PET/CT diagnostic value in suspicion of palatine tonsils’ lymphoma recurrence

Wartość diagnostyczna PET/CT w podejrzeniu nawrotu chłoniaka migdałków podniebiennych

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ABSTRACT:

Introduction: Diffuse large B-cell lymphoma (DLBCL) is a non-homogenous group of neoplasms of the lymphatic system in terms of morphology, genetics, and clinical aspects. The follow-up of patients treated for lymphoma includes the following examinations: clinical, laboratory, and imaging. According to the recommendation of the National Comprehensive Cancer Network (NCCN) from 2020, the observation of patients with DLBCL is mostly based on the PET/CT examination with 18 F-FDG, especially when suspecting the extranodal lymphoma recurrence.

Aim: The aim of the study was to define the predictive value of the PET/CT examination in the evaluation of the recurrence of DLBCL in the palatine tonsils.

Material and methods: The analysis of the medical documentation of patients treated in our Department was performed. Research material included patients with suspicion of local recurrence of DLBCL in the palatine tonsils. Thirty-three patients were included in the study: 22 women and 11 men. The age range was 23–73 years with a mean of 53 years.

Results: The confirmation of the local recurrence of DLBCL in the histological examination was obtained in 11 patients – 7 women and 4 men aged 58–73 years (μ = 65.4). SUV max in the palatine tonsil in those patients ranged: for the right tonsil 3.6–9.5 (μ = 6.0), and for the left tonsil 3.8–9.5 (μ = 6.1). The second group of the patients did not present any local recurrence of DLBCL in the palatine tonsils. The histological diagnosis was chronic tonsillitis. The age of those patients ranged from 23 up to 73 years (μ = 43.1 years). SUV max ranged: for the right palatine tonsil 2.8–27.7 (μ = 8.62), for the left palatine tonsil 3.8–27.4 (μ = 8.60). The sensitivity of PET/CT in the recurrence assessment in our study was 100%, while the specificity was 33.3%. The additional predictive value was 0.33.

KEYWORDS: chronic tonsillitis, DLBCL, lymphoma follow-up, PET-CT

STRESZCZENIE:

Wstęp: Chłoniak rozłany z dużych komórek B (DLBCL) jest niejednorodną pod względem morfologicznym, genetycznym i klinicznym grupą nowotworów układu limfatycznego. Obserwacja chorych po leczeniu chłoniaka obejmuje badania: kliniczne, laboratoryjne i obrazowe. Zgodnie z zaleceniem National Comprehensive Cancer Network (NCCN) z 2020 r., obserwacja pacjentów z DLBCL opiera się głównie na badaniu PET/CT z 18 F-FDG, zwłaszcza przy podejrzeniu pozawęzłowej wznowy chłoniaka.

Cel: Celem pracy było określenie wartości predykcyjnej badania PET/CT w ocenie nawrotu DLBCL w migdałkach podniebiennych.

Materiał i metody: Przeprowadzono analizę dokumentacji medycznej pacjentów leczonych w naszej Klinice. Grupę badaną stanowili pacjenci z podejrzeniem wznowy miejscowej DLBCL w palatynach. Trzydzieści trzy pacjentów włączono w badanie: 22 kobiety i 11 mężczyzn. Wiek chorych wahał się od 23 do 73 lat, średnia wieku 53 lata.

Wyniki: Potwierdzenie miejscowej wznowy w histologicznym badaniu uzyskano u 11 pacjentów – 7 kobiet i 4 mężczyzn w wieku 58–73 lat (średnia 65,4). SUV max w palatynach u tych pacjentów wynosił: dla prawego 3,6–9,5 (średnia 6,0), dla lewego 3,8–9,5 (średnia 6,1). Drugą grupę pacjentów nie stwierdzono żadnej miejscowej wznowy DLBCL w palatynach. Diagnoza histologiczna to przewlekła zapalność. Wiek tych pacjentów wahał się od 23 do 73 lat (średnia 43,1). SUV max wynosiło: dla prawego migdałka 2,8–27,7 (średnio 8,62), dla lewego migdałka 3,8–27,4 (średnio 8,60). Wrażliwość PET/CT w ocenie nawrotów w naszym badaniu wyniosła 100%, a specyficzność 33,3%. Dodatkowa wartość predykcyjna to 0,33.

