

Short Communication

Radioguided Pelvic Lymphadenectomy - The Rescue in Recurrence Prostate Cancer - one New Tool for Detection of Metastases

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Keywords

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- Radioguided surgery
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Abstract

Background: The prostate cancer is the most common tumor in man, and even after the initial therapy an important part of the affected population also presents recurrence of the tumor. The identification of metastasis sites through this nuclear medicine exam allows the extrapolation of its use, previously only diagnostic, to still act as an experimental model in the therapeutic field

Methodology: Case report of a 79 years old patient with a initial serum PSA 9.4 was diagnosed with prostate cancer with a biopsy showing a Gleason 7 (3+4). He underwent a radical prostatectomy with standard lymphadenectomy in 2010. It evolves uneventfully until in 2014 a biochemical recurrence was diagnosed and was then submitted to salvage radiotherapy. After 2 years of radiotherapy, he returned to have a new elevation of PSA and a PET-PSMA, which showed pelvic lymph node enlargement. He was submitted in an experimental protocol of radioguided pelvic lymphadenectomy with PSMA - 99mTc.

Conclusion: Although it is a recent technology, radioguided surgery is an effective way to identify small metastases in patients undergoing salvage lymphadenectomy, helping the surgeon to detect diseased lymph nodes and not adding morbidity and mortality to the procedure

INTRODUCTION

The prostate cancer is the most common tumor in man, and even after the initial therapy an important part of the affected population also presents recurrence of the tumor [1,2]. The treatment of recurrence could involve radiotherapy or salvage surgery. Metastatic patients usually receive androgen deprivation therapy [3]. In patients with a not detected metastasis or low volume metastasis and with a good health, they can benefit from local salvage treatments, positively influencing progression-free survival and delaying the initiation of more aggressive systemic therapies [4,5].

Lymph nodes represent one of the most frequently sites affected by recurrent prostate cancer. Originally, the lymphatic architecture is preserved in the presence of prostate cancer, but it can vary significantly between individuals and undergo alterations or deviations secondary to tumor blocks in its normal pathway. After radical prostatectomy or radiotherapy, important changes can occur in the lymphatic drainage. For this reason, metastases may appear in unexpected locations and outside the classic field of pelvic lymph node dissection. Recognizing

the exact status and extent of lymphatic spread is a complex challenge [6,7].

The image field tomography by positron emission tomography (PET) advanced substantially with the prostate-specific membrane antigen (PSMA) imaging. The identification of metastasis sites through this nuclear medicine exam allows the extrapolation of its use, previously only diagnostic, to still act as an experimental model in the therapeutic field. The use of gamma probe and for identification of membrane markers (PSMA) during surgery allows a more accurate location of lymph nodes affected by cancer.

MATERIALS AND METHODS

Case Description

Patient JLN, male, 79 years old, initial serum PSA 9.4, was diagnosed in 2010 with prostate Gleason 7 (3 + 4). He underwent a radical prostatectomy with standard lymphadenectomy still in 2010. Results of the pathological anatomy of the surgical specimen showed: Gleason 7 (4+3), free margins, T2cN0M0, no

lymph nodes involved. It evolves uneventfully until in 2014 a biochemical recurrence was diagnosed and was then submitted to salvage radiotherapy (7000GY, 35 sections), with a nadir of 0.25 in May 2015. After 2 years of radiotherapy, he returned to have a new elevation of PSA, and in 2019 it had a PSA doubling time less than 6 months. He was restaged with a PET-PSMA (Figure 1), which showed pelvic lymph node enlargement in the right external iliac chain, measuring 2.5 cm in the longest axes, coexisting another lymph node of 0.5 cm immediately below the bifurcation of the ipsilateral common iliac artery, without other distant injuries. As the patient in question had good clinical status and had no evidence of other metastases, we opted for inclusion in the experimental protocol of radioguided pelvic lymphadenectomy with PSMA - 99mTc.

Description of procedure

A kit HYNIC-PSMA – SN (Nucleus-Equip HYNIC-PSMA – SN) “Commercial name” manufactured by ININ (National Institute of Nuclear Investigations) was labeled with 99mTc-Technetium eluate, with quality control that guaranteed its radionuclide purity. 740 MBq of the material were injected, and images were taken after 2 and 22 hours to ensure adequate labeling with 99mTc-Technetium of the lymph nodes previously seen in PET/CT PSMA-Ga-68.

The surgery was performed in a minimally invasive way by laparoscopy. For this procedure, the patient was positioned in horizontal dorsal decubitus. Four small abdominal incisions were made (Figure 2). In the umbilical region was positioned a 10mm trocar for the camera, a trocar 10mm in the left iliac fossa aimed use of bipolar laparoscopic forceps and laparoscopic clip applier, a 5mm trocar in the above region pubic to a grasper

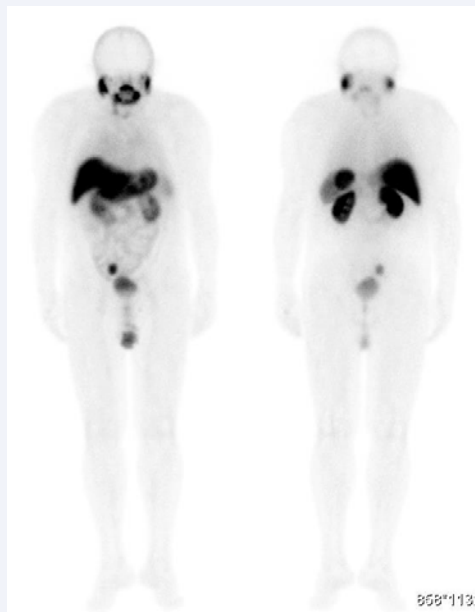


Figure 1 Whole-body PSMA-99mTc scintigraphy images in anterior and posterior projections, demonstrating uptake in the right pelvic lymph node.

