

# Amyloid Mimicking Myeloma: A Diagnostic Trap

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## Abstract

### Keywords

- ▶ <sup>18</sup>F-FDG PET/CT
- ▶ multiple myeloma
- ▶ amyloid
- ▶ plasmacytoma
- ▶ paramedullary

We present the case of a 54-year-old male with relapsing multiple myeloma (MM) complicated by biopsy-proven amyloid deposition, monitored over a span of 13 years with serial <sup>18</sup>F-FDG PET/CT imaging. The patient experienced multiple treatment interruptions and disease relapses, with evolving imaging features ranging from widespread skeletal involvement to soft tissue plasmacytoma formation and associated amyloid deposition. This case highlights the evolving role of <sup>18</sup>F-FDG PET/CT in detecting disease progression and treatment response in plasma cell dyscrasias with coexisting amyloidosis.

## Introduction

Multiple myeloma (MM) is a clonal plasma cell malignancy frequently associated with lytic bone lesions and, less commonly, with amyloid deposition. Amyloidosis may complicate the disease course and alter clinical behavior. While <sup>18</sup>F-FDG PET/CT is widely used to evaluate disease burden and treatment response in MM, its utility in detecting amyloid-related complications remains under exploration. We report a case of relapsing MM with histologically proven amyloid deposition, demonstrating the dynamic role of PET/CT in monitoring disease progression.

## Case Report

A 54-year-old male first presented in 2012 with backache. Initial laboratory workup revealed markedly elevated serum kappa free light chains (1,720 mg/L), lambda light chains (32 mg/L), and a kappa/lambda ratio suggestive of light-chain MM. Beta-2 microglobulin was 6.98 mg/L. Initial <sup>18</sup>F-FDG PET/CT (▶ **Fig. 1**) was done to evaluate disease burden; it revealed FDG-avid lytic expansile skeletal lesions (arrow) involving nearly the entire skeleton (SUV<sub>max</sub> up to 14.6), with no extramedullary or paramedullary disease. The utility of serial <sup>18</sup>F-FDG PET/CT in identifying disease transformation and in detecting skeletal involvement in plasma cell dyscrasias has been well established.<sup>1</sup>