SŁOWA KLUCZOWE: DLBCL, kontrola po leczeniu chłoniaka, PET-CT, przewlekłe zapalenie migdałków

STRESZCZENIE:
**INTRODUCTION**

Positron emission tomography (PET) in combination with computed tomography (CT) is a hybrid diagnostic tool (positron emission tomography/computed tomography PET/CT). Being a highly sensitive and specific examination, PET-CT is a widely used diagnostic tool in oncology and its importance cannot be left unappreciated. Otto Warburg’s discovery in the early 20$^{th}$ century of glucose metabolism in neoplastic cells contributed to the invention of the first prototypes of PET-CT in 70s [1].

In PET-CT, the most commonly used substrate is 18F-Fluorodeoxyglucose (18F-FDG) and its maximum uptake in the organs (maximum standardized uptake value \(SU V_{\text{max}}\)) is a semi-quantitative parameter. The parameter correlates with proliferation of the tumor’s cells and is used in oncology diagnostics to evaluate many different neoplasms [2, 3].

Up to date, it is hard to imagine diagnostics in oncology without the PET/CT examination. Indications for the PET-CT examination are strictly defined in the neoplastic disease [3, 4].

Diffuse large B-cell lymphoma (DLBCL) is a non-homogenous group of neoplasms of the lymphatic system in terms of morphology, genetics and clinical aspects. It arises from the peripheral B-type lymphocytes from the reproduction center [5]. DLBCL accounts for about 35% of the neoplasms of the lymphatic system and for 80% of all aggressive lymphomas [6, 7].

The follow-up of patients treated for lymphoma includes the following examinations: clinical, laboratory, and imaging. According to the recommendation of the National Comprehensive Cancer Network (NCCN) from 2020, the observation of patients with DLBCL is mostly based on the PET/CT examination with 18F-FDG, especially when suspecting the extranodal lymphoma recurrence [8]. Some authors suggest performing follow-up PET/CT in the 6th, 12th, 18th, and 24th months after the end of the treatment, and then once a year, which allows for early detection of the recurrence of the disease in up to 80% of the patients [9]. However, recommendations of the imaging examinations including PET/CT do not indicate performing that procedure in asymptomatic patients. The only exception is patients from the group of the risk of quick recurrence, who should have PET/CT performed six months from the end of the treatment. The following patients are included in the risk group:

- with score 4 and 5 in the Deauville scale – it is recommended to perform PET/CT after the second cycle of the chemotherapy,
- with score 3 in the Deauville scale – PET/CT is recommended after the end of the treatment,
- with primary occupation of extranodal areas (in particular: bone marrow, bones and lungs) [10–12].

**RESULTS**

Thirty-three patients were included in the study: 22 women and 11 men. The age range was 23–73 years with a mean of 53 years. The time from the end of treatment ranged from 2 to 7 years, 4 years on average. All of the patients had PET/CT examinations performed during their follow-up and the number of examinations without increased \(SU V_{\text{max}}\) values ranged from 2 to 6, on average.

The \(SU V_{\text{max}}\) value in the palatine tonsils ranged from 2.8 to 27.4 (\(\mu = 7.9\)): in the right tonsil – 2.8–27.4 (\(\mu = 7.92\)), in the left tonsil – 3.8–27.4 (\(\mu = 7.88\)).

Confirmation of local DLBCL recurrence in the histological examination was obtained in 11 patients – 7 women and 4 men aged 58-73 years (\(\mu = 65.4\)). The range of the \(SU V_{\text{max}}\) value in the palatine tonsils in those patients was: for the right tonsil 3.6–9.5 (\(\mu = 6.0\)), left tonsil 3.8–9.5 (\(\mu = 6.1\)).

The second group of patients did not present any local recurrence of DLBCL in the palatine tonsils. The histological diagnosis was chronic tonsillitis. The age of those patients ranged from 23 to 73 years (\(\mu = 43.1\) years). The \(SU V_{\text{max}}\) value range was: for the right palatine tonsil 2.8–27.7 (\(\mu = 8.62\)), left palatine tonsil 3.8–27.4 (\(\mu = 8.60\)).
The sensitivity of PET/CT in recurrence assessment in our study was 100%, while the specificity was 33.3%. The additional predictive value was 0.33.

DISCUSSION

The proper interpretation of imaging examination results in combination with anamnesis and laboratory examination outcomes allows for taking appropriate diagnostic and therapeutic decisions. In case of DLBCL, there are recommendations of the American NCCN [8], European Society for Medical Oncology (ESMO) [13], Polish Lymphoma Research Group [14], and other organizations and associations of national and international range. Most of the associations depend on the control PET/CT examination after DLBCL treatment evaluated according to the international Deauville scale (comparison of the $^{18}$F-FDG uptake in the mediastinum and palatine tonsils) and extranodal localization of the lymphoma. Those are the recommendations in asymptomatic patients while in case of suspected recurrence of DLBCL in the clinical examination, it is suggested to perform PET/CT [8, 13, 14].

