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Case Report / Приказ болесника

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^{18}F-fluorodeoxyglucose positron emission tomography / computed tomography in the diagnosis of secondary malignancies in a patient with Hodgkin lymphoma

Позитронска емисиона томографија / компјутерска томографија са^{18}Ф-флуородеоксиглукозом у дијагнози секундарних малигнитета код болесника са Хоџкиновим лимфомом

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SUMMARY

Introduction The incidence of a second cancer among patients who have been treated for Hodgkin lymphoma (HL) is higher than the incidence of cancer in the general population. ^{18}F-fluorodeoxyglucose (18F-FDG) positron emission tomography / computed tomography is used in the evaluation of a number of malignancies. The aim of the article is to emphasize the importance of including a second primary cancer as a differential diagnosis among patients at risk.

Case outline We present a case of a patient diagnosed with two separate malignancies almost two decades after the treatment of HL.

Conclusion In patients previously treated for HL, a biopsy of lesions that show high 18F-FDG uptake should be advised, particularly if the location of the lesion is unusual for the primary diagnosis.

Keywords: lymphoma, Hodgkin; positron emission tomography; second primary malignancy; chemotherapy; radiation therapy

САЖЕТАК

Увод Инциденца другог рака код болесника који су лечени од Хоџкиновог лимфома већа је од инциденце рака у општој популацији. Позитронска емисиона томографија / компјутерска томографија са ^{18}Ф-флуородеоксиглукозом се користи у евалуацији бројних малигнитета. Циљ рада је да се истакне важност укључивања другог примарног карцинома као диференцијалне дијагнозе код болесника са повећаним ризиком.

Приказ болесника Представљамо случај болесника са два одвојена малигна обољења дијагностификована скоро две деценије након лечења Хоџкиновог лимфома.

Закључак Код болесника који су претходно лечени од Хоџкиновог лимфома, требало би саветовати да се обави биопсија лезија које показују високо преузимање ^{18}Ф-флуородеоксиглукозе, посебно ако је локација лезије неуобичајена за примарну дијагнозу.

Кључне речи: Хоџкинов лимфом; позитронска емисиона томографија; други примарни малигнитет; хемотерапија; зрачна терапија

INTRODUCTION

Hodgkin lymphoma (HL) is a chronic malignant lymphoproliferative disease with a bimodal distribution of occurrence in the third decade of life as well as in the sixth decade. It has a good prognosis and a high cure rate [1]. Lung cancer, on the other hand, causes an estimated 1.8 million annual deaths globally, which is 18% of all deaths attributed to cancer, and it is the leading cause of cancer death [2]. Meanwhile, non-Hodgkin lymphoma (NHL) is the most common hematological malignancy worldwide, with diffuse large B-cell lymphoma (DLBCL) being the most frequent subtype [3].

Among the late complications, second malignancies (SMN) are a great concern in cancer survivors [4]. Although second cancers can reflect the influence of lifestyle factors, environmental exposures, genetic contributions, and host factors, the late sequelae of treatment are paramount [5]. The risk for SMN is particularly high in HL survivors. In 2023, Núñez-García et al. [6]

demonstrated the much higher than expected mortality in patients previously treated for HL, even when HL as the cause of death was eliminated, with patients younger than 30 years and women being especially vulnerable, most frequently secondary to SMN (37.8%). During the last three decades, the role of positron emission tomography / computed tomography (PET/CT) in diagnosis, staging, and follow-up of cancer patients has been revolutionary [7]. The majority of PET scans are performed using ^{18}F-fluorodeoxyglucose (18F-FDG), the gold standard of PET radiopharmaceuticals [8]. However, due to its non-specific nature, 18F-FDG PET/CT cannot distinguish between different types of cancer, and histopathological confirmation for lesions of an undetermined origin is a necessity.

In this case report, we present the development of two distinct malignancies two decades after the completion of Hodgkin lymphoma treatment.

