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Diagnosis of Multiple Myeloma Through an Atypical Serum Protein Electrophoresis Profile: A Case Report

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Abstract

Multiple myeloma (MM) is usually suspected when serum protein electrophoresis (SPEP) shows a monoclonal peak. However, the electrophoretic pattern can sometimes be hard to interpret at very high protein concentrations.

We report the case of a 72-year-old man who presented with non-traumatic neural compression at the L1 level. He had marked hyperproteinemia (total protein 112 g/L), anemia, and rouleaux formation. Initial capillary SPEP showed a broadened, distorted gamma-globulin region without a clearly delineated monoclonal peak. The monoclonal component was reported as exceeding the quantification threshold (>33 g/L). After dilution, repeat analysis showed a prominent monoclonal peak quantified at 55 g/L, and immunofixation identified it as IgG lambda. Bone marrow examination showed 35% plasma cells. Together with anemia, this met the International Myeloma Working Group (IMWG) criteria for MM. The change in the profile after dilution suggests a concentration-related analytical or interpretive limitation, but this mechanism was not formally demonstrated. When an atypical SPEP profile occurs with marked hyperproteinemia and clinical suspicion of a plasma cell disorder, the analytical findings should be reviewed and the sample reanalyzed after appropriate dilution. Immunofixation and bone marrow examination provide complementary diagnostic evidence. Beyond diagnosis, an accurate baseline M-protein value is essential for later assessment of treatment response.

Categories: Hematology, Pathology, Internal Medicine
Keywords: bone marrow plasmacytosis, dilution, immunofixation, monoclonal spike, multiple myeloma, serum protein electrophoresis

Introduction

Multiple myeloma (MM) is a plasma cell malignancy characterized by clonal proliferation of plasma cells in the bone marrow and production of a monoclonal immunoglobulin or its fragments [1]. It accounts for approximately 10% of hematological malignancies, and its incidence and outcomes vary across populations [1-3]. Diagnosis integrates clinical, biological, radiological, and bone marrow findings according to the IMWG criteria [4].

Serum protein electrophoresis (SPEP) separates serum proteins into albumin, alpha-1, alpha-2, beta, and gamma fractions. A monoclonal immunoglobulin typically appears as a narrow, well-defined peak, most often in the gamma region, and the area of this peak is used to quantify the monoclonal protein (M-protein) [5]. Many laboratories now use capillary zone electrophoresis, which provides automated separation and a densitometric-like tracing [6]. However, interpretation still relies on visual review of the tracing. A very large monoclonal component can broaden or distort the gamma region and make peak integration difficult. In addition, electrophoretic M-protein quantification can become nonlinear at high immunoglobulin concentrations, as shown with agarose gel electrophoresis [7]. These observations cannot be directly extrapolated to capillary systems, but they support careful review of tracings that are discordant with the clinical picture.

When the initial tracing is difficult to interpret, repeat analysis after dilution may bring the sample into a range where the peak is better resolved and quantified, and immunofixation confirms the monoclonal nature of the protein and identifies its isotype [8,9].

We report a case of IgG lambda MM in which the initial capillary SPEP profile was atypical and became clearly interpretable only after sample dilution. This case illustrates the value of reviewing discordant electrophoretic results and the importance of accurate baseline M-protein measurement for subsequent

response assessment.

Case Presentation

A 72-year-old man with no significant past medical history was admitted for progressive, non-traumatic neural compression. He reported worsening back pain with progressive weakness of the lower limbs and gait impairment. There was no recent trauma, fever, or known malignancy.

Neurological examination showed progressive lower-limb weakness, sensory disturbance in the proximal lower limbs, and gait impairment. Sphincter involvement was suspected clinically but not confirmed. Medical Research Council (MRC) muscle strength grades, the dermatomal sensory level, deep tendon reflexes, and objective sphincter findings (anal tone, perineal sensation, and post-void residual volume) were not documented in the medical records available for this report. Spinal magnetic resonance imaging (MRI) showed vertebral collapse with compressive involvement at the L1 level, consistent with compression at the level of the conus medullaris. The MRI report available for this case did not specify the degree of vertebral height loss, the extent of any epidural soft-tissue component, or the presence or absence of intramedullary signal change.

