

CASE REPORTS PRIKAZI SLUČAJEVA

ISOLATED ORBITAL RELAPSE OF FOLLICULAR LYMPHOMA DETECTED BY 18F-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY WITH COMPUTED TOMOGRAPHY – A CASE REPORT

IZOLOVANI ORBITALNI RELAPS FOLIKULARNOG LIMFOMA DETEKTOVAN 18F-FLUORODEOKSIGLUKOZOM POZITRONSKOM EMISIONOM TOMOGRAFIJOM SA KOMPJUTERIZOVANOM TOMOGRAFIJOM – PRIKAZ SLUČAJA

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Abstract

Introduction. Orbital localization of follicular lymphoma is exceedingly rare, and its diagnosis is often challenged due to a broad spectrum of ophthalmic differential diagnoses. We report a case of orbital relapse of follicular lymphoma detected five years after complete remission using 18F-fluorodeoxyglucose positron emission tomography with computed tomography. **Case Report.** A 53-year-old man diagnosed with follicular lymphoma in 2013 achieved complete remission following chemotherapy in 2017 and remained under routine follow-up for the subsequent five years. In 2022, he presented with a 10-day history of right orbital pain. Clinical examination revealed right-sided exophthalmos and eyelid ptosis. 18F-fluorodeoxyglucose positron emission tomography with computed tomography demonstrated increased metabolic activity in the right orbit, raising suspicion of disease relapse. Subsequent ophthalmologic assessment and additional imaging confirmed the presence of an orbital mass, which was surgically excised. Histopathological analysis verified a localized orbital recurrence of follicular lymphoma. The patient was subsequently treated with localized radiotherapy. Follow-up 18F-fluorodeoxyglucose positron emission tomography with computed tomography performed in 2023 demonstrated a complete metabolic response. **Conclusion.** The case highlights the important role of 18F-fluorodeoxyglucose positron emission tomography with computed tomography in detecting atypical and rare manifestations of follicular lymphoma. Integration of 18F-fluorodeoxyglucose positron emission tomography/computed tomography findings with ophthalmologic evaluation and histopathological confirmation is essential for accurate diagnosis and appropriate therapeutic decision-making.

Key words: Lymphoma, Follicular; Positron Emission Tomography Computed Tomography; Fluorodeoxyglucose F18; Recurrence; Orbital Neoplasms; Diagnosis; Radiotherapy

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Sažetak

Uvod. Intraorbitalna lokalizacija folikularnog limfoma je izuzetno retka, a postavljanje dijagnoze predstavlja izazov zbog širokog spektra mogućih oftalmoloških diferencijalnih dijagnoza. Prikazujemo slučaj pacijenta sa prethodno lečenim folikularnim limfomom, kod koga je pet godina nakon potpune remisije, detektovan relaps u desnoj orbiti putem 18F-fluorideoksiglukoze pozitronske emisije tomografije sa kompjuterizovanom tomografijom. **Prikaz slučaja.** Pacijent muškog pola i starosti 53 godine, kome je 2013. godine postavljena dijagnoza folikularnog limfoma, postigao je potpunu remisiju tokom 2017. godine, nakon sprovedene hemioterapije. Narednih pet godina bio je bez znakova relapsa osnovne bolesti. Tokom 2022. godine, pacijent je prijavio bol u desnom oku u trajanju od deset dana, dok su kliničkim pregledom ustanovljeni egzofthalmus i ptoza desnog kapka. Na 18F-fluorodeoksiglukozi pozitronskoj emisionoj tomografiji sa kompjuterizovanom tomografijom koja je sprovedena 2022. godine, prikazala se fokalna zona pojačanog nakupljanja fluorodeoksiglukoze u desnom oku, što je izazvalo sumnju na atipični relaps osnovne bolesti. Naknadna oftalmološka evaluacija ukazala je na intraorbitalni tumor, koji je hirurški uklonjen. Histopatološka analiza utvrdila je da se radi o orbitalnom relapsu folikularnog limfoma. Kod pacijenta je sprovedena radioterapija desnog oka. Kontrolna 18F-fluorodeoksiglukoza pozitronska emisiona tomografija sa kompjuterizovanom tomografijom iz 2023. godine pokazala je potpunu metaboličku regresiju prethodno opisane fokalne zone pojačane akumulacije radiofarmaka. **Zaključak.** Predstavljeni prikaz slučaja ukazuje da 18F-fluorodeoksiglukoza pozitronska emisiona tomografija sa kompjuterizovanom tomografijom ima važnu ulogu u otkrivanju atipičnih manifestacija folikularnog limfoma, dok je integracija nalaza 18F-fluorodeoksiglukoze pozitronske emisije tomografije sa oftalmološkom evaluacijom i patohistološkom analizom neophodna za postavljanje tačne dijagnoze i odabira optimalne terapije.

