Clinical Biochemistry 51 (2018) 48–55

Contents lists available at ScienceDirect

Clinical Biochemistry

journal homepage: www.elsevier.com/locate/clinbiochem

Review

Peaks and tails: Evaluation of irregularities in capillary serum protein electrophoresis

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ARTICLE INFO

Keywords:
Serum electrophoresis
Capillary electrophoresis
Irregularities
Monoclonal components
Monoclonal proteins

ABSTRACT

The increased analytical sensitivity of capillary electrophoresis detects additional irregularities that are suspicious for a monoclonal component. This is most noticeable in the beta-1-, beta-2- and gamma-globulin fractions. The causes of non-monoclonal irregularities are manifold, but are rarely reported back to the ordering physician. This article reviews the basic concepts to correctly identify irregularities, monoclonal and oligoclonal peaks by capillary electrophoresis. It then focuses on detecting and reporting typical non-monoclonal irregularities according to their electrophoresis fractions as well as their possible clinical implications.

1. Introduction

Protein electrophoresis provides information about the protein status of components that are present in large quantities, i.e. the g/L range in the human body. An altered relationship of these proteins provides surprisingly detailed disease information, for instance acute or chronic inflammation, antibody deficiency, protein synthesis/loss or nutritional status. The most common application today is, however, the detection of monoclonal components, i.e. immunoglobulins which are caused by the abnormal proliferation of plasma cells. A monoclonal component usually appears as and is called an additional band when it is visible on a gel. It is usually referred to as an additional peak when the sample is analyzed by densitometry after gel or capillary electrophoresis. Frequent synonyms are extragradient, extra-band, extra-peak, monoclonal fraction, monoclonal protein, monoclonal immunoglobulin, paraprotein, M-protein, M-spike, etc. Small monoclonal components sometimes do not present as distinct fractions, but rather appear with gel band deformations or shape irregularities of the densitometric curve. Various degrees of asymmetry are most frequent in the normally symmetrically alpha-2-, beta-1- and beta-2-fraction. These irregularities are usually named after their shape; for instance, tail, broadness, bridge, plateau, swell, shoulder, bump, bulge, wiggle, up-slant, downslope, depression, etc. The detection of a monoclonal component in the alpha-2-, beta-1- or beta-2-fraction is challenging if the electrophoretic mobility is nearly identical to the proteins regularly present in this fraction. This has been named comigration, masked or hidden monoclonal component. Often the corresponding fraction is elevated, presents with a very sharp peak or the beta-2-fraction may exceed the beta-1 fraction. Small amounts of monoclonal proteins may display no electrophoretic abnormalities and the monoclonal component is only visible in immunofixation. Monoclonal free light chains often do not present as distinct bands or peaks. Sometimes they present with a decrease of the gamma-globulin fraction. This requires additional, mandatory testing for free light chains and/or immunofixation in serum and urine. Non-monoclonal, so called pseudo-monoclonal substances may also cause additional bands or peaks and resemble monoclonal components. These also require immunofixation to rule out. (Refer to footnote[1] for details on the usage of terminology in this article)

Agarose or capillary protein electrophoresis has a detection limit for monoclonal proteins of 0.5–1 g/L while immunofixation detects bands down to the 50–100 mg/L range. Immunofixation therefore defines the absence of a monoclonal band and classifies therapeutic response categories [1].

A study with 5992 protein electrophoresis samples initiated reflex immunofixation in 13.2% of abnormal samples, which were considered suspicious for monoclonal components. Immunofixation identified 43% of the abnormalities as monoclonal (*100% of all M-spikes and 28% of the other SPE abnormalities*) [2]. There is some controversy whether immunofixation should run with every serum electrophoresis [1] or whether it may be only of benefit in clinical laboratories using poor

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[1] *Terminology* (as used in this text): **Extragradient**: Deviation from the regular shape of the curve – either defined by visual inspection or detected by software based on mathematical curve analysis. **Monoclonal component**: A monoclonal protein that has been verified by immunofixation or immunosubtraction. **Pseudo-monoclonal component**: Curve irregularity suspicious or resembling a monoclonal component but that has been excluded by immunofixation or immunosubtraction.

