LETTER TO THE EDITOR

Evaluation and characterization of monoclonal gammopathies using serum protein electrophoresis in a major urban population: one institution's experience

Introduction

Serum protein electrophoresis (SPEP) with serum protein immunofixation electrophoresis (SPIFE) are clinical laboratory techniques used to identify, evaluate and monitor a wide range of disease states where abnormal serum protein levels are observed.[1] Such disorders include solid tumors, lymphoproliferative disorders (eg, multiple myeloma (MM), monoclonal gammopathy of undetermined significance (MGUS), Waldenström macroglobulinemia, primary amyloidosis, chronic lymphocytic leukemia, lymphoma), acute and chronic infections, trauma, connective tissue diseases, and liver disorders.[2] Clinical indications for ordering SPEPs are varied: suspected lymphoproliferative disorders; unexplained back pain, anemia, weakness or fatigue; osteolytic lesions; unexplained renal insufficiency; hypercalcemia; unexplained peripheral neuropathy; elevated erythrocyte sedimentation rate; and recurrent infections.[2]

Changes observed in SPEPs follow predictable patterns guiding clinicians toward correct interpretation and diagnosis. Polyclonal gammaglobulin protein elevation typically results from reactive, inflammatory or infectious processes. Monoclonal gammaglobulin protein elevation (monoclonal gammopathy; MG) is typified by a sharp band or monoclonal spike (M-component) confined to the gammaglobulin region of the electrophoretogram; however, MG proteins can also be observed within α-1, α-2 and β-globulin regions.[1 2] These monoclonal bands result from a single abnormal plasma cell or B lymphocyte clone, which could be from a malignant (MM, Waldenström macroglobulinemia) or premalignant process (MGUS).[1 2] Initial SPEP evaluation is typically performed in conjunction with SPIFE to identify and confirm monoclonality, and determine the M-component immunoglobulin heavy and light chain class.

Several large studies looked at the characteristics and prevalence of patients with MG; however, the patients were primarily Caucasian and Asian.[3–5] Since our institution primarily serves black patients with Afro-Caribbean descent, and in light of recent evidence suggesting significant racial differences that MG affects blacks disproportionately more than Caucasians, we attempted to look at MG characteristics in our homogeneous patient population.[6–10] The aforementioned studies had more stringent inclusion/exclusion criteria, while this study is unique as it provides a cross-sectional analysis with inclusion criteria being that patients must have received an SPEP and are ≥18 years old.[6 8] Little data exist describing MG in Afro-Caribbean patients; thus, we aim to delineate the characteristics of patients receiving SPEP from our institution, and investigate whether a clonal proliferation or malignancy can be identified or excluded.

Materials and methods

Following institutional review board approval (#1005174–1), we performed a cross-sectional, retrospective review and analysis of medical records for 50 consecutive patients who were ≥18 years old who had SPEP and SPIFE studies performed during July 2015. Data included SPEP result pattern and interpretation, monoclonal immunoglobulin isotype, light chain immunoglobulin, clinical diagnoses, age and gender. SPEP and SPIFE analyses were performed using a Helena SPIFE® 3000 instrument utilizing agarose-gel five-band SPE assay and agarose-gel QuickGel Immuno-Fix assay, respectively (Helena Laboratories, Beaumont, Texas, USA). Univariate analysis was used to describe patient demographics. Patients were divided into groups based on whether or not their SPEP exhibited a monoclonal band. Parametric analysis (two-sample t-test) for normally distributed continuous variables was performed with Microsoft Excel (Microsoft, Redmond, Washington, USA) when comparing MG group with non-MG group.

Results

Patient ages ranged from 18 to 86 years (mean 61.8±17.7 years) and the male-to-female ratio was 1:3.5. SPEP patterns (table 1) identified that 1 (2%) patient had acute inflammation, 3 (6%) had chronic inflammation, 16 (32%) had monoclonal bands, 24 (48%) were non-diagnostic patterns, 3 (6%) had normal results and 3 (6%) had polyclonal bands. Of the patients with a monoclonal band, SPIFE identified IgG as the most common isotype (75%) and κ most common light chain (58%); IgG κ was most common (44%), consistent with literature values (table 2).[4] Abnormal serum free light chain (sFLC) ratios were identified in 13 patients (81%) within the MG group. Monoclonal IgA was seen in two patients: IgA κ and IgA λ. Monoclonal IgM was seen in two patients, consistent with Waldenström macroglobulinemia. For patients exhibiting a monoclonal band, the mean age was 68.7 years; for patients without a monoclonal band, the mean age was 58.2 years (p=0.013). Two patients without a monoclonal band exhibited abnormal sFLC ratios on SPIFE: one with κ-restricted pattern, the other with λ-restricted pattern.

MM was identified in 9 (18%) patients: eight (89%) had normal total protein levels and one (11%) showed increased total protein levels. A clinical diagnosis of

Table 1 Patient mean age and gender with corresponding serum protein electrophoresis pattern result

	Acute inflammation	Chronic inflammation	Monoclonal	Non-diagnostic	Normal	Polyclonal
Patients, n (%)	1 (2)	3 (6)	16 (32)	24 (48)	3 (6)	3 (6)
Age, mean (years)	37.0	47.7	68.7	59.1	69.0	58.0
Gender (male:female)	0:1	1:2	1:4.3	1:3	0:1	1:2

Table 2 Monoclonal isotype and light chain immunoglobulins (serum protein immunofixation electrophoresis)

Ig type	Patients, n (%)	κ, n (%)	λ, n (%)
IgG	12 (75)	7 (58)	5 (31)
IgA	2 (33)	1 (6)	1 (6)
IgM	2 (33)	1 (6)	1 (6)

neuropathy was seen in 7 (14%) patients: five (71%) exhibited a polyclonal gammaglobulin increase and one (14%) case with a co-HIV infection showed a monoclonal IgG κ spike. Seven (14%) patients had chronic kidney disease, four (8%) had HIV/AIDS, three (6%) had anemia, three (6%) had MGUS, one (2%) had systemic lupus erythematosus and the remaining sixteen (32%) had other comorbidities (ie, hypertension, diabetes mellitus, coronary artery disease).

