The role of PET/CT in diagnosing generalized lymphadenopathy in asymptomatic secondary syphilis

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Abstract

Objective: Syphilis is a well-known sexually transmitted disease, and has multiple stages and various symptoms. However, it is difficult to diagnose syphilis in patients without any clinical symptoms. Because of these reasons, there have been several case reports on misdiagnosis of syphilis. Generalized lymphadenopathy could be an indication of various diseases including malignancies or infections. **Conclusion:** We report a case of a patient with generalized lymphadenopathy detected on fluorine-18-fluorodeoxy glucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) images without any clinical symptom. This case was diagnosed by clinical examination and serologic tests at an early stage of secondary syphilis.

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Introduction

Syphilis is a systemic sexually transmitted disease caused by treponema pallidum. According to World Health Organization (WHO) report, the global incidence of syphilis is about 10.6% [1]. The clinical manifestations of syphilis are variable and have been described for centuries. Syphilis is divided into primary and secondary (SS) [2]. Secondary syphilis can present with various clinical symptoms including generalized lymphadenopathy [2]. Furthermore, SS usually presents with several systemic symptoms and should be treated more intensively than primary syphilis [2]. However, there have been only few case reports using fluorine-18-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) to describe cases of SS with generalized lymphadenopathy [3, 4].

In this paper, we present a case report of an early stage of SS which showed generalized lymphadenopathy on ^{18}F-FDG PET/CT without clinical symptoms.

Case Report

A 49 years old man visited the health screening center of our hospital for cancer screening. The patient's vital signs were stable (pulse rate: 61/min, systolic blood pressure: 122mmHg, diastolic blood pressure: 74mmHg). Liver function tests were normal (aspartate aminotransferase: 20IU/L, normal range: 0-40IU/L, alanine transaminase: 37IU/L, normal range: 0-40IU/L). Other laboratory studies were within normal limits (hemoglobin: 15.5g%, normal range: 13.0%-18.0g%, white blood cell count: 8,930%, normal range: 4,000%-10,800%, platelet count: 264,000%, normal range: 130,000%-400,000%). Other cancer screening studies like colonoscopy, gastroduodenoscopy, chest X-rays, abdominal ultrasonography showed negative findings.

Positron emission tomography/CT images showed enlarged lymph nodes with intensely increased ^{18}F-FDG uptake in both submandibular areas, right neck level III, left internal and external iliac areas (Figure 1). Furthermore, multiple enlarged lymph nodes with mildly increased ^{18}F-FDG uptake were seen at the right neck level III, mediastinum, bilateral axillae, hepatic hilum,, left internal iliac area, bilateral external iliac area, and bila-

teral inguinal area. For evaluation of the generalized lymphadenopathy, the patient visited the department of hematology/oncology. On physical examination, a single painless ulcer was found on his penis. He reported a history of travel to China with a sexual contact 6 months ago. However, the patient had no remarkable clinical symptoms such as fever or rash.

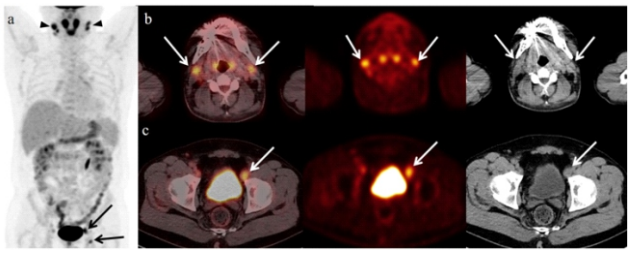

Figure 1. Maximum intensity projection image showed: a) generalized lymphadenopathy with increased ^{18}F-FDG uptake in both submandibular areas, right neck level III (arrow heads), left internal and external iliac areas (arrows) and left inguinal areas. Transaxial ^{18}F-FDG PET/CT images showed multiple lymph nodes with increased ^{18}F-FDG uptake in b) bilateral submandibular areas (maximum standardized uptake value of 7.12, upper row-arrows) and c) left external iliac area (maximum standardized uptake value of 6.22, lower row-arrows).

To rule out syphilis we used the rapid plasma reagin (RPR) test, known as non-treponemal test, which showed a high titer (1:128, normal range: less than 1:8). Additional fluorescent treponemal antibody absorption (FTA-AB) immunoglobulin G and M tests were also positive.

He was diagnosed with SS and treated with benzathine penicillin via intramuscular injection.

Two months after treatment, a follow-up RPR test showed decreased titer and FTA-AB test showed negative conversion of immunoglobulin M. Furthermore, the follow-up abdomen CT and neck ultrasonography showed decreased size of the lymph nodes seen before on the ^{18}F-FDG PET/CT images.

This study was approved by the Institutional Review Board of Soonchunhyang University Cheonan Hospital and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The Institutional Review Board of our university waived the need to obtain patients' informed consent.