http://dx.doi.org/10.1016/j.clinbiochem.2017.09.017
Received 5 March 2017; Received in revised form 20 September 2017; Accepted 20 September 2017
Available online 28 September 2017
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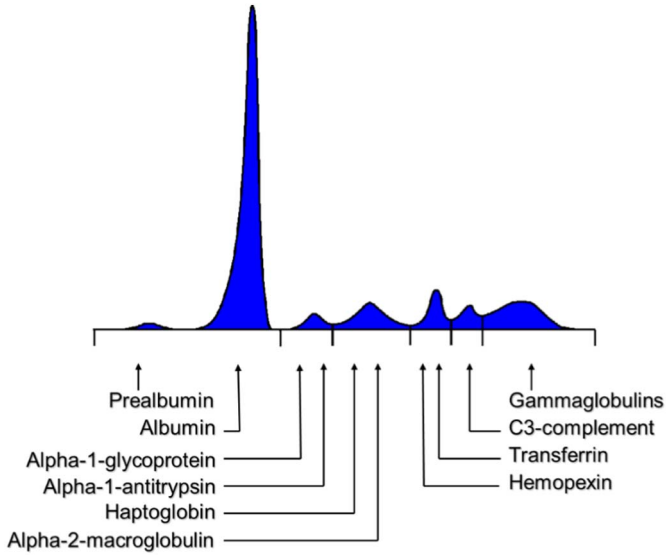

Fig. 1. Major human proteins present in capillary serum electrophoresis.

resolution electrophoresis in the beta region, where it assists in the detection of mainly IgA monoclonal protein. Immunofixation may also increase the detection of trace bands of questionable clinical significance which represent transient phenomena in infectious and autoimmune conditions or very low risk MGUS [3–5].

The detection of monoclonal components has been largely improved by capillary electrophoresis. Capillary electrophoresis estimates monoclonal peaks more accurately, because there are no varying dye binding affinities of proteins as seen with agarose gel electrophoresis [6]. The better differentiation of the beta region into beta-1- and beta-2-globulin fractions also improves their detection [7,8]. If a monoclonal component has been excluded by immunofixation, the origin of the irregularity is rarely reported back to the ordering physician, because this requires profound knowledge within the reporting laboratory.

Here, we review non-monoclonal causes of irregularities in capillary serum protein electrophoresis and their possible clinical implications. The terms used in laboratory medicine are not standardized and differ between individuals, hospitals, countries and languages. This is definitely an area of laboratory medicine that requires standardization and would be a worthwhile task for the IFCC Working Group on Harmonization of Interpretive Commenting. Here we use the terms we established in our institutions, i.e. extragradient, monoclonal component and M-gradient to describe the irregularities present in capillary electrophoresis.

2. Basics of capillary serum protein electrophoresis interpretation

In order to recognize relevant alterations in protein electrophoresis the assessor must not only know the location of the proteins physiologically present (Fig. 1) but also interpret their most common variants. There are numerous influences that determine the presence of a protein and thus the curve in the electrophoresis graph: phenotypic variants (genes), age; synthesis (liver function, antibody deficiency syndrome), malnutrition, renal diseases, enteral malabsorption, dermal loss, inflammation, malignancy, hormones (pregnancy, contraceptives, thyroid) or medication (immunosuppressants). In addition, increases or decreases may be seen not only with single proteins but appear also as typical group protein reactions, for instance as acute phase response.

A valid interpretation of the electrophoresis curve includes the measurement of total protein. The percentual value of each protein fraction should be converted to g/L. However, the reporting of electrophoresis values only as percentages still exists today, although the quantification of monoclonal gradients requires absolute values and absolute numbers are well established in laboratory medicine. A blood differential of 40% granulocytes and 50% lymphocytes, for instance, does not distinguish neutropenia from lymphocytosis without their absolute values. Equally, absolute concentrations are mandatory to correctly interpret electrophoresis. An albumin concentration of 50.8% (decreased) and a gamma fraction of 18.6% (elevated) will yield different reference range and abnormal absolute values even if total protein only varies within its reference range (66–83 g/L, Fig. 2).

