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Evaluation of immunofixation electrophoresis data of Ankara Etlik City Hospital

Ankara Etlik Şehir Hastanesi immünfiksasyon elektroforezi verilerinin değerlendirilmesi

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ABSTRACT

Objective: Monoclonal gammopathy is the abnormal proliferation of a single clone of B cell lineages, producing monoclonal immunoglobulin (M-protein). Serum protein electrophoresis (SPE) and immunofixation electrophoresis (IFE) are commonly used to detect M-protein. IFE is mainly used to detect M-protein types and clonality. The results of urine and serum immunofixation electrophoresis (IFE) tests performed in the laboratory of our newly established hospital were retrospectively evaluated.

Methods: The study included 962 serum immunofixation electrophoresis results analyzed with Hydrasis 2 (Sebia, France) between November 1, 2022, and May 1, 2023, in our laboratory. In addition, the results of 51 samples from patients who had paraprotein bands in serum immunofixation electrophoresis and who requested urine immunofixation electrophoresis were included.

Results: Paraprotein band was detected in 220 (22.9%) of 962 serum immunofixation electrophoresis results. A paraprotein band was detected in

ÖZET

Amaç: Monoklonal gammopati, monoklonal immünoglobulin (M-protein) üreten tek bir B hücre klonunun anormal çoğalmasıdır. Serum protein elektroforezi (SPE) ve immünofiksasyon elektroforezi (IFE) M-proteinini tespit etmek için yaygın olarak kullanılır. IFE esas olarak, M-protein tiplerini ve klonaliteyi tespit etmek için kullanılır. Yeni kurulan hastanemizin laboratuvarında analiz edilmiş idrar ve serum IFE testlerinin sonuçları retrospektif olarak değerlendirilmiştir.

Yöntem: Çalışmaya laboratuvarımızda 1 Kasım 2022 ile 1 Mayıs 2023 tarihleri arasında Hydrasis 2 (Sebia, Fransa) ile analiz edilen 962 serum immünfiksasyon elektroforezi sonucu dahil edilmiştir. Ayrıca, serum immünfiksasyon elektroforezinde paraprotein bantları olan ve idrar immünfiksasyon elektroforezi istenen hastalardan alınan 51 örneğin sonuçları da dahil edilmiştir.

Bulgular: Toplam 962 serum immünfiksasyon elektroforezi sonucunun 220 (%22,9)'sinde paraprotein bandı tespit edilmiştir. Serum immünfiksasyon

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the urine immunofixation electrophoresis of 18 (34.6%) of 52 patients with paraprotein bands in serum immunofixation electrophoresis. In serum immunofixation electrophoresis, IgG kappa monoclonal band in 66 (30%) patients, IgG lambda monoclonal band in 50 (22.7%) patients, IgA kappa monoclonal band in 19 (8.6%) patients, IgA lambda monoclonal band in 14 (6.4%) patients, free light chain band in 22 (%10) patients were detected.

Conclusion: We detected IgG kappa as the most common paraprotein band and IgG lambda as the second most common paraprotein band. Our study provided an opportunity to predict the frequency and type of monoclonal gammopathy detected in our newly established hospital laboratory and to compare it with literature data. Moreover, the data obtained in the study has enabled opportunities for comparison with hospital laboratories to be established in the future.

Key Words: Monoclonal gammopathy, immunofixation electrophoresis, plasma cell dyscrasias, paraproteinaemias

elektroforezinde paraprotein bandı saptanan 52 hastanın 18 (%34,6)'inin idrar immünfiksasyon elektroforezinde paraprotein bandı saptanmıştır. Serum immünfiksasyon elektroforezinde 66 (%30) hastada IgG kappa monoklonal bant, 50 (%22,7) hastada IgG lambda monoklonal bant, 19 (%8,6) hastada IgA kappa monoklonal bant, 14 (%6,4) hastada IgA lambda monoklonal bant, 22 (%10) hastada serbest hafif zincir bandı tespit edilmiştir.

