Clin. Lab. 2026;72:XXX-XXX

CASE REPORT

Proposed Solutions for a Multiple Myeloma Case with Unobtainable Serum

Zeliha Kocaismail [1], Ceylan Bal [1], Gülsüm Özet [2], Özcan Erel [1]

[1] *Department of Medical Biochemistry, Ankara Bilkent City Hospital, Ankara, Türkiye*
[2] *Department of Hematology, Ankara Bilkent City Hospital, Ankara, Türkiye*

ABSTRACT

Background: **Multiple myeloma (MM) is a plasma cell malignancy characterized by monoclonal protein secretion. Excessive immunoglobulin production increases blood viscosity, impairing serum separation and complicating laboratory analyses. We present a case of a 54-year-old male MM patient with hyperviscous samples, describing the laboratory solutions applied.**
Methods: **To extract a sufficient liquid compartment from the initial sample, several approaches were planned: repeated or extended centrifugation using serum separator tubes (SST), collection in heparinized tubes, use of plain tubes with dilution at 1/2 and 1/4 ratios, and mechanical separator tube (MST) usage.**
Results: **Repeated or prolonged centrifugation in SSTs did not produce sufficient serum. Blood collected in a heparinized tube also failed to yield adequate plasma. Sampling into a plain tube with dilution enabled sufficient serum collection, and MST provided the required plasma volume. MST test results were consistent with the patient's clinical status, whereas increasing the dilution ratio in plain tubes led to greater percentage differences compared with MST results.**
Conclusions: **MST provided optimal and clinically reliable results. If MST is unavailable, we recommend diluting hyperviscous samples in plain tubes, beginning with a 1/2 ratio.**
(Clin. Lab. 2026;72:xx-xx. DOI: 10.7754/Clin.Lab.2025.250834)

Correspondence:
Zeliha Kocaismail
Ankara Bilkent City Hospital
Department of Medical Biochemistry
Üniversiteler Mahallesi
Bilkent Cad. No: 1
06800, Ankara
Türkiye
Email: zelihakocaismail96@gmail.com
https://orcid.org/0009-0003-6712-485X

Case Report accepted September 11, 2025

KEYWORDS

blood viscosity, multiple myeloma, mechanical separator tube

INTRODUCTION

Multiple myeloma (MM) is a hematologic malignancy characterized by the clonal proliferation of plasma cells within the bone marrow, accompanied by the presence of monoclonal proteins in the blood or urine, and associated organ dysfunction [1]. About 1% of all cancers and 10% of hematologic malignancies are attributed to multiple myeloma, which is recognized as the second most common hematologic malignancy in adults [2,3]. Clinical presentations in MM patients are diverse, including anemia, hypercalcemia, bone pain, renal insufficiency, and immunosuppression, which collectively contribute to diagnostic complexity [3]. Given these challenges, the role of laboratory investigations is criti-

cal for the early identification and diagnosis of MM. Malignant plasma cell clones produce excessive amounts of abnormal immunoglobulins, which increase blood viscosity and hence make thrombosis more likely in MM patients [4]. Moreover, the elevated total protein concentration, particularly hyperimmunoglobulinemia, results in altered serum density, complicating serum separation from collected blood [5]. The serum fraction is critical for conducting biochemical analyses, and serum separator tubes (SSTs) are commonly employed to isolate the serum compartment after centrifugation. However, extracting serum fragments from protein-rich samples of MM patients is extremely challenging due to their elevated serum density and/or viscosity. A frequent issue encountered is improper gel positioning within SSTs following centrifugation, underscoring the difficulty of obtaining serum samples from these patients [6].

In this report, we present a case with an excessively viscous sample, which resulted in difficulties in obtaining serum after blood collection and centrifugation despite multiple attempts, together with various methods applied in our laboratory during the preanalytical phase to resolve the issue and obtain the patient's results. Considering the clinical significance of this condition, we believe that reporting alternative solutions may assist healthcare professionals and enhance patient benefits.