and, for last, a trocar 12mm 4cm to the right of the umbilical trocar through which the long gamma probe was passed, properly protected with sterile plastic. Pelvic lymphadenectomy was performed in the region previously identified by PET/PSMA - the right external iliac region and right common iliac bifurcation - and with the aid of the gamma probe, we identified the two affected lymph nodes. The excision of the lymph node tissue was completely performed (Figure 3). Healthy fat tissue samples were also removed so that ex - vivo the comparison could also be made in obtaining the gamma probe signals and once again confirming the correct removal of the affected tissue. The signal value emitted in the fat tissue serves as an analysis parameter. It is considered as diseased tissue, one that emits at least twice the value of the unaffected tissue.

The patient evolved uneventfully and was discharged less than 24 hours after surgery. The result of the anatomopathological exam confirmed metastasis of prostate adenocarcinoma in both lymph nodes. The control PSA test performed 45 days after surgery was 0.87 ng/mL.



Figure 2 Trocar placement. Two trocars of 10mm (optics and grasper). One trocar 12mm for removal of parts and passage of probe. Two trocars of 5mm for passage of accessory clamps.



Figure 3 Probe showing 168 SUV in pelvic lymphadenectomy product piece.

DISCUSSION

With the increasing use of PET/PSMA in prostate cancer recurrence, treatments aimed at metastasis, such as rescue lymphadenectomy, are becoming more feasible. However, accurate identification of small and/or atypically located lesions during salvage lymphadenectomy can be challenging considering previous treatments and manipulations. In this context, radioguided surgery can be an advantage [8]. This surgery detects prostate cancer recurrences expressing PSMA with a high sensitivity (92.3%) and specificity (93.5%) [9,10].

Maurer et al. [9], were able to show in 31 patients who underwent radioguided surgery with ^{99m}Tc-PSMA that all lesions previously seen on imaging with ⁶⁸GaPSMA PET were also identified intraoperatively. In two patients, radioguided surgery was able to identify 3mm lymph node recurrences not seen in the previous imaging exam. Rasucher et al (2017) also found 5 suspicious lesions not seen on PET/CT in 3/31 patients.

Long-term data are still lacking to determine whether radioguided therapy would actually have as much positive impact as the therapies already in vogue. The use of the gamma probe has been investigated as a tool to aid in the removal of affected lymph nodes. Published studies show a positive predictive value ranging from 88% to approximately 100% ex vivo [9,10]. The study by Kniiper S. et al (2018) comparing patients undergoing conventional and radioguided lymphadenectomy found, in terms of short-term outcome, an overall PSA decline, PSA decline > 50% and > 90% within 6 weeks no additional treatment in 50%, 29% and 7% in the Conventional group and compared to 100%, 92% and 53% in the radioguided surgery group [8].

In line with the rationale observed in the literature review, it is essential to carefully choose the profile of patients who will undergo this procedure so that it really benefits cancer control and reduces the morbidity of the treatment. One of the eligibility criteria would be positive PET/PSMA, demonstrating locoregional disease and absence of distant metastases. Other factors, including the patient's clinical status and associated comorbidities, should also be taken into account.

Rigatti et al. [11], noted that the 5-year clinical recurrence-free survival was shorter for patients with positive lymph nodes in the retroperitoneum compared to patients in whom positive lymph nodes were detected only in the pelvis (11% vs 53%; $P < 0.001$), as well as the level of PSA < 4ng/mL compared to PSA \geq 4ng/mL (48% vs 13%). Patients with unfavorable factors may have a greater need for further treatments to control the clinical progression of the disease.

Several postoperative factors, including complete biochemical response and number of positive lymph nodes in salvage lymphadenectomy, are also established as independent predictors of clinical progression as well [10].

In the literature review, complications related to radio-pharmaceutical infusion were not observed and complications

related to the surgical procedure were mostly classified in the Clavien-Dindo scale as grade 1 - lymphorrhea (21%), fever (25-30%), prolonged ileum [4,10,11]. This reinforces the greater safety and reduced complications of the procedure compared to standard lymphadenectomies.

CONCLUSION

Recurrence of prostate cancer presents a challenge for urologists and oncologists. Although it is a recent technology, radioguided surgery is an effective way to identify small metastases in patients undergoing salvage lymphadenectomy, helping the surgeon to detect diseased lymph nodes and not adding morbidity and mortality to the procedure. In the short term, there seems to be a positive influence with a reduction in disease progression, as it makes it possible to detect subcentimeter lesions. In the long term, some patients may even achieve a cure and, in others, there may be the prospect of postponing systemic treatment.

SUMMARY

Question: Is radioguided surgery an effective way to identify small metastases in patients undergoing salvage lymphadenectomy?

Pertinent Findings: In this case report the use of the gamma probe remained as a tool to aid in the removal of affected lymph nodes. Thanks to the signals that came from affected disease and was collect by the gamma probe we could affirm that lymph node tissue was completely performed, still during the intraoperative period.

Implications For Patient Care: Radioguided surgery is an effective way to identify small metastases in patients undergoing salvage lymphadenectomy, helping the surgeon to detect diseased lymph nodes and not adding morbidity and mortality to the procedure.

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