Sonuç: En sık görülen paraprotein bandı olarak IgG kappa ve ikinci en sık görülen paraprotein bandı olarak IgG lambda tespit ettik. Çalışmamız, yeni kurulan hastane laboratuvarımızda tespit edilen monoklonal gammopati sıklığını ve tipini tahmin etme ve literatür verileri ile karşılaştırma imkanı vermiştir. Ayrıca, çalışmada elde edilen veriler, gelecekte kurulacak hastane laboratuvarları ile karşılaştırma yapılmasına olanak sağlamıştır.

Anahtar Kelimeler: Monoklonal gammopati, immünfiksasyon elektroforezi, plazma hücre diskrazileri, paraproteinemiler

INTRODUCTION

A monoclonal gammopathy is defined as the electrophoretically and antigenically homogeneous monoclonal protein production (M-protein, paraprotein) of a single clone of B lymphocytes and/or plasma cells that has proliferated beyond the limits of normal control mechanisms (1). Monoclonal gammopathy-associated disorders can be divided into several categories, including plasma cell dyscrasias (such as multiple myeloma, smoldering multiple myeloma, and monoclonal gammopathy of undetermined significance), B-cell lymphoproliferative disorders (such as non-Hodgkin's lymphoma, chronic lymphocytic leukemia, and Waldenstrom's macroglobulinemia), connective tissue disorders (such as rheumatoid arthritis and systemic lupus erythematosus), infections (such as hepatitis C and HIV), dermatological disorders (such as diffuse plane xanthomatosis and subcorneal pustular dermatosis), renal disorders (such as anti-glomerular basement membrane disease and dense deposit disease), neurological disorders (such as sporadic late-onset nemaline myopathy and corneal copper deposition), and other disorders (such as cryoglobulinemia, capillary leak syndrome, and cold agglutinin disease) (2).

Serum protein electrophoresis (SPE) and immunofixation electrophoresis (IFE) are commonly used to detect M-protein (3). While SPE is a relatively inexpensive and straightforward method for detecting M-protein, it has some limitations in detecting low

levels of M-protein or other abnormalities that are difficult to separate from normal protein bands (4). In such cases, additional tests such as IFE and serum free light chain assay may be required to confirm the presence of abnormal proteins. IFE is a laboratory technique that uses electrophoresis and immunoprecipitation methods to separate and identify proteins in a patient's blood or urine sample. It provides greater sensitivity and specificity, higher resolution, and the ability to detect low levels of target proteins compared to traditional electrophoresis (5).

In this study, we evaluated the results of urine and serum IFE tests performed in our newly established hospital laboratory retrospectively. Our objectives were to determine the number of patients with paraprotein bands detected in serum and urine IFE test results, the types of paraprotein bands detected, and whether patients with or without paraprotein bands had a history of plasma cell dyscrasia or a de novo diagnosis.

MATERIAL and METHOD

We included 962 serum immunofixation electrophoresis results that were analyzed in our Ankara Etlik City Hospital laboratory between 01/11/2022 and 01/05/2023. In addition, 51 specimen results from patients who had positive bands on serum immunofixation electrophoresis and were requested to undergo urine immunofixation electrophoresis were included. Initial results from patients with more than one IFE result were included. All samples were analyzed in our laboratory using the Hydrasys 2 analyser (Sebia, France). Final diagnoses of patients were reviewed. Patients' clinical diagnoses and investigations were obtained from our hospital's hospital information management system. All percentages in the study are given at 95% confidence interval (CI). All calculations were made from the website (https://www.openepi.com/Proportion/Proportion.htm).

The study was approved by the Etlik City Hospital Clinical Research Ethics Committee (Date: 17.05.2023 and Number: AEŞH-EK1-2023-155).

RESULTS

The mean age of patients included in the study was 62.3 years. 498 were female, and 464 were male of the 962 patients included in the study.

Paraprotein band was detected in 220 (22.9% [95%CI: 20.3%-25.6%]) of 962 serum IFE results. A paraprotein band was detected in the urine IFE of 18 of 52 (34.6% [95%CI: 22.7%-48.2%]) patients with paraprotein band in serum IFE.

