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FDG-PET probe-guided surgery for recurrent retroperitoneal testicular tumor recurrences

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Abstract

Aim: Tumor marker based recurrences of previously treated testicular cancer are generally detected with CT scan. They sometimes cannot be visualized with conventional morphologic imaging. FDG-PET has the ability to detect these recurrences. PET probe-guided surgery, may facilitate the extent of surgery and optimize the surgical resection.
Methods: Three patients with resectable 2nd or 3rd recurrent testicular cancer based on elevated tumor markers after previous various chemotherapy schedules and resections of residual retroperitoneal tumor masses were included in this study. A diagnostic FDG-PET was performed and a hotspot in previously operated area of the retroperitoneal space in all three patients was visualized . PET probe-guided surgery was performed using a high-energy gamma probe 3 h post-injection of 500 MBq FDG.
Results: All patients showed extended adhesions and scar tissue in the retroperitoneal area due to the previous surgeries. Pre-operative PET/CT scan showed a good correlation with intra-operative PET probe-guided detection of recurrent lesions. There was a high target to background ratio (TGB) of 5:1 during the procedure. In one patient, a 2 cm large lesion, which did not show on pre-operative FDG-PET scan, was detected with the PET probe. Histopathologic tissue evaluation demonstrated recurrent vital tumor in all PET probe positive lesions.
Conclusions: PET probe-guided surgery seems to be a promising tool to localize FDG-PET positive lesion in recurrent testicular cancer in hardly accessible surgical locations. PET probe-guided surgery might be a useful technique in surgical oncology for recurrent testicular cancer and has the potential to be applied in surgery of other malignant diseases.

Keywords: Cancer; Testis cancer; Non-seminoma; PET; Handheld PET probe; Retroperitoneal

Introduction

Testicular cancer is the most common cancer diagnosis in men between the ages of 15 and 35 years, with approximately 2850 new cases detected in the Netherlands each year. Long-term cure can be achieved in 70–80 percent of patients with metastatic non-seminomatous testicular germ cell tumors (NSTGCT) with cisplatin based chemotherapy.[1,2] After completion of first-line chemotherapy, residual masses consisting of necrosis, fibrosis, vital carcinoma or mature teratoma are found in approximately 40% of patients. Since CT imaging and serum tumor markers have low specificity in predicting the presence of vital carcinoma or mature teratoma in residual masses, complete surgical resection is the only diagnostic and curative treatment option.[3]

Positron emission tomography (PET) using [^{18}F]fluorodeoxy-glucose (FDG) has been used in seminomatous and non-seminomatous germ cells cancer in trying to improve the differentiation between vital and nonvital tumor tissue in residual masses.[4–7] However, in a recent report by Oechsle and colleagues, FDG-PET showed no additional value compared to CT imaging and serum tumor markers in pre-operative staging of 121 patients with primary stage IIC or III NSTGCT.[3] In recurrent testicular cancer it can be difficult to locate tumor lesions due to extensive scar tissue formation of previous surgery. Multimodality FDG-PET/CT scanning could be of additional value to locate PET positive lesions pre-operatively. To relocate these

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FDG-PET positive hot spots intra-operatively PET probe-guided surgery could be of additional value. In the last years PET probe-guided surgery has emerged as a new technique to improve intra-operative staging and localize sites of occult disease in cancers of the colon, stomach, lung, breast and thyroid.[8,9]

In the current study, pre-operative PET/CT imaging and intra-operative PET probe-guided surgery have been combined to improve the localization and resection of recurrent retroperitoneal testicular cancer after previous extensive surgery.

Patients and methods

Patients

Three patients with resectable 2nd or 3rd recurrent testicular cancer that were evaluated by the Department of Surgical Oncology at the University Medical Center Groningen for PET probe-guided surgery.

Primary surgery for retroperitoneal residual tumor tissue consisted of laparoscopic full template retroperitoneal lymph node dissection (RPLND). Retroperitoneal recurrences were treated by open resection of tumor mass with surrounding tissue.

The first patient was diagnosed at the age of 22 year with disseminated NSTGCT and received polychemotherapy (3x bleomycin, etoposide and cisplatin (BEP) and 1x EP) and residual disease was resected and showed mature teratoma. Two years later an isolated retroperitoneal recurrence was resected and histology revealed mature teratoma. After three years a second isolated retroperitoneal recurrence was radically resected. Histology showed a yolk sac tumor. Subsequently the patient developed severe renal insufficiency precluding the use of intravenous contrast medium. A year later FDG-PET and CT showed a retroperitoneal recurrence at the corpus vertebra of L2.

The second patient was diagnosed at the age of 21 years in 2001 with a stage IIC seminoma testicular germ cell tumor (STGCT) and treated with polychemotherapy (4x cyclophosphamide, vincristine and carboplatin (COC)) with a complete response. After four years the patient developed a retroperitoneal recurrence and received four courses polychemotherapy (4x paclitaxel, ifosfamide, cisplatin (TIP)) with a complete response. One year later a recurrence in the mesentery of the small bowel was resected. The patient recurred in the previous surgical area four months after the previous surgery, documented on PET and CT.

