

PORT-SITE METASTASIS AFTER LAPAROSCOPIC RADICAL NEPHRECTOMY FOR RENAL CELL CARCINOMA: REPORT OF 2 CASES AND REVIEW OF THE LITERATURE

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Port site metastasis (PSM) after laparoscopic Surgery for Renal Cell Carcinoma is asporadic disease. At Viet Duc Friendship Hospital, the first case of renal cell carcinoma was operated by laparoscopic surgery in 2006. Since then, we have only recorded 2 cases of PSM. Case 1: Tumor recurred 17 months after laparoscopic radical nephrectomy with the diagnosis of sarcomatoid RCC T1bN0M0; Case 2: Tumor recurred three months after laparoscopic radical nephrectomy with the diagnosis of clear cell RCC T1bN0M0. We take this opportunity to review similar recurrence cases mentioned in the literature to understand further the causes, treatment methods, and experience in preventing this pathological phenomenon.

Keywords: Laparoscopic, radical nephrectomy, recurrence, trocar, port-site metastasis.

I. INTRODUCTION

Laparoscopic surgery for the treatment of renal cell carcinoma has become routine and has shown many advantages over open surgery. The rate of port-site metastasis after laparoscopic surgery for urinary tract cancer is generally estimated at 0.09-0.73% which is considered as very rare.^{1,2} Literature search revealed, studies and reports on the

risk of metastasis, pathology, and methods to prevent recurrence of port-site metastasis after laparoscopic renal cancer surgery. We also shared the experience of two cases of tumor recurrence at the port-site after laparoscopic radical nephrectomy for renal cell carcinoma.

II. CASE REPORT

1. Case 1

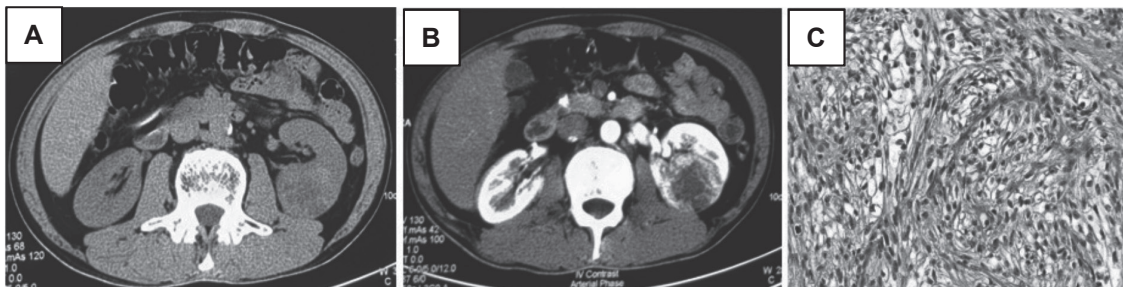


Fig 1. MSCT pre- (A) and post- contrast injection (B). Histopathology (C)

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A 53-year-old male patient, diagnosed with left RCC (Renal cell carcinoma) stage T_{1b}N₀M₀ (Figure 1 A + B), underwent laparoscopic radical left nephrectomy on May 9, 2014. The specimen was taken intactly in a homemade

plastic bag through an additional skin incision. The pathology results after the first surgery were sarcomatoid RCC (Figure 1 C), stage pT_{1b}N₀M₀. Patients did not receive supportive treatment after the surgery, he was periodically monitored by ultrasound.

Ater 17 months post surgery, there was appearance of a mass at the site of the abdominal wall incision from October 2015, but the mass was negligible and painless. However, the abdominal wall mass gradually increased and grew rapidly and painfully, causing the patient to be re-admitted in the hospital.

Physical examination on admission was

average vital signs were stable, there was a solid, painful 5 x 5cm mass on the abdominal wall. MSCT (Multi-slice computed tomography) showed the left anterior abdominal wall has a substantial, highly angiogenic mass, 49x49x53 mm, with blood supply from the branch of the left common femoral artery, invading the rectus muscle and surrounding fatty tissue, encroaching on the abdominal wall peritoneum and bordering with the viscera in the abdominal cavity (Figure 2). There was no thrombosis in the inferior vena cava, and no local recurrence was observed. Other laboratory parameters were within normal limits.

