



Metabolically Silent Diffuse Hepatic Involvement in Multiple Myeloma: An ¹⁸F-FDG-PET/CT Pitfall

Multipl Miyelomda Metabolik Olarak Sessiz Diffüz Hepatik Tutulum: ¹⁸F-FDG- PET/ BT'de Bir Tanısal Tuzak

Seçkin Bilgiç¹, Merve Okuyan², Efraim İbrahim¹

¹Bursa Uludağ University Faculty of Medicine, Department of Nuclear Medicine, Bursa, Türkiye

²Recep Tayyip Erdoğan University Training and Research Hospital, Clinic of Nuclear Medicine, Rize, Türkiye

Abstract

Diffuse hepatic involvement in multiple myeloma is rare and may present a diagnostic challenge. ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography (¹⁸F-FDG PET/CT). We present the case of a 59-year-old man with a 3-year history of multiple myeloma who developed progressive hepatomegaly and perihepatic ascites. ¹⁸F-FDG PET/CT demonstrated marked diffuse liver enlargement without any focal or diffuse hepatic ¹⁸F-FDG uptake, while mild diffuse skeletal uptake suggested a globally ¹⁸F-FDG-low myeloma phenotype. Given the discordance between severe morphological findings and the absence of hepatic metabolic activity, a liver biopsy was performed, which revealed diffuse sinusoidal infiltration by CD138-positive, lambda-restricted plasma cells and excluded hepatic amyloidosis. Following systemic therapy, hepatomegaly and ascites regressed, while hepatic ¹⁸F-FDG uptake remained absent. Written informed consent for publication was obtained from the patient. This case highlights an important limitation of ¹⁸F-FDG PET/CT in detecting diffuse hepatic myeloma and emphasizes the need for multimodal diagnostic integration.

Keywords: ¹⁸F-FDG PET/CT, hepatic myeloma, diagnostic pitfall, multiple myeloma, hepatomegaly, liver biopsy

Öz

Multipl miyelomda diffüz hepatic tutulum nadirdir ve ¹⁸F-florodeoksiglukoz pozitron emisyon tomografisi/bilgisayarlı tomografi (¹⁸F-FDG PET/BT) tanısal güçlük oluşturabilir. Bu yazıda, üç yıldır multipl miyelom tanısı bulunan ve progresif hepatomegali ile perihepatik asit gelişen 59 yaşında bir erkek hasta sunulmaktadır. ¹⁸F-FDG PET/BT'de karaciğerde belirgin diffüz büyüme izlenmesine karşın, fokal ya da diffüz hepatic ¹⁸F-FDG tutulumu saptanmamış; iskelette izlenen hafif diffüz ¹⁸F-FDG tutulumu ise global ¹⁸F-FDG düşük bir miyelom fenotipini düşündürmüştür. Belirgin morfolojik bulgular ile hepatic metabolik aktivitenin yokluğu arasındaki uyumsuzluk nedeniyle karaciğer biyopsisi yapılmış ve CD138 pozitif, lambda ile sınırlı plazma hücrelerinin diffüz sinüzoidal infiltrasyonu saptanarak hepatic amiloidoz dışlanmıştır. Sistemik tedavi sonrası hepatomegali ve asitte gerileme izlenirken, hepatic ¹⁸F-FDG tutulumu olmaması devam etmiştir. Yayın için hastadan yazılı bilgilendirilmiş onam alınmıştır. Bu olgu, diffüz hepatic miyelom tutulumunun saptanmasında ¹⁸F-FDG PET/BT'nin önemli bir sınırlılığını ortaya koymakta ve tanıda multimodal yaklaşımın gerekliliğini vurgulamaktadır.

Anahtar kelimeler: ¹⁸F-FDG PET/BT, karaciğer miyelomu, tanı hatası, multipl miyelom, hepatomegali, karaciğer biyopsisi

Address for Correspondence: Seçkin Bilgiç, Bursa Uludağ University Faculty of Medicine, Department of Nuclear Medicine, Bursa, Türkiye

E-mail: seckinbilgic@uludag.edu.tr **ORCID ID:** orcid.org/0000-0002-3429-7549

Received: 11.12.2025 **Accepted:** 10.02.2026 **Epub:** 06.03.2026

Cite this article as: Bilgiç S, Okuyan M, İbrahim E. Metabolically silent diffuse hepatic involvement in multiple myeloma: an ¹⁸F-FDG-PET/CT pitfall. Mol Imaging Radionucl Ther. [Epub Ahead of Print]



Copyright© 2026 The Author(s). Published by Galenos Publishing House on behalf of the Turkish Society of Nuclear Medicine. This is an open access article under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 (CC BY-NC-ND) International License.

