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# Capillary Electrophoresis Not Detecting Elevated Concentrations of Monoclonal Free Light Chains

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## Abstract

The most common exam ordered when monoclonal gammopathy (MG) is suspected is serum protein electrophoresis (SPEP). Capillary Zone Electrophoresis (CZE) is commonly used for its automation and speed. It is well known that it fails to detect free light chains because of lower concentrations falling below CZE sensitivity. We report a case of a serum sample of a 69-year-old woman during the follow-up of a free light chain multiple myeloma. CZE was normal while serum FLC-Kappa was elevated at 6392 mg/L. Serum Immunofixation (SIFE) revealed free lights kappa chains. Capillary immunotyping showed no abnormalities. This observation highlights the limitations of CZE to detect FLC even when they are elevated and the need to avoid CZE alone. Compliance with recent guidelines by combining exams for screening, diagnosis and follow-up for MG is essential.

**Keywords:** Free light chains, Capillary zone electrophoresis, Monoclonal gammopathy, and Immunofixation.

## 1. Introduction

Serum Electrophoresis of Proteins (SPEP) is commonly performed using capillary zone electrophoresis (CZE) to detect monoclonal proteins when monoclonal gammopathy (MG) is suspected. During CZE, proteins migrate under an electroosmosis flow with direct integration of the fractions by spectrophotometry (Mondol *et al.*, 2018). It has been reported that CZE can fail to detect 5% of MG and 40% of light chain multiple myeloma (LCMM). When small free light chains (FLC) pass in the urine, the residual concentration in serum is too weak to be detected by CZE. Serum Immunofixation (sIFE), Bence Jones proteinuria and serum free light chains (sFLC) quantification assays perform better sensibility for the detection of free light chains. We

report a case of serum free light kappa chains at high concentrations that failed to be detected by CZE but detected by sFLC assays and sIFE.

## Case Report

In September 2025, we received a sample of a 69-year-old woman for tests that were part of the follow-up of a light chain multiple myeloma (LCMM). Laboratory investigations from the sender laboratory showed a hemoglobinemia of 8.4 g/dL (reference interval (RI): 11.8 – 15.8 g/dL) with associated thrombocytopenia 20 G/mm<sup>3</sup> (RI: 150 G/mm<sup>3</sup> – 450 G/mm<sup>3</sup>), total serum protein: 67 g/L (RI: 64 - 83 g/L). Creatinine blood levels 4.20 mg/dl (RI: 0.5 mg/dl-1 mg/dl), the estimated GFR by 2021 CKD-EPI Creatinine was 11 ml/min/1.73 m<sup>2</sup> (RI:

greater than 90). Erythrocyte sedimentation rate accelerated at 92 mm.

SPEP by CZE and immunotyping were performed by using respectively Capillarys system and Capillarys immunotyping on Capillarys Octa (Sebia, Lisses, France). They showed no abnormalities, as no monoclonal spikes on the electropherogram (**Fig. 1**) and no subtraction on all immunotyping frames (**Fig. 2**). Serum Immunofixation was performed using HYDRASYS 2 scan system (Sebia, Lisses, France). It showed free kappa light chains (**Fig. 3**). sFLC was performed on the Architect c4100 instrument (Abbott) using the Diazyme turbidimetric immunoassay (Diazyme Laboratories). Results showed an elevated serum FLC-kappa: 6392.8 mg/L (RI: 2.37 – 20.73 mg/L), serum FLC-lambda: 107.1 mg/L (RI: 4.23 – 27.69 mg/L), and a high FLC-kappa/FLC-lambda ratio of 59.70 (RI: 0.37 – 3.10).

## 2. Discussion

Monoclonal gammopathies (MG) are defined by the increased production of a monoclonal protein (MP), following an abnormal production of a plasma cells clone. The MP can be an intact immunoglobulin (with both a heavy chain and a light chain) or an isolated light chain referred to as free light chain (FLC). MG consist in a wide range of diseases such as: MGUS (Monoclonal Gammopathy of Undetermined Significance), multiple myeloma, Waldenström's macroglobulinemia, light chain amyloidosis, light chain deposition disease, solitary plasmacytoma and other plasma cell leukemias and lymphomas.

