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Axillary lymph nodes' response to pneumococcal polysaccharide vaccination on FDG-PET/CT examination: Two case reports

Y.M. Chi[1] and C.C. Chang[1,2,3*]

[1]Department of Nuclear Medicine, Kaohsiung Medical University Hospital, Kaohsiung 807, Taiwan
[2]School of Medicine, Kaohsiung Medical University, Kaohsiung 807, Taiwan
[3]Neuroscience Research Center, Kaohsiung Medical University, Kaohsiung 80756, Taiwan

► ***Case report***

Corresponding author:
Dr. Chin-Chuan Chang,
E-mail: *chinuan@gmail.com*

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ABSTRACT

Positron emission tomography/computed tomography (PET/CT) with radioactive Fluorine-18 fluorodeoxyglucose (FDG) is a highly sensitive tool that is used for detecting malignancy. However, it can sometimes produce false positive results if done after vaccination. To prove this, we present two cases of individuals who received pneumococcal polysaccharide vaccination (PPV) and later showed FDG accumulation in the axillary lymph nodes during PET/CT scans. The first case involves a 69-year-old man who underwent a PET/CT scan for a health checkup. The scan revealed low-grade FDG uptake in the left axillary lymph nodes. A thorough examination of his medical history revealed that the patient had received PPV in his left upper arm eight days prior to the checkup. The vaccination was suspected to have caused left axillary lymphadenopathy. The second case involves a 66-year-old woman who also underwent a PET/CT scan for a health checkup. The scan showed FDG-avid lymph nodes in the left axillary region and increased FDG uptake in the spleen. After further questioning, it was discovered that the patient had received PPV in her left upper arm eight days prior to the checkup. Seven days after the PET/CT scan, when a complete blood count with differential was performed on the second case, it revealed that all data were within normal limits. Further, an abdominal ultrasound was conducted, which showed normal findings in the spleen. Based on these results, the medical team concluded that the prior vaccination was the cause of the observed benign findings and emphasized the importance of carefully reviewing patient history to differentiate between benign findings and malignant lesions.

INTRODUCTION

Positron emission tomography/computed tomography (PET/CT) with radioactive Fluorine-18 fluorodeoxyglucose (FDG) is a diagnostic exam that is widely used to detect malignant tumors by observing changes in glucose metabolism. However, an FDG-PET scan showing changes in glucose metabolism and FDG accumulation does not necessarily indicate the presence of cancerous lesions. Such changes may also occur in normal physiological, infectious, and inflammatory conditions, or after various medical treatments [1]. Clinicians should study FDG-PET results based on detailed patient history and chart review, and be aware of the possibility of unexpected findings. Certain medical treatments may result in unexpected FDG-PET findings, which are rarely reported. In this paper, we present two cases of axillary lymph node accumulation of FDG (manufactured by Positron Scientific Company Ltd, Kaohsiung, Taiwan) after pneumococcal polysaccharide vaccination (PPV).

In Taiwan, two types of pneumococcal vaccines are used-pneumococcal conjugate vaccine (PCV13) and pneumococcal polysaccharide vaccine (PPV). The two patients in our cases had received PPV, which is manufactured in the Netherlands and marketed by Merck Sharp and Dohme from the United States of America as Pneumovax 23 in Taiwan. PPV is an unconjugated vaccine that contains 23 capsular polysaccharide serotypes against pneumococcal disease. The most common adverse reactions reported previously in patients vaccinated with PPV include headache, pain, swelling, tenderness, soreness, induration, erythema of the injection site, asthenia/fatigue and myalgia [2].

Different types of vaccines, including smallpox, anthrax, and Bacille Calmette-Guerin (BCG), have been reported to cause lymphadenopathy [3]. Literature reports show that COVID-19, seasonal influenza, H1N1, human papillomaviruses, Pediarix (a combination of diphtheria, tetanus toxoids, acellular pertussis, recombinant hepatitis B, and inactivated poliovirus) and carcinoembryonic antigen vaccines

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cause FDG-PET accumulation [4-8]. To the authors' knowledge, no literature has reported similar immune responses to PPV detected through FDG-PET/CT.

Case Descriptions

Case 1

A 69-year-old man, who had no prior personal or family history of malignance, went in for a health checkup at our PET center. During FDG-PET/CT (GE Discovery MI DR, GE Medical System, Waukesha, Wisconsin, USA), low-grade FDG uptake was observed in the left axillary lymph nodes with a maximal standardized uptake value (SUVmax) of 2.3 (figure 1). Upon further investigation, it was revealed that the patient had received Pneumovax 23 (Merck, USA) in his left upper arm eight days before the FDG-PET examination. The vaccination was suspected to have caused left axillary lymphadenopathy.