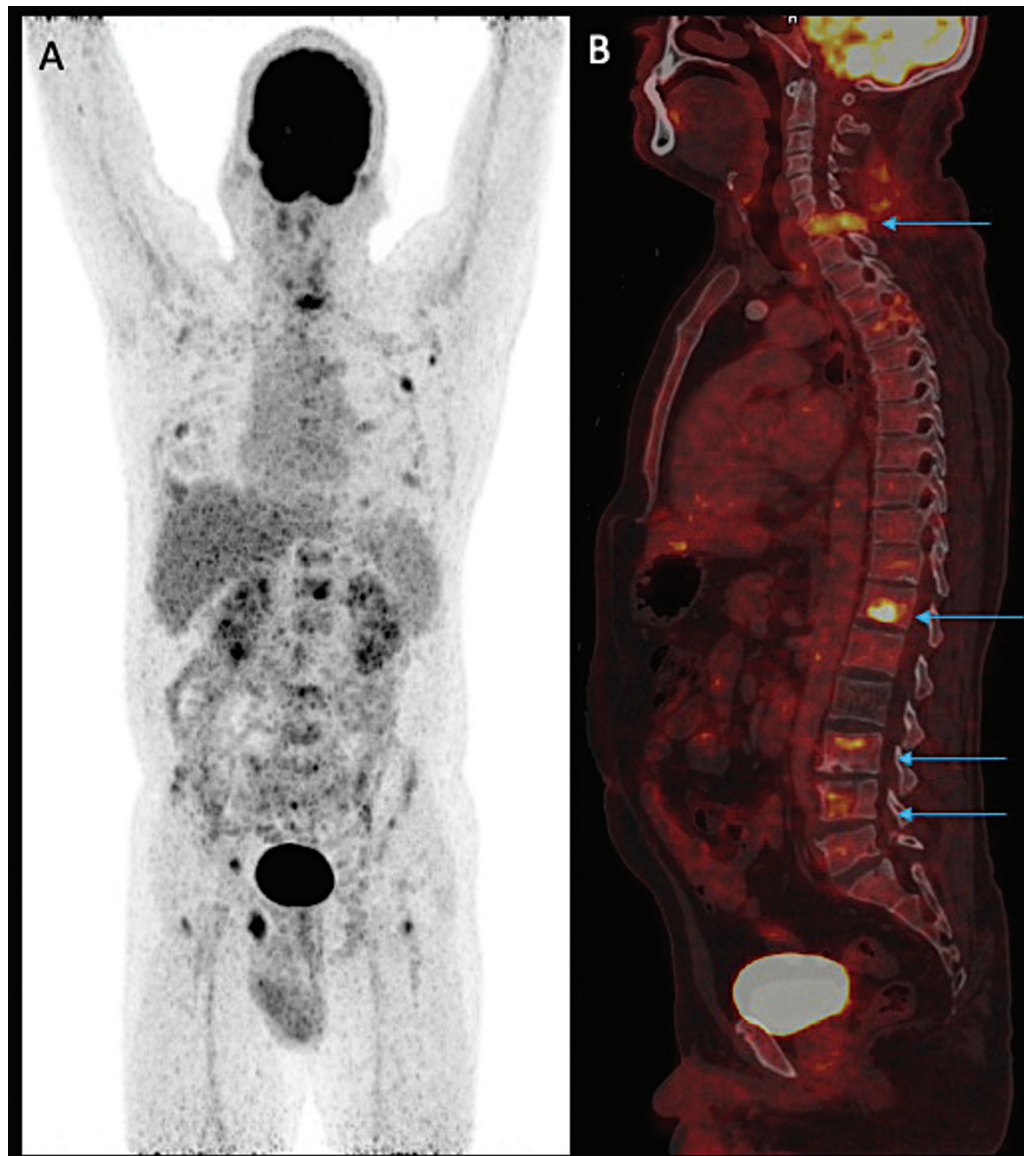
The patient received thalidomide but discontinued therapy after four cycles. Following a 3-year treatment hiatus, he received three cycles of bortezomib, again defaulting for 4 years. He re-presented with lower abdominal pain. A CT scan revealed multiple lytic lesions and bilateral sacral masses. He was initiated on a bortezomib, cyclophosphamide, and dexamethasone (VCD) regimen but defaulted again for 2 years and returned with worsening abdominal discomfort. <sup>18</sup>F-FDG PET/CT (▶ **Fig. 2**) showed uptake (SUV<sub>max</sub> 7.9) in multiple lytic expansile skeletal lesions along with two large FDG-avid (SUV<sub>max</sub> 9.9) soft tissue masses (arrow), appearing to arise from L5 and the sacrum and abutting the anterior abdominal wall. The lesions were initially suspected to represent paramedullary disease. Soft tissue lesions in MM, particularly in the pelvis or abdomen, may mimic extramedullary disease but may also represent amyloid deposits, necessitating histopathological correlation.<sup>2,3</sup>

However, a biopsy (▶ **Fig. 3**) from the pelvic mass revealed sheets of atypical plasma cells with perivascular and interstitial extracellular pale material, confirmed as amyloid on hematoxylin–eosin staining. On immunohistochemistry, CD138 highlights sheets and clusters of plasma cells and exhibits kappa clonality. These plasma cells are negative for CD20 and lambda light chains. Amyloid itself is not typically FDG-avid;<sup>4</sup> however, when admixed with plasma cells, it may show increased uptake. Up to 12 to 15% of patients with

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**Fig. 1** Initial  $^{18}\text{F}$ -FDG PET/CT. (A) Maximum intensity projection image of the whole body. (B) Sagittal view of the vertebrae showing multiple FDG avid ( $\text{SUV}_{\text{max}}$  14.6) lytic skeletal lesions (blue arrow). CT, computed tomography; PET, positron emission tomography; SUV, standardized uptake value.

