

Case Report

Serum B-Cell Maturation Antigen Reflects Disease Status in a Patient Who Developed Nonsecretory Multiple Myeloma: A Case Report

Ryan Danis^a Bernard Regidor^a Sean Bujarski^{a, b} Scott Jew^{a, b}
Marissa-Skye Goldwater^{b, c} Regina Swift^a Benjamin Mark Eades^a
Marsiye Emamy-Sadr^a Ashley Del Dosso^d James Berenson^{a, b, c, d}

^aBerenson Cancer Center, West Hollywood, CA, USA; ^bInstitute for Myeloma and Bone Cancer Research, West Hollywood, CA, USA; ^cONCotracker, West Hollywood, CA, USA;

^dONCotherapeutics, West Hollywood, CA, USA

Keywords

Multiple myeloma · Nonsecretory disease · Serum B-cell maturation antigen · Case report

Abstract

Introduction: Multiple myeloma (MM) is an incurable bone marrow (BM)-based cancer involving clonal plasma cells. Most patients show elevated levels of serum monoclonal protein (sMP) and kappa or lambda serum free light chains (sFLCs) at diagnosis. However, around 1–2% of patients, termed nonsecretory, do not produce these biomarkers. As the disease progresses, more patients may become unevaluable using conventional markers, requiring invasive and expensive procedures like BM biopsies and positron emission tomography-computed tomography (PET-CT) scans for assessment and highlighting the need for alternative methods to monitor disease progression. **Case Presentation:** We present a case report of an MM patient who developed nonsecretory disease during his second line of treatment when he complained of new rib pain; progressive disease was then confirmed on a PET-CT scan. The patient showed an increase in his serum B-cell maturation antigen (sBCMA) levels whereas his conventional myeloma markers did not detect disease activity (sMP remained undetectable and involved sFLC level was normal). After starting a new treatment regimen, his rib pain disappeared, PET-CT scan improved, and sBCMA levels decreased. Upon relapse, he developed increased rib pain with a rising sBCMA level; his conventional myeloma markers did not detect disease activity. After changing to a new regimen, his rib pain improved, and this was accompanied by a decrease in his sBCMA levels. **Conclusion:** Thus, this case exemplifies the potential for sBCMA to provide a non-invasive method for monitoring MM patients who develop nonsecretory disease.

© 2024 The Author(s).
Published by S. Karger AG, Basel

Correspondence to:
James Berenson, jberenson@berensoncancercenter.com

Introduction

Multiple myeloma (MM) is a bone marrow (BM)-based malignancy of clonal plasma cells and remains incurable. At diagnosis, most patients present with a serum monoclonal protein (sMP) and elevated levels of kappa or lambda serum free light chains (sFLCs). Approximately 1–2% of patients fail to produce these biomarkers and are referred to as nonsecretory [1]. The proportion of patients that develop nonsecretory disease and become unevaluable with conventional markers increases over the course of the disease. Evaluation of these patients necessitates the use of invasive and costly procedures including BM biopsies and positron emission tomography-computed tomography (PET-CT) scans. Serum B-cell maturation antigen (sBCMA) has a universal reference interval of <82.59 ng/mL in healthy individuals with levels becoming elevated in both secretory and nonsecretory newly diagnosed MM patients, providing a novel biomarker for monitoring their disease status [2–5]. Changes in sBCMA levels during treatment correlate with changes in the conventional biomarkers sMP and sFLC. However, despite undetectable levels of sMP and sFLC, patients with nonsecretory disease continue to have elevated sBCMA levels, which correlate with changes in their PET-CT scans and plasma cell percentage in the BM and can, therefore, be used as a novel biomarker to track their disease [2, 4, 6, 7]. This is the first report demonstrating a role for sBCMA in disease monitoring for an initially secretory MM patient who developed nonsecretory disease during their disease course. The CARE Checklist has been completed for this case report and is attached as supplementary material (for all online suppl. material, see <https://doi.org/10.1159/000539814>).

Case Report

On May 1, 2021, a 55-year-old white male with no significant medical history presented to the emergency room with bilateral chest and sternal pain. A chest CT scan and angiogram both revealed lytic rib lesions, and his laboratories 4 days later showed the following: sMP 0.8 g/dL, IgG 1,042 mg/dL, IgA 111 mg/dL, IgM 47 mg/dL, sFLC kappa 10.2 mg/L, sFLC lambda 253.0 mg/L, hemoglobin 7.7 g/dL, platelet count 289,000/ μ L, creatinine 1.12 mg/dL, and serum albumin 4.1 g/L. Serum immunofixation confirmed the sMP to be an IgG lambda monoclonal protein. A rib biopsy confirmed a plasma cell tumor with lambda light chain restriction. A chest CT was repeated on June 15, 2020, which revealed lytic lesions with soft tissue masses in his right 7th, 11th, and 12th ribs and right scapula and a large 8.4 cm lesion in his right posterior back soft tissues. He underwent a BM biopsy the following day, which showed 10% CD138-positive plasma cells with lambda light chain restriction, confirming the diagnosis of MM. No cytogenetics or FISH were performed on the specimen. He then came to clinic on June 26, 2020, and had blood drawn, which revealed an sBCMA level of 515 ng/mL.