CASE PRESENTATION

A 54-year-old male presented to the Ankara Bilkent City Hospital Hematology Clinics with complaints of back pain, generalized weakness, and fatigue on March 4, 2025. Laboratory tests and imaging modalities are ordered accordingly. The imaging techniques suggest a suspicion of MM lesions in the skeletal structures. Blood samples collected for laboratory analysis were insufficient in volume due to their hyperviscous state. Due to the difficulty of obtaining serum from a highly viscous sample, the clinics referred the case to the Department of Biochemistry of the same hospital to resolve the problem. To extract an adequate volume of liquid compartment, such as serum or plasma from collected blood, a plan was established based on literature research, and the solutions listed in Table 1 were subsequently implemented. Various analyses could then be performed, including serum protein electrophoresis (SPE), which revealed the presence of M-protein (Figure 1a), and immunofixation electrophoresis (IFE), which identified this protein as IgG–Kappa (Figure 1b). Therefore, the assay results confirmed the diagnosis of multiple myeloma (MM), and a treatment plan was established. All blood collection tubes used in the laboratory were manufactured by BD (Becton, Dickinson and Company, Franklin Lakes, NJ, USA). The study protocol received approval from the Ankara Bilkent City Hospital Ethics Committee, with the decision number 2-25-1347.

RESULTS

Repeating the centrifugation process or extending the duration of centrifugation in SST did not result in sufficient serum volume to carry out the laboratory analysis. Collecting blood into a heparinized tube did not yield an adequate amount of plasma, as the sample shown in Figure 2a became noticeably viscous quickly after centrifugation. The other method involved sampling in-to a plain tube with dilution at 1/2 and 1/4 ratios. Centrifugation of the sample resulted in a sufficient amount of serum (Figure 2b, 2c). The necessary amount of plasma is obtained using a mechanical separator tube (MST) (Figure 2d). The laboratory results obtained using a MST and diluted samples in plain tubes are presented in Table 2.

We calculated the percentage differences (% difference) between the results of MST and the diluted samples at 1/2 and 1/4 ratios. These differences are then categorized as less than or equal to 10% and greater than 10% across the tubes. We evaluated a total of 24 parameters. When comparing the results from MST and the 1/2 diluted sample, we found that 13 of them showed a difference of ≤ 10%. These parameters include: Albumin, Alkaline phosphatase (ALP), Alanine transaminase (ALT), Amylase, Calcium, Total cholesterol, Creatine Kinase (CK), Glucose, Lipase, Magnesium, Total protein, Uric Acid, and High Density Lipoprotein (HDL). Results indicating a difference of less than 10% between 1/2 diluted sample and MST showed consistency in terms of reference range which means that the results either fell within the reference range or were above or below the reference limits, but were consistently in the same direction.

The remaining 11 parameters showed a difference of more than 10% between MST results and those of a 1/2 diluted sample including Aspartate aminotransferase (AST), Creatinine, Total and Direct Bilirubin, Gamma-glutamyl transferase (GGT), Phosphate, Iron (Fe), Lactate Dehydrogenase (LDH), Triglyceride, Urea and C-Reactive Protein (CRP). Another comparison of the MST results with a 1/4 diluted sample revealed that this time the group with > 10% difference contains 20 parameters and additionally includes ALP, ALT, Amylase, Calcium, CK, Magnesium, Total protein, Uric Acid and HDL when the dilution factor increases.

DISCUSSION

Malignant clones of plasma cells produce and release M-protein into the bloodstream that can interfere with laboratory assays. Frequently reported interferences may involve a direct mechanism in which the precipitation of M-proteins affects chemical assays that rely on turbidimetry or absorbance for measurement. M-protein may also interfere with the gel positioning of SST upon centrifugation. This gel dislocation may be attributed to the increased viscosity of the sample, which can occur

Table 1. Laboratory Examinations.