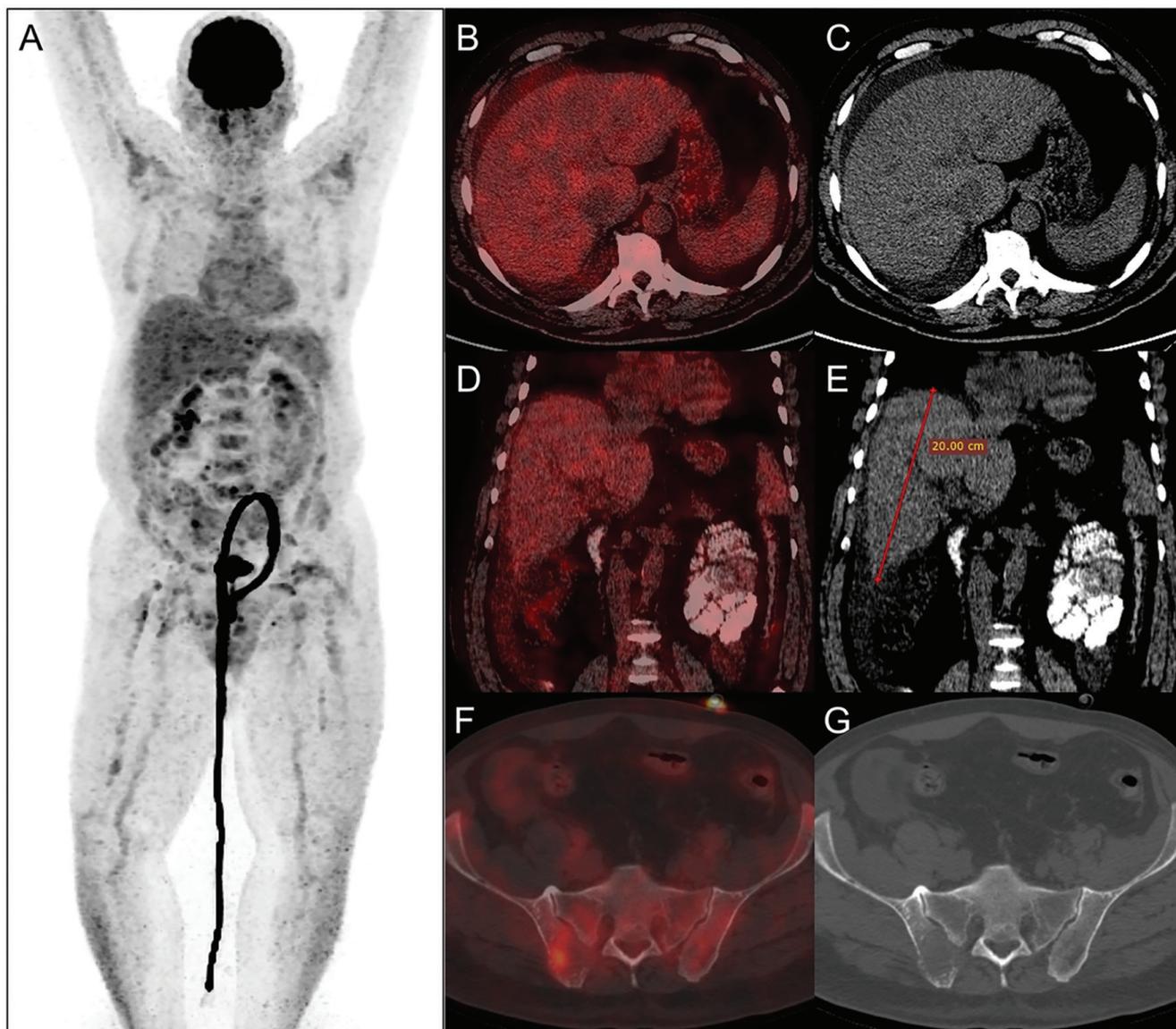


Figure 1. ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography (¹⁸F-FDG PET/CT) findings in a 59-year-old male with a 3-year history of multiple myeloma who developed progressive hepatomegaly and perihepatic ascites 1A. Maximum-intensity projection image demonstrates marked hepatomegaly with no abnormal hepatic ¹⁸F-FDG uptake 1B,C. Axial fused ¹⁸F-FDG PET/CT and CT images show diffuse hepatic enlargement and mild parenchymal heterogeneity without abnormal metabolic activity 1D-E. Coronal fused ¹⁸F-FDG PET/CT and CT images illustrate hepatomegaly with a craniocaudal measurement of approximately 20 cm 1F-G. Axial fused ¹⁸F-FDG PET/CT and CT images at the pelvic level reveal mild-low ¹⁸F-FDG-avid lytic lesions in the posterior iliac bones. Given the absence of focal hypermetabolic lesions and the low-grade, diffuse pattern of skeletal uptake, these findings are compatible with a globally ¹⁸F-FDG -low myeloma phenotype rather than highly active focal disease (1,2).

According to the IMWG-endorsed Italian Myeloma Criteria for PET Use (IMPETUs), the imaging findings were consistent with a low-¹⁸F-FDG-avid myeloma phenotype. Bone marrow uptake demonstrated a Deauville score of 3 (BM3) with a mixed diffuse-focal pattern. Six lytic lesions were identified (L3 group), with the highest ¹⁸F-FDG uptake at the iliac bone biopsy site [maximum standardized uptake value (SUV_{max}): 4.8], comparable to hepatic reference activity (SUV_{max}: 4.1). No paramedullary or extramedullary metabolically active disease was detected. Overall, the IMPETUs profile was classified as BM3 Sp F2 L3. Bone marrow biopsy demonstrated marked plasma-cell infiltration (approximately 85% of marrow cellularity) with CD138 and MUM1 positivity and lambda light-chain restriction (kappa/lambda ratio 1/80), consistent with relapsed plasma cell myeloma.