Glavne reči: folikularni limfom; PET/CT; FDG; relaps; tumori orbite; dijagnoza; radioterapija

Abbreviations

FL	– follicular lymphoma
NHL	– non-Hodgkin lymphoma
FDG PET/CT	– Fluorodeoxyglucose positron emission tomography/Computed Tomography
PET/CT	– Positron Emission Tomography/Computed Tomography

Introduction

Follicular lymphoma (FL) is the most common indolent subtype of non-Hodgkin lymphoma (NHL) and typically presents with lymphadenopathy. Extranodal involvement in FL is uncommon and most frequently affects the gastrointestinal tract, skin, or central nervous system [1–5]. Intraorbital localization of FL relapse is exceedingly rare and represents a considerable diagnostic challenge, particularly in patients without prior orbital involvement [6]. This diagnostic complexity arises from a broad spectrum of differential diagnoses, including inflammatory conditions, primary intraorbital tumors, and metastatic lesions. Early recognition of such atypical presentations is therefore essential for timely intervention and appropriate therapeutic decision-making.

¹⁸F-Fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) plays a central role in the management of lymphoma across different disease stages, including initial staging, assessment of suspected relapse, and evaluation of treatment response [7].

We report the case of a patient with previously treated FL who developed right orbital pain, exophthalmos, and eyelid ptosis five years after achieving complete remission. The relapse was ultimately diagnosed as intraorbital FL recurrence. The aim of this report is to highlight the diagnostic value of the FDG PET/CT in disease staging and treatment monitoring in patients with rare extranodal manifestations of FL.

Case report

A 53-year-old man was diagnosed with FL in 2013 based on histopathological examination and was treated with systemic chemotherapy. At the time of diagnosis, FDG PET/CT demonstrated involvement of the submandibular, cervical, and mediastinal lymph nodes. Complete remission was achieved in 2017. Over the subsequent five years, the patient remained asymptomatic and underwent regular follow-up with FDG PET/CT examinations, without requiring additional treatment.

In 2022, five years after achieving disease remission, the patient presented for a routine follow-up FDG PET/CT examination. During medical history

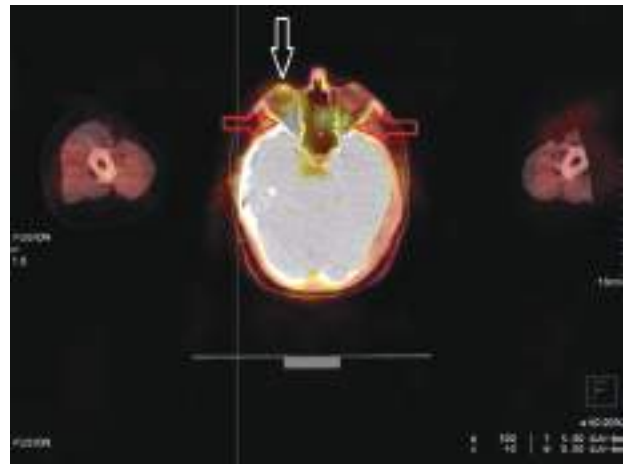


Figure 1. Fluorodeoxyglucose positron emission tomography/Computed Tomography before radiotherapy shows apparent focal FDG uptake within the right eye (white arrow) (SUVmax 5.1) – histopathologically confirmed as follicular lymphoma, while symmetric retrobulbar hypermetabolism can be seen bilaterally (red arrows) (SUVmax up to 8.1).

assessment, he reported a 10-day history of right eye pain. Clinical examination revealed right-sided exophthalmos and ptosis of the upper eyelid.

Whole-body FDG PET/CT imaging was performed using a 64-slice Biograph True64 PET/CT hybrid system (Siemens Medical Solutions USA Inc., Malvern, PA, USA), 90 minutes after intravenous administration of 269 MBq of ¹⁸F-FDG. The images revealed a focal area of increased FDG uptake in the right orbit. Given the non-specific nature of FDG accumulation, the findings raised suspicion for several possible etiologies, including relapse of FL, a primary orbital malignancy, or an inflammatory process (**Figure 1**). Additionally, symmetrical retrobulbar regions of increased glucose metabolism were observed bilaterally. Although these findings were most consistent with physiological uptake, pathological causes could not be entirely excluded (**Figure 1**). An ophthalmological consultation was therefore recommended.