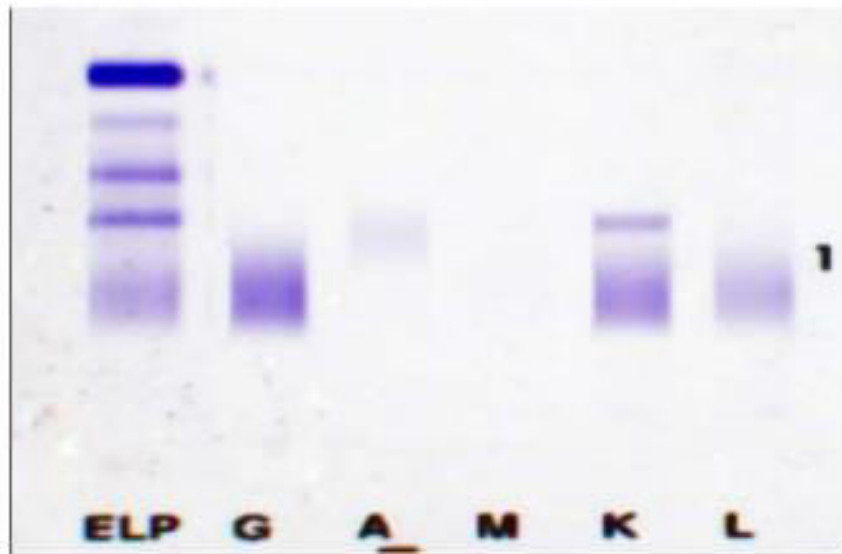
Serum protein electrophoresis (SPEP) is a common test used once a monoclonal gammopathy is suspected. SPEP separates serum protein based on their size and charges. CZE has been widely adopted to perform SPEP as the technique is automated and sensitive (Bossuyt *et al.*, 2003). Monoclonal protein appears as a peak, usually in the gamma region. While it can detect and quantify the size of a monoclonal protein, it has its limitations. The CZE by Sebia we used can detect a monoclonal protein as low as 19 mg/dL (Sebia, 2022.). The manufacturer also states that this sensitivity may vary according to the mobility of the monoclonal component and polyclonal background. A well-known pitfall of CZE is its limited ability to detect monoclonal FLCs which are the sole products of LCMM (Dispenzieri *et al.*, 2010).

It is indeed known that CZE produces false negatives for serum FLC. This has been attributed to weak serum concentrations below the sensitivity range (Bakshi *et al.*, 2005a; Biaz *et al.*, 2022; Ellidag *et al.*, 2015; Jenner, 2014). Free chains monoclonal proteins have low serum concentrations due to FLC readily passing in urine. The false negative in CZE might also be a consequence of the FLC's low molecular weight affecting their electrophoretic mobility. They can produce a modest peak or can be invisible if they co-migrate in other normal fractions (Carrère *et al.*, 2019; Ellidag *et al.*, 2015). It has been suggested that due to their low molecular weight, they can migrate before the start of the reading signal or remain immobile in the capillary (Biaz *et al.*, 2022).

In our case, the concentration of monoclonal kappa free chains of 6392.8 mg/L is above the level of detection of the manufacturer. Capillary techniques (CZE and immunotyping) were strictly normal. This observation suggests that the failure to detect serum FLC with CZE is not strictly related to their low serum levels. On the other hand, sIFE which has the 10-fold sensitivity of SPEP was able to detect the monoclonal FLC-kappa as a thick band in the kappa lane. Our case illustrates that FLC at concentrations over CZE level of detection can remain invisible on the electropherogram, as well as in immunotyping. It also indicates the added value of sFLC quantifications assays in the panels of laboratory tests for MG patients. sFLC quantifications assays are replacing the Bence Jones proteinuria test.

