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REVIEW ARTICLE

Demonstrations of AIDS-associated malignancies and infections at FDG PET-CT

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Abstract HIV infection results in profound alterations of immunologic function that render the patient severely immunocompromised, and susceptible to malignancies and opportunistic infections. Three AIDS-defining malignancies include Kaposi's sarcoma (KS), non-Hodgkin's lymphoma (NHL) and invasive cervical cancer. In AIDS patients, KS is often aggressive and multifocal, with visceral involvement and widespread cutaneous and nodal spread; NHL is always high grade and often widely disseminated at the time of diagnosis with frequent involvement of extranodal sites; cervical cancer is invasive and has greater likelihood of progression and metastasis. Although there are very sparse systemic data available in the literature, limited studies has shown that FDG PET-CT is a valuable imaging technique in the diagnosis, staging, restaging and monitoring therapeutic response in these malignancies. In addition, a unique application of FDG PET/CT is the differentiation of cerebral lesions between lymphoma and toxoplasmosis in AIDS patients, which cannot be reliably achieved with either CT or MRI. HIV-associated opportunistic infections may involve different pathogens and multiple tissues, organs or systems. Some preliminary observations have revealed a promising role of FDG PET-CT in the diagnosis and identification of these infections such as tuberculosis, fever of unknown origin, pneumocystis pneumonia and candidiasis. However, it should be stressed that FDG PET-CT alone has no role in identifying the pathology of abnormalities. FDG PET-CT, at best, can localize the sites of abnormalities and impact on patient's management in clinical decision making.

Keywords Human immunodeficiency virus (HIV) · Acquired immunodeficiency syndrome (AIDS) · Positron emission tomography/computed tomography (PET-CT) · Kaposi's sarcoma (KS) · Non-Hodgkin's lymphoma (NHL) · Opportunistic infection

Introduction

Acquired immunodeficiency syndrome (AIDS) is a disorder of cell-mediated immunity that causes certain multiple characteristic malignancies and opportunistic infections, which result from infection with human immunodeficiency virus (HIV). More than 1.1 million people are living with HIV in the USA, and more than 56,000 Americans become infected with HIV each year [1]. HIV primarily infects and kills helper T lymphocytes. Although most patients are asymptomatic for years, the process of viral infection, replication and T-helper cell destruction remains active throughout the course of the disease. Ultimately, HIV infection results in profound alterations of immunologic function that render the patient severely immunocompromised and susceptible to malignancies and opportunistic infections [2, 3]. Management of AIDS has undergone a transformation with the introduction of a variety of antiretroviral agents, in particular the highly active antiretroviral treatment (HAART), which uses a range of these agents together. These treatment regimens have resulted in prolongation of life. On the other hand, extended life expectancy is associated with increased incidence of malignancies or opportunistic infections.

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Positron emission tomography (PET) with fluorine-18 fluorodeoxyglucose (FDG) is a quantitative imaging technique that visualizes biochemical and physiological processes in vivo. Combined PET and computed tomography (CT) scanning provides better disease localization and attenuation correction. Today, PET/CT has been wisely used for a variety of malignancies and is also under clinical trials for infections. But in radiology literature, there are very sparse systemic data regarding the applications of FDG PET/CT for AIDS-related disease. This article reviews and illustrates the role of FDG PET-CT in the most common AIDS-associated malignancies and infections.

Kaposi's sarcoma

Kaposi's sarcoma (KS) is the most common AIDS-defining tumor, seen in approximately 15–20% of cases [4, 5]. The lifetime prevalence may be as high as 50% among homosexual male AIDS patients [6, 7].

KS lesions are characterized histologically by neoangiogenesis and proliferating spindle-shaped cells admixed with an inflammatory infiltrate of lymphocytes, plasma cells and macrophages [8]. Multiple factors likely contribute to the development of KS. Infections with human herpes virus-8 (HHV8) has been detected in all forms of KS and deemed the causative agent of both AIDS-defining and non-AIDS related KS [9]. In addition, the HIV virus itself may play a direct role in KS tumorigenesis [10]. Infections with HHV and HIV cause the activation of numerous preexistent and virus-specific signal transduction pathways [11].

In patients with AIDS, KS is often aggressive and multifocal, with visceral involvement and widespread cutaneous and nodal spread. Common sites of involvement by KS include skin, lymph nodes, gastrointestinal tract, oral cavity, lung, liver and spleen. Visceral dissemination is present at the time of diagnosis in more than 50% of cases [12]. Gastrointestinal involvement has been reported in 40% of cases at initial diagnosis and up to 80% at autopsy [13]. KS in the oral cavity occurs in 33% of cases [13]. Almost no organ is spared from the involvement with KS.

Diagnosis of cutaneous lesions of KS is usually made by direct biopsy. Multiple imaging modalities are used for evaluation of non-cutaneous lesions, such as CT, MRI and scintigraphy with sequential thallium and gallium. AIDS-related KS is frequently disseminated or involves multiple organs, particularly the oral cavity, pulmonary system and gastrointestinal tract, and visceral lesions can be asymptomatic. The role of CT or MRI is significantly limited with its focal, regional imaging rather than whole-body investigation. One of the significant advantages of FDG PET/CT is its routine whole-body acquisition, which is ideal for systemic disease such as KS. In the radiology literature, there were a few case reports about applications of FDG PET/CT for AIDS-defining KS, which all suggested that FDG PET-CT was effective in detecting clinically occult KS lesions that were difficult to diagnose with traditional imaging techniques in more advanced stages of KS [14–18].

There is the overlap in FDG positive nodal lesions between AIDS-defining KS and lymphadenopathy syndrome. FDG avidity in lymph nodes should be interpreted with caution because it may also be caused by HIV viremia in the absence of HAART [19]. Lymphadenopathy secondary to only HIV viremia is often mild. Bulky nodal enlargement is often suggestive of a neoplastic process. However, without biopsy, it is impossible to distinguish adenopathy in KS from that in lymphoma.

Figures 1 and 2 illustrate cutaneous and non-cutaneous lesions of KS.

Lymphoma

Lymphoma is the second most common malignant neoplasm in AIDS patients. Non-Hodgkin's lymphoma (NHL) is the AIDS-defining condition in approximately 3% of patients. The risk of developing lymphoma is about 60 times greater in patients with AIDS than in the general population, and it increases 1–2% each year after development of AIDS or symptomatic HIV infection [20]. Systemic NHL generally occurs late in the course of HIV infection, when the CD4 count has fallen to less than 200 cells/mm^3. In all lymphomas, diffuse large B-cell lymphoma (DLBCL) and Burkitt's lymphoma represent the overwhelming majority (>90%) of patients [8, 21]. Primary central nervous system lymphoma (PCNSL) represents a distinct extranodal presentation of DLBCL in AIDS patients, usually of the immunoblastic type and associated with severe immunosuppression and a poor prognosis. PCNSL is typically confined to the craniospinal axis without systemic involvement [22].