MM develop secondary AL amyloidosis,<sup>5</sup> and both MM and AL amyloidosis are plasma cell dyscrasias.<sup>6</sup>

Posttreatment  $^{18}\text{F}$ -FDG PET/CT (**Fig. 4**) reveals interval reduction in metabolic activity ( $\text{SUV}_{\text{max}}$  4.7) of the previously noted abdominopelvic masses and skeletal lesions following 11 cycles of carfilzomib, suggesting partial metabolic response. Systemic AL amyloidosis occurs more frequently than previously recognized, especially in patients with underlying plasma cell dyscrasias.<sup>7</sup> Accurate posttreatment PET/CT assessment is crucial for longitudinal monitoring.<sup>8</sup>

However, follow-up  $^{18}\text{F}$ -FDG PET/CT (**Fig. 5**) after 1 year demonstrated disease progression with increased uptake ( $\text{SUV}_{\text{max}}$  11.6) in the abdominopelvic masses and mild increased uptake in the skeletal lesions, consistent with evolving disease activity.

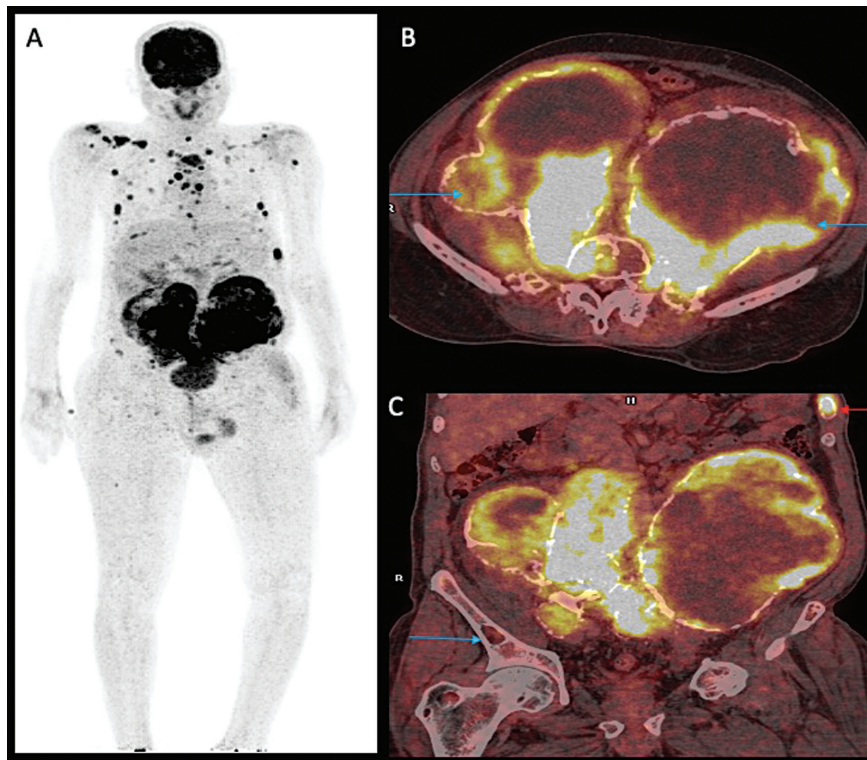
The patient is currently on oral pomalidomide (Day 1–21) and is clinically stable.

While extramedullary myeloma is associated with aggressive disease, distinguishing it from amyloid is essential, as treatment and prognosis differ significantly.<sup>9</sup> The 2022 update on MM management recommends incorporating imaging, especially PET/CT, to differentiate these disease entities early in the course.<sup>8</sup>