The interpretation of the PET/CT examination is dependent on many factors that may affect the uptake of $^{18}$F-FDG. Increased uptake of $^{18}$F-FDG in the palatine tonsils and hence over-interpretation of the results indicating a potential focus of the neoplasm may have many causes, among them being: active or past acute infection, chronic infection, trauma of the tissues, surgical trauma, retrograde laryngeal nerve palsy on the opposite site, or the technical aspects of the procedure, for example patient’s movements during the PET/CT examination. Chemotherapy may modulate the uptake of $^{18}$F-FDG in both ways — by increasing or decreasing it [15]. Even radiotherapy, leading to increased inflammatory lesions in soft tissues during early and late radiation reactions may be the reason for the changed uptake of $^{18}$F-FDG [16].

Misinterpretation of the results may also be the consequence of the presence of teeth implants. Rarely, a lower uptake of $^{18}$F-FDG is observed as a result of physiologically decreased glucose metabolism or omission of the lesion due to the low resolution of the examination tool [17].

A variable physiological uptake of $^{18}$F-FDG is commonly observed in the Waldeyer’s lymphatic ring. The uptake of $^{18}$F-FDG in the palatine tonsils is usually described as low to moderate and symmetrical. However, due to the presence of macrophages and lymphocytes, the uptake may be much higher than expected. Another difficulty with interpretation is the presence of the asymmetry of uptake in the palatine tonsils. It mostly occurs when PET/CT examination is performed in patients with metastases to the lymph nodes (with unknown primary focus), or if the recurrence of the disease is suspected. In this case, it is recommended to perform a thorough clinical examination to exclude a possible inflammation-type lesion. It is also recommended to compare the PET/CT examination results with CT or MR scans which present higher resolution. However, always in case of any doubts, the most important examination remains the histological study of the lesion.

In our research, only 11 of 33 patients treated previously due to DLBCL were confirmed with recurrence in the histological examination after a suspicious PET/CT result. The uptake of $^{18}$F-FDG in the palatine tonsils ranged from 2.8 to 27.4 and the mean uptake was 7.92. Interestingly, the patient with the highest SUV$_{max}$ value in the palatine tonsils was not confirmed to have a local recurrence of DLBCL but chronic tonsillitis. Birkin et. al. [18] found the uptake was higher in the right palatine tonsil (4.63) than in the left one (4.47), and that the value was different for non-smokers and for smokers. Okuyama et. al. [15] stated that in the group of juvenile patients treated with chemotherapy due to lymphoma for 6–12 months, there was an increased uptake of $^{18}$F-FDG in control PET/CT examinations although the palatine tonsils were not enlarged. The authors explain it with a reactive increase of $^{18}$F-FDG uptake that is not connected to the recurrence of lymphoma. The sensitivity of PET/CT is evaluated as very high — in our study it was 100%, but the specificity was only 33.3%. Such a low specificity of PET/CT in the evaluation of lymphoma recurrence in the palatine tonsils may be caused by the metabolic activity connected with the accumulation of macrophages and lymphocytes — both in the tissues and tonsil crypts — as well as past infection in the Waldeyer’s ring [17]. An alternative to tonsillec-toomy in case of a suspected local recurrence in the tonsils might be fine needle aspiration cytology (FNAC) or surgical biopsy but the overall usefulness of both methods is low in case of lymphoma [19–21]. However, due to the fact that a full immunohistochemical staining panel is needed to identify lymphoma, tonsillec-toomy remains the method of choice in this case [22–24]. The combination of the clinical examination with additional examinations such as imaging tests, as well as thorough monitoring of patients following DLBCL treatment may improve the odds of reaching a correct diagnosis.

CONCLUSIONS

1. Sensitivity of PET/CT examination in evaluation of the recurrence of DLBCL in palatine tonsils is high but the specificity is low (analogously in our study: 100% and 33.3%);
2. The predictive value of the PET/CT examination in evaluation of the recurrence of DLBCL in tonsil tissue is positive (in our study it is 0.33);
3. The final diagnosis of the recurrence of DLBCL is only possible after histological examination of the material, where it is suspected to occur the development of neoplastic disease in the follow-up PET/CT examination.
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