Subsequent ophthalmological evaluation prompted additional radiological imaging, which demonstrated a tumorous mass within the right orbit. The report indicated no pathological changes involving the right eyeball itself. **Figure 2** outlines the chronological diagnostic steps leading to the final diagnosis.

Surgical exploration of the right orbit was performed via a superotemporal skin incision below the superior orbital rim. The lesion was completely excised, and the specimen was submitted for histopathological analysis. However, available radiological and surgical documentation did not allow precise determination of the lesion's exact anatomical localization within the orbital compartment.

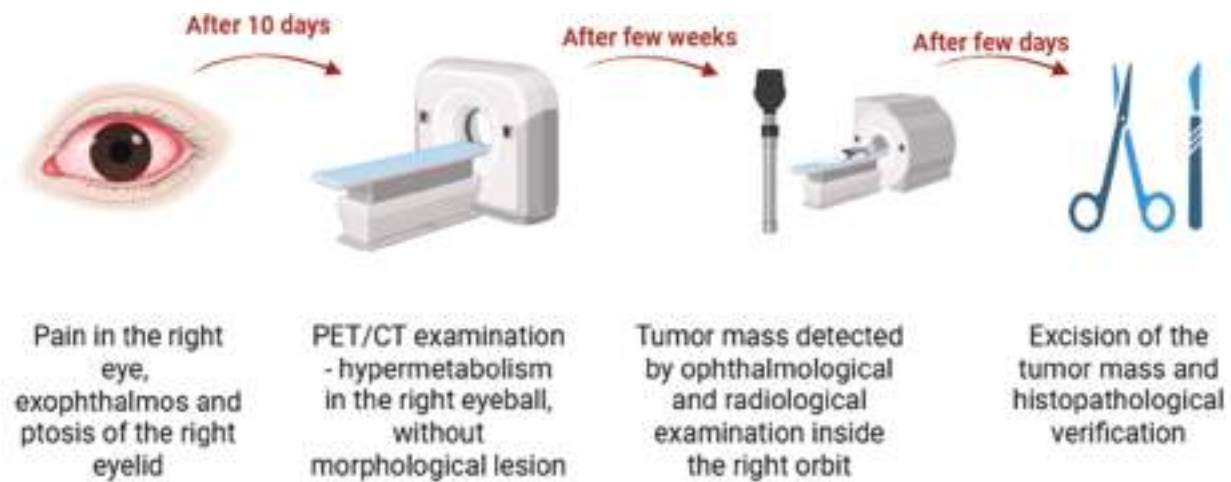


Figure 2. Timeline of diagnostics in right orbital follicular lymphoma relapse

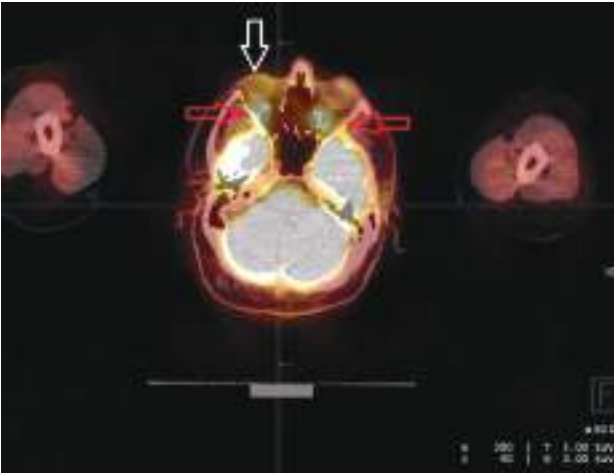


Figure 3. On post-radiotherapy Fluorodeoxyglucose positron emission tomography/Computed Tomography, the previously noted focal FDG uptake is no longer visible (white arrow), while symmetric retrobulbar FDG uptake, representing physiological uptake, is still observed (red arrows) (SUVmax up to 7.7)

Histopathological examination revealed a lymphoid neoplasm with a predominantly follicular growth pattern and infiltration of adjacent tissues. The tumor consisted mainly of centrocyte-like cells with admixed centroblasts. Immunohistochemical analysis demonstrated positivity for CD20, PAX5,

CD79a, CD10, BCL2, and BCL6, and negativity for CD3, CD5, Cyclin D1, and MUM1. The Ki-67 proliferation index was approximately 20%, with focal increase up to 40%. These findings were consistent with grade 3A follicular lymphoma.

The patient subsequently underwent local radiotherapy, receiving a total of 25.5 Gy in 17 fractions. Four months after completion of radiotherapy, a follow-up FDG PET/CT examination was performed.

