Asia Oceania Journal of Nuclear Medicine & Biology
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AOJNMB

Herpes zoster infection mimicking pelvic lymph node metastasis on FDG-PET/CT in a patient with cervical cancer

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ARTICLEINFO

Article type:
Case report

Article history:
Received: 18 Jan 2021
Revised: 2 Apr 2021
Accepted: 10 May 2021

Keywords:
Varicella zoster
Herpes zoster
FDG-PET
Cervical cancer

ABSTRACT

Although ^{18}F-fluorodeoxyglucose-positron emission tomography/computed tomography (FDG-PET/CT) is an established method for the staging of malignancies, benign lesions (e.g, active inflammatory lesions) often show increased metabolic activity. Herpes zoster is the clinical manifestation of the activation and replication of dormant varicella-zoster virus (VZV) in individuals with decreased cell-mediated immunity. Although the diagnosis of herpes zoster is clinical, it is sometimes observed incidentally during imaging for another disease. We describe the case of a 67-year-old Japanese female patient diagnosed with cervical cancer in whom FDG-PET/CT revealed herpes zoster manifestations: hypermetabolic cutaneous lesions in the buttock and pelvic lymph node involvement. The resected lymph nodes showed no malignant lesions but revealed lymphoid follicle formation, probably related to viral infection. There has been no report comparing FDG-PET findings of lymph nodes with histologic findings; the present findings are compatible with a clinically VZV-induced inflammatory reaction in regional lymph nodes, which increased FDG accumulation. Active infection with VZV displays increased FDG uptake in regional lymph nodes and may lead to incorrect malignant disease management in oncology. Misdiagnoses can be avoided by a careful interpretation by experienced nuclear medicine physicians as well as proper clinical evaluation.

Please cite this paper as:

Harashima K, Watanabe S, Okazaki N, Endo D, Uchiyama Y, Kato F, Hirata K, Kudo K. Herpes zoster infection mimicking pelvic lymph node metastasis on FDG-PET/CT in a patient with cervical cancer. Asia Ocean J Nucl Med Biol. 2021; 9(2): 183-187. doi: 10.22038/AOJNMB.2021.55050.1378

Introduction

Although ^{18}F-fluorodeoxyglucose-positron emission tomography/computed tomography (FDG-PET/CT) is an established method for the staging of malignancies, benign lesions (such as active inflammatory lesions) often show increased metabolic activity. Herpes zoster is the clinical manifestation of the activation and replication of dormant varicella-zoster virus (VZV) in an individual with decreased cell-mediated immunity. Although the diagnosis of herpes zoster is clinical, it is sometimes identified incidentally during imaging for another disease. Here, we present the case of a patient diagnosed with cervical cancer in whom FDG-PET/CT revealed herpes zoster virus manifestation, i.e., hypermetabolic cutaneous lesions in the right buttock and pelvic lymph node involvement.

Case report

A 67-year-old Japanese female was diagnosed with cervical squamous cell carcinoma at another

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hospital. She underwent an FDG-PET/CT examination for the staging of the primary disease. The examination revealed an FDG-avid mass in the uterine cervix (SUV_{max}=13.8, Figure 1), and multiple lymphadenopathies with abnormal FDG uptake extending to both inguinal lymph nodes, the external iliac lymph nodes, the right common iliac lymph node, and the para-aortic region, which was concerning regarding the possibility of lymph node metastasis from the patient's uterine cervical carcinoma (SUV_{max}= 10.0, Figure 1). There was also subtle but abnormal FDG uptake in the skin overlying the buttock (SUV_{max}=1.6, Figure 1).