1. Repeating centrifugation	**The samples are routinely centrifuged at 4,000 RPM for 10 minutes in the laboratory. This procedure is repeated twice in SST.**
2. Extended Centrifugation Duration	**The sample is centrifuged for 20 minutes in SST.**
3. Using a heparinized tube	**The routine centrifugation process is carried out in a heparinized tube to yield plasma.**
4. Using a plain tube and diluting the sample	**After collection, the complete blood sample is quickly diluted at 1/2 and 1/4 ratios by using a 0.9% isotonic saline solution in plain tubes.**
5. Mechanical separator tube usage	**A special centrifugation process is performed at 2,400 x g (relative centrifugal force) for 10 minutes to yield plasma in MST.**
6. Precipitation with polyethylene glycol solution	**The procedure is planned but could not be performed due to insufficient sample volume.**

Table 2. The laboratory results of the patient for biochemical parameters.

Parameters	Results of MST *	Results of PT # 1/2 dilution	Results of PT # 1/4 dilution	Reference range
Albumin (g/L)	**36.6**	**34.1**	**33.4**	**32 - 48**
ALP (U/L)	**32.0**	**30.0**	**22.5**	**56 - 119**
AST (U/L)	**23.5**	**26.5**	**11.7**	**< 35**
ALT (U/L)	**39.0**	**37.5**	**22.5**	**< 50**
Amylase (U/L)	**199**	**177**	**144**	**30 - 118**
Ca (mg/dL)	**9.61**	**9.15**	**7.56**	**8.7 - 10.4**
Total Cholesterol (mg/dL)	**97.0**	**92.5**	**94.5**	**< 200**
CK (U/L)	**92.0**	**90.0**	**72.0**	**32 - 294**
Creatinine (mg/dL)	**1.27**	**0.57**	**0**	**0.7 - 1.3**
Total Bilirubin (mg/dL)	**0.42**	**0.29**	**0.36**	**0.3 - 1.2**
Direct Bilirubin (mg/dL)	**0.12**	**0.10**	**0.10**	**< 0.3**
GGT (U/L)	**34.0**	**27.5**	**22.5**	**< 73**
Glucose (mg/dL)	**93.0**	**88.0**	**92.0**	**70 - 99**
Phosphate (mg/dL)	**4.70**	**4.15**	**3.46**	**2.4 - 5.1**
Iron (ug/dL)	**42.0**	**36.0**	**31.5**	**65 - 175**
LDH (U/L)	**171**	**207**	**112**	**120 - 246**
Lipase (U/L)	**66.0**	**61.7**	**70.0**	**12 - 53**
Mg (mg/dL)	**1.71**	**1.62**	**1.17**	**1.3 - 2.7**
Total Protein (g/L)	**114**	**102**	**92**	**57 - 82**
Triglyceride (mg/dL)	**58.0**	**47.5**	**67.5**	**< 150**
Uric Acid (mg/dL)	**7.90**	**7.75**	**6.75**	**3.7 - 9.2**
Urea (mg/dL)	**50.0**	**64.0**	**58.0**	**19 - 49**
CRP (mg/L)	**7.60**	**3.0**	**0.50**	**0 - 5**
HDL (mg/dL)	**25.4**	**27.1**	**20.9**	**> 40**

*** MST: Mechanical seperator tube, # PT: Plain tube.**

in monoclonal gammopathies with marked hyperproteinemia and, especially, hyperimmunoglobulinemia [5-7]. Moreover, studies reported that laboratories utilizing automated pre-analytical processes, like centrifugation and sample transport to analyzers, face issues with serum samples that are not fully separated in SSTs. A key problem is probe occlusion caused by hyperviscous samples that are integrated into analytical systems with-