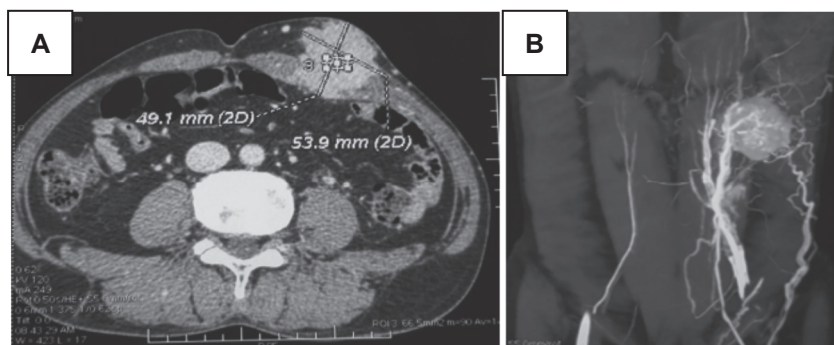


Fig 2. PSM on MSCT

Diagnosis: Abdominal wall recurrence after surgery for a left kidney tumor. The patient was operated on December 16, 2015. Examination: The tumor invaded the abdominal peritoneum, a large part of the omentum was attached to the tumor, and there was no metastasis in other sites. The patient had a complete resection of the recurrent tumor and partial resection of the large omentum attached to the tumor. The immediate pathology in the resection did not show any malignant cells. Postoperatively, the patient's condition progressed well, and he was discharged after seven days. Pathological results of the abdominal wall metastases are clear cell RCC type infiltrating the abdominal

wall and small blood vessels, Fuhrman grade 3. The patient was consulted but declined postoperative adjuvant treatment. Eight months after the second surgery, the patient was diagnosed with a secondary metastasis in the brain's left hemisphere. The patient died one month after the brain damage was discovered.

2. Case 2

A 70-year-old male, diagnosed with RCC stage T1bN0M0 (Figure 3 A+B), underwent laparoscopic right radical nephrectomy on January 22, 2018. The specimen was obtained by morcellating after being placed in a homemade bag. After the first surgery, the pathology results were RCC clear cell

type; Fuhrman grade 4 (Figure 3 C); stage T1bN0M0. Patients received no supportive

treatment after the surgery, he was periodically examined and monitored by ultrasound.

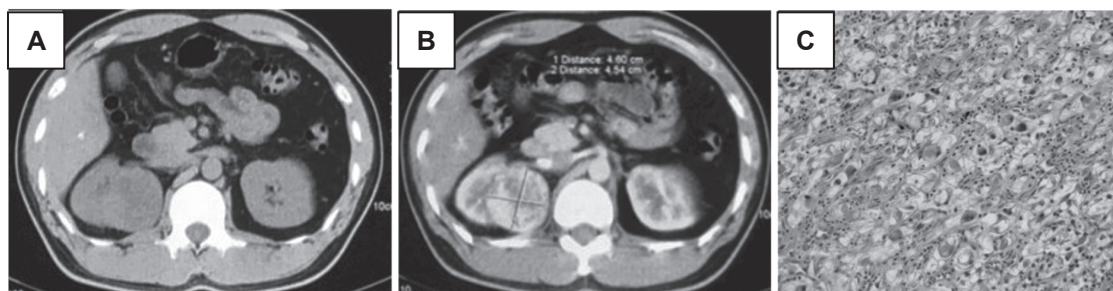


Fig 3. MSCT before and after contrast injection

The patient began to notice a mass at the abdominal incision site after three months post surgery from May 2018, but it was small and painless and coincided with the surgical scar, so it was not noticeable until it gradually enlarged fast but remained painless.