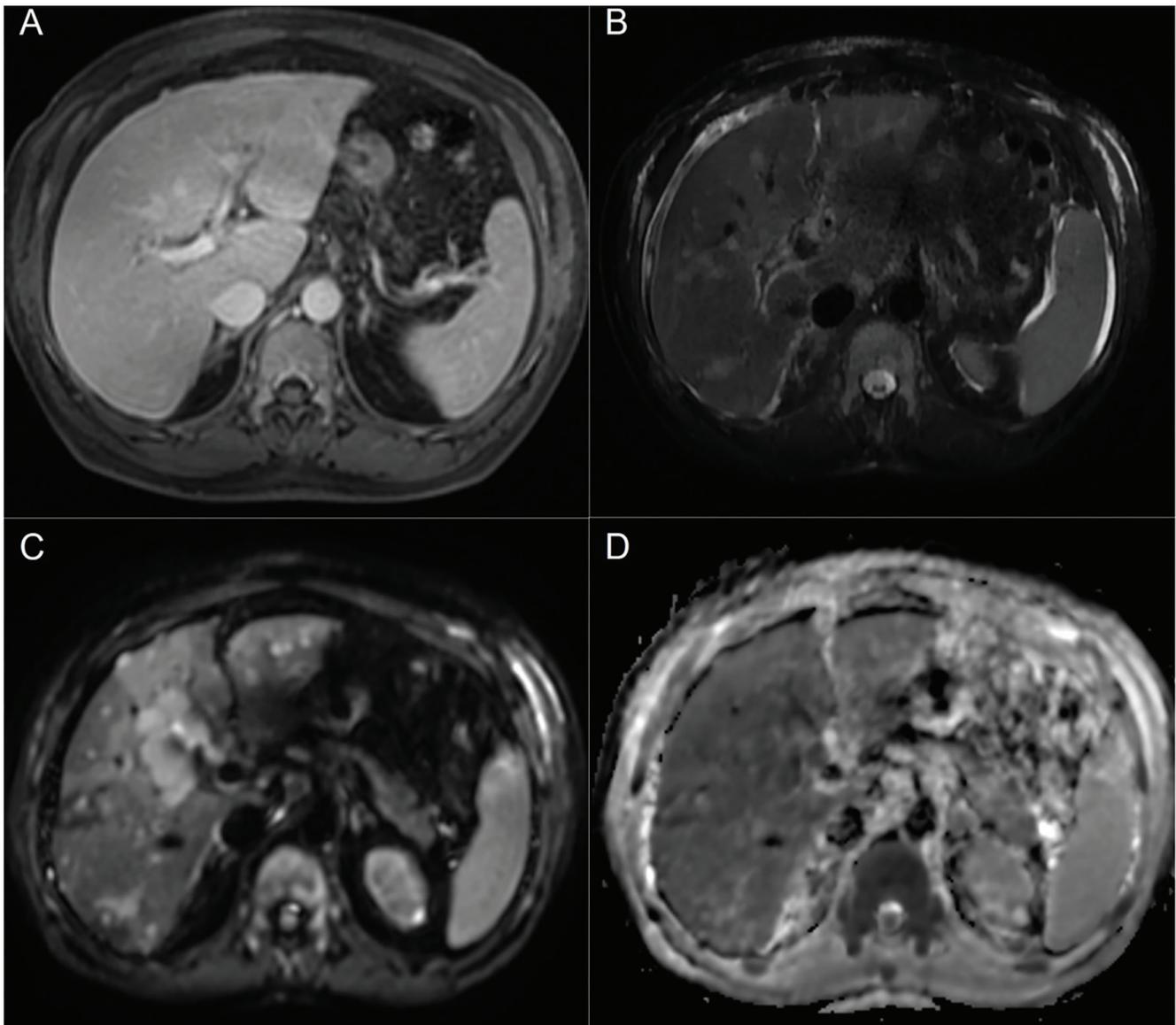


Figure 2. Liver magnetic resonance imaging demonstrating diffuse hepatic infiltration in multiple myeloma 2A. Axial contrast-enhanced T1-weighted image shows heterogeneous parenchymal enhancement without discrete focal lesion 2B. Axial T2-weighted image demonstrates hepatomegaly with heterogeneous, mildly increased parenchymal signal intensity without discrete focal lesions 2C. Diffusion-weighted image ($b=800$) shows heterogeneous parenchymal hyperintensity without discrete focal lesions 2D. Apparent diffusion coefficient map shows diffusely reduced signal intensity, supporting restricted diffusion in keeping with diffuse plasma-cell infiltration. As previously reported in the literature, magnetic resonance images findings of diffuse hepatic myeloma may be subtle and non-specific, often manifesting as heterogeneous parenchymal signal alterations without discrete mass formation (3,4).

Hepatic involvement in multiple myeloma is uncommon, and tumor-forming hepatic lesions are particularly rare. Reported histopathological patterns include extramedullary plasmacytoma, light-chain deposition disease, amyloidosis, and diffuse infiltrative forms such as sinusoidal plasma-cell infiltration, which may present radiologically as hepatomegaly with ascites in the absence of discrete focal lesions (3).

The striking discrepancy between severe hepatomegaly with ascites and complete absence of hepatic ^{18}F -fluorodeoxyglucose uptake prompted further diagnostic evaluation. Percutaneous liver biopsy demonstrated diffuse sinusoidal infiltration by plasma cells with strong CD138 expression and lambda light-chain restriction, confirming hepatic involvement by multiple myeloma. Congo red staining was negative, excluding hepatic amyloidosis (5,6).