In serum IFE, IgG kappa monoclonal band in 66 (30.0% [95%CI: 24.2%-36.3%]) patients, IgG lambda monoclonal band in 50 (22.7% [95%CI: 17.6%-28.6%]) patients, IgA kappa monoclonal band in 19 (8.6% [95%CI: 5.4%-12.9%]) patients, IgA lambda monoclonal band in 14 (6.4% [95%CI: 3.7%-10.2%]) patients, free light chain band in 22 (10.0% [95%CI: 6.5%-14.5%]) patients were detected (Table 1). Among the the types of monoclonal bands detected in urine IFE, kappa free light chain bands were detected in seven (38.9% [95%CI: 18.9%-62.3%]) patients, lambda free light chain bands were detected in six (33.3% [95%CI: 14.8%-56.9%]) patients, and heavy + light chain monoclonal bands were detected in five (27.8% [95%CI: 11.0%-51.3%]) patients. Of the patients with paraprotein bands detected in serum IFE, 65.9% (95%CI: 59.5%-72.0%) were previously diagnosed or newly diagnosed with plasma cell dyscrasias. Of the patients with bands not detected in serum IFE, 11.3% (95%CI: 9.2%-13.8%) were previously diagnosed or newly diagnosed with plasma cell dyscrasia.

DISCUSSION

An abnormal amount of M-protein production characterizes monoclonal gammopathies. The M-protein produced can cause many serious complications. These M protein-related complications can take the form of nephropathy and neuropathy (6,7). Nephropathy can result from tubular

Table 1. Paraproteinemia types detected by serum immunofixation electrophoresis

Paraprotein type	Number	Percentage (%)
IgG-Kappa	66	30.0% (95%CI: 24.2%-36.3%)
IgG-Lambda	50	22.7% (95%CI: 17.6%-28.6%)
IgA-Kappa	19	8.6% (95%CI: 5.4%-12.9%)
IgA-Lambda	14	6.4% (95%CI: 3.7%-10.2%)
IgM-Kappa	12	5.5% (95%CI: 3.0%-9.1%)
IgM-Lambda	8	3.6% (95%CI: 1.7%-6.8%)
Biclonal IgG-Kappa	7	3.2% (95%CI: 1.4%-6.2%)
Biclonal IgG-Lambda	2	0.9% (95%CI: 0.2%-3.0%)
IgG-Kappa + Free light chain	7	3.2% (95%CI: 1.4%-6.2%)
IgG-Lambda + Free light chain	3	1.4% (95%CI: 0.4%-3.7%)
Biclonal IgA-Lambda	3	1.4% (95%CI: 0.4%-3.7%)
Biclonal IgG-Kappa + IgG-Lambda	3	1.4% (95%CI: 0.4%-3.7%)
Biclonal IgM-Kappa	2	0.9% (95%CI: 0.2%-3.0%)
IgM-Kappa + Free light chain	2	0.9% (95%CI: 0.2%-3.0%)
Free light chain	22 (16 lambda, 6 kappa)	10.0% (95%CI: 6.5%-14.5%)

Table showing serum IFE results. The most common type of paraprotein was IgG kappa, and the second most common type was IgG lambda. All percentages are presented with 95% confidence intervals.

dysfunction caused by M-proteins accumulation in the renal tubules (7). IFE is used to evaluate paraproteinemia diagnosis and follow-up and monitor paraproteinemia-related complications. Plasma cell dyscrasias are among the causes of monoclonal gammopathy. IFE is used for the diagnosis and treatment monitoring of plasma cell dyscrasias and is the gold standard diagnostic method for determining M protein type and clonality. Determination of M-protein type is essential for assessing prognosis and treatment options in multiple myeloma (MM). IgD-secreting MM has a worse prognosis than other MM subtypes (8). In our study, we evaluated the results of IFE analyzed in our newly established hospital laboratory from the start of analyses until May 2023.