In the following month, he initiated therapy consisting of bortezomib 1.3 mg/m² intravenously (IV), dexamethasone 40 mg IV, and pegylated liposomal doxorubicin 5 mg/m² IV all given on days 1, 4, 8, and 11 of 28-day cycles. His sFLC lambda was 334.6 mg/L at that time. After 8 cycles of this therapy, his sMP, sFLC lambda, and sBCMA levels decreased to 0.33 g/dL, 152.1 mg/L, and 207.6 ng/mL, respectively. The pegylated liposomal doxorubicin was then discontinued, and he received 1 month of maintenance therapy with bortezomib 1.3 mg/m² and dexamethasone 40 mg IV on days 1 and 15 with methylprednisolone 20 mg orally every other day not to be taken within 48 h of dexamethasone infusion. However, he experienced new-onset chest pain in March 2021. Magnetic resonance imaging showed a new lower rib lesion measuring 5 cm and expansile lesions in his right ilium and left posterior ilium. At that time, his sMP, sFLC, and sBCMA levels increased to 0.36 g/dL, 172.8 mg/L, and 515 ng/mL,

respectively. His treatment was subsequently changed to 28-day cycles of the following: daratumumab 16 mg/kg IV weekly for cycles 1 and 2, every other week for cycles 2–6, and once per cycle for cycles 7 and each cycle thereafter, along with lenalidomide 10 mg orally on days 1–21 and dexamethasone 40 mg IV administered on daratumumab days. Starting with cycle 3, 20 mg oral methylprednisolone was added every other day not to be taken within 48 h of dexamethasone infusion. In December 2021 after 8 cycles, his chest pain had markedly improved; his sMP became undetectable and lambda sFLC and sBCMA decreased to 6.8 mg/L and 317 ng/mL, respectively. A BM biopsy was performed and showed no evidence of increased plasma cells, confirming the patient's complete remission.

Two months later, he presented with worsening right rib and sternal pain, and his sBCMA levels increased to 452 ng/mL. By March of 2022, he had developed lower back and left rib pain, and his sBCMA further increased to 468 ng/mL, but his sMP remained undetectable and lambda sFLC remained low at 4.8 mg/mL. He obtained a PET-CT scan, which showed new MM involvement in his right 12th rib (SUV 9) and right L3 transverse process (SUV 4.2). His treatment was then changed to 28-day cycles of the following: elotuzumab 10 mg/kg IV weekly for cycles 1 and 2 followed by every other week for cycle 3 and each cycle thereafter, pomalidomide 3 mg orally on days 1–21. He received dexamethasone 28 mg orally before each elotuzumab infusion and an additional 8 mg IV just prior to the infusion. Starting with cycle 3, 20 mg oral methylprednisolone was added every other day not to be taken within 48 h of dexamethasone infusion. After 4 cycles of this treatment, he obtained a repeat PET-CT scan that showed decreased MM activity in his right 12th rib (SUV 1.5) and right L3 transverse process (SUV 1.4). At this time, his sBCMA levels decreased to 90 ng/mL. In November 2022, the patient stated that his pain had markedly improved, and his sBCMA levels further decreased to 49 ng/mL.

In December 2022, he complained of new rib pain. His sBCMA levels rose to 131 ng/mL and 171 ng/mL in December 2022 and January 2023, respectively. Despite rises in his sBCMA levels, his sMP remained undetectable and his lambda sFLC was normal (8.8 mg/L) in January 2023. A PET-CT scan in February 2023 revealed new activity within the left hilum with an SUV of 8.8, a hypermetabolic left posterior pleural soft tissue mass with SUV 30.2, and increased activity in the right anterior 8th rib with SUV 4.9. His sBCMA level increased to 610 ng/mL on March 9, 2023, and he subsequently began treatment with 28-day cycles of the following: isatuximab 10 mg/kg weekly during cycle 1 followed by days 1 and 15 for each cycle thereafter, carfilzomib 56 mg/m² on days 1, 8, and 15 with a reduced 20 mg/m² dose on day 1 of cycle 1, and dexamethasone 40 mg IV weekly. During his course of this therapy, the patient reported improvement in his rib pain, and sBCMA levels decreased to 248 ng/mL by April 11, 2023, and further decreased to 110 ng/mL by June 19, 2023. On December 28, 2023, after 8 cycles of this therapy, he transitioned to a maintenance schedule of this therapy at which time the frequency of both dexamethasone and carfilzomib was changed to days 1 and 15 of each cycle and 20 mg oral methylprednisolone was added every other day not to be taken within 48 h of dexamethasone infusion. When he began this maintenance therapy, his sBCMA had further decreased to 87 ng/mL. A visual representation for the timeline of key events related to disease progression, laboratory assessments, and treatment regimens is depicted in Figure 1.