The third patient was diagnosed at the age of 40 years in 1998 with an NSTGCT with retroperitoneal and lung metastases. Patient received 4 courses polychemotherapy (BEP) with a complete tumor marker and CT response. Seven years later the patient was diagnosed with an isolated retroperitoneal recurrence, which was resected. The pathology revealed a microscopically irradical resected yolk sac tumor. The patient received adjuvant polychemotherapy (4xTIP). Two half years later the patient was diagnosed with a small 2nd recurrence retroperitoneally in the previous surgical resected area and selected for PET probe-guided surgery.

FDG-PET and CT scan imaging

FDG-PET imaging was only used in case of elevated serum tumor markers during follow-up. FDG-PET imaging was performed on an ECAT HR + PET camera. Patient fasted approximately 6 h prior to intravenous injection of 5 MBq FDG/kg bodyweight. Images were obtained 60 min after intravenous injection of FDG. FDG-PET images were fused with stand-alone CT contrast images to obtain optimal anatomical information of the FDG-PET positive lesions. FDG-PET positive lesions had a mean SUVmax of 8.1 (corrected for blood glucose level) (Range 3.3–11.2).

FDG-PET probe-guided surgery

Patients received an intravenous injection of 5 MBq FDG/kg bodyweight 3 h before surgery. All patients received a urinary catheter prior to administration of FDG to avoid contamination of the operation field with FDG positive urine. No glucose containing IV fluids were given prior of during surgery. PET probe-guided surgery was performed using a high-energy gamma probe (y Locator DXI, GF&E Tech GmbH, Seeheim, Germany) 3 h post-injection of FDG. A target to background ratio of 1.5 and above was used for confirmation of the target localization. This probe is in effect a multi-detector probe without mechanical collimation. Its focusing properties achieved by a parameterization of the count rates from the different detectors inside the probe. So no mechanical collimator is used on the PET probe (Fig. 1). During the surgical procedure, the PET probe was used to frequently scan the operation area for FDG activity. The highest FDG activity was compared with normal surrounding tissue to calculate the target to background ratio. After resection of the FDG-PET positive lesions the operation area was scanned for residual FDG-PET activity.

Results

All three patient showed one hot spot on the pre-operative FDG-PET scan (Fig. 2). During the surgical procedure, all patients showed extended adhesions and scar tissue in the retroperitoneal area due to the previous surgeries. The pre-operative FDG-PET hotspots and CT scan lesions showed a good correlation with the intra-operative PET probe-guided detection of recurrent lesions.

In the first patient who underwent two previous resections of retroperitoneal non-seminoma testis recurrence, showed a 3 cm large PET probe positive lesion corresponding with the pre-operative PET/CT scan. A second 1.5 cm large lesion, which did not show on the pre-operative FDG-

Figure 1. High-energy gamma probe.

PET scan, showed a high signal with the PET probe. This lesion was located at a distance of 5 cm of the lesion detected on the pre-operative PET scan and identified as suspected of tumor metastasis. After resection of these lesions, histopathologic tissue evaluation demonstrated recurrent vital tumor glandular yolk sac in both lesions. The patient received postoperative 50 Gy radiotherapy and died 6 months later from disseminated testicular cancer.

The second patient underwent a previous resection of recurrent seminoma testis tumor of the retroperitoneum and small bowel. Pre-operative PET/CT scan showed a 7 cm large tumor in close proximity of the superior mesenteric artery. During surgery the tumor was PET probe positive. The tumor was clearly visible and palpable and could be removed on without the use of the PET probe. No additional lesions could be detected with the PET probe during surgery. Histopathologic evaluation demonstrated vital tumor in the resected tissue and the patient received 40 Gy postoperative radiotherapy. Within a few months the patient died of disseminated seminoma testicular cancer.

The third patient with a 2nd retroperitoneal recurrence of non-seminoma testis tumor showed one PET/CT positive lesion between the aorta and caval vein. During surgery, the infra-renal part of the aorta and caval vein were encapsulated in fibrotic tissue. The tumor could not be detected on visual inspection or palpation. The handheld PET probe could easily detect the area with high FDG-PET activity. The resected PET positive tissue showed vital tumor on histopathological examination. Two month after PET probe-guided surgery the patient showed progressive disease, retroperitoneally and distantly, received palliative chemotherapy (Oxaliplatin/Gemcitabine) and died 6 months later.

After resection of the PET probe positive lesions, no activity was detected with the PET probe in all three patients. There was a sufficiently high target to background ratio of 5:1 or greater during all procedure.

