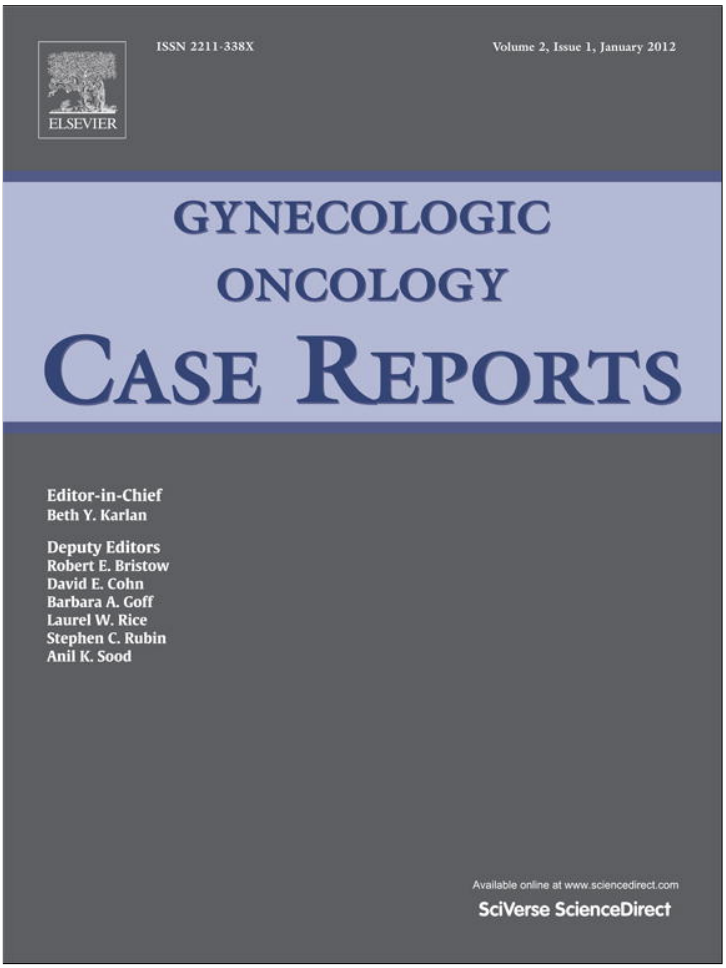

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Gynecologic Oncology Reports 4 (2013) 29–31

Contents lists available at SciVerse ScienceDirect

Gynecologic Oncology Reports

journal homepage: www.elsevier.com/locate/gynor

Case Report

False positive PET–CT scan and clinical examination in a patient with locally advanced vulvar cancer

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ARTICLE INFO

Article history:
Received 2 November 2012
Accepted 27 December 2012
Available online 6 January 2013

Keywords:
Inguinofemoral metastasis
PET–CT scan
Vulvar cancer

Introduction

In the United States, 4490 new malignant vulvar tumors and 950 deaths are expected secondary to vulvar malignancy in 2012 (Siegel et al., 2012). The most common histologic type is the squamous cell carcinoma. The presence of inguinofemoral lymph node metastasis is the hallmark of FIGO stage III vulvar cancer. At this stage, 5-year survival rates vary from 20% to 60% depending on the number and location of involved lymph nodes (Rutledge et al., 1991). Clinical prediction of lymph node spread can be inaccurate, so lymph node status is best determined surgically (Micheletti et al., 1990). Systematic, complete inguinofemoral lymphadenectomy is the historical gold standard for evaluating metastasis (Micheletti et al., 1990). However, this procedure carries a high complication rate, including lymphedema, especially if chemoradiation is needed due to pathologically proven metastases (Homesley et al., 1986).

Along with clinical assessment, fluorine-18, deoxy-2-fluoro-D-glucose positron emission tomography (PET)–computerized tomography (CT) (PET–CT) scan can be used preoperatively to diagnose possible regional inguinofemoral lymph node or distant metastasis (Cohn et al., 2002). In the absence of inguinofemoral metastasis on a PET–CT scan, the surgical approach is to perform radical vulvectomy with systematic complete inguinofemoral lymphadenectomy (to confirm PET scan results). If a metastasis is found in the inguinofemoral lymph node basin by PET–CT scan, many surgeons will debulk the positive lymph node, and follow the surgery by adjuvant chemoradiation therapy.

We present a patient with invasive vulvar carcinoma with bilateral inguinofemoral lymph nodes that are both clinically palpable and PET–CT scan positive. Removal of the inguinofemoral lymph nodes was then performed. This case demonstrates limitations of this radiologic technique.

Case

A 34 year-old female presented with a six-month history of vulvar pain and discharge. Vulvar examination revealed a 10 cm bilateral ulcerated mass, extending to the distal portion of the vagina and surrounding the anus. She was then referred to the university gynecologic oncology clinic.