The pathogenesis of AIDS-related NHL is unclear. Mutation in oncogenes or tumor suppressor genes, and continuous release of various growth factor and cytokines induced by HIV or EB-virus infection are considered to lead to the development of B-cell proliferation [23]. AIDS-defining NHLs are always high grade, aggressive and often widely disseminated at the time of diagnosis with frequent involvement of extranodal sites. The response to treatment is also poor, with unfavorable prognosis [20]. In AIDS-associated lymphoma, treatment of lymphoma is complicated with pre-existing immunodeficiency disease. Patient's immune status such as CD4 count and treatment history for AIDS are more important predictors of clinical

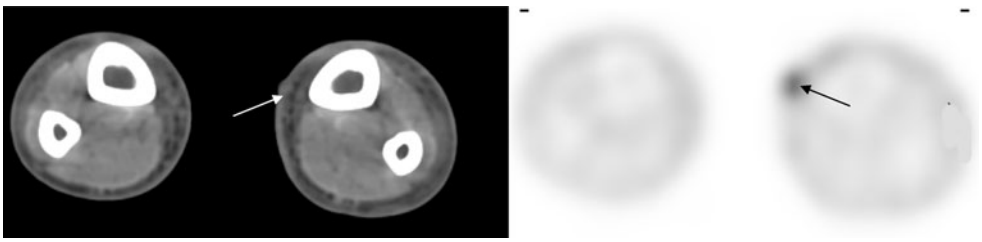

Fig. 1 Skin KS in a 45-year-old man with AIDS. Transaxial images of FDG PET-CT demonstrate a skin lesion with moderate uptake (SUV 3.8) in the left medial thigh (*arrows*). Skin lesion of KS is usually popular, and less frequently plaque-like. FDG uptake is often mild to moderate mainly due to small size

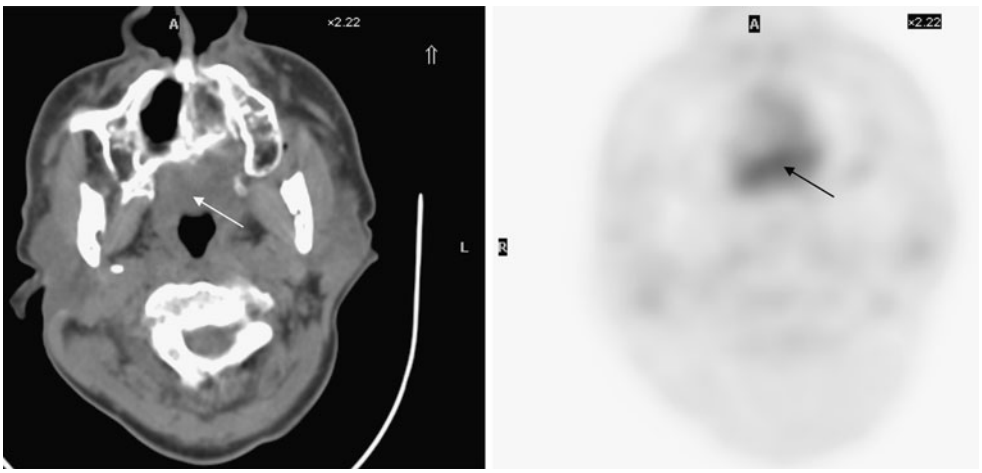

Fig. 2 Soft palate KS in a 57-year-old man with AIDS. Transaxial images of FDG PET-CT show intense uptake (SUV 8.0) in the soft palate (*arrows*). KS lesion in the month is usually macular rather than a well-marginated discrete mass

outcome than the features associated with lymphoma such as stage, lactic dehydrogenase concentration, etc. [7, 24]. Clinical trials have demonstrated a better outcome with chemotherapy for AIDS-associated lymphoma since the introduction of HAART [24].

FDG PET is widely used for initial staging, restaging and monitoring of therapeutic response in lymphoma. There is a substantial body of evidence that shows the accuracy of staging with FDG PET/CT. There is promising data to suggest that the result of early restaging with PET is an important prognostic factor in terms of predicting final response; PET can detect recurrent disease before clinical symptoms or signs, laboratory results or CT imaging have been able to detect relapse [25, 26]. Although there is very scant literature regarding the specific role of FDG PET/CT in AIDS-defining lymphoma, it is believed that PET/CT is a choice of imaging technique during the course of the lymphomatous disease in AIDS patients, same as in non-HIV patients. A study in 13 AIDS-related Burkitt's lymphoma found that FDG PET/CT provided accurate initial staging with detection of more lesions compared to conventional workup; it was useful to monitor treatment response, as regression of initial disease could be observed early and it had prognostic value, as a negative scan was always associated with a favorable outcome [27]. Another report in a seven patient series also suggested that PET/CT accurately detected lymphoma in patients with HIV infection, and had been used confidently as a management tool in the patient group [28].

Regarding the lymphadenopathy, the differentiation between lymphoma and HIV viremia-related lymph nodes can be difficult. Some pitfalls are helpful for interpretation. The lymphadenopathy in lymphoma is usually bulky, conglomerate and significantly enlarged with intense FDG uptake, but lymph nodes secondary to viremia are typically slightly enlarged and mild FDG avid [29]. However, practically there is no cutoff of the size or standardized uptake value (SUV) which can be reliably used to differentiate a benign from malignant lymphadenopathy. The locations of the lymph nodes may be also different between two entities. The viremia-induced lymphadenopathy is more superficially distributed, such as in the neck, axilla or inguinal region. In contrast, large retroperitoneal or mesenteric nodes are more likely suggestive of lymphoma. The finally, identification of extranodal lesions such as in the liver or spleen is most likely consistent with lymphoma.

Figures 3, 4 and 5 illustrate three AIDS-defining diffuse large B-cell lymphomas in the different locations.

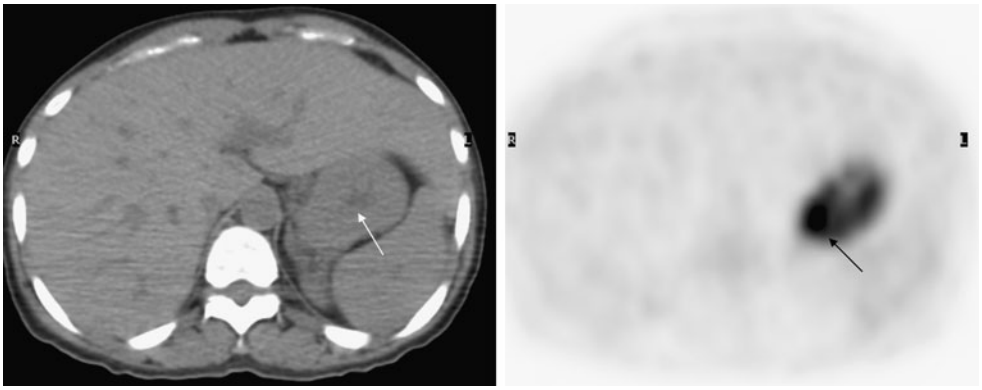

Fig. 3 Gastric NHL in a 30-year-old woman with AIDS. Transaxial images of FDG PET-CT show diffuse thickening with intense uptake (SUV 12) in the gastric wall (*arrows*). Lymphomatous infiltration of the gastric wall produces morphologic appearances as diffuse infiltrative, ulcerative, or nodular thickening on endoscopic examination or CT imaging