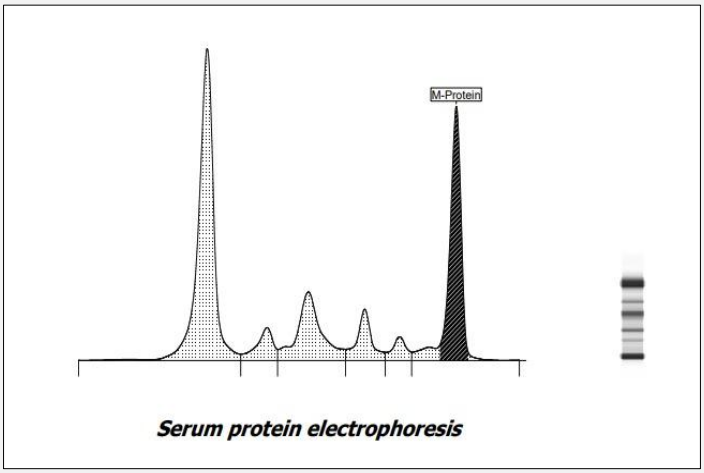

Figure 1a. Serum Protein Electrophoresis result.

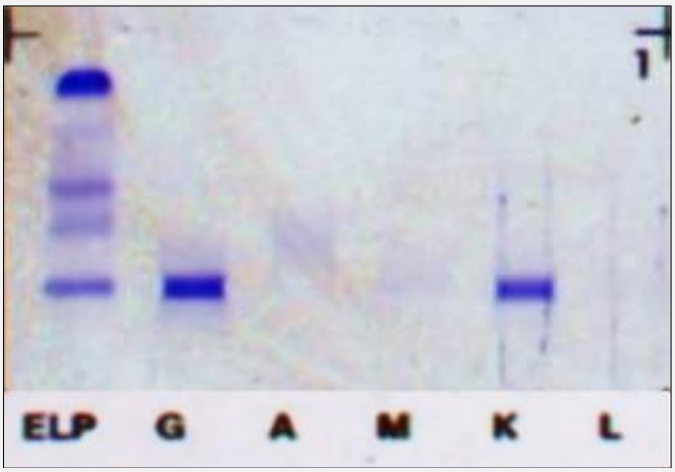

Figure 1b. Immunofixation electrophoresis result.

out visual inspection [8].

All these factors create challenges in laboratory analyses and in obtaining serum from highly viscous samples of MM patients. The study by Zaharudin et al. showed that prolonging the centrifugation time to eliminate insufficient centrifugal force as a cause for not obtaining an adequate serum volume did not resolve the problem [6]. Birdi et al. found that repeated centrifugation did not resolve the hyperviscosity issues in their sample. Consequently, they diluted the sample at a 1/10 ratio, which allowed them to obtain the results [9]. To yield a sufficient amount of serum, Zhang et al. and Gerin et al. used a plain blank tube, and Rico Rios et al. utilized a lithium heparin tube for biochemical analyses, which has been reported to be more effective than SST [4,10,11].

Based on our literature review, we initially repeated the centrifugation process and increased the duration of