Discussion

Accurate localization and resection of recurrent tumor after previous surgery can be difficult in testicular cancer patients. Up till now, intra-operative visual inspection and palpation of the pre-operative identified area on CT scan was the only method to identify the recurrent tumor sites. However, due to extensive scar tissue formation of previous surgery, discrimination between vital tumor and fibrosis is almost impossible. It was therefore necessary to resect all suspected and fibrotic tissue. However, due to the close proximity of vital structures, like blood vessel, nerves tissue and the urethra to the fibrotic tissue, this could be a cumbersome task. In the last years PET probe-guided surgery has shown to be of additional help in cancer surgery. PET probe-guided surgery with the use of FDG as a PET tracer has been used in melanoma, ovarian, gastric, colon, lung, breast and thyroid cancer to aid intra-operative tumor localization.[9–12]

In our current study, intra-operative PET probe-guided localization of recurrent tumor correlated well with pre-operative FDG-PET imaging. However, pre-operative FDG-PET imaging on our PET camera is limited by the size of the lesion to about 1 cm. In this series, intra-operative PET probe detected an additional tumor of 1.5 cm in one of three patients. This is in line with a study of Sarikaya

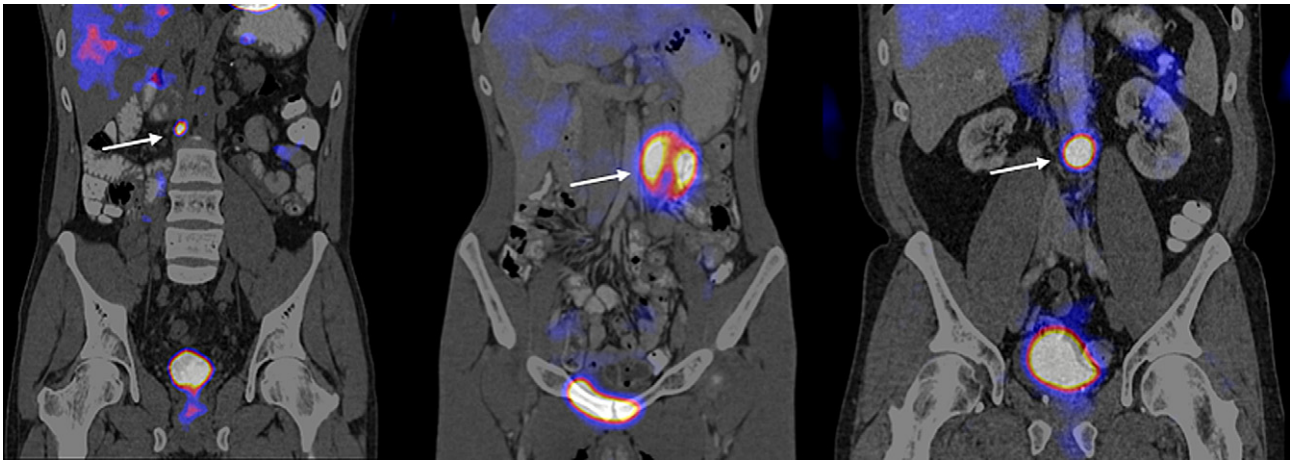

Figure 2. FDG-PET positive abdominal lesion in patient 1 (left), patient 2 (middle) and patient 3 (right).

and colleagues[8] of 24 patients with recurrent colorectal carcinoma where a handheld PET probe detected 6 additional tumor foci that were not identified on pre-operative FDG-PET scan. All foci were less than 1 cm in size and were generally located within the omentum and deep pelvis. Recent PET-CT cameras systems show better resolution, up to 3–5 mm, and this may improve pre-operative detection of smaller lesions.

Pitfalls of FDG-PET in testicular cancer

There are some pitfalls in the use of FDG-PET scanning for follow-up of patients with testicular cancer. False negative FDG-PET scans can occur if the residual lesion contains only mature teratoma tissue. False positive FDG-PET results can be obtained as a result of persistent inflammation after chemotherapy. In the study of Oechsle et al. FDG-PET scan showed a negative predictive value of 51% and a positive predictive value of 59% for predicting viable tumor.[3] However, in case of elevated serum tumor markers, FDG-PET/CT can be helpful in anatomical localization of the recurrent tumor lesion. Thereafter, a handheld PET probe may be useful for intra-operative localization of the FDG positive lesions.

Value of PET probe

A disadvantage of PET probe-guided surgery is the relative diffuse signal of a PET positive lesion. Due to the nature of a PET signal, acquiring a focused signal is hardly possible with the standard collimated probe. Changing the collimator to a Tungsten collimator improved the directional properties of the standard probe. The electronic collimation as achieved in this multi-detector 511 keV probe outperforms the traditional mechanical collimated probe although improving surgical resection margins in fibrotic areas with the use of this electronically collimated PET probe is therefore still difficult.

Safety of FDG-PET probe-guided surgery

Heckathorne and colleagues[13] investigated the radiation exposure to the surgical team and nursing staff during FDG-PET guided surgery. For surgeries performed between 1 and 3 h after injection of 10 mCi (370 MBq) of ^{18}FDG the effective radiation dose to the surgeon is 59 μSv and to the nursing staff 22 μSv. This will allow the surgeon to perform 800 procedures per year without exceeding the occupational dose limit of 50 mSv.

Conclusion

In conclusion PET probe-guided surgery seems to be a promising tool to localize FDG-PET positive lesion in recurrent testicular cancer. However since sensitivity of handheld PET probe on microscopic lesions is not available, improving resection margins and prognosis of patient with recurrent testicular cancer is not proven.

Conflict of interest

The authors declare that they have no conflict of interest.

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