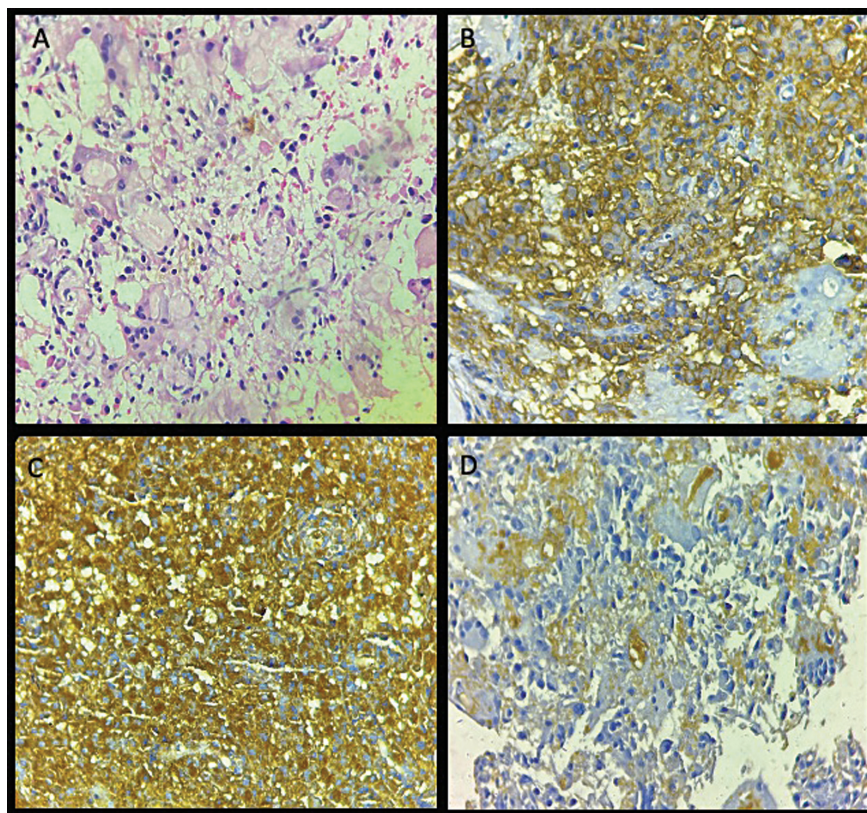
## Discussion

MM with concurrent amyloidosis (most commonly AL type) is a known, although underdiagnosed entity. In this case, relapsing myeloma with poor treatment adherence led to the formation of amyloid deposits.

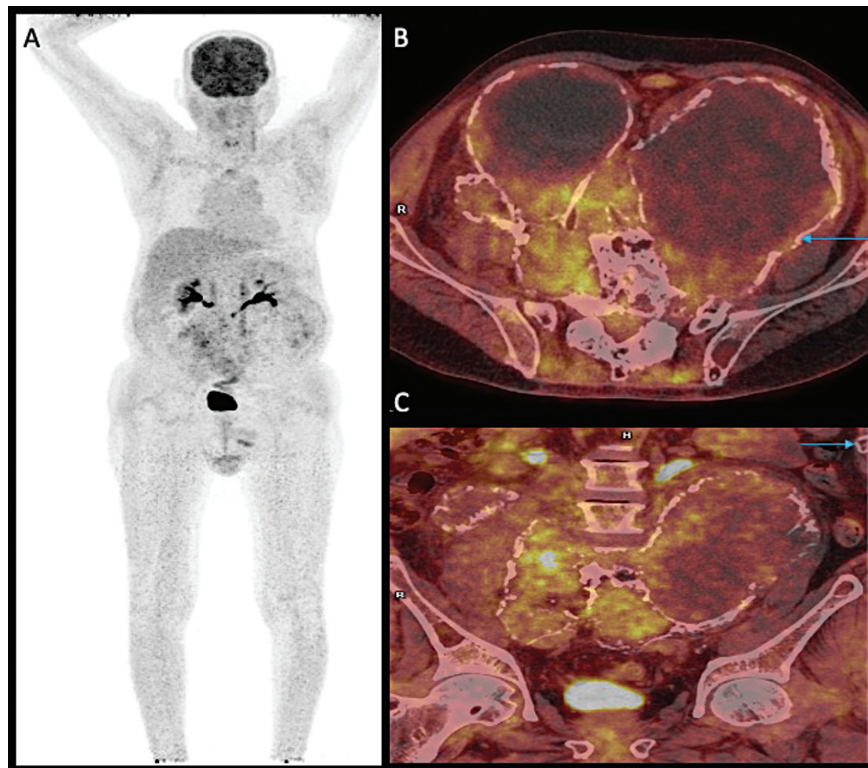
The evolving imaging pattern from diffuse skeletal involvement to bulky soft tissue masses underscores the utility of serial  $^{18}\text{F}$ -FDG PET/CT in identifying disease transformation.<sup>10</sup> Notably, amyloid itself is not typically FDG-avid;