CASE REPORT

A 62-year-old female patient was sent for an 18FDG PET/CT examination at the Center for Nuclear Medicine with Positron Emission Tomography of the University Clinical Center of Serbia for the initial staging of DLBCL, diagnosed 19 years after the patient had been treated for HL with chemotherapy (CTx) and radiation therapy (RTx). Previously, a sample of enlarged submandibular lymph nodes was taken. Histopathological specimens revealed pathological findings resembling DLBCL, the most common subtype of NHL. Therefore, the patient was scheduled for a PET/CT. Meanwhile, a standard-dose CT showed a mass in the right lung, without a definitive conclusion regarding the etiology. The patient complained of fatigue and coughing.

A three-dimensional PET scan and a low-dose non-enhanced CT scan were acquired from the base of the skull to the mid-thigh. On PET/CT exam, we found an increased metabolism of glucose in a lesion in the posterobasal segment of the right lower lobe of the lungs (Figure 1), previously seen on a standard-dose CT, and in the subcarinal lymph node (Figure 2). Dimensions of the pulmonary lesion were 42 × 38 × 41 mm with the maximum standardized uptake value (SUVmax) of 22.2, while the subcarinal lymph node measured 16 × 9 mm in diameter with the SUVmax of 4.7. Primary carcinoma of the lungs was suspected, without the exclusion of a lymphoma as a possible cause. PET/CT examination also disclosed an increased accumulation of FDG in the right tonsil and right cervical lymph nodes (Figure 3), up to 36 × 20 mm in size with SUVmax of 36.4, which showed an increased metabolism due to DLBCL, and a

focal zone of an increased metabolism of glucose in a soft tissue mass in the cervix of the uterus (Figure 4), 22 × 17 mm in diameter with SUVmax of 14.7. Later on, bronchoscopy was performed, and a biopsy of the pulmonary lesion revealed squamous cell carcinoma. Specimens from both the submandibular lymph nodes and a pulmonary lesion were sent for revision, and the findings confirmed two separate malignancies of different locations and histological types. Afterwards, the gynecology specialist did a comprehensive evaluation. The patient stated that she noticed blood spots on her underwear in the last seven days. Ultrasound confirmed a soft tissue mass in the projection of the cervix. The sample of the lesion was taken. Based on the morphological and immunohistochemical analysis of the tumor cells, the pathologist concluded that infiltration by the previously diagnosed DLBCL was most likely. Two weeks later, the patient arrived at the emergency department with family members who reported that the patient was disoriented and could not walk. CT of the head was performed. A scan revealed an oval, hypodense lesion in the frontobasal region of the right cerebral hemisphere, suspected to be a metastasis. Further treatment will be planned based on the decision of the lung cancer council.

A decision (668/6) dated April 19, 2018, by the University Clinical Center of Serbia's Ethics Committee allows employees of the Center for Nuclear Medicine with PET of the University Clinical Center of Serbia to use anonymous data and obtained patient results for scientific research purposes.

DISCUSSION

Hodgkin lymphoma, a type of cancer that arises from B-lymphocytic cells, is one of the most curable malignancies [9]. In recent years, the use of lower doses of alkylating CTx and RTx, limited to smaller volumes and at lower doses, has improved survival of patients with HL, such that the cure rate for this disease currently exceeds 80% [6]. However, as more patients survive longer, the impact of late complications of treatment is increasingly clear, with second primary malignancy (SPM) and cardiovascular, pulmonary, and infectious diseases being the leading cause of mortality in survivors of HL [10]. NHL and lung cancer are among the most common SPMs in patients previously treated for HL [11], both of which occurred in the case we presented. Moreover, the patient received CTx and RTx, both of which increase the risk for SPM in HL survivors. 18FDG PET/CT at baseline has proven to be highly sensitive in determining sites of disease for DLBCL [12], an aggressive lymphoma subtype. It shows higher sensitivity, specificity, and accuracy compared to contrast-enhanced CT in the initial assessment and

staging of lymphoma [13]. However, since a large percentage of malignant lesions show 18FDG avidity, the type of cancer cannot be determined based on 18FDG-PET/CT findings alone, and further evaluation is needed if SMN is suspected. Furthermore, most non-cancerous cells use glucose as the main source of energy. Consequently, the increased glucose metabolism is not only specific for malignant neoplastic lesions but is also observed in many other sites, such as pathologically benign lesions, especially inflammatory lesions, and normal organs [14].