By MSCT the right abdominal wall has substantial tissue enhancement, increased angiogenesis, by 39x57 mm which invaded the abdominal wall muscle, and bordered with intra-abdominal viscera. No other metastases were found. Biopsy was diagnosed as RCC metastasis. The patient was admitted to the hospital on January 2, 2019; the physical condition was average with stable vital signs, no peripheral lymph nodes; there was a solid mass of about 4x6cm at the abdominal wall; it was painless, the remaining two trocars are standard. Other tests are within normal ranges.

The patient was operated on January 4, 2019. The tumor invaded the abdominal wall muscle, other organs showed no metastasis, no recurrence at the old surgical site of nephrectomy. The patient had a complete resection of the recurrent tumor and had an abdominal wall reconstruction. Postoperatively, the patient progressed well and patient was discharged after seven days. Pathological results images are consistent with metastatic

lesions of the abdominal wall of clear cell type RCC. Postoperative follow-up: 15 months after the second surgery (May 2020), CT scan detected recurrent mass (size: 35x65mm) in the previous nephrectomy site. This recurrent mass invaded the inferior vena cava and surgery was no longer indicated.

III. DISCUSSION

Risk factors of port-site metastasis

Pathologically, the authors believe that port-site metastasis is an early relapsing tumor lesion. This lesion develops in the abdominal wall concurrently with the healing of the trocar port-site. Tumor metastasis at the trocar port is not associated with peritoneal metastasis. Metastasis to the trocar port site has occasionally been reported, especially in cases of gallbladder cancer (7-17%), colorectal cancer (5%), and gynecological cancer (4%).³ The rate of metastasis to the port-site after urological laparoscopic surgery is scant.⁴ Micali (2004): reported 13 cases of trocar site recurrence. The incidence was 0.12% (13 out of 10,912).⁵ Among these 13 cases, there were 4 cases of metastatic adrenal carcinoma, 4 cases of lower tract urothelial carcinoma, 3 cases of upper tract urothelial carcinoma, 1 case after dissection of retroperitoneal lymph nodes testicular cancer,

and 1 case of lymph node dissection for penile cancer. This study also included 2604 cases of laparoscopic radical nephrectomy and 555 cases of laparoscopic partial nephrectomy, but no recurrence of the trocar site was observed.⁵

According to few research, the rate of port-site metastasis after surgery for urological cancer is generally 0.5-2%, while with open surgery is 0.8-1.6%. Patients with port-site metastases are often a poor prognostic factor. The 1-year survival prognosis in these patients is about 31.8%, while in metastatic kidney cancer, 1-year survival is 50%.⁶

The first case of tumor metastasis to the port-site in urological laparoscopic was recorded in 1994, and this is the case of metastasis after laparoscopic pelvic lymphadenectomy. The first case of port-site metastasis after laparoscopic renal treatment cancer was reported by Fentie DD et al. in 2000.⁷

The cause of this metastasis is still not clear, the authors admit to many different factors such as the initial tumor status, port-site status, immunity status, specimen collection method, laparoscopic surgery with CO₂ circulating throughout the abdomen, and exiting the trocar hole can also be the cause of cancer cells spreading. In order to prevent the seeding of cancer cells, specimen collection bags are recommended. In the presence of ascites, laparoscopic surgery is not recommended.⁸

Tumor type:

Joseph Song (2014) reviewed 16 cases of recurrence at the trocar port-site after RCC surgery, counting seven patients related to surgical technique, nine patients related to the initial tumor status. Histopathological results include clear cells (11), papillary bodies (4), and RCC chromatophores (1).⁶ Shimokihara K (2017) reports 1 case of laparoscopic radical

nephrectomy diagnosed as cRCC, pT1a, low grade and without technical problems, the tumor was removed through the specimen bag without tearing, relatively low risk compared to previous reports that most of the reported cases were high-grade carcinoma (Fuhrman grade 3, 4).⁹ Our first patient is a case of sarcomatoid kidney cancer with high malignancy. Time to detect recurrence 18 months, no recurrence was detected at a location other than the trocar port-site. Thus, the factor related to tumor recurrence here is probably related to the original tumor status. Our second patient also had a pathological result of high-grade renal cell carcinoma with a Fuhrman grade 4.