Discussion

Nonsecretory MM patients have shorter median progression-free survival compared to those with measurable disease [8, 9]. MM patients with nonsecretory disease are challenging to monitor and require the use of expensive and invasive procedures such as BM biopsies and

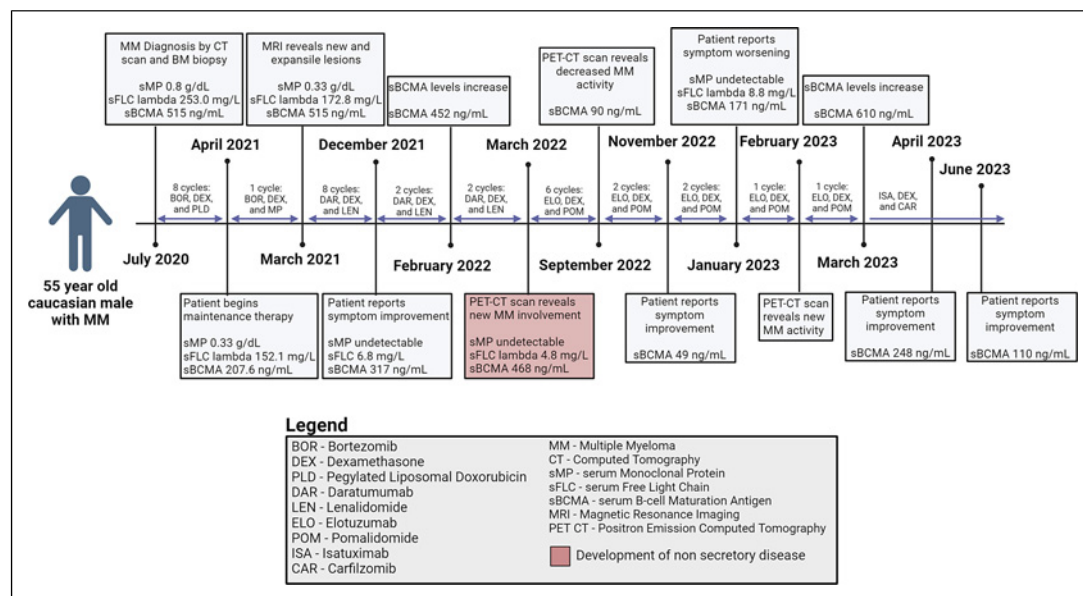


Fig. 1. Timeline of clinical events. A visual representation for the timeline of key events related to disease progression, laboratory assessments, and treatment regimens. The development of nonsecretory disease is denoted by the red coloring.

PET-CT scans; and, as a result, these monitoring procedures are performed less frequently than the conventional blood and urine biomarker-based assays. Moreover, results from BM examinations may not accurately assess changes in the clinical status of these patients given the characteristically heterogeneous involvement of MM in the BM [10]. The testing of sBCMA levels is minimally invasive with only 4 μ L of serum required for measurement using the currently available ELISA kits [3]. The development of nonsecretory disease may also delay or not allow for the discovery of progressive disease, which requires urgent therapeutic intervention. A recent retrospective analysis of 1,347 patients demonstrated that MM patients who initiate new therapy at biochemical progression have a longer overall survival from relapse compared to those who initiate new therapy at clinical relapse. Therefore, sBCMA testing could utilize increases in patients' sBCMA levels to indicate biochemical relapse in patients who develop nonsecretory disease, allowing for an earlier detection of disease progression resulting in improved clinical outcomes from being able to start a new line of therapy sooner [11]. Moreover, these patients and those with oligosecretory disease, where the monoclonal immune markers are detectable but below threshold levels (>1 g/dL for sMP and >100 mg/L for sFLC) [9], are ineligible for clinical trials because they are not considered evaluable. However, the use of sBCMA to accurately and easily assess biochemical progression may permit these patients to participate in clinical trials.