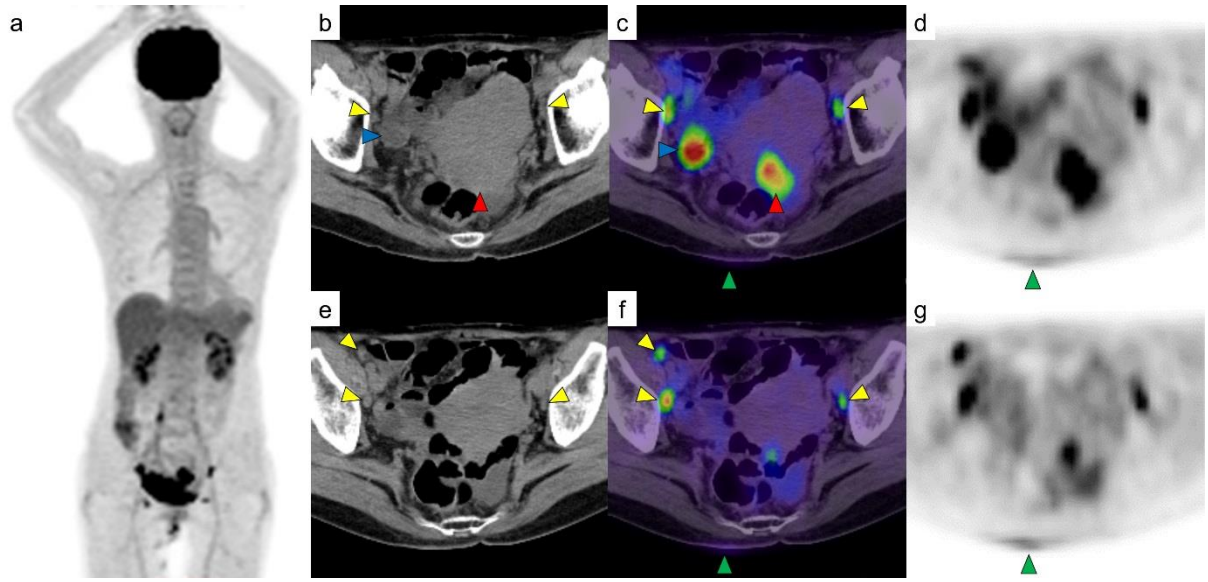

Figure 1. FDG-PET/CT image of the patient, a 67-year-old woman diagnosed with cervical cancer. **a**: Maximum intensity projection (MIP) image of PET (SUV range:0-5). **b**: CT. **c**: Fused slice (SUV range:0-5) showing an FDG-avid mass in the uterine cervix. **d**: FDG PET image (SUV range:0-3) showing the abnormal FDG uptake in the skin overlying the buttock. **e,f,g**: A different slice showing skin lesions of the buttock and bilateral pelvic lymph nodes. Red arrowhead: Cervical cancer. Yellow arrowheads: Lymph nodes. Green arrowheads: Skin lesions of the buttock. Blue arrowhead: Bladder

However, magnetic resonance imaging (MRI) performed 2 weeks before this FDG-PET/CT examination showed a mass mainly on the posterior wall of the cervix as the primary lesion, and there was no significant lymph node enlargement in the abdomen or pelvis in the images (Figure 2). Three days before the FDG-PET/CT exam, the patient was diagnosed with herpes zoster based on the appearance of eczema on her buttocks and pubic area, and treatment with amenamevir was initiated. In light of the above findings, we determined that the lymph node lesions that appeared on FDG-PET/CT reflected herpes zoster at the time of writing the radiology report.

