Türk Klinik Biyokimya Derg 2025; 23(3): 143-147

https://doi.org/10.56615/tkbd.2025.18

Olgu Sunumu / *Case Report*

From Laboratory Clue to Diagnosis: Multiple Myeloma

Laboratuvar İpucundan Tanıya: Multipl Miyelom

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Received / Başvuru Tarihi: 13.10.2025 *Accepted* / Kabul Tarihi: 11.11.2025

ABSTRACT

Preanalytical irregularities in serum separator tubes are frequently regarded as technical artifacts. In this case, repeated failure of serum separation led to the diagnosis of multiple myeloma. A 77-year-old woman presented with chest pain and fatigue, and successive serum samples failed to form an adequate gel barrier, yielding only minimal serum despite prolonged centrifugation. Biochemical analyses revealed hypoalbuminemia, elevated total protein, increased IgA with suppressed IgM and IgG levels, and a markedly decreased kappa/lambda ratio. Serum and urine immunofixation identified an IgA–lambda monoclonal band. PET-CT demonstrated multiple lytic bone lesions. Bone marrow biopsy revealed a hypercellular marrow with 80% plasma cell infiltration, confirming the diagnosis of multiple myeloma. These findings underscore that abnormal serum separation, often dismissed as a technical issue, may serve as an early indicator of underlying hematologic malignancy.

Keywords: Multiple myeloma, Serum separator tube, Preanalytical error, Immunofixation, Hyperproteinemia.

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Etik onay: Hastadan bilgilendirilmiş onam formu alınmıştır

ÖZET

Serum ayırıcı tüplerde görülen preanalitik düzensizlikler sıklıkla teknik artefaktlar olarak değerlendirilir. Bu olguda, tekrarlayan serum ayrışma başarısızlığı multipl miyelom tanısına yol açmıştır. Yetmiş yedi yaşındaki bir kadın hasta göğüs ağrısı ve halsizlik şikâyetleriyle başvurmuş, ardışık serum örneklerinde yeterli jel bariyer oluşmamış ve uzun süreli santrifügasyona rağmen yalnızca minimal miktarda serum elde edilmiştir. Biyokimyasal analizlerde hipoalbuminemi, artmış total protein, IgM ve IgG baskılanması ile birlikte artmış IgA düzeyi ve belirgin derecede azalmış kappa/lambda oranı saptanmıştır. Serum ve idrar immünfiksasyonunda IgA–lambda monoklonal bant tespit edilmiştir. PET-BT incelemesinde çok sayıda litik kemik lezyonu gösterilmiştir. Kemik iliği biyopsisinde %80 plazma hücresi infiltrasyonu ile hipersellüler bir kemik iliği saptanmış ve multipl miyelom tanısı doğrulanmıştır. Bu bulgular, sıklıkla teknik bir sorun olarak göz ardı edilen anormal serum ayrışmasının, altta yatan hematolojik malignitenin erken bir göstergesi olabileceğini vurgulamaktadır.

Anahtar Kelimeler: Multipl miyelom, Serum ayırıcı tüp, Preanalitik hata, İmmünfiksasyon, Hiperproteinemi.

INTRODUCTION

Gel barrier displacement or failure to form in serum separator tubes is predominantly considered a pre-analytical artifact (1). Nevertheless, such anomalies may occasionally serve as harbingers of underlying severe pathologies (2). The localization of the gel barrier is influenced by multiple factors, including sample viscosity, specific gravity, tube composition, and laboratory handling conditions. Additionally, patient-specific variables such as heparin therapy, anemia, elevated plasma protein concentrations, or sample contamination may precipitate gel barrier failure (3). This case report delineates the diagnosis of multiple myeloma in a 77-year-old female patient, subsequent to recurrent gel barrier failure in serum separator tubes.

Case Presentation

A 77-year-old female patient initially presented to an external medical center with complaints of chest pain, fatigue, generalized weakness, and musculoskeletal pain, mainly affecting both legs. She reported increased sleep duration, loss of appetite, and approximately 7 kg of weight loss over the past three months. In addition, she described recurrent episodes of nasal bleeding and severe leg pain during the last three days.

On physical examination, no jaundice, cyanosis, or clubbing was observed. Vital signs were stable (heart rate: 84/min, blood pressure: 130/80 mmHg). Cardiovascular and abdominal examinations were within normal limits. Based on the initial evaluation at the external center, a need for blood transfusion was identified, and the patient was referred to our hospital for further investigation and management.