The follow-up imaging demonstrated complete metabolic regression of the disease, corresponding to a Deauville score of 2. This conclusion was based on the complete resolution of previously observed pathological FDG uptake in the right orbital region, indicating a complete local therapeutic response (**Figure 3**). The symmetrical retrobulbar hypermetabolic areas remained unchanged compared to the prior examination, confirming their physiological nature (Figure 3). Key FDG PET/CT findings before and after radiotherapy are summarized in **Table 1**, illustrating complete metabolic response in the right orbit with no evidence of new pathological uptake elsewhere.

Discussion

The present case illustrates an exceptionally rare relapse of follicular lymphoma (FL) involving the

Table 1. Comparative presentation of metabolic activity on initial and follow-up Fluorodeoxyglucose positron emission tomography/Computed Tomography

Findings	Before RT FDG PET/CT	After RT FDG PET/CT
FDG uptake in the right eye	Pathological focal uptake	No pathological uptake
FDG uptake in retrobulbar region	Symmetric hypermetabolism	Symmetric hypermetabolism
FDG pathological uptake in other parts of the body	None	None
Clinical correlation	Relapse of follicular lymphoma confirmed by histopathology	Complete metabolic response

RT – radiotherapy; FDG – 18F-Fluorodeoxyglucose; PET/CT – Positron Emission Tomography/Computed Tomography

right orbit following a prolonged disease-free interval and achievement of complete remission. Its clinical relevance lies in emphasizing the necessity of long-term surveillance, as FL may relapse even after several years of stable remission [8]. Importantly, relapse can occur despite an initially favorable therapeutic response and may involve anatomical sites not previously affected by the disease.

FDG PET/CT played a pivotal role in this case by detecting focally increased FDG uptake in the right ocular region, which prompted further diagnostic investigation. On the initial examination, the increased uptake appeared to be localized within the right eyeball and was interpreted as focal intraocular hypermetabolism. However, subsequent radiological assessment identified an intraorbital mass that was not clearly delineated on the FDG PET/CT images.

This apparent discrepancy can be explained by the spillover effect of metabolic activity from the adjacent intraorbital tumor, combined with reactive metabolic changes in displaced ocular structures and the inherent spatial resolution limitations of PET imaging. Consequently, FDG uptake originating from the intraorbital lesion may have been projected onto the globe, creating the false impression of intraocular involvement on PET/CT images [9,10]. Additionally, the retrobulbar mass detected by other imaging modalities may not have been sufficiently large at the time of the FDG PET/CT examination to be visualized on the low-dose, non-contrast CT component of the hybrid scan. This explanation is supported by the short duration of symptoms – only 10 days prior to imaging – suggesting that the orbital lesion was in an early stage of development.

It is well recognized that FDG PET/CT may demonstrate physiological FDG uptake in the ocular region, particularly within the extraocular muscles. Nevertheless, asymmetrical focal FDG accumulation in one eye relative to the contralateral side should raise suspicion for an underlying pathological process. FDG PET/CT is highly sensitive for the detection of extranodal lymphoma and frequently identifies disease sites that may be overlooked by other diag-

nostic modalities [11]. In the present case, the symmetrical retrobulbar FDG uptake observed bilaterally was deemed physiological, and it remained unchanged on follow-up imaging, whereas the pathological hypermetabolic focus in the right orbital region completely resolved after radiotherapy.

The differential diagnosis in this case was broad and included FL recurrence, primary intraocular malignancies such as uveal melanoma, idiopathic inflammatory orbital disease, and infectious processes [12]. Consequently, comprehensive ophthalmological evaluation and surgical excision of the lesion were required, enabling definitive histopathological confirmation of FL relapse. Although FDG PET/CT is an invaluable tool in the assessment of lymphoma, histopathological analysis remains the diagnostic gold standard, as imaging alone cannot reliably distinguish lymphoma from other intraocular pathologies.

Despite the inability of FDG PET/CT to initially visualize the orbital mass directly – likely due to spatial resolution constraints and early lesion size – the identification of abnormal hypermetabolism in the right ocular region during routine follow-up was crucial. This finding led to a timely referral for further diagnostic procedures, allowing prompt visualization, surgical excision, and initiation of appropriate therapy. Subsequent FDG PET/CT demonstrated complete metabolic response, underscoring the additional value of this modality in monitoring therapeutic efficacy.

Conclusion

The case highlights several important clinical points: (1) Follicular lymphoma may relapse after a prolonged period of remission and may present in exceptionally rare extranodal locations; (2) Fluorodeoxyglucose positron emission tomography plays a crucial role in the detection of atypical extranodal manifestations of lymphoma; and (3) Accurate diagnosis and optimal treatment selection require integration of Fluorodeoxyglucose positron emission tomography findings with ophthalmological assessment and histopathological confirmation.

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