A nuclear medicine specialist should be aware of a possibility of two or more different types of malignant lesions in a patient, especially in patients who have an increased risk thereof due to earlier treatment. In cases where the etiology of the lesion is uncertain, a biopsy should be advised, in order to determine a proper therapeutic strategy.

Conflict of interest: None declared.

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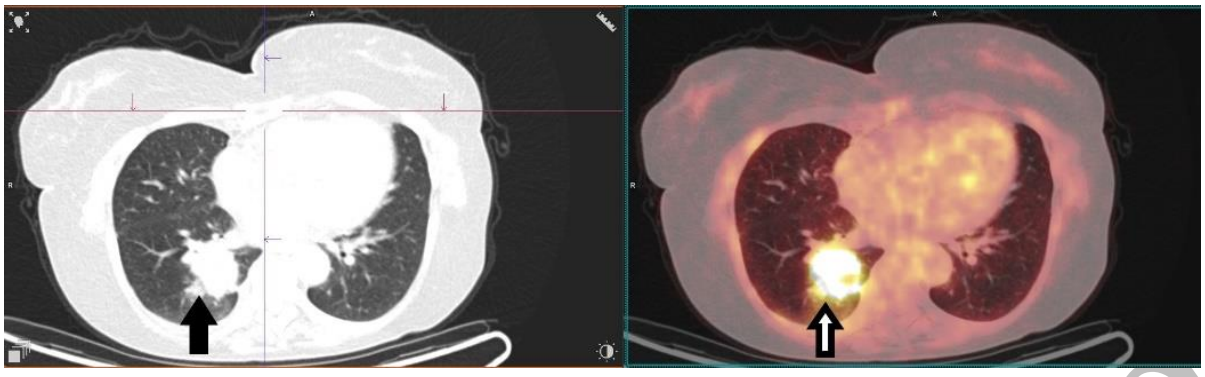

Figure 1. ^{18}F-fluorodeoxyglucose positron emission tomography / computed tomography: the axial image depicts a lesion in the posterobasal segment of the right lower lobe of the lungs on the low-dose CT (black arrow) and an increased accumulation of a radiopharmaceutical on the fused image (white arrow); histopathology revealed squamous cell carcinoma

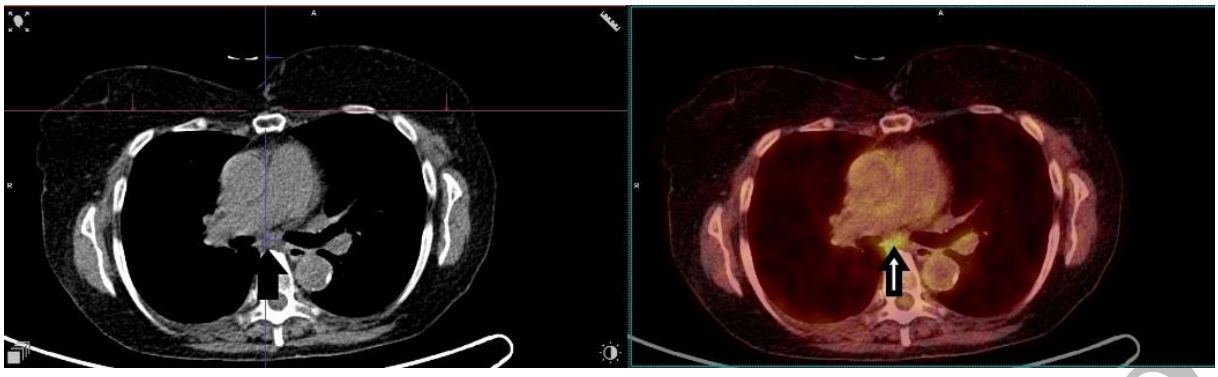

Figure 2. ^{18}F-fluorodeoxyglucose positron emission tomography / computed tomography: the axial image depicts an enlarged subcarinal lymph node on the low-dose CT (black arrow) and an increased accumulation of a radiopharmaceutical on the fused image (white arrow)