The initial blood sample was collected in a Greiner Bio-One VACUETTE Serum Sep Clot Activator tube (Lot A240839S) and centrifuged at 2000 × g for 10 minutes. Post-centrifugation, gel barrier formation was absent. Despite prolonging the centrifugation duration, the anomaly persisted. (Figure 1) A subsequent blood draw yielded minimal serum from the upper fraction. Biochemical analyses, including albumin, total protein, immunoglobulins, and free light chains, were performed using the Beckman Coulter AU5800 analyzer (Beckman Coulter Inc., Brea, CA, USA). Serum and urine immunofixation electrophoresis were performed using the Helena SAS-1 Plus system (Helena Biosciences, Sunderland, UK).

Oncologic PET using F-18 fluorodeoxyglucose (FDG), performed at diagnosis, revealed a mildly hypermetabolic lytic lesion measuring 30 × 17 mm located at the anterior aspect of the right iliac bone. Additionally, multiple lytic hypodense lesions exhibiting mild to minimal intramedullary hypermetabolism were observed throughout the skeletal system, with more prominent

involvement of the calvarium, bilateral humeri, pelvic bones, and femora. Subsequently, a bone marrow biopsy was performed.

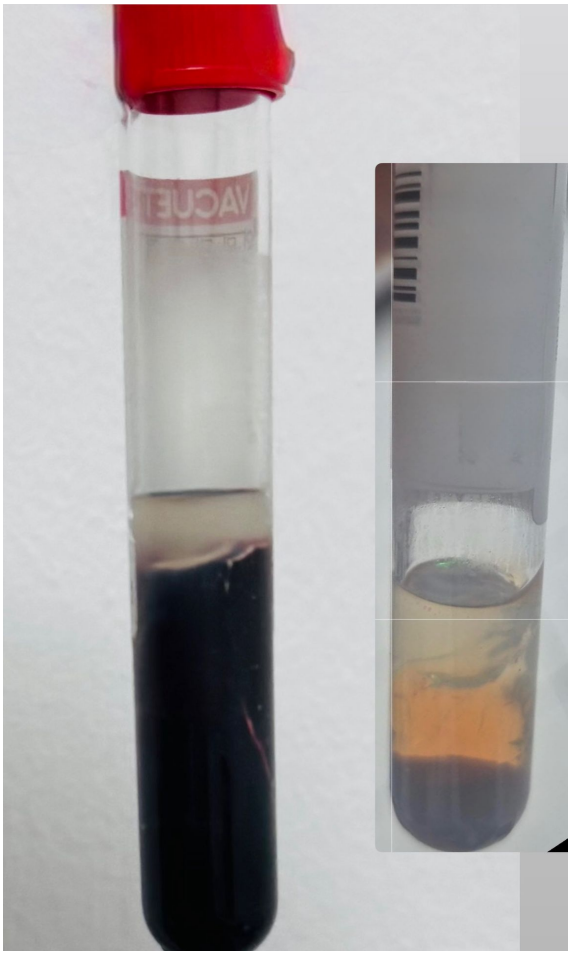

Figure 1. Abnormal floating separator gel.
Şekil 1. Ayırıcı Jelde Anormal Konumlanma

Laboratory Findings

Serum biochemistry revealed hypoalbuminemia (23 g/L; reference range: 35–52 g/L) concomitant with hyperproteinemia (119 g/L; reference range: 66–83 g/L). Immunoglobulin profiling demonstrated markedly elevated IgA (16.68 g/L; reference range: 0.7–4 g/L), with depressed IgM (0.20 g/L; reference range: 0.4–2.3 g/L) and IgG (2.07 g/L; reference range: 7–16 g/L) concentrations. Free light chain assays showed reduced kappa chains (1.48 mg/L; reference range: 2.37–20.73 mg/L) and normal lambda chains (26.42 mg/L; reference range: 4.23–27.69 mg/L), resulting in a markedly decreased kappa/lambda ratio of 0.056 (reference range: 0.22–1.74). Serum and urine immunofixation electrophoresis revealed an IgA lambda monoclonal band, representing a laboratory finding compatible with a monoclonal gammopathy (Figure 2). A differential diagnosis of multiple myeloma was considered, and to confirm it, a bone marrow biopsy was performed, which revealed plasma cell dyscrasia consistent with multiple myeloma. Additionally, the bone marrow biopsy showed a hypercellular marrow with 80% plasma cells and 3% blasts. Based on these findings, a definitive diagnosis of multiple myeloma was established.

