



# <sup>68</sup>Ga-PENTIXAFOR PET/CT Captures Superscan in Refractory Multiple Myeloma

## <sup>68</sup>Ga-PENTIXAFOR PET/BT Refrakter Multiple Miyelomada Süper Scan Paternini Gösterir

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### Abstract

We present a case of a 40-year-old male with refractory multiple myeloma, assessed using <sup>68</sup>Gallium-PENTIXAFOR positron emission tomography/computed tomography (<sup>68</sup>Ga-PENTIXAFOR PET/CT), revealing widespread and intense C-X-C motif chemokine receptor 4 (CXCR4) expression in multiple osteolytic lesions across axial and appendicular skeletons, including bone marrow deposits. Despite undergoing autologous hematopoietic stem cell transplantation and multiple lines of maintenance therapy, the patient experienced disease relapse and progression. The term "superscan" typically refers to diffuse skeletal uptake in conventional bone scans, primarily seen in advanced metastatic cancers or metabolic bone diseases. CXCR4, crucial for tumor growth and metastasis, binds C-X-C motif chemokine 12 (CXCL12) to promote cancer progression. PENTIXAFOR, a CXCR4-targeted PET agent, facilitates imaging of such malignancies. While superscans using PET/CT are rare, our case underscores the utility of <sup>68</sup>Ga-PENTIXAFOR PET/CT in evaluating CXCR4 expression in multiple myeloma, highlighting its potential as a diagnostic and prognostic tool in refractory disease management.

**Keywords:** PENTIXAFOR, C-X-C motif chemokine receptor 4, positron emission tomography/computed tomography, superscan, multiple myeloma

### Öz

<sup>68</sup>Galyum-PENTIXAFOR pozitron emisyon tomografisi/bilgisayarlı tomografi (<sup>68</sup>Ga-PENTIXAFOR PET/BT) kullanılarak değerlendirilen, kemik iliği tutulumları da dahil olmak üzere aksiyel ve apendiküler iskeletlerde çoklu osteolitik lezyonlarda yaygın ve yoğun C-X-C motif kemokin reseptörü 4 (CXCR4) ekspresyonu gösteren, refrakter multipl miyelomlu 40 yaşında bir erkek hastayı sunuyoruz. Otolog hematopoietik kök hücre nakli ve çoklu idame tedavisine rağmen hastalık nüksetti ve progrese oldu. "süper scan" terimi genellikle konvansiyonel kemik taramalarında yaygın iskelet tutulumunu ifade eder ve öncelikli olarak ileri metastatik kanserlerde veya metabolik kemik hastalıklarında görülür. Tümör büyümesi ve metastaz için kritik öneme sahip olan CXCR4, kanser ilerlemesini desteklemek için C-X-C motif kemokin 12'ye (CXCL12) bağlanır. CXCR4 hedefli bir PET ajanı olan PENTIXAFOR, bu tür malignitelerin görüntülenmesini kolaylaştırır. PET/BT kullanan süper scanler nadir olsa da, olgumuz <sup>68</sup>Ga-PENTIXAFOR PET/BT'nin multipl miyelomda CXCR4 ekspresyonunu değerlendirmedeki faydasını vurgulayarak, dirençli hastalık yönetiminde tanı ve prognoz aracı olarak potansiyelini vurgulamaktadır.

**Anahtar kelimeler:** PENTIXAFOR, C-X-C motif kemokin reseptörü 4, pozitron emisyon tomografisi/bilgisayarlı tomografi, süper scan, multiple miyelom