Laboratory investigations

Initial laboratory tests showed marked hyperproteinemia and hypoalbuminemia, anemia, an elevated erythrocyte sedimentation rate, elevated serum creatinine, and rouleaux formation on the peripheral blood smear.

The leukocyte count was at the upper limit of the reference interval, with mild absolute lymphocytosis. Serum calcium was normal, including after correction for albumin. Using the 2021 CKD-EPI creatinine equation, the estimated glomerular filtration rate (eGFR) was approximately 43 mL/min/1.73 m^2. Results are summarized in Table *1*.

Parameter	Patient result	Unit	Reference interval/expected finding
Total serum protein	112	g/L	60-80
Serum albumin	28	g/L	35-50
Calculated globulins (total protein - albumin)	84	g/L	-
Hemoglobin	10	g/dL	13-17
Erythrocyte sedimentation rate, first hour	116	mm/h	≤20-30
Serum creatinine	149	µmol/L	60-110
eGFR (CKD-EPI 2021)	≈43	mL/min/1.73 m²	>90
Serum calcium	2.20	mmol/L	2.15-2.55
Albumin-corrected calcium	2.44	mmol/L	2.15-2.55
Leukocyte count	11,000	cells/µL	4,000-11,000
Absolute lymphocyte count	5,000	cells/µL	1,000-4,800
Serum IgG	>41.8 (above measuring range)	g/L	7-16
Serum IgA	0.59	g/L	0.7-4.0
Serum IgM	0.37	g/L	0.4-2.3
Monoclonal component, initial SPEP	>33 (above reported quantification threshold)	g/L	No monoclonal component expected
Monoclonal component, SPEP after dilution (dilution-corrected)	55	g/L	No monoclonal component expected
Serum immunofixation	Monoclonal IgG lambda	-	No monoclonal band expected
Bone marrow plasma cells	35	%	≤5
Peripheral blood smear	Rouleaux formation	-	Absent
Serum free light chains	Assay unavailable at diagnosis	-	-

TABLE 1: Laboratory findings at diagnosis

eGFR was calculated with the race-free CKD-EPI 2021 creatinine equation. Corrected calcium = measured calcium + 0.02 × (40 - albumin in g/L).

SPEP: serum protein electrophoresis; eGFR: estimated glomerular filtration rate

SPEP and dilution

SPEP was performed by capillary zone electrophoresis on the CAPILLARYS 3 OCTA system (Sebia, Lisses, France) [10]. The initial tracing showed marked broadening and distortion of the gamma-globulin region without a clearly delineated narrow monoclonal peak (Figure *1*).

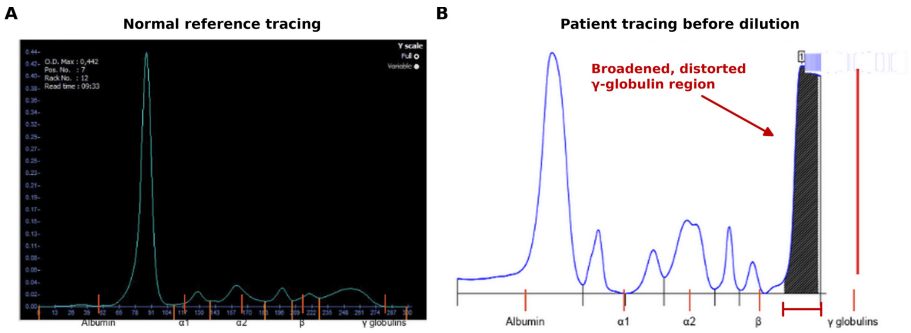


FIGURE 1: Serum protein electrophoresis before dilution

Capillary zone electrophoresis (CAPILLARYS 3 OCTA, Sebia). (A) Normal reference tracing: predominant albumin peak with smaller alpha-1, alpha-2, beta, and gamma fractions. (B) Patient tracing before dilution: broadened and distorted gamma-globulin region (arrow and bracket) without a clearly delineated narrow monoclonal peak. The monoclonal component was reported as exceeding the quantification threshold (>33 g/L).

The monoclonal component was reported as exceeding the quantification threshold (>33 g/L), which corresponds to the upper limit above which the analyser could not provide a precise numerical value on the undiluted sample. The atypical appearance of the tracing, combined with marked hyperproteinemia and strong clinical suspicion, raised concern for a concentration-related analytical or interpretive limitation and led to repeat analysis after dilution.