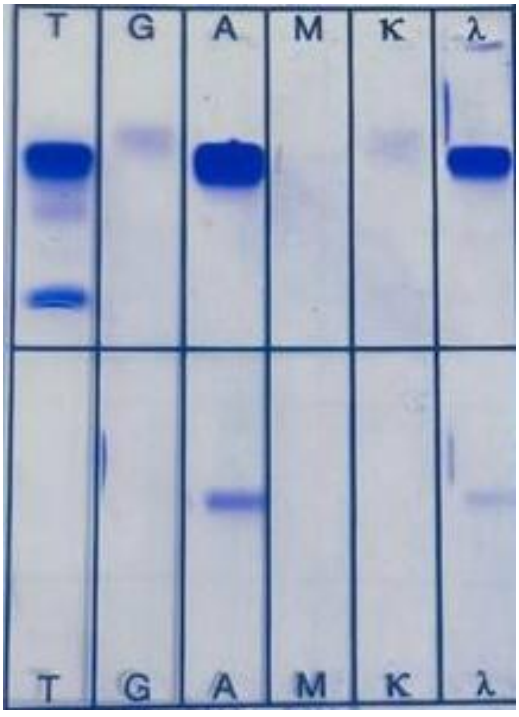

Figure 2. IgA lambda monoclonal band on serum and urine immunofixation electrophoresis.
Şekil 2. Serum ve idrar immünofiksasyon elektroforezinde IgA lambda monoklonal band.

DISCUSSION

Failure or aberrant positioning of the gel barrier in serum separator tubes is commonly attributed to preanalytical technical errors. However, accumulating evidence suggests that such abnormalities may serve as early indicators of hematologic

malignancies and other serious clinical conditions (1,2,4). In particular, gel barrier failure has been repeatedly reported in patients with multiple myeloma, a disorder characterized by excessive paraprotein production and increased plasma viscosity (3,5,6).

In multiple myeloma, overproduction of monoclonal immunoglobulins and free light chains alters the physicochemical properties of serum, including density and viscosity, thereby interfering with normal gel barrier migration during centrifugation. Tan et al. described serum separator tube gel failures associated with elevated IgA concentrations, findings that closely parallel the present case and emphasize the importance of heightened awareness in clinical laboratory practice (1).

Similarly, Kim et al demonstrated that discrepancies between serum separator and plasma tubes in immunoglobulin measurement are influenced by both tube composition and serum viscosity, highlighting the critical role of appropriate tube selection in laboratory diagnostics (2). Demir et al. reported abnormal gel flotation in hemodialysis patients with hyperproteinemia, further supporting the notion that elevated protein concentrations disrupt proper gel positioning (3).

Increased serum viscosity, a hallmark of hyperproteinemic states, has been strongly implicated in serum separator tube failures. Kisselev et al. identified hyperviscosity syndrome as a key contributor to separation errors, adversely affecting assay reliability (5). Likewise, Smith et al. demonstrated that elevated viscosity promotes gel barrier displacement during centrifugation, underscoring its relevance to preanalytical quality control (7). Collectively, these findings indicate that excessive serum protein levels disturb the physicochemical equilibrium within serum separator tubes.

In addition to patient-related factors, variability in tube manufacturing and gel composition may influence gel barrier performance. Jones et al. showed that differences in gel chemistry and density among manufacturers affect gel stability and protein electrophoresis outcomes (8). Lee et al. further reported reduced reliability of certain tube brands in samples with high protein content, often necessitating repeat testing (9). These observations underscore the importance of judicious tube selection in clinical laboratories.

In the present case, all samples were collected using the same type of serum separator tube, ensuring consistency in tube composition. Therefore, the observed gel barrier failure cannot be attributed to inter-tube variability. Nevertheless, samples were obtained at different time points during the patient's clinical evaluation. Minor temporal changes in serum viscosity—potentially related to fluctuations in paraprotein concentrations or slight delays between sample collection and centrifugation—may have contributed to variations in gel migration. Despite these potential factors, the predominant cause of the abnormal separation was most likely the markedly elevated serum protein concentration associated with multiple myeloma.

Brown et al. emphasized the diagnostic value of preanalytical abnormalities in serum separator tubes as early warning signs of hematologic malignancies. Prompt recognition of such anomalies may facilitate earlier diagnosis and improve clinical outcomes (10).

Additional patient-related factors, including anemia, anticoagulant therapy, and contamination with contrast agents, may also contribute to gel barrier abnormalities (11,12). Accordingly, preanalytical protocols should be adapted to account for individual patient characteristics.

In conclusion, heightened awareness of serum separator gel anomalies during the pre-analytical phase is essential for laboratory personnel. Such vigilance facilitates the early detection of life-threatening conditions like multiple myeloma.

Limitations and Contributions

A limitation of this study is that it is based on a single patient case, which constrains the assessment of variability in pre-analytical and analytical conditions. Factors such as serum viscosity, sample handling, and centrifugation parameters were observed qualitatively rather than systematically quantified. Despite this, the study underscores the importance of monitoring gel barrier behavior as apotential indicator of altered serum physicochemical properties, such as those seen in multiple myeloma. By linking repeated gel barrier failure to a specific hematologic malignancy, this report contributes methodologically by highlighting a practical pre-analytical clue that can inform laboratory quality control and early diagnostic vigilance.

Research Funding

This study did not receive any external funding.

Conflict of Interest

The authors declare no conflicts of interest.

Informed consent was obtained from the participant.

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