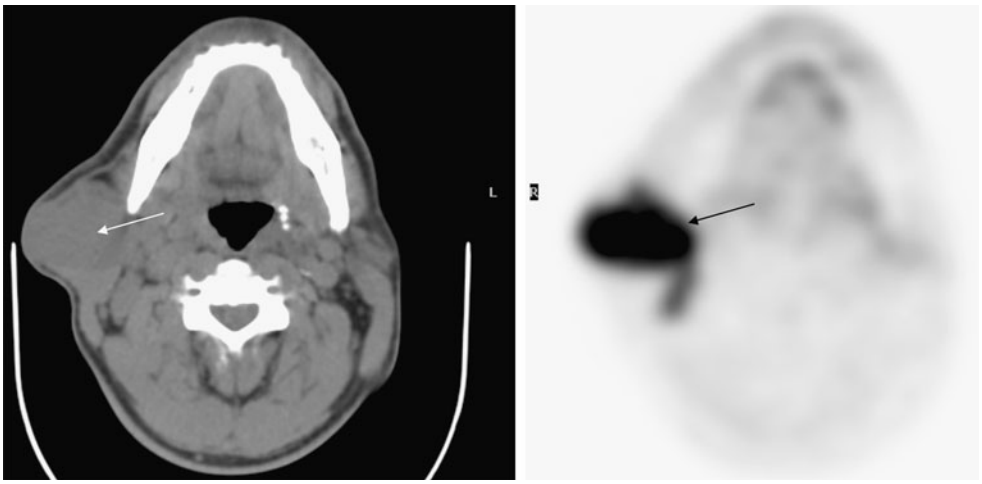

Fig. 4 Parotid NHL in a 49-year-old man with AIDS. Transaxial images of FDG PET-CT show a large mass with intense uptake (SUV 13) in the right parotid gland (*arrows*). Parotid is the most frequently involved salivary gland in NHL

A unique application of FDG PET/CT is differentiation of cerebral lesions and identification of PCNSL in AIDS patients. PCNSL is the second most common cerebral mass lesion in AIDS patient. On CT, lymphomatous lesion often demonstrates central necrosis and ring enhancement. On MRI, lymphoma is generally seen as a hypointense lesion on T1-weighted images and isointense or hyperintense on T2-weighted sequences. However, neither CT nor MRI can reliably distinguish between PCNSL and cerebral toxoplasmosis, the most common cause of focal cerebral lesions in AIDS patients. FDG PET/CT has been used for this differentiation with excellent results [29–34]. The FDG uptake within the lesion was compared to that of the contralateral brain area using qualitative visual interpretation and/or semiquantitative SUV, and SUV ratio could be calculated between the lesion and normal contralateral brain area. All studies demonstrated significantly increased FDG uptake in the lymphomas and decreased uptake in nonmalignant diseases such as toxoplasmosis or tuberculosis, with no overlap of the SUVs. In all case series, FDG PET correctly characterized the brain lesions and therefore guided the clinical management of the patients. High focal FDG uptake of a brain lesion in AIDS patient most likely represents a malignant process, which should be biopsied for confirmation rather than treated presumptively as infection [35].

Figure 6 illustrates an AIDS-defining PCNSL.

Invasive cervical cancer

Invasive cervical cancer was included as an AIDS-defining malignancy in 1993, and there is good epidemiological evidence that the precursor lesions, cervical intraepithelial neoplasm (CIN) and squamous intraepithelial lesion (SIL) also occur more frequently in women with AIDS [36].

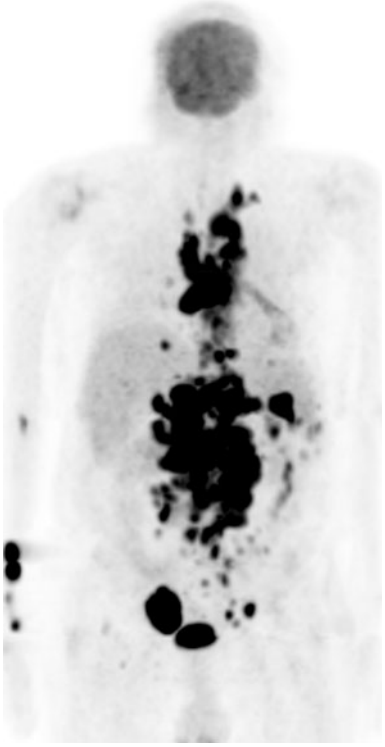

Fig. 5 NHL in a 50-year-old man with AIDS and progression of lymphadenopathy. Maximum intensity projection imaging of the whole-body FDG PET shows extensive bulky mediastinal and retroperitoneal nodes with intense uptake (SUV 20). Biopsy of mediastinal nodes suggested NHL. Large, conglomerate FDG avid nodal lesions are often indicative of a neoplastic rather than infectious/inflammatory process

Human papilloma virus (HPV) has a central role in the pathogenesis of both CIN and invasive cervical cancer. HIV is associated with not only a higher prevalence of HPV in the cervix, but also a higher prevalence of CIN/SIL and greater likelihood of lesion progression [7]. Unlike the other AIDS-defining malignancies, there was no impact of HAART on the incidence of cervical cancer in a large Swiss HIV cohort study [37]. Both preinvasive disease and invasive cervical cancer have been reported to have a much poorer outcome in HIV-infected women than in the general population [38, 39]. In a South Africa-based study, HIV-infected women presented with cervical cancer at a younger age and poorer histological differentiation of the tumors, but same disease stage as non-HIV infected women [40].

The role of FDG PET/CT in cervical cancer has been well established. FDG PET/CT demonstrates abnormal cervical uptake in virtually all patients with cervical cancer (Fig. 7), and the current state-of-the-art PET software allows for the three-dimensional volumetric analysis of the tumor, which has been shown to be of more prognostic significance than clinical stage of disease [41, 42]. For locally advanced untreated cervical cancer, FDG PET/CT is more sensitive than CT in detecting metastatic lymph node deposits in the pelvic, para-aortic and supraclavicular regions [43], which is of utmost importance in determination of radiation field and management of patient. In patients receiving irradiation, PET/CT can be utilized to outline the irradiation targets for the FDG-avid lesions [44, 45].