Discussion

We have looked at the characteristics of 50 consecutive patients who were screened for a diverse set of disorders using SPEP and SPIFE. Various disease states were observed, suggesting the wide application that SPEP studies are used at our institution. Since it is well known that MG disproportionately affects blacks more than Caucasians and Asians, we looked at SPEP/SPIFE characteristics within our unique, homogeneous Afro-Caribbean patient population, where little data exist.

With patients exhibiting a monoclonal band, IgG was the most common isotype (75%); κ was the most common light chain (58%). On average, patients with MG were 10.5 years older than patients without MG. This finding is consistent with the literature—as MG incidence rapidly increases with age[6]—however, absolute age difference is not clearly defined. Additionally, female tended to be affected more than male (M:F, 1:4.3), a finding discordant with the literature and warrants further investigation.[10]

Limitations include its small sample size, the nature of retrospective analysis and homogeneous patient population. Since SPEP orders did not discriminate between patients with a known history of a lymphoproliferative disorder who were being monitored for relapse and/or treatment response compared with a patient initially being evaluated for an immunoproliferative disorder, the results positively favor a higher observed MG incidence rate (32%) than reported in the literature for blacks (8.4%) and Caucasians (0.5%–3.8%).[4 6] However, when isolating only the newly diagnosed MG cases, three patients (6%) were identified, which is similar to reported rates seen in other black populations. Further study should increase the number of patients and clinical outcome follow-up, and interrogate significance of female predominance.

Derek B Laskar,[1] Khurram Shafique,[1] Chuanyong Lu,[2] Alejandro Zuretti[1]

[1]Department of Pathology, SUNY Downstate Medical Center, Brooklyn, New York, USA
[2]Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, USA

Correspondence to
Dr Derek B Laskar, Department of Pathology, State of New York Downstate Medical Center, 450 Clarkson Avenue, MSC 25, Brooklyn, NY 11203, USA;
Derek.Laskar@downstate.edu

Contributors DBL contributed to study design, data collection, data analysis and interpretation and manuscript review. CL contributed to data analysis and interpretation and manuscript review. AZ contributed to study design and manuscript review.

Competing interests None declared.

Ethics approval SUNY Downstate Medical Center Institutional Review Board (#1005174-1).

Provenance and peer review Not commissioned; externally peer reviewed.

To cite Laskar DB, Shafique K, Lu C, *et al*. *J Investig Med* Published Online First: [*please include* Day Month Year]. doi:10.1136/jim-2017-000446

Accepted 29 July 2017

J Investig Med 2017;**0**:1–2. doi:10.1136/jim-2017-000446

REFERENCES

1 Attaelmannan M, Levinson SS. Understanding and identifying monoclonal gammopathies. *Clin Chem* 2000;46:1230–8.
2 O'Connell TX, Horita TJ, Kasravi B. Understanding and interpreting serum protein electrophoresis. *Am Fam Physician* 2005;71:105–12.
3 Iwanaga M, Tagawa M, Tsukasaki K, *et al*. Prevalence of monoclonal gammopathy of undetermined significance: study of 52,802 persons in Nagasaki City, Japan. *Mayo Clin Proc* 2007;82:1474–9.
4 Kyle RA, Therneau TM, Rajkumar SV, *et al*. Prevalence of monoclonal gammopathy of undetermined significance. *N Engl J Med* 2006;354:1362–9.
5 Park HK, Lee KR, Kim YJ, *et al*. Prevalence of monoclonal gammopathy of undetermined significance in an elderly urban Korean population. *Am J Hematol* 2011;86:752–5.
6 Cohen HJ, Crawford J, Rao MK, *et al*. Racial differences in the prevalence of monoclonal gammopathy in a community-based sample of the elderly. *Am J Med* 1998;104:439–44.
7 Brown LM, Gridley G, Check D, *et al*. Risk of multiple myeloma and monoclonal gammopathy of undetermined significance among white and black male United States veterans with prior autoimmune, infectious, inflammatory, and allergic disorders. *Blood* 2008;111:3388–94.
8 Landgren O, Gridley G, Turesson I, *et al*. Risk of monoclonal gammopathy of undetermined significance (MGUS) and subsequent multiple myeloma among African American and white veterans in the United States. *Blood* 2006;107:904–6.
9 Landgren O, Weiss BM. Patterns of monoclonal gammopathy of undetermined significance and multiple myeloma in various ethnic/racial groups: support for genetic factors in pathogenesis. *Leukemia* 2009;23:1691–7.
10 Landgren O, Graubard BI, Katzmann JA, *et al*. Racial disparities in the prevalence of monoclonal gammopathies: a population-based study of 12,482 persons from the National Health and Nutritional Examination Survey. *Leukemia* 2014;28:1537–42.