It highlights the need to comply with the recent guidelines for laboratory detection and initial diagnosis of MG as well as diagnosis and follow-up of multiple myeloma. In a screening situation, performing CZE alone would have resulted in a missed or delayed diagnosis. We also suggest clinicians comply by ordering tests accordingly. Algorithms involve at least SPEP and sFLC quantification assays (Keren *et al.*, 2022; Rajkumar, 2022) and sometimes sIFE is added (Dimopoulos *et al.*, 2021; Mohammad *et al.*, 2020; Keren *et al.*, 2022) to increase detection sensitivity. Additionally, for laboratories, combining SPEP and sFLC into a unique test order has shown to increase compliance with the International Myeloma Working Group (IMWG) guidelines (O'Brien *et al.*, 2023). Such changes improved the detection of MG, where early





**Fig. 3:** The Serum Immunofixation gel showing a monoclonal band in Kappa.

### 3. Conclusion

CZE is a widely adopted test in clinical laboratories for its speed, its automation and sensitivity. It is vastly prescribed when a clinician suspects a monoclonal gammopathy as a screening test as well as for monitoring therapy for already diagnosed patients because CZE allows the quantification of the monoclonal protein. However, CZE has inherently limits detecting serum free light chains. This pitfall is frequently explained by the lower concentration of MP constituted of serum free light chains readily passing in the urine. In our case report, CZE and Capillary Immunotyping failed to detect free light chains kappa MP although the concentrations are over the limit of detection stated by the manufacturer. Our observation illustrates that the false negatives for sFLC in capillary electrophoresis is not only a matter of concentrations but might also involve of a particular interaction of sFLC during the capillary electrophoresis procedure. Overall, such false negatives should be avoided for patients in order not to miss diagnosis or delay treatments. Clinicians should comply with international recommendations when ordering tests by combining serum electrophoresis with sIFE or quantification of sFLC anytime MG is evoked. sIFE and serum quantifications perform better detecting MP constituted of FLC. Clinical laboratories could help enhance such compliance by combining those tests into one. Meanwhile, in clinical setups where compliance with international recommendations is not man-

datory, CZE clinical laboratory reports should include a note reminding clinicians that SPEP alone can fail to detect monoclonal protein.

### 4. Ethical Clearance

We declare that all text, data, figures/tables, or other illustrations presented in the manuscript are completely original and do not contain or include material taken from other copyrighted sources and affirm that the work does not contravene any proprietary or own rights of others. We state that the article submitted has neither been previously published nor submitted elsewhere in any form or for simultaneous consideration in any other journal, and we will not reuse this previously published work without making substantial alterations and without desire to address. We state that we have substantially participated in the research and in preparation of the manuscript and that it represents original work adequate to claim authorship, and we agree that no author can publish anywhere else unless it has been changed substantially.

### 5. Author Contributions

K.K.: analysis, data collection, figure preparation, manuscript writing. M.A: Manuscript review and final approval. B.Y.: Manuscript review and final approval.

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## 7. Conflicts of Interest

The authors declare that they have no conflicts of interest, financial or otherwise, that could have influenced the conduct or outcomes of this study.