Discussion

Syphilis can be divided into acquired or congenital, primary or secondary. Acquired syphilis is usually sexually transmitted [2]. Primary syphilis begins with the development of a chancre located usually on the genital organs, mouth or skin that heals by itself. As syphilis progresses, symptoms can be more aggressive [2]. Secondary syphilis is characterized by multisystemic symptoms such as fever, generalized lymphadenopathy, hepatitis, and splenomegaly due to its hematogenous spread [5]. Furthermore, SS can present with variable symptoms including, generalized fatigue, anorexia, myalgia and hair loss [6]. Clinical findings of SS are, skin rash on the hands and feet, and multiple patterns of skin lesions in the mouth, vagina, penis and skin folds [2].

Because of the various clinical features, syphilis, was described as "the greater imitator" by Sir William Osler [3]. Previous studies reported that the most common clinical misdiagnoses of syphilis were pityriasis lichenoides, psoriasis, eczema, insect bites, sarcoidosis, Leishmaniasis, and lymphoma [7, 8]. Thus, generalized lymphadenopathy without typical symptoms can be easily misdiagnosed.

Our patient at first denied any suspicious sexual contact, had no abnormal signs or symptoms such as fever, general illness, weight loss, skin rash, or respiratory symptoms and his first routine laboratory studies were also normal. However, he had unexplained generalized lymphadenopathy, detected by ^{18}F-FDG PET/CT [9].

Fluorine-18-FDG accumulation in tissues is proportional to the amount of glucose utilization and so increased glucose absorption is found in most cancers and infections [10]. Our patient could thus be diagnosed early although he had no clinical symptoms. Park et al. reported a case of generalized lymphadenopathy due to SS which was misdiagnosed as malignant lymphoma, and to the best of our knowledge, that was the first case report on ^{18}F-FDG PET/CT features of SS in Korea [3]. This patient had clinical findings of SS similar to symptoms of beta cells lymphoma including progressive weakness, fever and weight loss [3]. The above authors concluded that clinicians should have a high index of suspicion for syphilis in patients with unexplained lymphadenopathy and should remember that potential nonmalignant conditions can also show increased ^{18}F-FDG uptake on PET/CT [3]. Our patient's history of sexual contact 6 months earlier, the chancre on his penis, serum tests and the favorable effect of treatment supported the diagnosis. Furthermore, our ^{18}F-FDG PET findings showed hypermetabolic lymphadenopathy [3, 4].

In conclusion, this case shows that secondary syphilis can be present without any symptoms but with generalized lymphadenopathy detected by ^{18}F-FDG PET/CT. After 2 months of treatment the size of the lymph nodes decreased. In such cases, differential diagnosis with malignancy is necessary.

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The authors declare that they have no conflicts of interest

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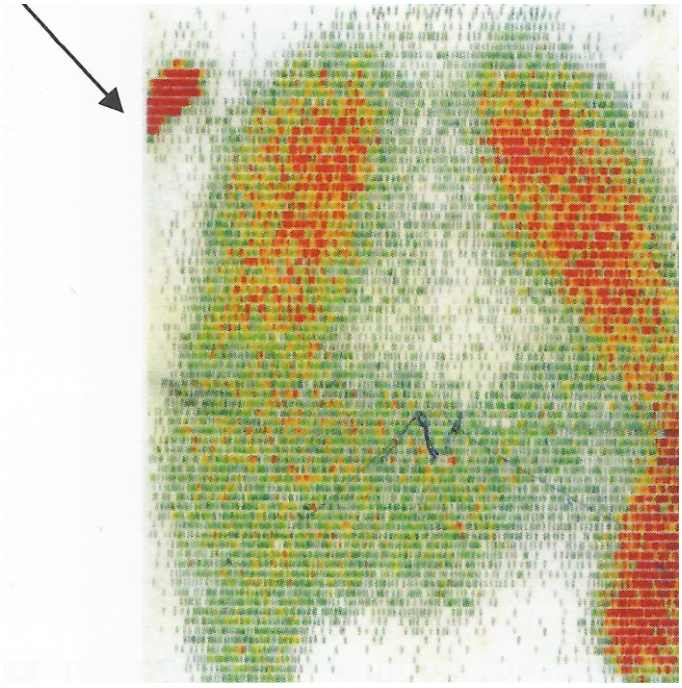

Male 73 years. Liver scan with ^{99m}Tc-S-colloid. One can see a large thrombus in the right bronchial artery (arrow) and uneven distribution of the radiopharmaceutical in the lungs possibly due to small infarcts. Signs of liver insufficiency and "hot" enlarged hypertrophic spleen. After 3 days the patient died from a large pulmonary embolus. (From: Nuclear Medicine 5th edn. P. Grammaticos, 2014; p398.