The sample was then re-analysed on the same CAPILLARYS 3 OCTA system using the analyser's automated 1:10 dilution function without manual pre-dilution. It showed a prominent, well-delineated monoclonal peak in the gamma region, quantified at 55 g/L after correction for the dilution factor (Figure *2*).

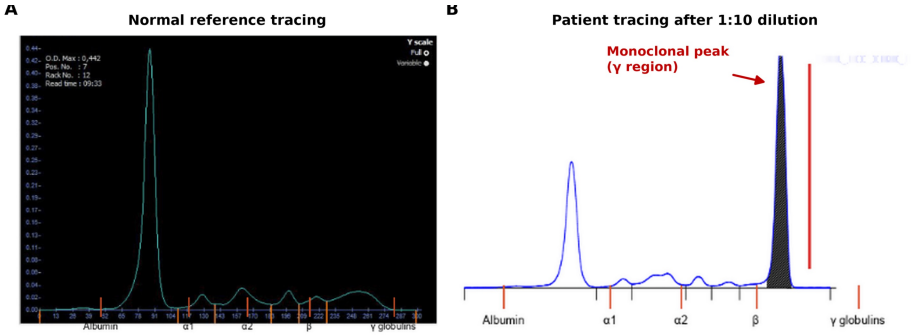


FIGURE 2: Serum protein electrophoresis after sample dilution

Capillary zone electrophoresis performed on the same system (CAPILLARYS 3 OCTA, Sebia). (A) Normal reference tracing. (B) Patient tracing after automated 1:10 dilution by the analyser: prominent, well-delineated monoclonal peak in the gamma-globulin region (arrow), quantified at 55 g/L after correction for the dilution factor.

These values are internally consistent. Calculated globulins were 84 g/L (total protein 112 g/L minus albumin 28 g/L), which can accommodate a 55 g/L monoclonal component plus the residual alpha, beta, and polyclonal gamma fractions. The IgG concentration (>41.8 g/L) was also above the measuring range of the immunoassay.

Immunofixation and bone marrow examination

Serum immunofixation electrophoresis showed a discrete band in the IgG and lambda lanes, consistent with a monoclonal IgG lambda protein (Figure *3*). IgA (0.59 g/L) and IgM (0.37 g/L) were reduced, consistent with immunoparesis. A serum free light chain assay was not available at diagnosis. Bone marrow cytology showed approximately 35% plasma cells.

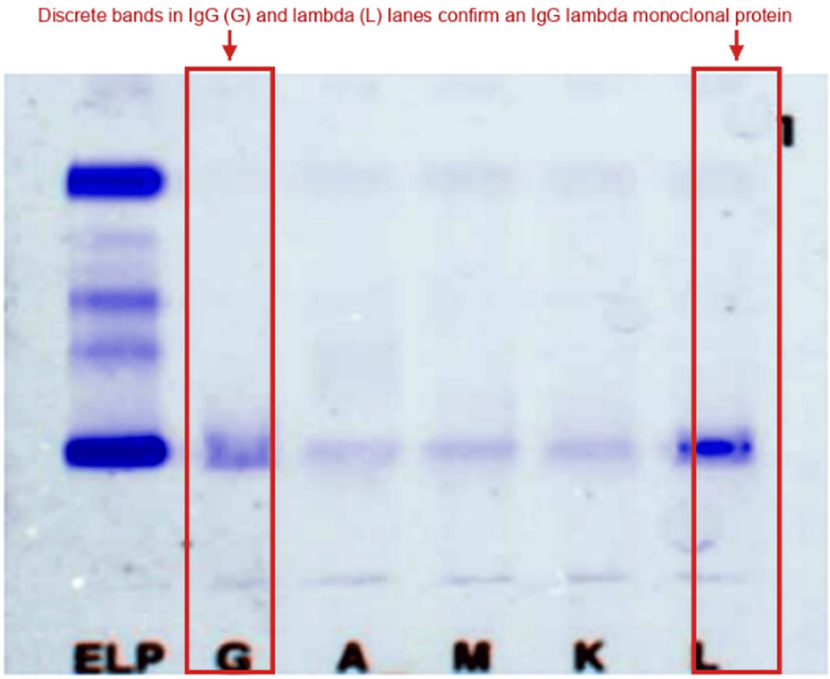


FIGURE 3: Serum immunofixation electrophoresis

Monoclonal bands in the IgG (G) and lambda (L) lanes identify a monoclonal IgG lambda protein. No corresponding band is seen in the IgA (A), IgM (M), or kappa (K) lanes.