At the clinic, a thorough examination revealed the mass extending from the lower half of the left labia through the perineal body, to the lower half of the right labia. It also involved the lower half of the posterior vaginal wall and the skin around the anus. Although it was close to the anal sphincter, it did not invade the rectovaginal septum or the anal sphincter itself. Examination also showed two palpable and firm inguinal lymph nodes in the left groin measuring 1 and 2 cm in diameter and a 1 cm lymph node on the right side. A punch biopsy of the primary lesion was taken that later revealed invasive squamous cell carcinoma.

PET–CT scan highlighted the vulvar lesion as well as several prominent bilateral inguinal lymph nodes — all with positive uptake, suggesting inguinofemoral metastasis without apparent distant metastasis (Fig. 1). The initial diagnosis was a T3 vulvar lesion with bilateral lymph node involvement.

Due to the extent of the vulvar lesion and close proximity to the anal sphincter, the decision was made to surgically debulk the inguinofemoral lymph nodes without operating on the primary tumor. Surgery would be followed by primary chemoradiation therapy to the vulvar mass and to both inguinofemoral lymph node basins.

Debulking of the lymph nodes was uncomplicated. Four enlarged nodes were found on the left, the largest being 2.1 cm. On the right, there were 3 small palpable lymph nodes approximately 0.5 to 1 cm in size. All suspicious lymph nodes were removed. Because of the multiplicity and size of the affected nodes, a complete bilateral

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2211-338X/$ – see front matter
http://dx.doi.org/10.1016/j.gynor.2012.12.009

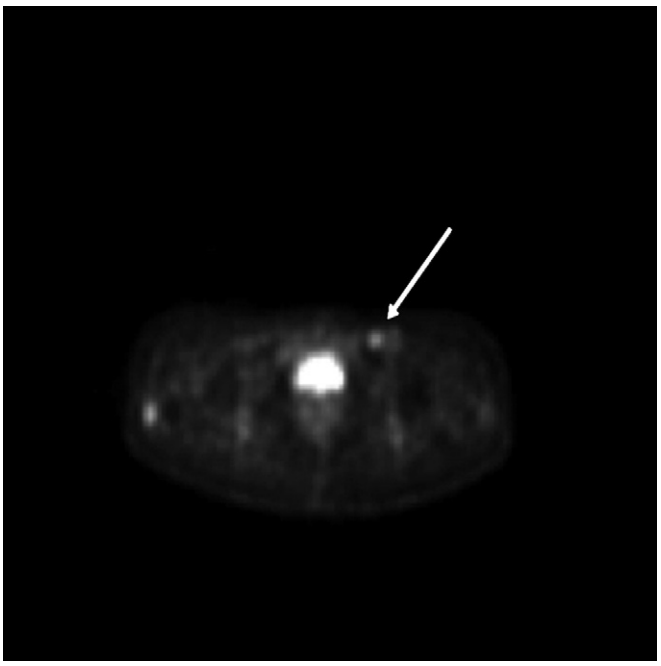

Fig. 1. PET positive lymph node in the left inguinofemoral region.

lymphadenectomy was performed instead of the intended lymph node debulking. No frozen section analysis was deemed necessary.

Final pathologic examination revealed eleven left inguinal lymph nodes, ranging in size from 0.3–2.1 cm, all negative for metastatic cancer (Fig. 2). On the right side, there were nine inguinal lymph nodes, ranging in size from 0.5–1.5 cm, which were also all negative for metastatic cancer. The patient's final diagnosis was stage II vulvar squamous cell carcinoma.

