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Dept. Pathol. & Parasitol.,
Fac. Vet. Med., Alex. Univ.

A COMPARATIVE STUDY ON TUMOUR SPREADING FOLLOWING LAPAROTOMY AND LAPAROSCOPY

(With 1 Table and 2 Figures)

By

E. EL-MANAKHLY and M. SULTAN*

*: Dept. Surgery, Fac. Med., Zagazig Univ.

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دراسة مقارنة على الإنتشار السرطانى الذى يعقب شق البطن أو استخدام التنظير الجراحى

السيد المناخلى ، محمد سلطان

تمت هذه الدراسة المعملية حيث تم حقن عدد من فئران التجارب بخلايا سرطانية خبيثة فى جدار البطن وعقب ذلك تم تمزيق الورم الناتج عن طريق التنظير الجراحى فى مجموعة وتمزيق الورم عن طريق الشق الجراحى للبطن فى مجموعة اخرى وقد توصل البحث الى نتائج تتلخص فى ان حجم الورم قد تزايد بنسبة اكبر فى مجموعة تنظير البطن عن طريقة الشق الجراحى. كذلك كان معدل الإنتشار السرطانى الثانوى فى جدار البطن اكبر ما يكون فى مجموعة تنظير البطن عنه فى مجموعة شق البطن وبخاصة فى الجرح الذى استخدم لتمزيق الورم اثناء التنظير الجراحى. وبفحص باقى الأنسجة والأعضاء الداخلية لم يلاحظ سواء بالفحص الظاهرى أو المجهرى ان هناك انتشار للورم عن طريق الدم أو السائل الليمفوى فى أى من المجموعتين.

SUMMARY

Albino rats, in which an implanted abdominal cancer was lacerated during laparotomy or laparoscopy, were used to evaluate the rate of tumour spreading following both techniques. The postmortem examination revealed that infiltration of the primary tumour was higher in rats exposed to laparoscopy than laparotomy. Microscopically, the incidence of secondary implantation was greater after laparoscopic laceration than after tumour laceration by laparotomy, particularly at the wound from which laparoscopic lacerating instruments were introduced. However,

both treated groups showed neither macroscopic nor microscopic evidence of metastasis in any organ beyond the laparotomy or laparoscopy wounds.

Keywords: *Tumour, Laparotomy, Laparoscopy.*

INTRODUCTION

The concept of cancer recurrence at the site of a surgical wound is not new (Gerster, 1885). Recurrence at the site of cannula insertion following laparoscopy is also a recognized phenomenon (Dobronte et al., 1978).

Recently, several reports described metastasis in wounds created for the introduction of laparoscopic instruments into the abdominal and thoracic cavities following tumour resection (Ciracco et al., 1994; Birkett, 1995; Jorgensen et al., 1995 and Watson, 1996). As a consequence, many surgeons have expressed concern about the application of laparoscopic technique to the surgical treatment of malignancy.

Although many cancer cells are transplantable, their invasive and metastatic potential depends on both their intrinsic properties and the host environment at the site of inoculation (Filder, 1990). In addition, orthotopic injection (injection of tumor cells into the tissue or organ of their origin) often enhances metastatic potential (Kozlowski et al., 1984).

Having established that surgery for cancer is often associated with implantation of viable malignant cells, one must turn the question of whether laparoscopy is associated with any additional specific risks. Most of laparoscopic surgeons would probably agree that the nature of current instrumentation means that operative manoeuvers are much less dexterous than at open surgery. The lack of tactile feedback in laparoscopy could mean that unsuspected malignancies may undergo unnecessary manipulation before a histopathological diagnosis made leading to spillage of more malignant cells. Pazet and Fondrinier (1992) attributed cutaneous implantation at the periumbilical cannula site.

The aim of this study was to determine whether laparoscopic treatment of a malignant abdominal disease in rat, in comparison to laparoscopy, increases the risk of tumour spreading.

MATERIAL and METHODS

Sixty adult female albino rats (220 ± 20 g B.W.) were used, balanced diet and water were available ad libitum. They were classified into 4 equal groups designated GPs. 1, 2, 3 and 4. All rats, except GP.4 were intramuscularly injected with a suspension of viable mammary carcinoma cells (2×10^8 cells/rat in a volume of 0.2 ml sterile phosphate buffer saline) at the left flank. Rats of GP.4 (control negative) were injected as previously described with 0.2 ml sterile phosphate buffer saline (PBS).

The tumour cell suspension was prepared by aseptic collection of the tumour masses from carrier rats (spontaneous cases) which were histopathologically diagnosed as mammary carcinoma schirrous form (Fig. 1). The fresh tumour mass was cut into very small pieces, treated with trypsin solution (0.25% in PBS) and EDTA solution (0.02% in PBS). The cell suspension was filtered and the filtrate was centrifuged (800 rpm for 5 minutes) and suspended in PBS 3 times. Cell concentration was adjusted at 1×10^9/ml (Freshney, 1984).