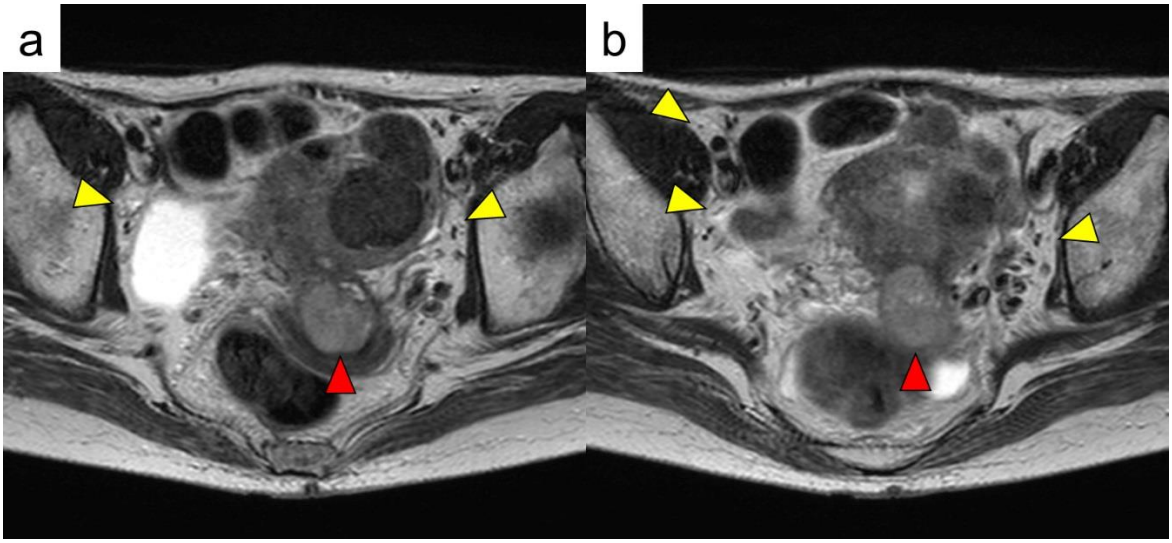

Figure 2. MRI image of the same slices of Figure 1. **a,b**: T2-weighted image showing no significant lymph node enlargement. Red arrowhead: Cervical cancer. Yellow arrowheads: Lymph nodes

One month after the FDG-PET/CT exam, the patient underwent a radical hysterectomy with bilateral adnexectomy and pelvic lymphadenectomy for cT1bN0M0 cervical cancer. Histopathologically, no malignant lesions were detected in the resected lymph nodes (pT1b1N0M0). Obturator lymph nodes showed follicular hyperplasia, which could be interpreted as the reactive process associated with the viral infection (Figure 3) (1).

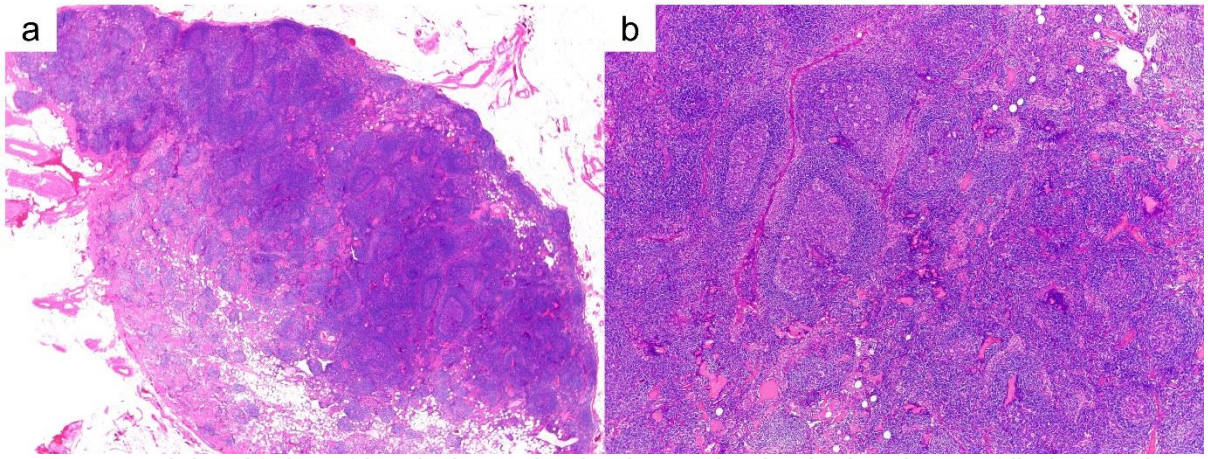

Figure 3. Histopathological findings of the right obturator lymph nodes. Some lymph nodes showed reactive follicular hyperplasia, associated with hyperplastic germinal centers. No metastatic tumor cells were found. Original magnification, **a**: ×1.25 and **b**: ×4, respectively. Hematoxylin-eosin stain

Discussion

The present case of uterine cervical carcinoma showed increased FDG uptake in abdominal or pelvic lymph nodes, plus cutaneous lesions in the right buttock. As these lesions were not present on the MRI scan 2 weeks earlier (Figure 2), the clinical manifestations suggested reactive changes associated with VZV infection, and no malignant lesions were identified histopathologically.