Grey shaded circles indicate reference range values for albumin (35–53 g/L) and gamma-globulin (5.6–15.0 g/L), red circles indicate pathological values. A sample with a fixed relative albumin concentration of 50.8% (decreased) and gamma-globulin of 18.6% (increased) yields different absolute normal or pathological results when total protein is varying within the reference range (66–83 g/L): Albumin decreases below 35 g/L when total protein is below 70 g/L, while gamma-globulin is increased above the reference range in samples with a total protein above 78 g/L. Albumin as well as the gamma-globulins are reference range when the total protein concentrations is between 70 and 78 g/L.

Surprisingly, absolute reference ranges established under IFCC

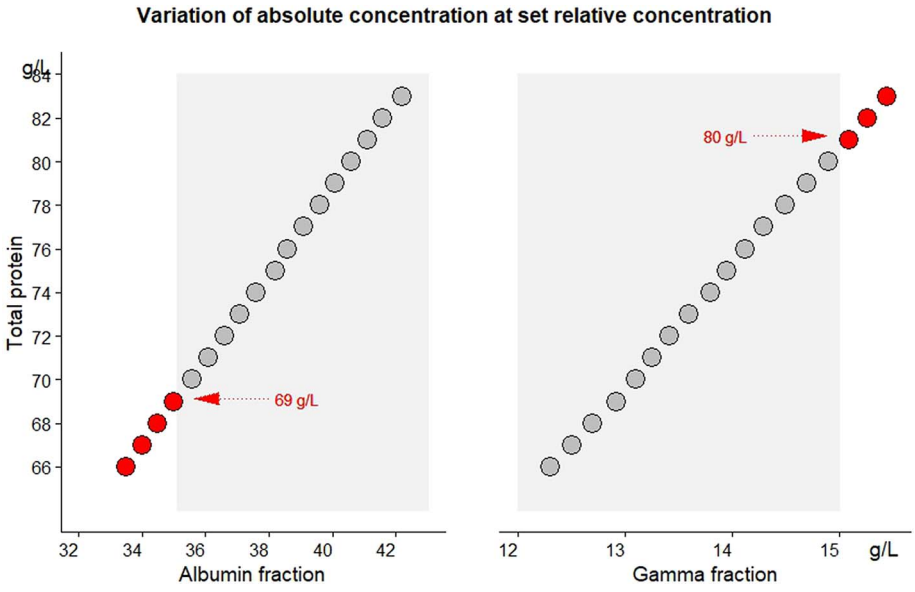

Fig. 2. Albumin and gamma-globulin variation of absolute concentrations at fixed relative values (albumin 50.8%, gamma-globulin 18.6%).

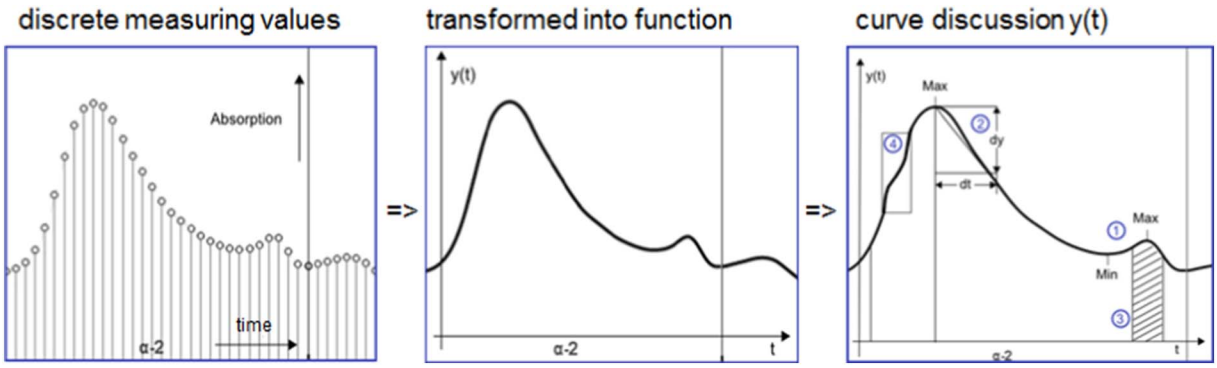

Fig. 3. Transformation of measurements into function and curve analysis for: Extremes of max/min ①, "steepness"of absorption peaks ②, area under the curve ③, curve regularity ④.

criteria (minimum of 120 samples and analysis by nonparametric statistical methods [9]) under rigid selection of the reference population (e.g. normal values for kidney and liver parameters, ferritin, CRP, cholesterol and triglycerides) are not available for serum protein electrophoresis. Our own reference range study of > 500 working subjects covering an age range from 17 to 93 years yielded different from the published results. The main difference was in the albumin concentration that was substantially lower in subjects older than 60 years (data prepared for publication) [10].