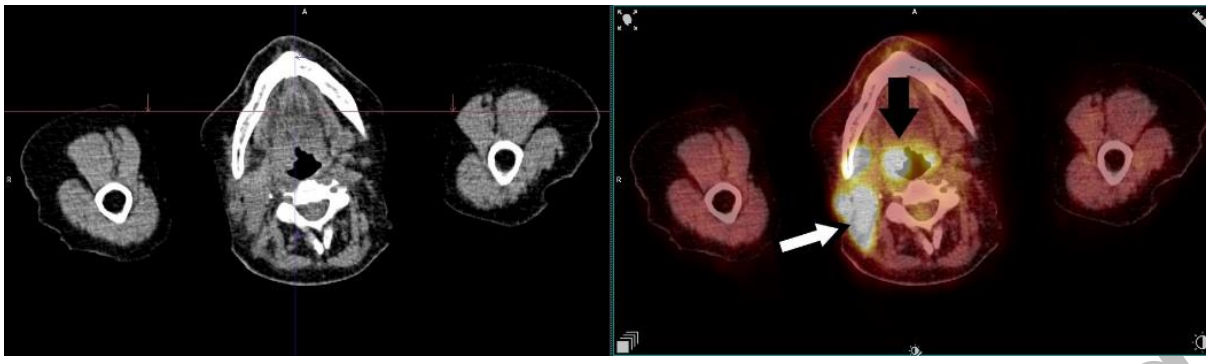

Figure 3. ^{18}F-fluorodeoxyglucose positron emission tomography / computed tomography: the axial image depicts an increased accumulation of a radiopharmaceutical in the right tonsil (black arrow) and in enlarged right cervical lymph nodes (white arrow); histopathology revealed diffuse large B-cell lymphoma

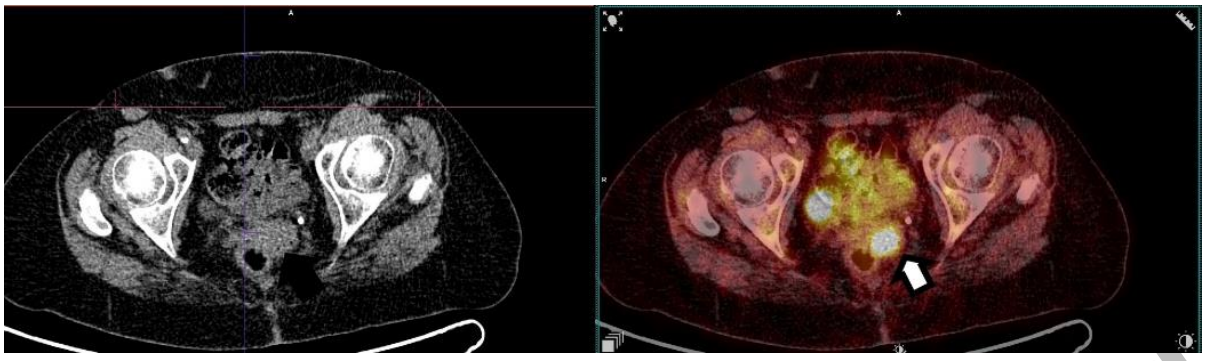

Figure 4. ^{18}F-fluorodeoxyglucose positron emission tomography / computed tomography: the axial image depicts a soft tissue mass in the cervix of the uterus on the low-dose CT (black arrow) and an increased accumulation of a radiopharmaceutical on the fused image (white arrow); histopathology revealed diffuse large B-cell lymphoma