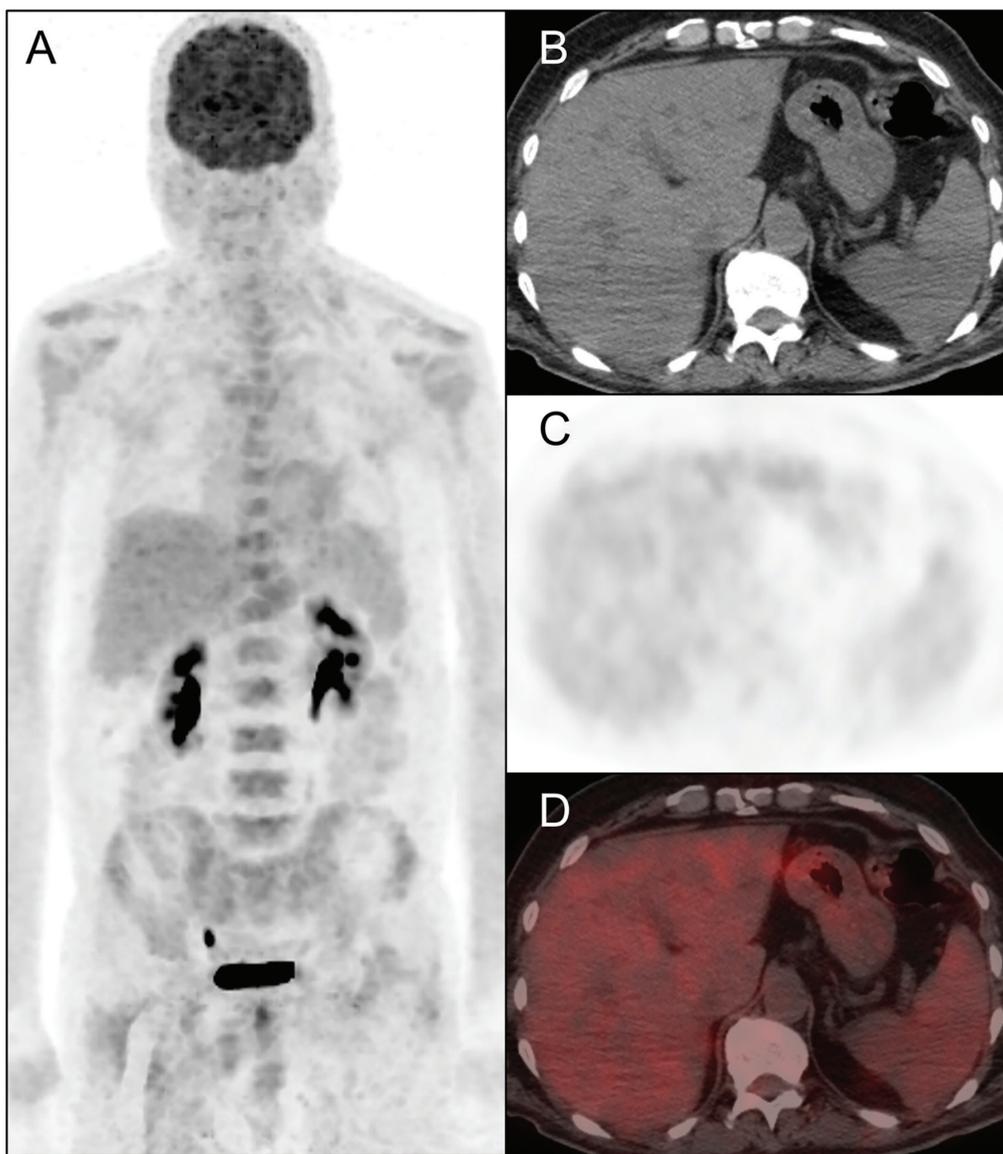


Figure 3. Follow-up ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography (¹⁸F-FDG PET/CT) findings after systemic therapy 3A. MIP image demonstrates interval decrease in diffuse skeletal ¹⁸F-FDG uptake compared with baseline, with no newly emerged focal hypermetabolic lesions. Hepatic¹⁸F-FDG activity remains homogeneous and within physiological limits 3B. Axial low-dose CT image shows regression of hepatomegaly with improved hepatic contour and parenchymal homogeneity, with the craniocaudal liver length measuring approximately 15.6 cm 3C. Axial PET image at the hepatic level demonstrates persistently low-grade, diffuse ¹⁸F-FDG uptake within the liver parenchyma, without abnormal focal activity. 3D. Axial fused ¹⁸F-FDG PET/CT image confirms the absence of focal hepatic ¹⁸F-FDG uptake and demonstrates interval improvement of hepatic findings following systemic therapy, in keeping with the observed clinical improvement.

Hepatic involvement in multiple myeloma is uncommon, with reported frequencies ranging from approximately 0.3-3%, and diffuse infiltrative patterns are far less frequently encountered than focal plasmacytomas. Histopathological manifestations include diffuse sinusoidal plasma-cell infiltration, light-chain deposition disease, amyloidosis, and less commonly tumor-forming lesions. This case illustrates a well-recognized but underappreciated limitation of ¹⁸F-FDG PET/CT in detecting diffuse hepatic involvement; low ¹⁸F-FDG avidity in such presentations has been proposed to relate to reduced hexokinase-2 expression and alternative metabolic pathways in certain plasma-cell phenotypes, as supported by prior translational and imaging studies rather than being directly demonstrated in the present case (7,8,9). In patients presenting with unexplained hepatomegaly and discordant metabolic imaging findings, histopathological confirmation remains essential. In this context, alternative PET tracers most notably CXCR4-targeted agents and, more recently, fluorocholine PET may provide complementary information in ¹⁸F-FDG -low myeloma phenotypes (10,11,12).

Ethics

Informed Consent: Written informed consent for publication was obtained from the patient.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.B., Concept: S.B., E.A.İ., Design: S.B., M.O., E.A.İ., Data Collection or Processing: S.B., E.A.İ., Analysis or Interpretation: S.B., E.A.İ., Literature Search: M.O., E.A.İ., Writing: S.B., M.O., E.A.İ.

Conflict of Interest: No conflicts of interest were declared by the authors.