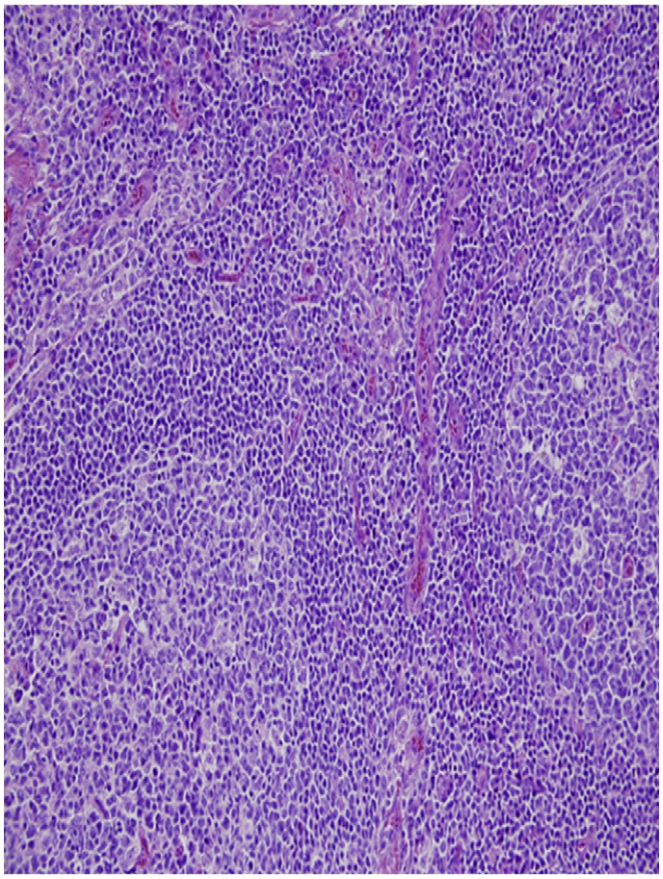

Fig. 2. Histologically negative PET positive lymph node.

Comment

Our case details a patient with extensive vulvar cancer and clinically large and suspicious bilateral inguinofemoral lymph nodes consistent with metastatic disease and confirmed by PET–CT scan. Pathologically, however, none of the lymph nodes showed cancer metastasis. This report highlights the limitations of PET–CT scanning in its ability to predict lymph node metastasis, even in the setting of clinically large and suspicious nodes.

Since the staging of vulvar cancer is performed surgically, it depends on the result of a systematic and complete inguinofemoral lymphadenectomy. Metastasis to these lymph nodes signifies stage III vulvar cancer. It is known that 10% to 20% of patients with disease confined to the vulva will show clinically occult inguinofemoral lymph node metastases, depending mainly on the depth of invasion of the primary site (Binder et al., 1990). However, inguinofemoral lymphadenectomy while imperative to the evaluation of lymph nodes, has a relatively high complication rate. To lower the incidence of complications, three strategies have been suggested: intraoperative frozen section analysis of suspicious lymph nodes (and omission of full lymphadenectomy) (McGee and Covens, 2009), sentinel lymph node (SLN) dissection (McGee and Covens, 2009), and PET–CT scan to detect metastasis prior to surgery (Basu et al., 2009).

Frozen section has good accuracy in evaluation of lymph nodes, but its utilization is generally limited to those incidences when the surgeon palpates a suspicious lymph node during surgery (Brunner et al., 2008). The second strategy of SLN dissection is currently undergoing clinical investigation. Recent studies show evidence indicating that it appears safe to omit inguinofemoral lymphadenectomy in the case of a negative SLN, with a high negative predictive value (Oonk et al., 2010). SLN dissection has not yet been universally adopted as a standard of care in the United States (van der Steen et al., 2010). The third strategy (preoperative use of a PET–CT scan) can help modify the technique of inguinofemoral lymphadenectomy. It is adopted in our practice in combination with intraoperative frozen section analysis. It also helps quantify distant occult metastasis if present.

The principle of PET scanning is based upon human tissue uptake of a glucose analog that has been tagged with a positron-emitting isotope (fluorine-18). This process is intensified in malignant cells, but can also occur in any metabolically active tissue such as brain, liver, reticulo-endothelial, and even inflammation. Both infection and inflammation are known causes of false-positive scan results. In our patient, it is possible that her clinically enlarged lymph nodes were secondary to vulvar or vaginal bacterial infection, given the large size of the tumor and likely areas of necrosis. Other potential causes for a false positive PET–CT scan include: active fibrosis, granulomatosis, sarcoidosis, hemangiomas or even ectopic endocrine tissue. Therefore, PET positivity is not specific to malignant cells. The combination of PET and CT scanning can increase specificity as well as the positive predictive value (Schmidt et al., 2007). For detecting metastasis of vulvar cancer, PET–CT is found to have a sensitivity of 80%, specificity of 90%, positive predictive value of 80%, and negative predictive value of 90% (Cohn et al., 2002). For detecting inguinofemoral lymph node metastasis specifically, PET–CT has a sensitivity rate of 67%, specificity of 95%, positive predictive value of 86%, and negative predictive value of 86% (Cohn et al., 2002).

The positive and the negative prediction values of the PET–CT scan in patients with clinically large and suspicious lymph nodes are unknown, however. Most of our knowledge about the accuracy of the PET–CT scan comes from vulvar cancer patients with normal sized lymph nodes. Future studies to examine this particular matter are needed. Until these values are determined, frozen section analysis

should be performed at the time of surgery for clinically suspicious nodes.

In conclusion, this case illustrates that if further treatment management is dependent upon the presence of a positive lymph node, it is imperative to obtain intraoperative frozen section analysis for suspicious inguinofemoral lymph nodes, even if they are known to be PET–CT scan positive. The possible future adoption of SLN dissection in vulvar cancer has the potential to limit the PET–CT scan to a screening tool for distant metastasis only.

Consent

In accordance with University of Wisconsin's IRB policy, written informed consent was not obtained for publication of this case.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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