (1 case) in the open arm. Among 534 cases of laparoscopic colectomies for cancer studied in COLOR trial (3) 7 cases of PSM (1.3 %) were documented at 5-year interval, from which 5 were "true" PSM, localized on the trocar insertion sites, and 2 were extraction minilaparotomy metastases, as it was the case with our patient. UK MRC CLASICC trial (4,5) which analysed 526 laparoscopic colorectal resection versus 268 open resection for patients with colon and rectal cancer in all TNM stages, including cases with liver metastases, reported at 5 years, 9 cases of PSMs (2.5 %), of which only one (0.2 %) was a "true" PSM, and the other 8 cases retrieval site recurrences. The authors emphasized the need for an adequate protection during specimen extraction (4).

Etiology of PSM

Although the etiology of PSM is not completely understood, it is accepted that it has a multifactorial etiology, two main factors being involved: pneumoperitoneum and inadequate handling of the tumor with direct contamination of parietal wound sites (18). Pneumoperitoneum plays a role in the exfoliation of malignant cells from the tumor surface into the intraperitoneal gaseous atmosphere by aerosolization, some of these free cells being viable and having a metastatic potential. These tumor cells are driven by so-called "chimney-effect" (18),

20-24), especially when the gas pressure suddenly drops due to dessufflation or leakages around the trocars, and preferentially transported to trocar/wound sites where peritoneum is traumatized. It is proved that a high pneumoperitoneal pressure increases the risk of tumor cell aerosolization and instrument contamination, whereas a low insufflation and constant pressure reduce this risk (19,22-24). Although, CO₂ is suggested to be one of the major factors leading to PSMs by releasing inflammatory mediators, causing acidosis or impairing macrophage function, it remains the safest gas that could be used for pneumoperitoneum in terms of side effects compared with other studied gases like helium (18,20,23,24). It should be noted that PSMs occur also after thoracoscopy or gasless laparoscopy, during which no CO₂ is used. Hematogenous spread of malignant cells is another suggested mechanism. It is possible that some malignant cells are liberated into portal blood stream due to tumor manipulation and theoretically reach the wound trocar sites where peritoneal barrier is breached. At this level there is a poor local immune response, local ischaemia, increased secretion of growth factors, and fibrin excess which could stimulate adhesion and growth of the cells implanted here (21,23-25). However, during laparoscopy, the splanchnic circulation is altered with a 30 % reduction of portal flux, just 1% of malignant cells that reach the general circulation survive, and only 0,1 % of them are able to induce metastases (24,26). One study revealed that after intravenously inoculation of tumor cells the incidence of PSM was 0% while direct peritoneal inoculation resulted in an incidence of 63% of PSM (27). Probably the most significant issue is the inadequate surgical technique by direct brutal manipulation and repeated traumatization of the tumor as a result of lack of laparoscopic surgical experience and technical mistakes (18,22-24). On contrary, the meticulous "no-touch" dissection technique and avoidance of direct contact between tumor or contaminated instruments and trocar or wound sites are associated with a low risk of PSMs (22-24).

PSMs may still occur even when there is no direct handling of tumor, as it is the case in staging laparoscopy, or after laparoscopic operation for another abdominal pathology where a synchronous cancer was missed, thus demonstrating that these metastases may also have another etiology (18,28,29). It is demonstrated that an intact peritoneum is more resistant to implantation of tumor cells, whereas a traumatised peritoneum by trocar insertion or an unsutured peritoneum at the port-site orifices is predisposed to PSM occurrence (22,24). Laparoscopic instruments contamination has also a great impact in peritoneal dissemination by transporting and putting the tumor cells in contact with trocar or wound sites (18,23,30,31). The contamination is more important for the operating surgeon surgical tools than the assisting one (18,30,32). Modern surgical dissection instruments, as Harmonic scalpel or Ligasure, appear to be less contaminating compared to usual diathermy instrument (18,24,33). The repeated removal and insertion of trocars or working surgical tools are associated with a greater risk of PSM (22-24).

The singular case of PSM in our series could be

explained by the aggressive histological form of colon cancer (pT4a, pN1, G3), which it made possible for malignant cells to be exfoliated in CO₂ atmosphere and directed preferentially to the port-site. However, a direct tumor cell contamination of extraction site during specimen retrieval cannot be excluded despite the wound protection we performed.

Preventive measures of PSM

There are many identified efficient actions to be taken before, during and after laparoscopic resections for colorectal cancer (34).

On this regard a proper selection of the patients (excluding voluminous and/or locally advanced tumors), a skilled laparoscopic surgical team, and an irreproachable surgical technique with respect for oncologic surgical principles are mandatory (23).

Protection of extraction wound sites and usage of specimen bags are simple and facile methods of PSM prevention. Nevertheless, there are reported cases of PSMs occurred even in protected sites where no direct contact with the specimen was done, questioning the benefits of these measures (18,23,24). Although routine protection of retrieval wound and extraction of the specimen inside a bag are recommended due to oncological safety (18-20), many surgeons might not pay much attention to these measures considering this is time-consuming.

Other suggested measures for reducing the risk of PSMs are: (1) avoidance of "chimney effect" by trocar fixation and control of gas leakages around trocars, (2) usage of low and constant pneumoperitoneal pressure during operation, (3) drainage of abdominal cavity before deflation to prevent "slosh" phenomenon, (4) complete gas exsufflation with trocars left in place (18,21-24,34).

Excision of port sites has been also recommended to decrease PSM frequency, but it was declared ineffective by some authors (18,20,23,24). Instead, peritoneal trocar site closure has a demonstrated role in prevention of PSMs (35). Peritoneal and port sites washing with 5% betadine or tauridine solution is credited with a theoretical role in decreasing PSM incidence due to its tumoricidal properties (18,22,24). Although its tumoricidal effect is not clearly proved, betadine washing is recommended to be used at the end of trocar site closure, at least for the prevention of wound infection due to its demonstrated very good antiseptic property.

Conclusions

The stigma of the early reported high incidence of PSMs in laparoscopic surgery for colorectal cancer has presently become a myth. Current data from large randomized trials have shown an acceptable low incidence of PSMs occurrence, which is statistically equivalent to that of wound metastases after open surgery. However, PSM still represents a reality that should be taken into consideration by any laparoscopic surgeon. Even if the diagnosis of PSMs is mainly clinical, imaging investigations are mandatory to rule out other local and distant

recurrences. Every effort should be made to decrease PSM incidence by proper selection of the patients, adequate surgical technique respecting the oncologic principles, and strictly following the recommended prevention methods.

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