Among 12/16 cases evaluated by Fuhrman grade in Joseph Song's literature there were 9 cases at grade 3, 4 and only 3 cases of Fuhrman grade 2 and there are related technical factors that can lead to PSM (specimens of 1 patient were taken without using a bag, specimens of 2 patients were morcellated). Therefore, in cases unrelated to surgical techniques, tumors with a high histological grade are more likely to metastasize further.⁶ Chuang also suggested that tumor type rather than technical factors are responsible for PSM formation.¹⁰

Specimens Extractor:

Joseph Song determined the factors related to port-site metastasis in 7/16 cases were: morcellate the tumor into small pieces (3 patients), no usage of the laparoscopic bag (2 patients), rupture of the tumor at collection (2 patients); there were 9 cases where there was no clear technical cause for the PSM condition. The average time of tumor appearance was 16 months (3-39 months).⁶ Our first patient received an intact specimen through an additional incision, while the second patient was obtained by morcellating. However, because there is no standard specimen bag, in both these cases,

we used a homemade sample bag made from a plastic camera bag, which is very thin, easy to tear, and not sealed. However, the first patient relapsed 18 months after surgery, probably not related to the specimen collection technique, whereas the second patient relapsed early after surgery (3 months), more likely the cause was related to small cutting specimens.

According to Tsivian A, there are 4/9 cases of PSM related to the morphology of small cut specimens after laparoscopic renal cell cancer.¹¹

To prevent seeding at the port site, specimens removed by morcellating should be stored in double-layer, waterproof, thick, and tough specimen bags such as LapSac. However, it is often challenging to put specimens into this type of bag, especially with large specimens. Although the bag is very sturdy, perforation can always occur when the specimen collection technique is poor.¹² Other patient bags, such as EndoCatch II (US Surgical, Norwalk, CT), have thin walls and are prone to tearing, therefore, it is contraindicated for morcellating specimens and is commonly used to remove intact specimens. Morcellating malignancies without a qualified pouch are considered poor practice in surgery. Removal of intact specimens has not been recognized to be associated with an increased risk of local recurrence or metastasis.¹³

Masterson pointed out that tumor ablation is a factor in PSM.¹⁴ Shortly after that, Greco reported RCC PSM after the specimen was morcellated. Both cases indicated that the large tumor was morcellated or ruptured as a possible cause of tumor cell seeding.¹⁵ Barrett and Fentie reported a case of recurrence at the trocar port 25 months after radical nephrectomy and microscopic specimen collection. Seeding can occur through lacerations of the specimen bag created by the blade during morcellating, especially with large specimen.¹⁶

Radical or partial nephrectomy:

In 2008, Masterson TA published a case of metastasis at the trocar port-site for partial nephrectomy with the pathology result of pRCC.¹⁴ In 2012, Chaturvedi S published 4 cases of metastasis at the trocar hole after laparoscopic radical nephrectomy.¹⁷ In 2013, Song JB published 1 case of PSM after laparoscopic partial nephrectomy,³ and Ploumidis published 1 case after laparoscopic radical nephrectomy with pRCC.¹⁸ In 2014, Joseph Song recorded 16 clinical cases: PSM appeared after radical nephrectomy laparoscopic (12), partial nephrectomy (3), and one case of robotic-assisted partial nephrectomy (3).⁶ Radical nephrectomy usually does not reveal the tumor but removes the perirenal fat tissue and the tumor with the kidney into one mass, so the possibility of seeding is lower with partial nephrectomy.