ELP: reference serum protein electrophoresis lane; G: anti-IgG; A: anti-IgA; M: anti-IgM; K: anti-kappa light chain; L: anti-lambda light chain.

Application of the IMWG diagnostic criteria

The IMWG definition of MM requires clonal bone marrow plasma cells ⩾10% (or a biopsy-proven plasmacytoma) plus at least one myeloma-defining event [4]. In this patient, clonal bone marrow plasma cells accounted for 35%, which meets the ⩾10% requirement. Clonality was supported by the monoclonal IgG lambda protein. The anemia criterion was met, as hemoglobin was 10 g/dL, which was 3 g/dL below the lower reference limit of 13 g/dL. The IMWG threshold is more than 2 g/dL below the lower limit of normal or <10 g/dL. The renal insufficiency criterion was not met, as serum creatinine was 149 µmol/L (threshold >177 µmol/L) and eGFR was approximately 43 mL/min/1.73 m² (threshold creatinine clearance <40 mL/min). Although mild renal impairment was present, it did not reach the IMWG criterion. The hypercalcemia criterion was not met, as albumin-corrected calcium was 2.44 mmol/L. Regarding bone disease, MRI showed vertebral collapse with compression at L1. The IMWG bone criterion requires one or more osteolytic lesions on skeletal radiography, CT, or PET-CT, and vertebral collapse alone is not specific. The diagnosis was therefore not based on the bone criterion. Biomarkers of malignancy could not be fully assessed. Bone marrow plasma cells were <60%, serum free light chains were unavailable, and MRI focal lesions were not enumerated. The diagnosis of IgG lambda MM therefore met IMWG criteria based on 35% clonal bone marrow plasma cells and anemia attributable to the plasma cell disorder.

Differential diagnosis

Non-traumatic compression at the thoracolumbar junction in an older adult raises several possibilities: vertebral metastasis, lymphoma, infectious spondylodiscitis, and plasma cell neoplasms. The diagnosis of MM rested on positive findings: marked hyperproteinemia with rouleaux formation, a monoclonal IgG lambda protein on immunofixation, immunoparesis, and 35% bone marrow plasma cells with anemia.

The absence of fever does not by itself exclude vertebral infection. A monoclonal gammopathy can also coexist with another cause of spinal compression. Within the information available for this report, no alternative diagnosis was formally confirmed or excluded by dedicated microbiological or histopathological investigation of the vertebral lesion. We therefore present the vertebral involvement as consistent with, but not histologically proven to be, myeloma bone disease.

Treatment, outcome, and follow-up

After diagnosis, the patient was transferred to the Internal Medicine Department. Anti-myeloma

chemotherapy was started according to the institutional protocol, together with supportive care and clinical and biological monitoring. The laboratory records used for this report did not include the specific regimen, the interval between diagnosis and treatment, the urgent management of the neural compression, or the exact duration of follow-up. Clinical follow-up showed stabilization after treatment began. At the time of manuscript preparation, the patient was alive and under regular clinical and laboratory follow-up.

Discussion

SPEP remains a cornerstone of the evaluation of monoclonal gammopathies. In most patients, it shows a narrow monoclonal peak that can be detected and quantified [5]. This case shows that, at very high protein concentrations, the capillary electrophoresis tracing can look atypical, and the M-protein may be reported only as above a quantification threshold.

In this patient, the initial tracing showed a broadened, distorted gamma region without a clearly delineated peak, and the M-protein was reported as >33 g/L. After dilution, a well-delineated peak was quantified at 55 g/L. This concentration-dependent change is consistent with an analytical or interpretive limitation at high protein concentration. Several explanations are possible: the tracing exceeded the optimal analytical response range at this protein load, the high concentration of monoclonal IgG distorted the gamma region, the software had difficulty integrating a very large, broad peak, or a combination of these factors.

We could not distinguish between these explanations. No instrument-specific analytical study was performed, and our data do not demonstrate a saturation mechanism. Murray et al. showed nonlinearity of M-protein quantification at high IgG concentrations with agarose gel electrophoresis [7]. Because the separation and detection principles differ, those findings cannot validate a specific mechanism or threshold on the CAPILLARYS 3 OCTA system [6,10]. We therefore describe a suspected concentration-related artefact, not a demonstrated saturation effect.