The reference concept so commonly used in laboratory medicine, however, is only partially applicable to the interpretation of protein electrophoresis. An increased globulin fraction may indicate presence of a monoclonal gammopathy but irregularities will only be detected by the time-consuming visual evaluation of each electrophoresis curve. This should include inspection for an additional fraction or peak in the curve (extragradient), an unusual fraction shape (asymmetry) or an unusual elevation of a fraction (comigration). Extragradient evaluation, though, is non-standardized and method as well as user skill dependent. This challenging task can be automated by mathematical curve analysis [11], which we improved and expanded in our software (Fig. 3, see details in Section 4).

In addition, the best electrophoretic quantification method for monoclonal gradients, tangent skimming, provides a 10-fold improvement in precision but is rarely used [12,13].

2.1. Recognition of irregularities, monoclonal and oligoclonal peaks by capillary electrophoresis

Technically, capillary electrophoresis has some advantages over agarose electrophoresis. Immune complexes that can be misinterpreted on agarose gels and thus require treatment with 2-mercaptoethanol for complete resolution are mostly resolved in the liquid medium of capillary electrophoresis. Additional peaks are detected which improves the recognition of phenotypic variants and irregularities. Capillary electrophoresis provides higher resolution with more detailed curve data and increases sensitivity for the recognition of monoclonal proteins. However, some non-proteins can present as irregularities, because all substances absorbing at 200 nm are detected. This decreases specificity and complicates the interpretation of pathological samples. Other drawbacks are that smaller irregularities can still be missed during the visual evaluation of capillary electrophoresis, which requires a careful and time-consuming analysis with the zoom function of the sebia scan software. There are also some differences in the detection of pure light chain myelomas compared with the quantitative methods as well as a weakness detecting smaller IgM gammopathies. Also, "non-homogeneously stained" gamma regions on agarose electrophoresis and immunofixation are not always present in capillary electrophoresis [14–16]. These samples with unclear banding (also called "zoning" or "stained non-homogeneously") are usually resolved with immunofixation after 2-mercaptoethanol or dithiothreitol treatment. In our experience immunofixation on a high-resolution gel is far superior. The resolution of the electrophoresis improves with separation length which is crucial for the detection of minor bands. This usually either resolves the non-homogeneous staining or unclear banding or it identifies the monoclonal protein hiding within an oligoclonal pattern. In our own comparison 43 ambigious specimens investigated with routine immunofixation proved to be either artefacts (n = 15), oligoclonals (n = 12) or faint monoclonal fractions (n = 16) on a high-resolution gel [17].

3. Irregularities in electrophoresis fractions

3.1. Albumin fraction

Albumin functions primarily as a carrier protein. In capillary electrophoresis lipids usually migrate beneath the albumin fraction, but the quantified values are usually slightly lower when compared with agarose measurements [18,19]. Overall, albumin is more accurately quantified by capillary electrophoresis, whereas in agarose gel electrophoresis it varies substantially depending on the protein binding affinities of the applied colorant.

Increases: These are almost always caused by dehydration.

Decreases: A fraction decrease accompanies a relative increase of the other fractions (alpha, beta, gamma), while total protein usually remains in the reference range. A singular decreased fraction is seen in malnutrition, decreased synthesis or loss (nephrotic syndrome).

Irregularities (Fig. 4): This includes in the anodal part an increase of transthyretin ("prealbumin"), and the split albumin fraction present