Three weeks post inoculation, rats of GP.1 and 2 were subjected to tumour laceration at laparoscopy and laparotomy, respectively. However, rats of GP.3 (control positive) did not exposed to any surgical treatment. Both surgical treatments were done under anaesthesia for 30 minutes using a combination of halothane and nitrous oxide supplemented by oxygen via a close-fitting mask.

Regarding laparoscopy group, 2 punctures/rat were done. The first puncture was done at the umbilicus wherein a disposable laparoscopy cannula was introduced to provide access for a 2-mm minilaparoscope. The primary tumour was seen bulging into the peritoneal cavity. The second puncture was simultaneously done at the right abdominal wall opposite to the primary tumour, then a long needle was inserted through a 18-gauge intravenous cannula to create a single laceration in the tumour mass. The two punctures were closed with interrupted 3/0 prolene suture. In laparotomy group, a 3-cm incision was done at the right abdominal wall opposite to the primary tumour to expose the abdominal contents. The tumour mass was bulging into the peritoneal cavity and was covered by parietal peritoneum. The tumour was lacerated once using tip of an 18-gauge needle. The incision was

closed with 3/0 polypropylene sutures in two layers. The number of rats that developed primary implanted tumour as well as the size of the mass in both groups were recorded.

Six weeks postoperative, all rats were killed and the dimensions of the primary mass were measured. Furthermore, both laparoscopy and laparotomy access wounds, sites of inoculation as well as all the internal organs of all rats were grossly examined for evidence of metastasis and implantation before they were excised, at least 5 specimens from each organ, for fixation in 10% neutral buffered formalin and processing through the paraffin embedding technique. Five microns thick paraffin sections were stained with Mayer's hematoxylin and eosin (H,E).

RESULTS

Preoperatively, the primary implanted tumour mass in GPs. 1 and 2 was more or less spherical (20 ± 2 mm diameter), bulged into the peritoneal cavity and covered with the parietal peritoneum. At the end of the experiment, the size of the primary mass increased by infiltration, particularly in laparoscopy-treated rats (40 ± 2 mm) followed by laparotomy-treated ones (35 ± 2 mm). The minimal increase in size of the primary mass was seen in surgically untreated, control positive, rats (25 ± 2 mm). Rats of GP.4 (control negative) were free from primary tumours at the site of inoculation.

As shown in table (1), the pathologic examination of GP.1 revealed that 9 rats out of 15 (60%) developed secondary wound implantation. According to the size of the secondary implants, 5 of them were micromasses that only seen during the microscopic examination and the remaining 4 cases were macromasses. As for the location of the secondaries, 7 rats had secondary implants at the wound used for lacerating instruments (3 macro and 4 micromasses). The 8th rat showed a micromass at the wound used for minilaparoscope, the 9th rat had a macromass in both wounds (lacerating instruments and minilaparoscope wounds). In laparotomy group, only 3 rats of 15 (20%) developed secondary wound implantation, two of them were micromasses and one was a macromass.

Macroscopically, both the primary and secondary implants were grayish white, firm, lobulated and diskoid masses. Microscopically, the

most of secondaries appeared as mammary carcinoma schirrous form precisely as the excised tumor from carrier rats (Fig. 1); but, few masses from both treated groups changed to mammary carcinoma solid form (Fig. 2). In the schirrous form, the neoplastic cells occurred in thin cords or small clusters separated by fibrous stroma; however, in the solid form, the neoplastic cells occurred in large lobules separated by fibrous septa. On the other hand, rats of GP.3 (control positive) exhibited no secondary wound implantation.

Moreover, there were no macroscopic or microscopic evidence of tumour metastasis even in the lung or regional lymph nodes of any rat group.

Table 1: Incidence, form an location of secondary wound implantation in different experimental groups.

Form of	Laparotomy	Laparoscopic rats (GP.1) n = 15			Control
Secondary Implantation	Rats (GP.2) n = 15	Laparoscope wound	Lacerating instruments wound	Both wounds	Positive (GP.3)
Micromasses	2	1	4	--	--
Macromasses	1	--	3	1	-
Total	3 (20 %)	9 (60 %)			0 %

DISCUSSION

Abdominal wall implantation following laparoscopy may become an increasingly recognized problem. Unfortunately, there are few large-scale studies that allow comparison of the incidence of wound implantation following open surgery and laparoscopy. Eight cases of cutaneous seeding have been reported following laparoscopic colectomy and cholecystectomy (Pezet and Fondrinier, 1992; Alexander et al., 1993 and Clair et al., 1993). Moreover, implantation had also occurred in port wounds through which no tumour was extracted and even with no direct contact with resected tumour (Hsui et al., 1986; Jocabi et al., 1995 and Watson, 1996). In our study, all injected rats developed tumor implant at the site of inoculation of the neoplastic cells indicating their powerful tumorigenicity and invasiveness. On the other hand, the absence of wound metastasis supported the hypothesis that injection of cancer cells into tissue or organ different from their origin decreases the metastatic potential (Kozlowski et al., 1984).