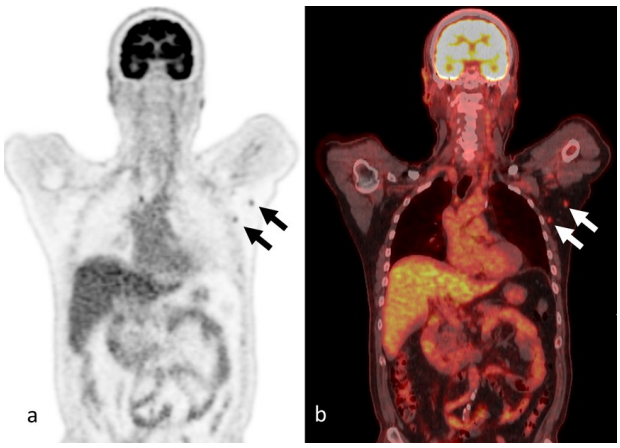

Figure 1. FDG PET/CT examination of case 1. A 69-year-old man, with no personal or family history of cancer, had received Pneumovax 23 in his left upper arm eight days before examination. Coronal images of **(a)** PET and **(b)** fused PET/CT showing axillary lymph nodes with FDG uptake in the left axillary (arrows).

Case 2

A 66-year-old woman without prior personal or family history of malignance came to our PET center for a health checkup. During FDG-PET/CT (GE Discovery MI DR, GE Medical System, Waukesha, Wisconsin, USA), some FDG-avid lymph nodes were observed in the left axillary region, with an SUVmax of 4.4 (figure 2). Additionally, an increased FDG uptake was noticed in the spleen with an SUVmax of 5.8. Upon further investigation, it was revealed that the patient had received Pneumovax 23 (Merck, USA) in her left upper arm eight days before the FDG-PET examination. The vaccination was suspected to have caused the left axillary lymphadenopathy. Seven days after the FDG-PET examination, a complete blood count with the differential was done and all data were found to be within normal limits. In addition, an abdominal ultrasound was performed, which revealed unremarkable findings in the spleen.

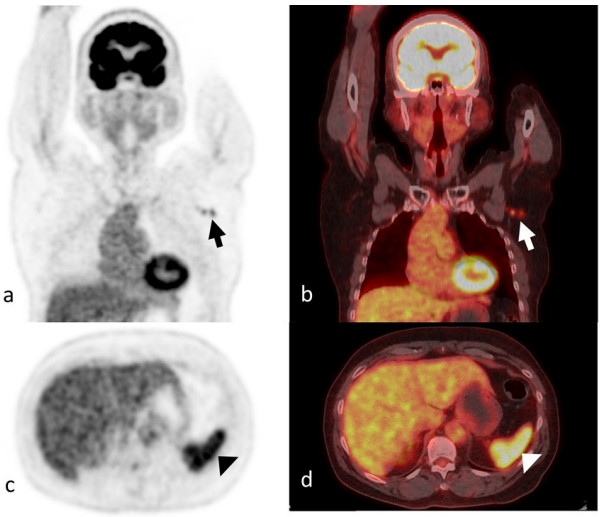

Figure 2. FDG PET/CT examination of case 2. A 66-year-old woman, with no personal or family history of cancer, had received Pneumovax 23 in her left upper arm eight days before examination. Coronal images of **(a)** PET and **(b)** fused PET/CT showing axillary lymph nodes with FDG uptake in the left axillary (arrows). Transaxial images of **(c)** PET and **(d)** fused PET/CT showing increased FDG uptake in the spleen (arrowhead).

DISCUSSION

FDG-PET results can sometimes show unilateral lymphadenopathy, which may be linked to malignancy, local infection, inflammation or previous medical treatment, such as vaccination. In this paper, we present two cases of patients who had received Pneumovax 23, an unconjugated vaccine from Merck that contains 23 capsular polysaccharide serotypes against pneumococcal disease. Lymphadenopathy was listed as one of the adverse reactions in post-marketing experience with an unknown frequency [2]. The axillary FDG nodal uptakes in our cases were likely due to prior PPV injections, which both had received on their ipsilateral arms before FDG-PET examinations.

Case 2 also demonstrated increased FDG uptake in the spleen, which may again be attributed to prior vaccination. A report has shown that intense splenic uptake was noted on FDG-PET after influenza vaccination. The influenza vaccine was thought to elicit a systemic immune-mediated response, which causes intense splenic FDG uptake [9]. PPV may have caused a systemic immune response in case 2, which must have resulted in the increased splenic FDG uptake. Some of the listed adverse reactions to PPV in the prescribing information were thrombocytopenia, hemolytic anemia and leukocytosis [2]. All these adverse reactions may have resulted in increased spleen function, which in turn caused increased FDG uptake in our patient. A limitation of this case was that no other test was done on the day of the FDG-PET examination to provide further insight. A follow-up FDG-PET examination was also not

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performed to prove the resolution of axillary lymph nodes and splenic FDG uptake.

CONCLUSION

FDG-PET is a highly sensitive diagnostic test for detecting cancer. However, it is important to note that FDG accumulation does not always indicate malignancy. It can also be observed in normal physiological, infectious, inflammatory conditions and after various medical treatments, such as PPV injection. Therefore, it is crucial for the reporting physician to carefully review the patient's medical history and identify any factors that could affect the FDG-PET results. This will ensure an accurate diagnosis.

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Conflicts of Interest: The authors declare that there is no conflict of interest.

Ethical Considerations: The reports in question were conducted in strict accordance with the ethical standards set forth in the Declaration of Helsinki. Moreover, the current study was approved by the Institutional Review Board of Kaohsiung Medical University Hospital (KMUHIRB-E(I)-20240153) on 25 -March-2024.

Authors' contributions: YC and CC participated in the study design and the literature search. YC collected the data and wrote the manuscript. YC and CC revised the manuscript. All authors have read and agreed to the published version of the manuscript.

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