We detected paraprotein bands in 220 of 962 serum IFE results included in the study. The most common type of paraprotein was IgG kappa, and the second most common type was IgG lambda. In a retrospective study by Dikker et al. evaluating 403 serum IFE results, the paraprotein band detection rate was, similar to our study. Furthermore, similar to our data, IgG kappa and IgG lambda were the most frequently detected paraprotein bands. In addition, paraprotein bands were detected in the urine IFE of 22.2% (95%CI: 20.4%-24.6%) of patients in whom paraprotein bands were detected in the serum IFE and urine IFE were requested (9). In a retrospective study by Ercan et al. evaluating 688 serum IFE results, the rate of paraprotein band detection was 17.9% (95%CI: 15.1%-20.9%). The most common paraprotein types detected were IgG kappa and IgG lambda. Our detection rate of both paraprotein bands was relatively low compared to the study by Ercan et al. This may be because the detection rates of the biclonal IgG kappa and IgG lambda paraprotein bands

detected in our study were reported under a separate heading (10). In a retrospective study by Civil et al. evaluating the serum IFE results of 6767 patients, the paraprotein band's detection rate was 21.4% (95%CI: 20.4%-22.4%). According to their data, the most common paraprotein bands detected were IgG kappa (29.5% [95%CI: 27.2%-31.9%]) and IgG lambda (12.7% [95%CI: 11.1%-14.5%]). In addition, paraprotein bands were detected in 27 (55.1% [95%CI: 41.1%-68.5%]) of 49 patients in whom paraprotein bands were detected in serum IFE and urine IFE were requested. In our study, this rate was 34.6% (95%CI: 22.7%-48.2%). When evaluating both the study by Civil et al. and our study, it is noteworthy that the rate of urine IFE request is low in patients with band positivity in serum IFE. This may explain the difference in the detection rates of paraprotein bands in urine IFE, as insufficient samples may have influenced the results (11). In general, IgG kappa is detected with the highest frequency and IgG lambda with the second highest frequency in the detection frequency of paraprotein band types, as our data, and also found in studies performed by retrospective evaluation of serum IFE results. One of the reasons for this situation may be that IgG immunoglobulin comes first when serum immunoglobulin levels are assessed. Another reason is that the most significant cause of monoclonal gammopathy is plasma cell dyscrasia. IgG subtypes are detected proportionally more often in M-protein typing in monoclonal gammopathy undetermined significance and multiple myeloma patients (12, 13). We found that 11.3% (95%CI: 9.2%-13.8%) of patients in whom we could not detect bands in serum IFE had a plasma cell dyscrasia diagnosis, which may be due to two reasons. Firstly, we did not differentiate between newly diagnosed and previously diagnosed patients and included patients in remission. The second reason may be due to non-secretory MM patients. Non-secretory MM has an incidence of 1-5% of all myelomas. These cases are characterized by the absence of M protein on SPE and serum IFE. Free light chain assays are more sensitive in non-secretory MM cases than SPE (14). We also found that 65.9% (95%CI: 59.5%-72.0%) of patients in whom we detected bands in serum IFE were diagnosed with plasma cell dyscrasia. Monoclonal gammopathy-related diseases other than the plasma cell dyscrasias mentioned in the introduction may have caused the remainder.

In laboratory applications, it is crucial to conduct verification and validation studies prior to the utilisation of new analyzers. Furthermore, it is essential to monitor the outcomes subsequent to the implementation of the analyzer. Our findings revealed that our results were consistent with the literature data, which provides reassurance regarding the reliability of a newly installed analyzer. We propose that every hospital laboratory should regularly monitor the results following the installation of a new electrophoresis device.

In conclusion, our study provided an opportunity to predict the frequency and type of monoclonal gammopathy detected in our newly established hospital laboratory and to compare it with literature data. It also contributed data to the literature.

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ETHICS COMMITTEE APPROVAL

* The study was approved by the Etlik City Hospital Clinical Research Ethics Committee (Date: 17.05.2023 and Number: AEŞH-EK1-2023-155).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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