Financial Disclosure: The authors declare that this study has received no financial support.

References

1. Cavo M, Terpos E, Nanni C, Moreau P, Lentzsch S, Zweegman S, Hillengass J, Engelhardt M, Usmani SZ, Vesole DH, San-Miguel J, Kumar SK, Richardson PG, Mikhael JR, da Costa FL, Dimopoulos MA, Zingaretti C, Abildgaard N, Goldschmidt H, Orłowski RZ, Chng WJ, Einsele H, Lonial S, Barlogie B, Anderson KC, Rajkumar SV, Durie BGM, Zamagni E. Role of ¹⁸F-FDG PET/CT in the diagnosis and management of multiple myeloma and other plasma cell disorders: a consensus statement by the International Myeloma Working Group. *Lancet Oncol*. 2017;18:e206-e217.
2. Tirumani SH, Sakellis C, Jacene H, Shinagare AB, Munshi NC, Ramaiya NH, Van den Abbeele AD. Role of FDG-PET/CT in extramedullary multiple myeloma: correlation of FDG-PET/CT findings with clinical outcome. *Clin Nucl Med*. 2016;41:e7-e13.
3. Tirotta D, Lena C, Torre M, Muratori P. Hematologic focal hepatic lesions in the absence of liver cirrhosis: consider lymphoma and myeloma. *Clin Res Hepatol Gastroenterol*. 2026;50:102749.
4. Tomasian A, Sandrasegaran K, Elsayes KM, Shanbhogue A, Shaaban A, Menias CO. Hematologic malignancies of the liver: spectrum of disease. *Radiographics*. 2015;35:71-86.
5. Pu Z, Zhan L, Zha Y, Li Y, Qiu S, He Y, Yang Y, Feng Z, Zhu X. Hepatic involvement as an initial manifestation of multiple myeloma: a case report with atypical imaging features. *Front Oncol*. 2025;15:1640981.
6. Singh M, Singh H, Pham P, Rizvi B, Rao R. Extramedullary multiple myeloma with hepatic involvement. *Cureus*. 2021;13:e13515.
7. Abe Y, Ikeda S, Kitadate A, Narita K, Kobayashi H, Miura D, Takeuchi M, O'uchi E, O'uchi T, Matsue K. Low hexokinase-2 expression-associated false-negative ¹⁸F-FDG PET/CT as a potential prognostic predictor in patients with multiple myeloma. *Eur J Nucl Med Mol Imaging*. 2019;46:1345-1350.
8. Rasche L, Angtuaco E, McDonald JE, Buros A, Stein C, Pawlyn C, Thanendrarajan S, Schinke C, Samant R, Yaccoby S, Walker BA, Epstein J, Zangari M, van Rhee F, Meissner T, Goldschmidt H, Hemminki K, Houlston R, Barlogie B, Davies FE, Morgan GJ, Weinhold N. Low expression of hexokinase-2 is associated with false-negative FDG-positron emission tomography in multiple myeloma. *Blood*. 2017;130:30-34.
9. Zamagni E, Patriarca F, Nanni C, Zannetti B, Englaro E, Pezzi A, Tacchetti P, Buttignol S, Perrone G, Brioli A, Pantani L, Terragna C, Carobolante F, Baccarani M, Fanin R, Fanti S, Cavo M. Prognostic relevance of ¹⁸F-FDG PET/CT in newly diagnosed multiple myeloma patients treated with up-front autologous transplantation. *Blood*. 2011;118:5989-5995.
10. Shekhawat AS, Singh B, Malhotra P, Watts A, Basher R, Kaur H, Hooda M, Radotra BD. Imaging CXCR4 receptors expression for staging multiple myeloma by using ⁶⁸Ga-pentixafor PET/CT: comparison with ¹⁸F-FDG PET/CT. *Br J Radiol*. 2022;95:20211272.
11. Kaya G, Akin S, Buyukasik Y, Bozkurt MF, Tuncel M, Kiratli PO. PET in myeloma redefined: a comparative imaging study with FDG and fluorocholine PET/CT. *Eur J Nucl Med Mol Imaging*. 2026;53:2325-2336.
12. Chavoshi M, Mirshahvalad SA, Kohan A, Ortega C, Metser U, Farag A, Kridel R, Hodgson D, Bhella S, Kukreti V, Veit-Haibach P. CXCR4-targeted PET imaging in hematologic malignancies: a systematic review and meta-analysis. *Clin Nucl Med*. 2025;50:e7-e16.