The diagnosis of MM was unlikely to have been missed in this patient. The clinical presentation, hyperproteinemia, rouleaux, immunofixation, and bone marrow findings all pointed to a plasma cell neoplasm, and other diagnostic tests were available. In our view, the main practical consequence of this pitfall is the quantification of the M-protein. The IMWG response criteria are based on the relative reduction in serum M-protein from baseline: at least 50% for partial response and at least 90% for very good partial response [11]. A baseline reported only as ">33 g/L" substantially underestimates the true concentration (55 g/L) and cannot serve as a reliable reference.

As a hypothetical example (not observed in this patient), a post-treatment value of 20 g/L would be a 64% reduction from 55 g/L (partial response). Compared with 33 g/L, it would be only a 39% reduction, which does not reach partial response. An accurate, dilution-corrected baseline is therefore essential for monitoring response, disease burden, and progression with serial measurements [5,7,11].

The novelty of this case is modest but practically relevant. It documents, on a capillary electrophoresis platform, an atypical gamma-region profile with an M-protein above the quantification threshold that became interpretable and quantifiable after dilution in a patient with marked hyperproteinemia and a myeloma-related neurological emergency. Diluting samples whose results exceed the measuring range is routine practice for many analytes. Our observation does not imply that dilution is required in every case or that dilution is the only explanation for an atypical gamma-region profile. Rather, the case supports a simple laboratory rule. When total protein is markedly elevated, or the M-protein exceeds the quantification threshold, the tracing should be reviewed and the sample re-analysed after appropriate dilution. When SPEP and the clinical picture are discordant, the laboratory should review the result and perform complementary testing rather than accept a non-diagnostic tracing.

Immunofixation confirms and characterizes a suspected M-protein, and published diagnostic algorithms combine SPEP, immunofixation, and serum free light chain testing [8,9]. In this case, immunofixation identified an IgG lambda protein, and bone marrow examination showed 35% plasma cells.

This report has several limitations. Serum free light chains were unavailable. The mechanism of the atypical initial tracing was not investigated experimentally. The MRI characterization of the vertebral lesion was limited, and the lesion was not confirmed histologically. The specific treatment regimen, the emergency management of the neural compression, and the duration of follow-up were not available in the records used for this report. In resource-limited settings, access to complementary investigations and formal dilution protocols may vary. Bone marrow clonality was inferred from the serum monoclonal IgG lambda protein. Light-chain restriction of bone marrow plasma cells was not assessed by flow cytometry or immunohistochemistry, and cytogenetic/FISH studies were not performed. Staging and prognostic markers (serum beta-2 microglobulin and lactate dehydrogenase) were not available in the records used for this report, so ISS and R-ISS stage could not be determined.

Conclusions

An atypical or apparently non-diagnostic SPEP profile should be interpreted together with the clinical

presentation, other laboratory findings, and confirmatory investigations. In a patient with marked hyperproteinemia and suspected plasma cell disorder, such a profile should prompt review of the tracing and repeat analysis after appropriate dilution. In this case, dilution made the monoclonal component interpretable and allowed it to be quantified. The underlying analytical mechanism, however, remains suspected rather than proven, and the diagnosis rested on immunofixation, bone marrow examination, and the IMWG criteria. An accurate, dilution-corrected baseline M-protein value is essential for later assessment of treatment response. Because the treatment regimen and follow-up M-protein values were not available, this consequence for response assessment was not observed in this patient and remains hypothetical.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Acquisition, analysis, or interpretation of data: Boutayna El Rhaffouli, Hicham Ez-zaidi, Dounia El Moujtahide, Elhoucine Sebbar, Mohammed Choukri

Drafting of the manuscript: Boutayna El Rhaffouli, Hicham Ez-zaidi, Dounia El Moujtahide, Elhoucine Sebbar, Mohammed Choukri

Critical review of the manuscript for important intellectual content: Boutayna El Rhaffouli, Hicham Ez-zaidi, Dounia El Moujtahide, Elhoucine Sebbar, Mohammed Choukri

Supervision: Dounia El Moujtahide, Elhoucine Sebbar, Mohammed Choukri

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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