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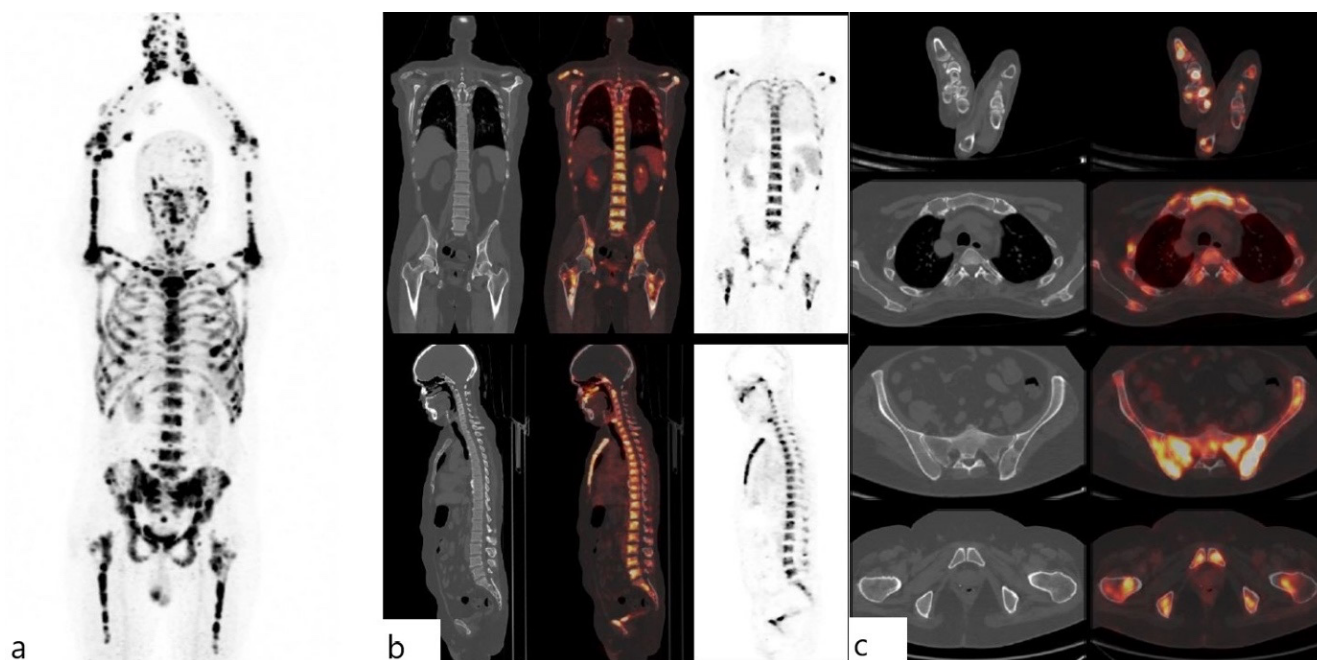
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**Figure 1.** <sup>68</sup>Gallium-PENTIXAFOR positron emission tomography/computed tomography (<sup>68</sup>Ga-PENTIXAFOR PET/CT)-maximum intensity projection image (a), coronal and sagittal (b) and axial sections (c) showing diffuse intensely increased C-X-C motif chemokine receptor 4 (CXCR4) expression in multiple osteolytic lesions throughout the visualised axial (including skull) and appendicular skeleton (including small bones of hands and feet) and bone marrow deposits in a 40-year-old male, known case of multiple myeloma, with renal impairment. He underwent autologous hematopoietic stem cell transplantation in 2021. Afterwards, he has been on multiple lines of maintenance therapy. He has had relapses and disease progression despite continuing therapy. The term “Superscan” (also “beautiful bone scan”) is generally used for <sup>99m</sup>Technetium-methylenediphosphonate bone scan when there is diffuse increased osseous activity noted in the bones, with reduced or faint visualisation of the bladder and kidneys. It is usually seen in diffuse metastatic carcinoma of the prostate or in the setting of metabolic bone disease (e.g. hyperparathyroidism, osteomalacia, Paget’s disease, etc.). CXCR4 is a chemokine receptor, which is widely expressed in hematopoietic cells (1). The abnormal expression of which is associated with tumor growth, dissemination, metastasis, and disease progression (2). CXCR4 binds specifically to C-X-C motif chemokine 12 (CXCL12) and this CXCL12/CXCR4 axis is critical for tumour growth. PENTIXAFOR is a novel PET agent that binds with high affinity to CXCR4. Hence, it has been useful in imaging multiple myeloma, myeloproliferative neoplasms, and aldosterone adenomas (3,4,5). It has been proven to show a greater extent of disease involvement than <sup>18</sup>F-fluorodeoxyglucose (<sup>18</sup>F-FDG) (3). A recent study by Chen et al. (6), demonstrated similar findings, demonstrating the ability of <sup>68</sup>Ga-PENTIXAFOR to more effectively predict disease progression (progression-free survival) in newly diagnosed multiple myeloma patients than <sup>18</sup>F-FDG. These developments have paved the way for possible use of alternative therapeutic strategies such as <sup>177</sup>[Lu]Pentixather for managing relapsed and refractory multiple myeloma in the future. Few superscans have been reported using PET/CT, but we found only two cases for multiple myeloma - one with fluorodeoxyglucose and one with PENTIXAFOR (7,8).

## Ethics

**Informed Consent:** Patient consent was obtained for this study.

## Footnotes

## Authorship Contributions

Concept: V.R.L., Design: S.K., H.G., Data Collection or Processing: S.K., N.S., Analysis or Interpretation: N.S., Literature Search: S.K., H.G., Writing: S.K.

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

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