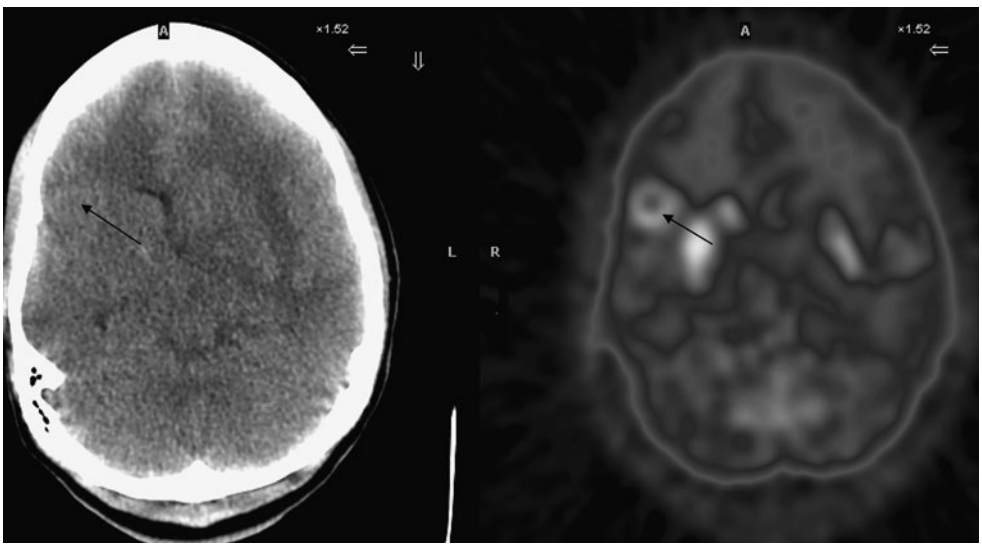

Fig. 6 Cerebral NHL in a 30-year-old man with AIDS. Transaxial images of FDG PET-CT show a 2.0-cm lesion with intense uptake (SUV 8.0) and photopenic center in the right frontal lobe (*arrows*). Pathology from craniotomy suggested NHL. FDG uptake is usually higher in NHL than that in gliomas or metastatic lesion. Benign brain lesion such as toxoplasmosis or TB often has no abnormally increased uptake

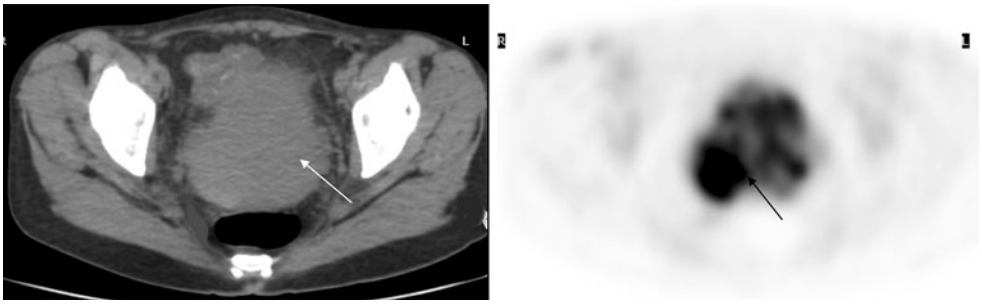

Fig. 7 Invasive cervical cancer in a 44-year-old woman with AIDS. Transaxial images of FDG PET-CT show a large bulky endocervical mass with intense uptake (SUV 15). There is parametrial and upper vaginal extension

Non-AIDS-defining malignancies

Individuals with HIV infection are at higher risk for the development of a wide variety of non-AIDS-defining cancers (NADCs) [46–48]. Several studies have documented an increased incidence of NADCs [46, 47]. NADC has emerged as an important cause of morbidity and mortality in AIDS patients. The development of NADC appears to be multifactorial.

Some common NADCs include Hodgkin's lymphoma, anal cancer, lung cancer, breast cancer, hepatocellular carcinoma, conjunctival cancer, prostate cancer, urinary cancer and plasma cell neoplasia. The role of FDG PET/CT in these NADCs is similar to that in non-HIV infected patients.

AIDS-related opportunistic infection

AIDS patients are vulnerable to a variety of opportunistic infections. The spectrum of HIV-associated opportunistic infections is broad and includes bacterial, mycobacterial, fungal, viral and parasitic pathogens. The infections may involve different or multiple tissues, organs or systems. Some preliminary studies have revealed a promising role of FDG PET-CT in the diagnosis and identification of HIV-associated infection and inflammation [49–54]. In HIV-infected patients, FDG PET has also shown that HIV-1 infection progresses by distinct anatomical steps, with involvement of the upper torso preceding involvement of the lower part of the body, and the degree of FDG uptake is related to viral load [35]. FDG uptake by the lymph nodes was found to be inversely related to CD4 count [52].

Tuberculosis

About one-third of HIV-infected persons are estimated to also be infected with mycobacterium tuberculosis (TB) [55, 56]. In HIV and TB co-infections, it is of cardinal importance to identify the patients correctly to start anti-TB treatment and, most importantly, to delay HAART, because it is common for patients with low CD4 counts and TB coinfection, who are treated with antiretroviral treatment, to develop immune reconstitution inflammatory syndrome (IRIS) and frequently die because of this condition [57].

However, diagnosis of active TB disease in HIV-infected persons is difficult, because patients with HIV-associated TB have fewer bacilli in their sputum than do HIV-uninfected patients with pulmonary TB [55]. In addition, HIV infection compromises the validity and effectiveness of chest radiography in the diagnosis of pulmonary TB. The presentation of TB in the HIV-infected patient is different from that observed in the HIV-negative patient: apical predominance is less pronounced, while consolidation and cavitations are less prevalent [50]. On FDG PET-CT, active pulmonary and extra-pulmonary TB always demonstrate increased uptake (Fig. 8). It is difficult to differentiate between a malignancy, HIV infection and TB, based on the intensity of FDG uptake only. Although some studies reported that double-phase FDG PET was helpful for differentiation between inflammation and malignancy, a study in HIV-infected children suggested that FDG PET scanning was unable to discriminate reliably between malignant and inflammatory pathology [58]. In most cases, diagnosis of TB is based on correlation of all information including CT appearance, FDG PET pattern, sputum and brachial washing stain and culture.

Detection of extra-pulmonary TB with or without concurrent lung involvement is usually difficult because of nonspecific symptoms. FDG PET-CT can help in the diagnosis with a single whole-body imaging (Fig. 9). A study revealed that FDG PET-CT correctly diagnosed presence or absence of active extra-pulmonary TB in all patients [59]. But in the presence of FDG avid abnormality, PET-CT cannot reliably differentiate an inflammatory process such as TB from neoplasm such as lymphoma.