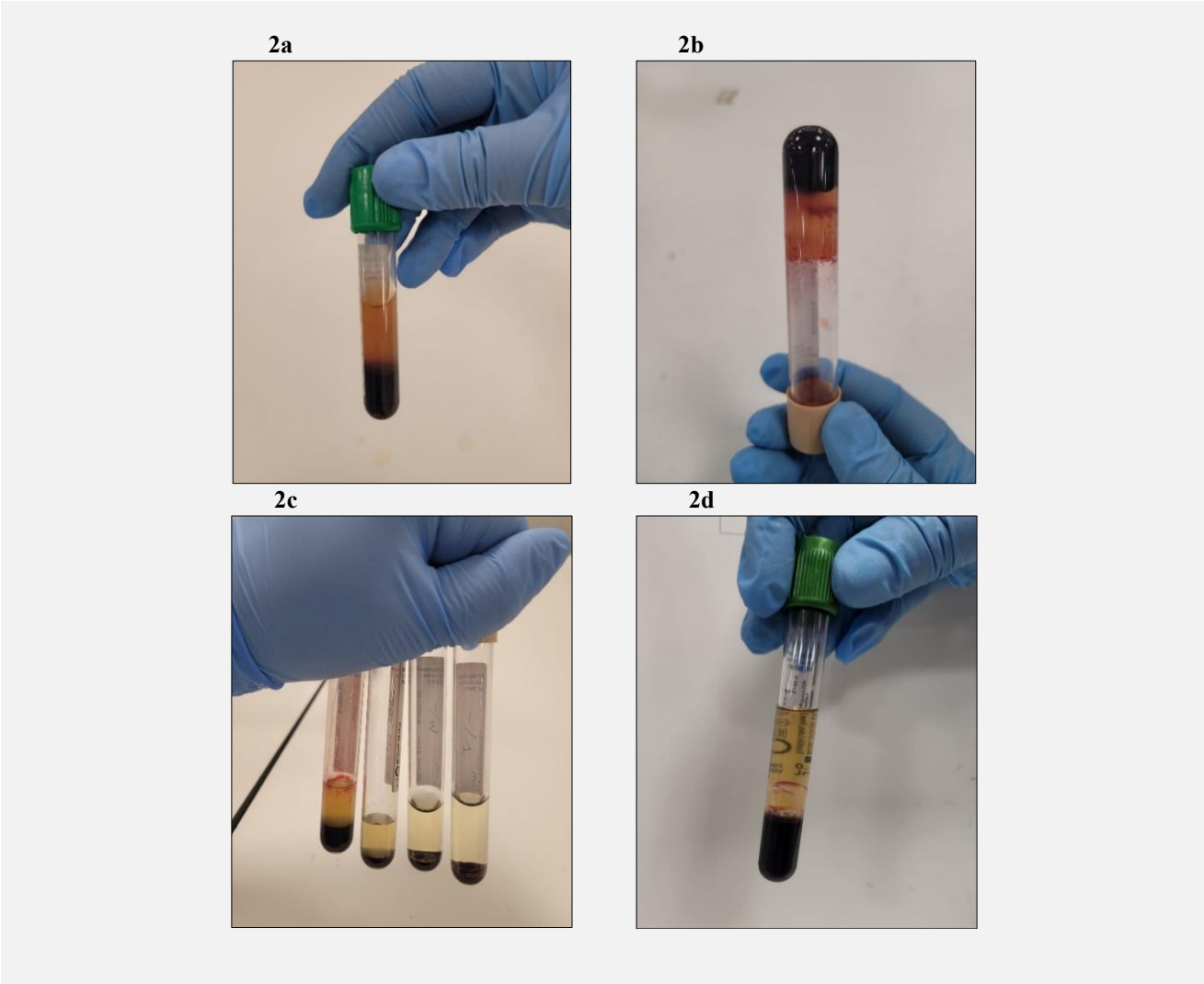

Figure 2. Laboratory examinations performed to obtain sufficient sample volume.

Figure 2a: Heparinized tube.
Figure 2b: Excessively viscous sample centrifuged in plain tube.
Figure 2c: Diluted and centrifuged samples in plain tubes.
Figure 2d: Mechanical seperator tube.

centrifugation. However, we were unable to obtain results due to the high viscosity, which is consistent with previous reports [6,9]. Then we utilized a heparinized tube, but could not obtain a sufficient portion of plasma. The reason we were unable to obtain results using a heparinized tube, while Rico Rios et al. did achieve results, may be due to differences in total protein and M-protein concentrations between the two cases at the time of measurement. Additionally, the sample from our case was collected before the initiation of treatment, which could also contribute to the greater viscosity of the sample [10]. We conducted laboratory analyses using a plain tube, in which we performed 1/2 and 1/4 dilutions, and a mechanical separator tube (MST), an additional procedure beyond the literature search. The reason for the trial of MST in this case was its advantageous features, such as a shorter centrifugation time without the need for a prior waiting step before centrifugation. This enables faster plasma collection, resulting in a reduced turnaround time for reporting results [12].

CONCLUSION

To our knowledge, there are no reports in the literature indicating that MST can be used to analyze hyperviscous samples. However, in our study, the optimal results closely related to the patient's clinical status were

obtained from MST, followed by diluted samples in plain tubes. A comparison of the MST results with diluted samples at 1/2 and 1/4 ratios showed that increasing the dilution factor led to greater discrepancies from the MST values and reduced the compatibility of the results. The most accurate results, in comparison to MST, were achieved with the 1/2 diluted sample, as indicated in Table 2.