CO2 factor:

While technical causes cannot be ruled out, there are several theories that the intrinsic etiology of laparoscopic surgery causes PSM. Mathew et al. suggested that CO2 injection significantly increased the risk of PSM compared with non-pneumatic laparoscopic surgery, as the intra-abdominal gas injection can cause air leakage that pulls tumor cells from the abdominal cavity to the abdominal organs. Furthermore, CO2 has a stimulating effect on tumor growth and inhibits protective factors.¹⁹ Wittich et al. showed that gas leakage could not carry sufficient tumor cells to cause tumor recurrence and concluded that gas leakage is not a significant factor in PSM formation and gas injection alone does not may play a role in PSM formation.²⁰

Biological factors:

Chaturvedi et al. identified 4 cases of RCC PSM with circulating metastasis. These

patients all used a sample collection bag, the tumor was not morcellated, and there were no other lesions. All four of these patients had metastases to multiple trocars ports and distant organs, suggesting that the patient had progressed to multiple sites, not only in the kidney.¹⁷ Similarly, Joseph Song PSM's report after robotic-assisted partial nephrectomy, no technical risk factors, and PSM appearance at the trocar portal was not related to specimen collection.³ In the reports of other authors and our two patients, after PSM treatment, the tumor then appeared to metastasize in many other locations such as the brain, lung, liver, kidney, and peritoneum. While inconclusive, these findings suggest that PSM may form by circulating metastasis, which is also the cause of distant metastases at other sites.

Local wound formation is known to increase the risk of tumor deposition 1000-times. The deposition of collagen on the surface during wound formation can stimulate tumor cells to grow. In addition, growth and angiogenesis factors also contribute to tumor growth. As a result, the port-site is an ideal site for circulating tumor cells in the blood to deposit and form tumors. Therefore, PSM may be a predictor of distant metastases at other sites.

Some research shows that in addition to the trocar site, there are some cases of abdominal wall metastasis unrelated to the location of the trocar port or the location of the old incision. In 1987 Yanagie H reported a case of metastasis to the left abdominal wall after resection of suitable renal cell carcinoma.²¹

Based on our 2 cases and the literature, we found that several causes increase the risk of PSM formation, such as morcellating specimens when there is no bag or unqualified bags, broken specimens for early PSM cases. For PSM cases that appear late, and no technical factors can

be found, the cause may come from the type of the tumor and the role of biological factors. There was no statistically significant difference between histopathological types, CO2 factor, surgical method, and port-site metastasis rate, which could explain that the sample size was not large enough. Because the number of cases is rare, and the mechanism is unclear, further studies are needed in the future.

PSM treatment

Surgical resection and radiation therapy have been reported for port-site metastatic after renal cell carcinoma. However, there is still no consensus on the optimal treatment method. In general, for metastatic renal cell carcinoma, complete surgical resection is the standard gold treatment when possible. For port-site metastases without visceral metastases, long relapse-free survival has been reported.²²

It is crucial to consider the possibility of Schloffer tumor in the differential diagnosis of port-site metastases. Schloffer tumors develop due to a reaction against a foreign body, such as surgical sutures, at the incision site. This inflammatory pseudotumor forms months to years after surgery. PET (Positron Emission Tomography) is sometimes performed to distinguish port-site metastases from Schloffer tumors.²² In the present case, due to the rare incidence of port-site metastases after radical nephrectomy, CT, ultrasonography, and PET-CT were performed to detect the type of the tumor. The tumor showed marked size progression on CT, spontaneous angiogenesis on ultrasound, and fluorodeoxyglucose uptake on PET-CT; Tumor excision was performed without needle biopsy due to the angiogenic nature of the tumor.

CONCLUSION

Port site metastasis after laparoscopic surgery for renal cell carcinoma is rare and has

a rate comparable to open surgery. At present time, all studies suggest that factors related to this phenomenon are initial tumor status, laparoscopic surgery technique, specimen collection method, and patient's condition. Prevention mainly requires the surgeon to perfect the surgical technique and be especially careful when removing the specimen.

Ethical approval

The study was approved by the Research Ethics Committee of Hanoi Medical University.

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Author contribution

Huy Hoang Nguyen: the primary doctor, conceived the original idea, wrote the manuscript. Van Hung LE: followed up, wrote the manuscript. Truong Thanh Do: operated the patients, summed up, revised manuscript. Long Hoang: operated the patients, summed up, revised manuscript.

Declaration of competing interest

The authors declare no known competing financial interests or personal relationships that could have influenced the work reported on this page.

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