Monitoring the efficacy of anti-TB treatment may be difficult based on symptoms and/or radiographic imaging. FDG PET-CT can quantitate the intensity of uptake, which provides information about metabolic alteration and allows

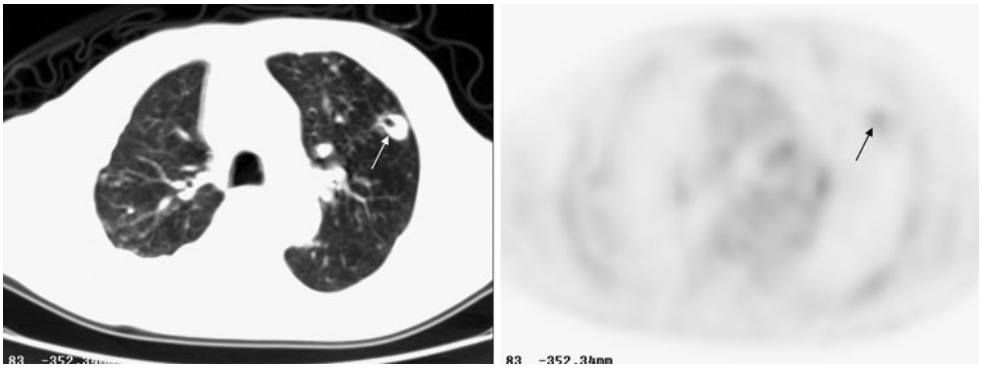

Fig. 8 Pulmonary TB in a 52-year-old man with AIDS and persistent cough. Transaxial images of FDG PET-CT show a 2.0-cm cavitary nodule with mild uptake (SUV 2.8) in the left lower lobe (*arrows*). Sputum stain and culture were positive for acid fast bacilli

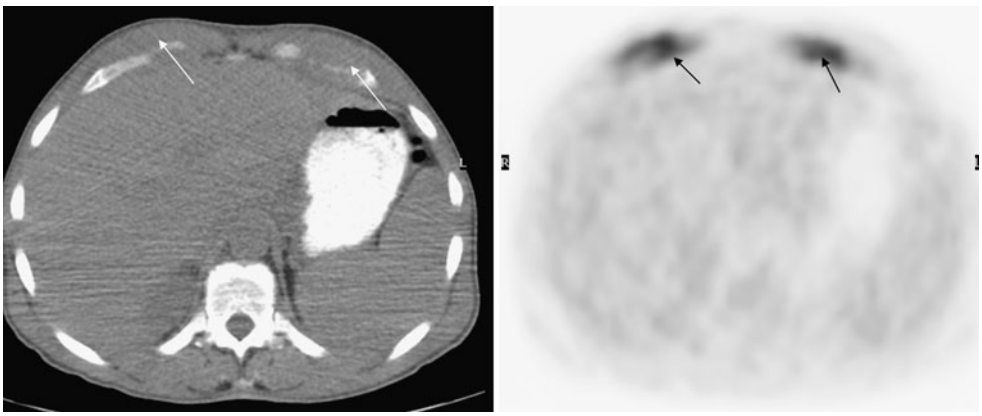

Fig. 9 Extra-pulmonary TB in a 56-year-old man with AIDS. Transaxial images of FDG PET-CT show intense uptake (SUV 8.2) in the anterior abdominal wall of the epigastric region, involving the rectus abdominis muscle and 6–7th costal cartilages (*arrows*). Biopsy with fine needle aspiration suggested TB infection

monitoring the activity of the disease [60]. Published report indicated the effectiveness of FDG PET-CT in the assessment of the state of disease activity in tuberculosis spondylitis and quantitative measurement of therapeutic response to anti-TB treatment [61].

Fever of unknown origin (FUO)

One of the most common symptoms resulted from a wide variety of opportunistic infections in AIDS patients is FUO without any localizing features. Although there were a few studies regarding application of FDG PET-CT in the workup of FUO in non-HIV infected patient population [62–65], the data on FDG PET-CT for FUO in AIDS patients are limited to only three reports. Santiago et al. [53] found a 76.4% sensitivity of FDG PET in identifying a lesion in 47 febrile AIDS patients. O'Doherty et al. investigated the usefulness of FDG PET in 57 HIV-positive patients with FUO and/or weight loss. The FDG PET was abnormal in 29 patients and the underlying diseases were malignancies and infections [29]. Castaigne et al. [66] reported that in 10 patients suffering from HIV-associated FUO, FDG PET-CT correctly diagnosed TB in 6 patients and neoplasm in 3 patients. In the series, FDG PET-CT directly suggested sites for biopsy in 6 cases. All these retrospective studies suggested that FDG PET-CT is helpful for diagnosis or exclusion of a focal pathologic etiology of HIV-associated FUO. Adding the CT anatomic landmarks to the PET findings allows easy localization for biopsy if histopathological diagnosis is needed. Figure 10 illustrates fungal pericarditis in an AIDS patient.

Pneumocystis pneumonia

The lungs are a principal target of HIV-associated opportunistic infections. Pneumocystis carinii pneumonia (PCP) remains one of the most frequent AIDS-defining infections in the USA, although its overall incidence is declining [67]. Approximately, 90–95% of cases of PCP occur in persons whose CD4 cell count is below 200 cells/mm^3. The clinical diagnosis of PCP is complicated by the nonspecific signs and symptoms of PCP and because pneumocystis is an intractable organism that currently cannot be isolated or sustained in culture [68]. The gold standard is microscopic

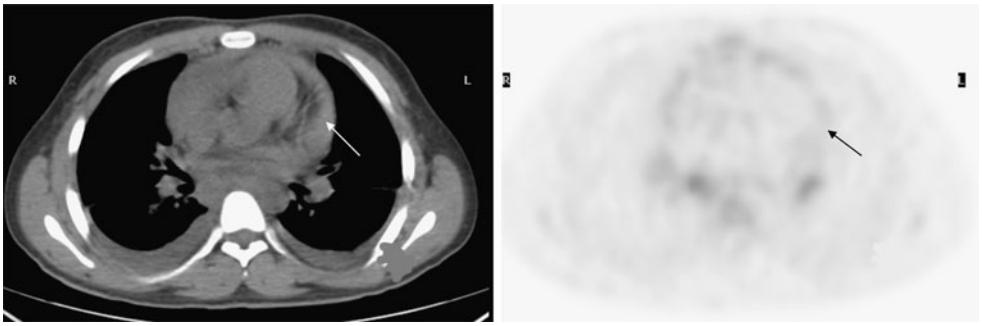

Fig. 10 Pericarditis in a 18-year-old man with AIDS and FUO. Transaxial FDG PET-CT show moderate pericardial effusion with mild uptake (SUV 2.3) (*arrows*). Subsequent blood culture was positive for fungi. The pericardial effusion resolved after anti-fungal therapy