Conclusions

This report demonstrates the potential for sBCMA to identify changes in the clinical status of patients whose disease has become nonsecretory. In addition, this new serum biomarker can also be used to accurately and more frequently monitor the course of these patients' disease than presently available modalities to determine changes in their clinical status. Further studies will be necessary to evaluate the role of this biomarker more completely in this growing subpopulation of myeloma patients.

Acknowledgments

The authors thank the patient for his contribution to the study and all healthcare professional staff involved in collecting clinical specimens. Figures were created with BioRender.com.

Statement of Ethics

This research was conducted ethically, in accordance with local Institutional Review Board requirements and the Declaration of Helsinki. Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

James Berenson has equity interests in OncoTracker. All other authors have no conflicts of interest to declare.

Funding Sources

No funding was received by any author for research relevant to this study.

Author Contributions

James Berenson designed the study. Regina Swift collected specimens for analysis. Marissa-Skye Goldwater, Sean Bujarski, Scott Jew, Ryan Danis, Bernard Regidor, Benjamin Mark Eades, and Marsiye Emamy-Sadr generated the data. James Berenson and Ryan Danis interpreted the results. Ryan Danis, Ashley Del Dosso, and James Berenson wrote the manuscript.

Data Availability Statement

All data generated and analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

- 1 Drayson M, Tang LX, Drew R, Mead GP, Carr-Smith H, Bradwell AR. Serum free light-chain measurements for identifying and monitoring patients with nonsecretory multiple myeloma. *Blood*. 2001;97(9):2900–2. <https://doi.org/10.1182/blood.v97.9.2900>
- 2 Bujarski S, Udd K, Soof C, Chen H, Spektor TM, Safaie T, et al. Baseline and changes in serum B-cell maturation antigen levels rapidly indicate changes in clinical status among patients with relapsed/refractory multiple myeloma starting new therapy. *Target Oncol*. 2021;16(4):503–15. <https://doi.org/10.1007/s11523-021-00821-6>

- 3 Sanchez E, Smith EJ, Yashar MA, Patil S, Li M, Porter AL, et al. The role of B-cell maturation antigen in the biology and management of, and as a potential therapeutic target in, multiple myeloma. *Target Oncol*. 2018; 13(1):39–47. <https://doi.org/10.1007/s11523-017-0538-x>
- 4 Ghermezi M, Li M, Vardanyan S, Harutyunyan NM, Gottlieb J, Berenson A, et al. Serum B-cell maturation antigen: a novel biomarker to predict outcomes for multiple myeloma patients. *Haematologica*. 2017;102(4): 785–95. <https://doi.org/10.3324/haematol.2016.150896>
- 5 Jew S, Bujarski S, Soof C, Chen H, Safaie T, Li M, et al. Estimating a normal reference range for serum B-cell maturation antigen levels for multiple myeloma patients. *Br J Haematol*. 2021;192(6):1064–7. <https://doi.org/10.1111/bjh.16673>
- 6 Sanchez E, Li M, Kitto A, Li J, Wang CS, Kirk DT, et al. Serum B-cell maturation antigen is elevated in multiple myeloma and correlates with disease status and survival. *Br J Haematol*. 2012;158(6):727–38. <https://doi.org/10.1111/j.1365-2141.2012.09241.x>
- 7 Udd K, Soof C, Eteessami S, Rahbari A, Gross Z, Casas C, et al. Changes in serum B-cell maturation antigen levels are a rapid and reliable indicator of treatment efficacy for patients with multiple myeloma. *Clin Lymphoma Myeloma Leuk*. 2017;17(1):e19–20. <https://doi.org/10.1016/j.clml.2017.03.033>
- 8 Cavo M, Galieni P, Gobbi M, Baldrati L, Leardini L, Baccarani M, et al. Nonsecretory multiple myeloma: presenting findings, clinical course and prognosis. *Acta Haematol*. 1985;74(1):27–30. <https://doi.org/10.1159/000206159>
- 9 Migkou M, Avivi I, Gavriatopoulou M, Cohen YC, Fotiou D, Kanellias N, et al. Clinical characteristics and outcomes of oligosecretory and non-secretory multiple myeloma. *Ann Hematol*. 2020;99(6):1251–5. <https://doi.org/10.1007/s00277-020-03984-w>
- 10 Singhal N, Singh T, Singh Z, Shome DK, Gaiha M. Histomorphology of multiple myeloma on bone marrow biopsy. *Indian J Pathol Microbiol*. 2004;47(3):359–63.
- 11 Goldman-Mazur S, Visram A, Kapoor P, Dispenzieri A, Lacy MQ, Gertz MA, et al. Outcomes after biochemical or clinical progression in patients with multiple myeloma. *Blood Adv*. 2023;7(6):909–17. <https://doi.org/10.1182/bloodadvances.2022007082>