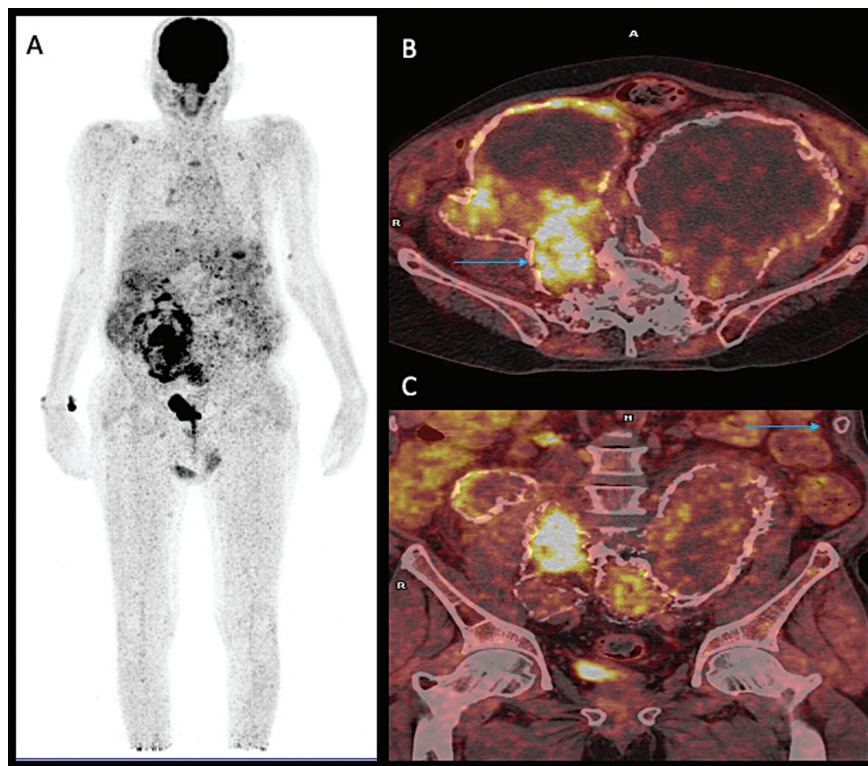
**Fig. 2**  $^{18}\text{F}$ -FDG PET/CT. (A) Maximum intensity projection image of the whole body. (B) Transverse axial section showing large FDG-avid ( $\text{SUV}_{\text{max}} -9.9$ ) abdominal/pelvic masses with necrosis and calcification (blue arrow). (C) Coronal section showing FDG avid (red arrow) and nonavid lytic skeletal lesions (blue arrow). CT, computed tomography; PET, positron emission tomography; SUV, standardized uptake value.



**Fig. 3** On microscopic examination (A) H&E-stained section shows multiple cores with sheets and aggregates of atypical plasma cells. Numerous multinucleated giant cells and abundant extracellular pale material (amyloid). On immunohistochemistry, (B) CD138 highlights sheets and clusters of plasma cells. (C) These plasma cells exhibit kappa clonality. (D) These plasma cells are negative for CD20 and Lambda light chains.



**Fig. 4**  $^{18}\text{F}$ -FDG PET/CT. (A) Maximum intensity projection image of the whole body. (B) Transverse axial section showing reduction in FDG avidity ( $\text{SUV}_{\text{max}}$  4.7) post-carfilzomib treatment (blue arrow). (C) Non-FDG avid lytic skeletal lesions (blue arrow). CT, computed tomography; PET, positron emission tomography; SUV, standardized uptake value.



**Fig. 5**  $^{18}\text{F}$ -FDG PET/CT. (A) Maximum intensity projection image of the whole body. (B) Transverse axial section showing progression of mass lesion (blue arrow) with increased FDG avidity ( $\text{SUV}_{\text{max}}$  11.6). (C) Non-FDG avid lytic skeletal lesions (blue arrow). CT, computed tomography; PET, positron emission tomography; SUV, standardized uptake value.

hence, PET/CT can help distinguish between metabolically active tumor tissue and inert amyloid matrix, aiding in biopsy guidance and response assessment.

This case illustrates the important role of  $^{18}\text{F}$ -FDG PET/CT in the longitudinal evaluation of relapsing MM with histologically confirmed amyloid deposition. It reinforces the value of PET/CT not only in detecting disease burden and extramedullary transformation but also in guiding treatment decisions in complex myeloma presentations.

#### Conflict of Interest

None declared.

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