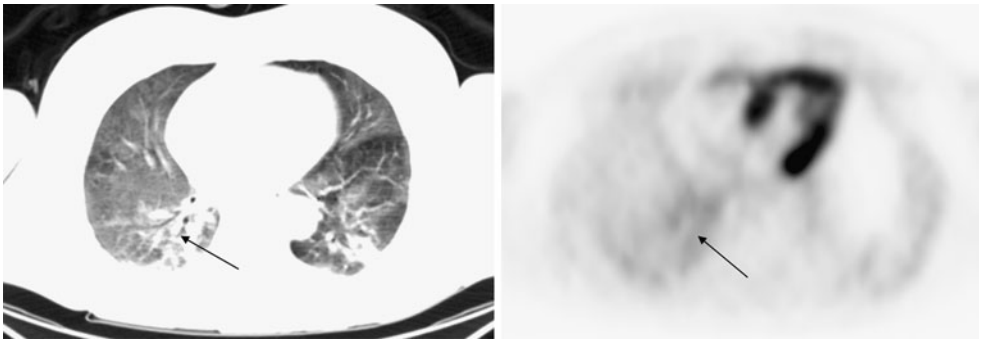

Fig. 11 PCP in a 58-year-old man with AIDS and cough. Transaxial images of FDG PET-CT show patchy areas of ground-glass opacities and consolidations with mild uptake in bilateral lungs, greater on the right (*arrows*). There is also interlobular septal thickening on the CT. Subsequent bronchial alveolar lavage cytology with Giemsa stain confirmed pneumocystis carinii organism

examination of stained bronchoalveolar lavage fluid or induced sputum. On chest radiography, classic PCP presents with bilateral, symmetric reticular or granular opacities [69] (Fig. 11). Less frequently, PCP may present with unilateral or asymmetric opacities. Traditionally, gallium scintigraphy is used to diagnose and monitor PCP, which often demonstrates diffuse pulmonary uptake. Published case reports suggested that FDG PET-CT might be preferred to gallium scintigraphy for PCP diagnosis and monitoring, due to its better resolution, higher target to background uptake, faster imaging time and lower radiation dose [70, 71].

Candidiasis

Oropharyngeal and/or esophageal candidiasis occur commonly and recur frequently. Oral candidiasis, the most common diagnosis and one of the earliest manifestations, affects more than 80% of AIDS patients and can be diagnosed by direct examination followed by histological evidence with biopsy [72, 73]. Patients with esophageal candidiasis usually complain of dysphagia and/or chest pain. FDG PET is very helpful for the diagnosis of esophagitis, even though it cannot identify the specific pathogen. Since there is minimal physiologic uptake in the esophagus, diffusely increased esophageal uptake is most likely suggestive of an inflammation/infection (Fig. 12).

Osteomyelitis and soft tissue abscess

Like in non-HIV infected patients, FDG PET-CT is a valuable tool for evaluation of osteomyelitis and soft tissue infection. For osteomyelitis, especially chronic osteomyelitis, FDG PET-CT is superior to MRI, more sensitive and specific than bone and white blood cell scintigraphy [74].

Conclusion

HIV infection results in profound alterations of immunologic function that render the patient severely immunocompromised and susceptible to malignancies and opportunistic infections. There are three AIDS-defining malignancies: KS, NHL and invasive cervical cancer. In AIDS patients, KS is often aggressive and multifocal, with visceral involvement and widespread cutaneous and nodal spread; NHL is always high grade and often widely disseminated at the time of diagnosis with frequent involvement of extranodal sites; cervical cancer is invasive and has greater likelihood of progression and metastasis. FDG

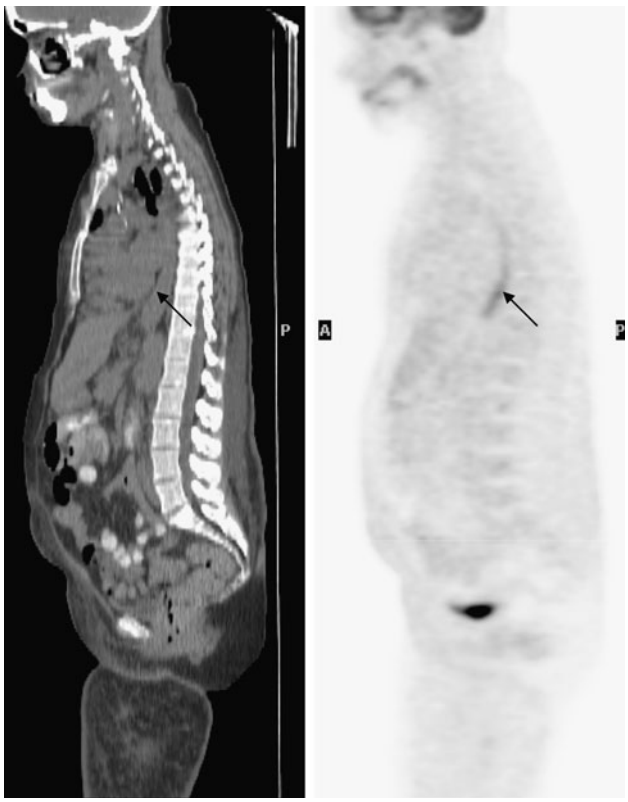

Fig. 12 Esophageal candidiasis in a 45-year-old woman with AIDS and dysphagia. Sagittal images of FDG PET-CT show diffuse esophageal thickening and uptake (SUV 5.6) (*arrows*), suspicious for esophagitis. Endoscopic biopsy suggested candidiasis with special stain

PET-CT has been shown to be a valuable imaging technique in the diagnosis, staging, restaging and monitoring therapeutic response for these malignancies. In addition, a unique application of FDG PET/CT is differentiation of cerebral lesions and identification of lymphoma in AIDS patients. The spectrum of HIV-associated opportunistic infections is broad and may involve different or multiple tissues, organs or systems. Some preliminary studies have revealed a promising role of whole-body FDG PET-CT in the diagnosis and identification of HIV-associated infections, such as TB, FUO, pneumocystis pneumonia and candidiasis. However, it should be stressed that FDG PET-CT alone has no role in identifying the pathology of abnormalities. FDG PET-CT, at best, can localize the sites of abnormalities and impact on patient's management in the clinical decision making.