As a neurotropic virus, VZV travels centripetally along sensory nerve endings from infected cutaneous and mucosal lesions to dorsal root and cranial nerve ganglia after the resolution of primary varicella infection in childhood and remains in the latent phase. The latent virus reactivates when cell-mediated immunity decreases due to an immunosuppressive state. The newly synthesized VZV transport along the sensory nerve is released into the cutaneous and/or mucosal sites and manifests as unilateral blisters or vesicular eruptions in one or two specific dermatomes in the innervations of the involved sensory nerve. This painful rash usually remains for 7–10 days, and the skin's normal appearance returns after 2–4 weeks (2). To our knowledge, there are 11 previously reported cases of FDG-PET/CT findings in herpes zoster, including a case of visceral disseminated VZV and brachial plexus neuritis caused by VZV (3). We have summarized the cases of these patients with skin and/or lymph node lesions in the Table 1. Of these patients, five showed FDG accumulation in skin lesions only and one showed FDG accumulation in lymph node lesions only. There are only four previous reports of FDG accumulation in both skin and lymph node lesions as in the present case, including three in the chest (4–6) and one in the pelvic region (2).

Herpes zoster causes FDG uptake through the intense viral replication in the subcutaneous tissue prior to eruption (7). Regional lymph nodes show high FDG uptake, which reflects heightened metabolic activity from the infiltration of lymphocytes into the regions infected by VZV (3). In our patient's case, the lymph nodes were surgically resected and the pathological examination demonstrated the absence of malignant cells, whereas reactive follicular hyperplasia was observed; this is consistent with an inflammatory response due to VZV infection (1). To the best of our knowledge, there has been no report comparing FDG-PET findings of lymph nodes with histologic findings, and our findings are compatible with a clinically VZV-induced inflammatory reaction in regional lymph nodes, which increased the FDG accumulation. It is likely that FDG-PET can reveal a VZV infection — especially without blisters or vesicular eruption — which is difficult to diagnosis clinically. Further reports of specific findings of FDG-PET in similar cases are necessary before any conclusions can be made.

Table1. Summary of the present case and previous reports of herpes zoster on FDG-PET/CT

Ref.	Age	Sex	location of skin lesion	Lymph node region	Clinical appearance	Treatment	Follow-up
Present case	67	F	right buttock	paraaortic and pelvic	3 days before PET	amenamevir	Surgically resected after 1 month
7	63	M	left flank	none	2 days after PET	none	Disappeared on PET after 2 weeks
8	unknown	unknown	unknown	unknown	unknown	unknown	unknown
9	71	M	left anterior chest wall	none	unknown	unknown	unknown
10	28	M	none	cervical, right hilar, and tracheobronchial	within 24 hr of PET	valacyclovir	Disappeared on PET after 1 month
5	50	M	right lower thoracic	bilateral axillary	2 days earlier	antiviral treatment	unknown
11	56	M	left mid back	none	2 months before the PET	valacyclovir	Disappeared on PET after 4 months
4	41	F	left breast	axillary	unknown	antiviral treatment	Disappeared on PET after 4 months
12	66	F	left lower thoracic	none	unknown	unknown	unknown
6	26	F	the right scapula	axillary	unknown	valacyclovir	Disappeared on PET after 4 months
2	45	F	right vulva, right thigh	right external iliac and right inguinal	during the examination	valacyclovir	Disappeared on PET after 11 months

Conclusion

Active infection with VZV displayed increased FDG uptake in regional lymph nodes in this patient, and similar cases may be misdiagnosed as a malignant disease. Misdiagnosis can be avoided by a careful interpretation by an experienced nuclear medicine physician as well as a proper clinical evaluation.

Acknowledgments

We thank all the members of the Department of Diagnostic and Interventional Radiology at the Hokkaido University Graduate School of Medicine and the Division of Radiology at the Hokkaido University Hospital.

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