The growth rate (infilterative power) of the primary implanted tumor was more rapid in surgically treated rats when compared with control ones. Alexander and Altemeier (1964) and Fisher (1965) confirmed that surgical trauma to the tissues enhanced the growth of the implanted tumour. Accordingly, open surgery is usually associated with much more trauma to tissues than do laparoscopy and subsequently more rapid tumour growth. However, the present study demonstrated more increase in tumour growth after laparoscopy than open surgery. A possible explanation of this is that laparoscopic techniques lead to more exfoliation of malignant cells from the surface of the laparoscopic instruments which come in direct contact with the surgical wound leading to implantation then proliferation of a high number of cancer cells. By contrast, in open surgery the cellular exfoliation is relatively minimal and the contact between the surgical instruments or even the resected tumour mass and the laparotomy wound is limited.

Furthermore, the present study showed that the highest rate of secondary wound implantation was noticed in laparoscopy group (60%) in comparison to laparotomy one (20%) and control positive group (0%). Mathew et al. (1996) reported a higher rate of port-site implantation following laparoscopy than open surgery. They concluded that the technical difficulties of laparoscopic dissection may lead to inadvertent tumour laceration more likely than open surgery with potentially more serious consequences as increased risk of wound implantation. The highest incidence of wound implantation in our study was seen in wound used for lacerating instruments during laparoscopy (7 cases) followed by laparotomy wound (3 cases) and wound used for minilaparoscope (1 case). This may be correlated with the number of exfoliated cancer cells indicating more spillage of these cells at the wound used for lacerating instruments.

In this study, the tumour used for induction of the primary implantation was diagnosed as schirrous form of mammary carcinoma. Few secondaries appeared as mammary carcinoma solid form. Weijer (1981) reported that the microscopic features of the secondaries of mammary gland carcinoma may differ from the primary growth. This change in the microscopic picture of the secondary tumour was noticed in both laparoscopy and laparotomy groups, so the surgical technique had no influence.

In conclusion, our results may added a weight to the argument that wound implantation following laparoscopic surgery of malignant abdominal tumours is an important clinical problem and until a clear picture emerges, we support the opinion that laparoscopic surgery for malignant diseases should be practiced only within well conducted prospective clinical trials.

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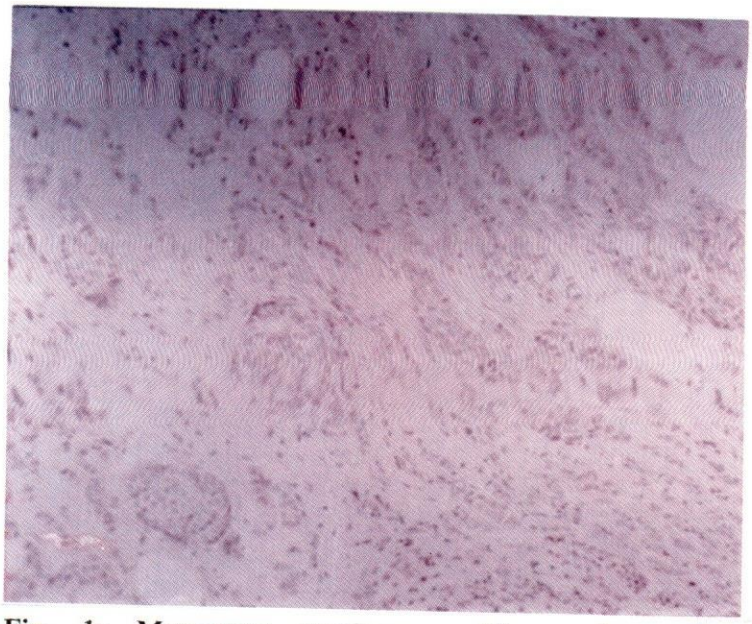

Fig. 1: Mammary carcinoma schirrous form: The neoplastic cells arranged in thin cords or small clusters separated by fibrous stroma. H,E (X 160).

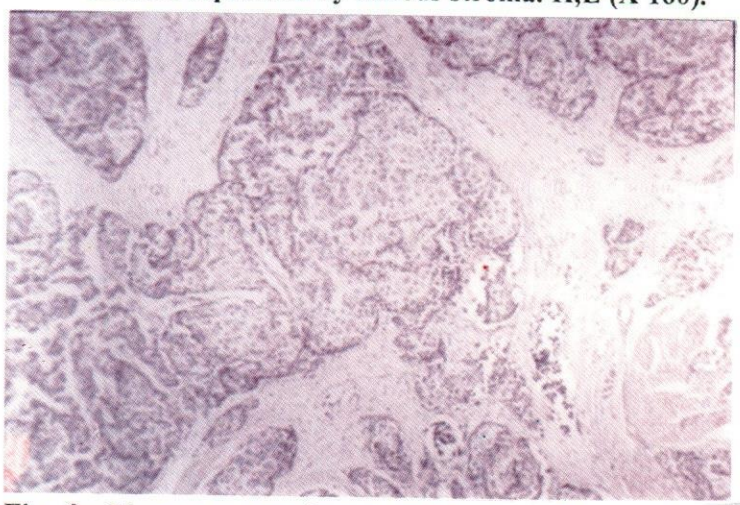

Fig. 2: Mammary carcinoma solid form: The neoplastic cells occurred in large lobular masses separated by fibrous septa. H,E (X 160).