References

1. Hall HI, Song K, Rhodes P, Prejean J, An Q, Lee LM, et al. Estimation of HIV incidence in the United States. JAMA. 2008;300:520–9.
2. Samuel R, Bettiker R, Suh B. AIDS related opportunistic infections, going but not gone. Arch Pharm Res. 2002;25:215–28.
3. Aoki Y, Tosato G. Neoplastic conditions in the context of HIV-1 infection. Curr HIV Res. 2004;2:343–9.
4. Restrepo C, Martinez S, Lemos JA, Carrillo JA, Lemos DF, Ojeda P, et al. Imaging manifestations of Kaposi sarcoma. RadioGraphics. 2006;26:1169–85.
5. Beral V, Peterman TA, Berkelman RL, Jaffe HW. Kaposi's sarcoma among persons with AIDS: a sexually transmitted infection? Lancet. 1990;335:123–8.
6. Katz MH, Hessol NA, Buchbinder SP, Hirozawa A, O'Malley P, Holmberg SD. Temporal trends of opportunistic infections and malignancies in homosexual men with AIDS. J Infect Dis. 1994;170:198–202.
7. Bower M, Palmieri C, Dhillon T. AIDS-related malignancies: changing epidemiology and the impact of highly active antiretroviral therapy. Curr Opin Infect Dis. 2006;19:14–9.
8. Cheung MC, Pantanowitz L, Dezube B. AIDS-related malignancies: emerging challenges in the era of highly active antiretroviral therapy. Oncologist. 2005;10:412–26.
9. Schwartz EJ, Dorfman RF, Kohler S. Human herpesvirus-8 latent nuclear antigen-1 expression in endemic Kaposi sarcoma: an immunohistochemical study of 16 cases. Am J Surg Pathol. 2003;27:1546–50.
10. Deregibus MC, Cantaluppi V, Doublier S, Brizzi MF, Deambrosis I, Albini A, et al. HIV-1-Tat protein activates phosphatidylinositol 3-kinase/AKT-dependent survival pathway in Kaposi sarcoma cells. J Biol Chem. 2002;277:25195–202.
11. Sullivan R, Dezube BJ, Koon HB. Signal transduction targets in Kaposi's sarcoma. Curr Opin Oncol. 2006;18:456–62.
12. Dezube BJ. Acquired immunodeficiency syndrome-related Kaposi's sarcoma: clinical features, staging, and treatment. Semin Oncol. 2000;27:424–30.
13. Dezube BJ, Pantanowitz L, Aboulafia DM. Management of AIDS-related Kaposi sarcoma: advances in target discovery and treatment. AIDS Read. 2004;14:236–8.
14. Kulasegaram R, Saunders K, Bradbeer CS, O'Doherty M. Is there a role for positron emission tomography scanning in HIV-positive patients with Kaposi's sarcoma and lymphadenopathy: two case reports. Int J STD AIDS. 1997;8:709–12.
15. Martinez S, McAdams HP, Youens KE. Kaposi sarcoma after bilateral lung transplantation. J Thorac Imaging. 2008;23:50–3.
16. van de Luijtgaarden A, van der Ven A, Leenders W, Kaal S, Flucke U, Oyen W, et al. Imaging of HIV-associated Kaposi sarcoma. F-18-FDG-PET/CT and In-111-bevacizumabscintigraphy. J AIDS. 2010;54:444–6.
17. Morooka M, Ito K, Kubota K, Minamimoto R, Shida Y, Hasuo K, et al. Whole-body 18F-fluorodeoxyglucose positron emission tomography/computed tomography images before and after chemotherapy for Kaposi sarcoma and highly active antiretrovirus therapy. Jpn J Radiol. 2010;28:759–62.
18. Morooka M, Ito K, Kubota K, Yanagisawa K, Teruya K, Kasuo K, et al. Usefulness of F-18 FDG PET/CT in a case of Kaposi sarcoma with an unexpected bone lesion. Clin Nucl Med. 2011;36:231–4.
19. Lucignani G, Orunesu E, Cesari M, Marzo K, Pacei M, Bechi G, et al. FDG-PET imaging in HIV-infected subjects: relation with therapy and immunovirological variables. Eur J Nucl Med Mol Imaging. 2009;36:640–7.
20. Goodman P. Imaging of the patient with AIDS: Clinical complications of HIV infection. Radiol Clin North Am. 1997;35:1021–6.
21. Levine AM, Seneviratne L, Espina BM, Wohl AR, Tulpule A, Nathwani BN, et al. Evolving characteristic of AIDS-related lymphoma. Blood. 2000;96:4084–90.