## 8. References

- Bakshi, N. A., Gulbranson, R., & Keren, D. F. (2005). Serum Free Light Chain (FLC) Measurement Can Aid Capillary Zone Electrophoresis in Detecting Subtle FLC-Producing M Proteins. *American J. of Clinical Pathology*, **124**(2), 214–218.  
<https://doi.org/10.1309/XE3UDARKW1B9EMWM>
- Biaz, A., Konzi, K., & Bouhsain, S. (2022). Monoclonal Immunoglobulin Associated with Monoclonal Free Light Chains Invisible on Capillary Electrophoresis. *Clinical Laboratory*, **68**(7).  
<https://doi.org/10.7754/CLIN.LAB.2021.211011>
- Bossuyt, X., Lissoir, B., & Wallemacq, P. (2003). Automated serum protein electrophoresis by Capillary. *Clinical Chemistry and Laboratory Medicine*, **41**(5), 704–710.  
<https://doi.org/10.1515/CCLM.2003.107>
- Carrère, F., Plasse, F., & Lellouche, F. (2019). Point sur les GMSI : interprétation des examens complémentaires et complications cliniques. *Annales de Biologie Clinique*, **77**(3), 245–254.  
<https://doi.org/10.1684/ABC.2019.1440>
- Dimopoulos, M. A., Moreau, P., & Mey, U. (2021). Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up †. *Annals of Oncology*, **32**(3), 309–322.  
<https://doi.org/10.1016/j.annonc.2020.11.014>
- Dispenzieri, A., Katzmann, J. A., and Rajkumar, S. V. (2010). Prevalence and risk of progression of light-chain monoclonal gammopathy of undetermined significance: a retrospective population-based cohort study. *The Lancet*, **375**(9727), 1721–1728.  
[https://doi.org/10.1016/S0140-6736\(10\)60482-5](https://doi.org/10.1016/S0140-6736(10)60482-5)
- Ellidag, H. Y., Eren, E., Aydin, O., & Yilmaz, N. (2015). Monoclonal Light Chains Can Remain Unnoticed in Protein Electrophoresis. *Indian J. of Clinical Biochemistry*, **30**(3), 363–364. *Springer India*.  
<https://doi.org/10.1007/s12291-015-0484-2>
- Holdings, S., Spradbery, D., & Shields, M. L. (2007). Combination of Serum Free Light Chain Analysis with Capillary Zone Electrophoresis Improves Screening for Monoclonal Gammopathies. *Blood*, **110**(11), 1497.  
<https://doi.org/10.1182/BLOOD.V110.11.1497.1497>
- Jenner, E. (2014). Serum free light chains in clinical laboratory diagnostics. *Clinica Chimica Acta*, Vol **427**, pp. 15–20.  
<https://doi.org/10.1016/j.cca.2013.08.018>
- Keren, D. F., Bocsi, G., & Ansari, M. Q. (2022). Laboratory Detection and Initial Diagnosis of Monoclonal gammopathies: Guidelines from the College of American Pathologists in Collaboration with the American Association for Clinical Chemistry and the American Society for Clinical Pathology. *Archives of Pathology and Laboratory Medicine*, **146**(5), 575–590. College of American Pathologists.  
<https://doi.org/10.5858/arpa.2020-0794-CP>
- Mohammad Zakerin Abedin, and Md. Ekhlas Uddin, (2020). Prevalence and in vitro antibiogram patterns of urinary tract pathogens in rural hospitals in Bangladesh, *Journal of Chemical, Biological and Physical Sciences*, **10**(3), 401-409.
- Mondol GC, Alam MG, and Uddin ME. (2018). Prevalence of Antibiotic Resistant *Staphylococcus aureus* Among Patients who come to Seek Treatment in a Hospital of Bangladesh. *Clinical Biotechnology and Microbiology*, **2**(5), 451- 455.  
<https://scientiaricerca.com/srcbmi/pdf/SRCBMI-02-00065.pdf>

O'Brien, T., Boughan, K. M., & Ansari, M. Q. (2023). M-Protein Analysis Test: Effects of Combining Serum Protein Electrophoresis and Free Light Chain Assay Tests into One Order. *Blood*, **142**(Supplement 1), 6759–6759. <https://doi.org/10.1182/blood-2023-190924>

Rajkumar, S. V. (2022). Multiple myeloma: 2022 update on diagnosis, risk stra-

tification, and management. *American J. of Hematology*, **97**(8), 1086–1107.

<https://doi.org/10.1002/ajh.26590>

Sebia. (2022). High-throughput serum protein electrophoresis, Accessed on October 22, 2025,

<https://www.sebia.com/tests/serum-protein-by-capillary-electrophoresis/>

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<https://doi.org/10.34104/10.34104/ejmhs.025.05870592>

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