Given the limited number of reports that address similar cases along with the potential negative impacts this condition may have on patient outcomes (where clinical decisions may vary based on inaccurate results) and costs (such as the need for probe renewal and interruptions to laboratory workflow), we aimed to share our experience and the solutions we implemented to resolve the issue and maximize patient benefits from healthcare. Upon considering the challenges and costs of utilizing MST in clinical laboratories, we concluded that using plain tubes and initiating the dilution at a 1/2 ratio as an alternative to MST may enable laboratories to obtain results that closely align with the patient's clinical status.

Declaration of Interest:

The authors listed above certify that they have no affiliations with or involvement in any organization or entity with any financial or non-financial interest in the materials discussed in this manuscript.

References:

1. Elbahoty MH, Papineni B, Samant RS. Multiple myeloma: clinical characteristics, current therapies and emerging innovative treatments targeting ribosome biogenesis dynamics. Clin Exp Metastasis 2024 Dec;41(6):829-42. (PMID: 39162964)

2. Rajkumar SV. Multiple myeloma: 2024 update on diagnosis, risk-stratification, and management. Am J Hematol 2024 Sep;99(9): 1802-24. (PMID: 38943315)

3. Monteith BE, Sandhu I, Lee AS. Management of Multiple Myeloma: A Review for General Practitioners in Oncology. Curr Oncol 2023 Apr 22;30(5):4382-401. (PMID: 37232792)

4. Zhang L, Lv H, Chen K, et al. Diagnosis of Multiple Myeloma from a Blood Sample Failed To Be Centrifuged: A Case Report. Neuropsychiatry 2018. https://www.jneuropsychiatry.org/peer-review/diagnosis-of-multiple-myeloma-from-a-blood-sample-failed-to-be-centrifuged-a-case-report.pdf

5. Pang L, Xing Y, Xing L, Miao L, An C, Li H. Contradictory Phenomenon Between Serum Separator Tube and Plasma Tube: A Case Report. Lab Med 2021 Sep 1;52(5):e125-8. (PMID: 33595087)

6. Zaharudin MR, C Thambiah S, Samsudin IN, A Hamid H. Serum separation abnormality in a multiple myeloma patient. Malays J Pathol 2023 Apr;45(1):123-7. (PMID: 37119252)

7. Chakraborty S, Chowdhury SR, Krishnan P, Sanyal S, Bhattacharya C, Sen S. Improper serum separation on gel tubes: a trivial laboratory problem or an indicator of monoclonal gammopathy? Clin Chem Lab Med 2014 Dec;52(12):e275-8. (PMID: 24964260)

8. van den Ouweland JM, Church S. High Total Protein Impairs Appropriate Gel Barrier Formation in BD Vacutainer Blood Collection Tubes. Clin Chem 2007 Feb;53(2):364-5. (PMID: 17259253)

9. Birdi A, Sinha A, Banerjee M, SelviN MK. Smouldering Myeloma: Chasing a Hyperviscous Sample. Ind J Clin Biochem 2023 Apr;38(2):279-83. (PMID: 37025433)

10. RicoRios N, Bowles L, Ayling RM. Multiple myeloma and acquired von Willebrand disease: a combined cause of preanalytical interference causing gel formation? Ann Clin Biochem 2018 Jan; 55(1):181-4. (PMID: 28490182)

11. Gerin F, Ramazan DC, Baykan O, Sirikci O, Haklar G. Abnormal gel flotation in a patient with apperant pneumonia diagnosis: a case report. Biochem Med (Zagreb) 2014 Feb 15;24(1):180-2. (PMID: 24627728)

12. Orhan B, Mercan H, Deniz L, Erdogan Z, Inal BB. Comparison of Barricor tube and serum separator tube in outpatients. Turkish Journal of Biochemistry 2022 47(6):719-26. https://www.researchgate.net/publication/364537512_Comparison_of_Barricor_tube_and_serum_separator_tube_in_outpatients