22. MacMahon EM, Glass JD, Hayward SD, Mann RB, Becker PS, Charache P, et al. Epstein–Barr virus in AIDS-related primary central nervous system lymphoma. Lancet. 1991;338:969–73.
23. Knowles DM. Etiology and pathogenesis of AIDS-related non-Hodgkin's lymphoma. Hematol Oncol Clin North Am. 2003;17:785–820.
24. Navarro W, Kaplan LD. AIDS-related lymphoproliferative disease. Blood. 2006;107:13–20.
25. Kirby AM, Mikhaeel G. The role of FDG PET in the management of lymphoma: practical guidelines. Nucl Med Commun. 2007;28:355–7.
26. Michallet AS, Trotman J, Tychyj-Pinel C. Role of early PET in the management of diffuse large B-cell lymphoma. Curr Opin Oncol. 2010;22:414–8.
27. Just PA, Fieschi C, Baillet G, Galicier L, Oksenhendler E, Moretti JL. 18F-fluorodeoxyglucose positron tomography/computed tomography in AIDS-related Burkitt lymphoma. AIDS Patient Care STDS. 2008;22:695–700.
28. Goshen E, Davidson T, Avigdor A, Zwas T, Levy I. PET/CT in the evaluation of lymphoma in patients with HIV-1 with suppressed viral loads. Clin Nucl Med. 2008;33:610–4.
29. O'Doherty MJ, Barrington SF, Campbell M, Lowe J, Bradbeer CS. PET scanning and the human immunodeficiency virus-positive patient. J Nucl Med. 1997;38:1575–83.
30. Hoffman JM, Waskin HA, Schifter T, Hanson MW, Gray L, Rosenfeld S, et al. FDG-PET in differentiating lymphoma from nonmalignant central nervous system lesions in patients with AIDS. J Nucl Med. 1993;34:567–75.
31. Villringer K, Jager H, Dichgans M, Ziegler S, Poppinger J, Herz M, et al. Differential diagnosis of CNS lesions in AIDS patients by FDG-PET. J Comput Assist Tomogr. 1995;19:532–6.
32. Pierce MA, Johnson MD, Maciunas RJ, Murray MJ, Allen GS, Harbison MA, et al. Evaluating contrast-enhancing brain lesions in patients with AIDS by using positron emission tomography. Ann Intern Med. 1995;123:594–8.
33. Menendez JA, Lilien DL, Nanda A, Polin RS. Use of fluorodeoxyglucose-positron emission tomography for the differentiation of cerebral lesions in patients with acquired immune deficiency syndrome. Neurosurg Focus. 2000;8:e2.
34. Heald A, Hoffman JM, Bartlett J, Waskin H. Differentiation of central nervous system lesions in AIDS patients using positron emission tomography (PET). Int J STD AIDS. 1996;7:337–46.
35. Sathekge M, Goethals I, Maes A, van de Wiele C. Positron emission tomography in patients suffering from HIV-1 infection. Eur J Nucl Med Mol Imaging. 2009;36:1176–84.
36. Ellerbrock TV, Chiasson MA, Bush TJ, Sun XW, Sawo D, Brudney K, et al. Incidence of cervical squamous intraepithelial lesions in HIV-infected women. JAMA. 2000;283:1031–7.
37. Clifford GM, Polesel J, Rickenbach M, Dal Maso L, Keiser O, Kofler A, et al. Cancer risk in the Swiss HIV Cohort Study: association with immunodeficiency, smoking, and highly active antiretroviral therapy. J Natl Cancer Inst. 2005;97:425–32.
38. Reimers LL, Sotardi S, Daniel D, Chiu LG, Van Arsdale A, Wieland DL, et al. Outcome after an excisional procedure for cervical intraepithelial neoplasia in HIV-infected women. Gynecol Oncol. 2010;119:92–7.
39. Lehtovirta P, Paavonen J, Heikinheimo O. Risk factors, diagnosis and prognosis of cervical intraepithelial neoplasia among HIV-infected women. Int J STD AIDS. 2008;19:118–20.
40. Moodley M, Mould S. Invasive cervical cancer and human immunodeficiency virus (HIV) infection in KwaZulu-Natal, South Africa. J Obstet Gynecol. 2005;25:706–10.
41. Kidd EA, Grigsby PW. Intratumoral metabolic heterogeneity of cervical cancer. Clin Cancer Res. 2008;14:5236–41.
42. Grigsby PW. Role of PET in gynecologic malignancy. Curr Opin Oncol. 2009;21:420–4.
43. Lai CH, Yen TC, Ng KK. Surgical and radiologic staging of cervical cancer. Curr Opin Obstet Gynecol. 2010;22:15–20.
44. Grigsby PW. PET/CT imaging to guide cervical cancer therapy. Future Oncol. 2009;5:953–8.
45. Esthappan J, Chaudhari S, Santanam L, Mutic S, Olsen J, Macdonald DM, et al. Prospective clinical trial of positron emission tomography/computed tomography image-guided intensity-modulated radiation therapy to cervical cancer with positive para-aortic lymph nodes. Int J Radiat Oncol Biol Phys. 2008;72:1134–9.
46. Stebbing J, Duru O, Bower M. Non-AIDS-defining cancers. Curr Opin infect Dis. 2009;22:7–10.
47. Pantanowitz L, Dezube BJ. Evolving spectrum and incidence of non-AIDS-defining malignancies. Curr Opin HIV AIDS. 2009;4:27–34.
48. Mounier N, Spina M, Spano J. Hodgkin lymphoma in HIV positive patients. Curr HIV Res. 2010;8:141–6.
49. Love C, Tomas MB, Tronco GG, Palestro CJ. FDG PET of infection and inflammation. RadioGraphics. 2005;25:1357–68.
50. Glaudemans AWJM, Signore A. FDG-PET/CT in infections: the imaging method of choice? Eur J Nucl Med Mol Imaging. 2010;37:1986–91.
51. Basu S, Chryssikos T, Moghadam-Kia S, Zhuang H, Torigian DA, Alavi A. Positron emission tomography as a diagnostic tool in infection: present role and future possibilities. Semin Nucl Med. 2009;39:36–51.
52. Sathekge M, Maes A, Kgomo M, van de Wiele C. Fluorodeoxyglucose uptake by lymph nodes of HIV patients is inversely related to CD4 cell count. Nucl Med Commun. 2010;31:137–40.
53. Santiago JF, Jana S, Gilbert HM, Salem S, Bellman PC, Hsu RS, et al. Role of fluorine-18-fluorodeoxyglucose in the work-up of febrile AIDS patients: experience with dual head coincidence imaging. Clin Positron Imaging. 1999;2:301–9.
54. O'Doherty MJ, Barrington SF, Klein JL. Opportunistic infection and nuclear medicine. Semin Nucl Med. 2009;39:88–102.
55. Getahun H, Gunneberg C, Granich R, Nunn P. HIV infection-associated tuberculosis: the epidemiology and the response. Clin Infect Dis. 2010;50:S201–7.
56. Sterling TR, Pham PA, Chaisson RE. HIV infection-related tuberculosis: clinical manifestation and treatment. Clin Infect Dis. 2010;50:S223–30.
57. Sathekge M, Maes A, Al-Nahhas A, Rubello D, Chiti A. What impact can fluorine-18 fluorodeoxyglucose PET/computed tomography have on HIV/AIDS and tuberculosis pandemic? Nucl Med Commun. 2009;30:255–7.
58. Hadley GP, Naude F. Malignant solid tumor, HIV infection and tuberculosis in children: an unholy triad. Pediatr Surg Int. 2009;25:697–701.
59. Liu RS, Shei HR, Chu YK, Feng CF, Su WJ. Detection of extrapulmonary tuberculosis with F-18 FDG PET. Rev Med Nucl Alasbimn J. 2002;17:504.
60. Ichiya Y, Kuwabara Y, Sasaki M. FDG-PET in infectious lesions: the detection and assessment of lesion activity. Ann Nucl Med. 1996;10:185–91.
61. Schmitz A, Kalicke T, Willkomm P. Use of fluorine-18 fluoro-2-deoxy-D-glucose positron emission tomography in assessing the process of tuberculosis spondylitis. J Spinal Discord. 2000;13:541–4.
62. Keidar Z, Gurman-Balbir A, Gaitini D, Israel O. Fever of unknown origin: the role of 18F-FDG PET/CT. J Nucl Med. 2008;49:1980–5.
63. Balink H, Collins J, Bruyn GA, Gemmel F. F18 FDG PET/CT: the diagnosis of fever of unknown origin. Clin Nucl Med. 2009;34:862–8.
64. KeiPL Kok TY, Padhy AK, Ng DC, Goh AS. 18F FDG PET/CT in patients with fever of unknown origin. A local experience. Nucl Med Commun. 2010;31:788–92.

65. Sheng JF, Sheng ZK, Shen XM, Bi S, Li JJ, Sheng GP, et al. Diagnostic value of fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography in patients with fever of unknown origin. Eur J Intern Med. 2011;22:112–6.
66. Castaigne C, Tondeur M, De Wit S, Hildebrand M, Clumeck N, Dusart M. Clinical value of FDG-PET/CT for the diagnosis of human immunodeficiency virus-associated fever of unknown origin: a retrospective study. Nucl Med Commun. 2009;30:41–7.
67. Thomas CF Jr, Limper AH. Pneumocystis pneumonia. N Engl J Med. 2004;350:2487–98.
68. Krajicek B, Thomas CF, Limper AH. Pneumocystis pneumonia: current concepts in pathogenesis, diagnosis, and treatment. Clin Chest Med. 2009;30:265–78.
69. Huang L, Crothers K. HIV-associated opportunistic pneumonias. Respirology. 2009;14:474–85.
70. Win Z, Todd J, Al-Nahhas A. FDG-PET imaging in pneumocystis carinii pneumonia. Clin Nucl Med. 2005;30:690–1.
71. Sojan SM, Chew G. Pneumocystis carinii pneumonia on F-18 FDG PET. Clin Nucl Med. 2005;30:763–4.
72. Marco CA, Rothman RE. HIV infection and complications in emergency medicine. Emerg Med Clin N Am. 2008;26:367–87.
73. Egusa H, Soysa N, Ellepola A, Yatani H, Samaranayake LP. Oral candidosis in HIV-infected patient. Curr HIV Res. 2008;6:485–99.
74. Gotthardt M, Bleeker-Rovers CP, Boerman OC, Oyen WJG. Imaging of inflammation by PET conventional scintigraphy and other imaging techniques. J Nucl Med. 2010;51:1937–49.