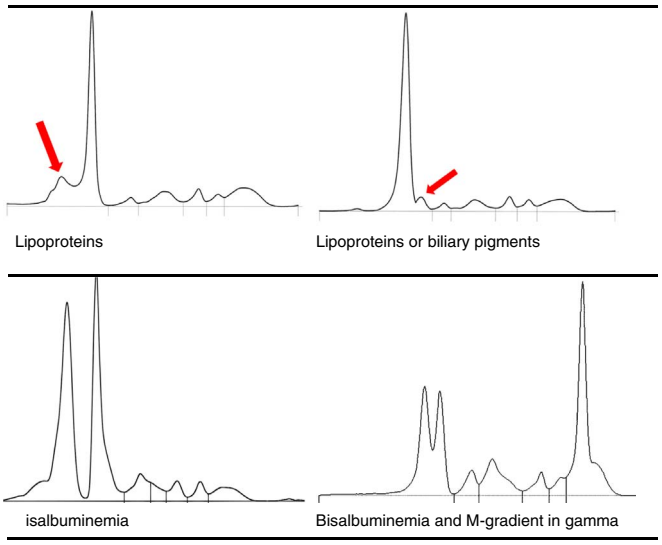

Fig. 4. Irregularities in the albumin fraction.

in bisalbuminemia [19–23].

Bisalbuminemia is a relatively rare, autosomal codominant genetic variant with a slight alteration in the albumin amino acid sequence and presents in capillary electrophoresis with a split albumin fraction. The only disorders which have been directly linked are familial dysalbuminemic hyperthyroxinemia (Arg218AEHis and Arg218AE Pro mutations) and hypertriiodothyroninemia (Leu66AEPro mutation) [22]. In acquired transient bisalbuminemia, the abnormal component of the albumin can be located in the anodal ("fast type") or cathodal part ("slow type"). A cathodic shoulder on the albumin side is commonly found with massive hyperlipidemia. Other irregularities have been observed with hyperbilirubinemia (presenting with an increased anodal front) [18,24], cirrhosis [25], tryptic digestion (pancreatic pseudo cysts, pancreatitis/malignancy) [26–28], viral infections (for instance mumps), meningococcal meningitis, sepsis or heavy metals intoxication, for instance with copper [18] or application of beta-lactam type antibiotics [28,29]. The exogenous application of sulfamethoxazole, ceftriaxone or salicylic acid is also a possible cause [18,19]. Aged capillaries may also cause an artefactual cathodal shoulder.

Monoclonal proteins are usually not present in the albumin fraction. One reported case of free monoclonal light chains showed an extragradient between albumin and the alpha-1 band on paper electrophoresis [30].

3.2. Alpha fraction

Acute phase proteins are found in the alpha-fractions. They increase 50–300% in acute inflammation and decrease with acute hepatitis, chronic active liver disease or protein loss [19,23].

3.2.1. Alpha-1-fraction

Decreases: Alpha1-antitrypsin is the main constituent of the alpha-1-globulin fraction. Evaluation of the alpha-1-globulin protein fraction usually receives little attention although a decreased fraction frequently indicates alpha-1-antitrypsin deficiency. As protein electrophoresis does not differentiate between alpha-1-antitrypsin deficiency and other minor proteins in the alpha-1 fraction, antitrypsin can be more directly and specifically measured using a nephelometric or immunoturbidimetric method and should be phenotyped for definitive diagnosis [31,32].

Increases: seen with acute phase response.

Irregularities (Fig. 5): Physiological irregularities can originate due to alpha-1-antitrypsin-phenotypic variants; alpha-1-acid glycoprotein (orosomucoid) [33] elevations accompanying chronic alcoholism, acute phase response, malignancy, chronic polyarthritis and autoimmune disorders (primary Sjögren's syndrome, systemic lupus erythematosus), Crohn's disease. A very high concentration of alpha-fetoprotein has also been reported to cause an extragradient in this region [18,19,26].

Monoclonals: Monoclonal components are extremely rare and are usually light chains [19,23].

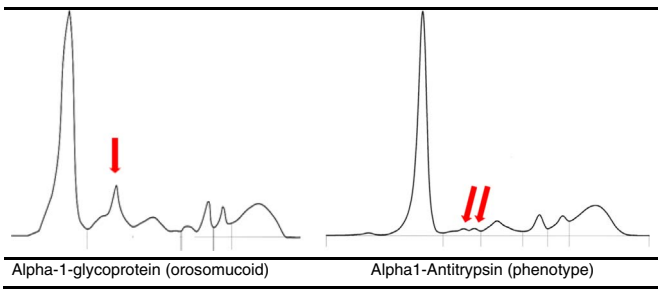

Fig. 5. Irregularities in the alpha-1-globulin fraction.

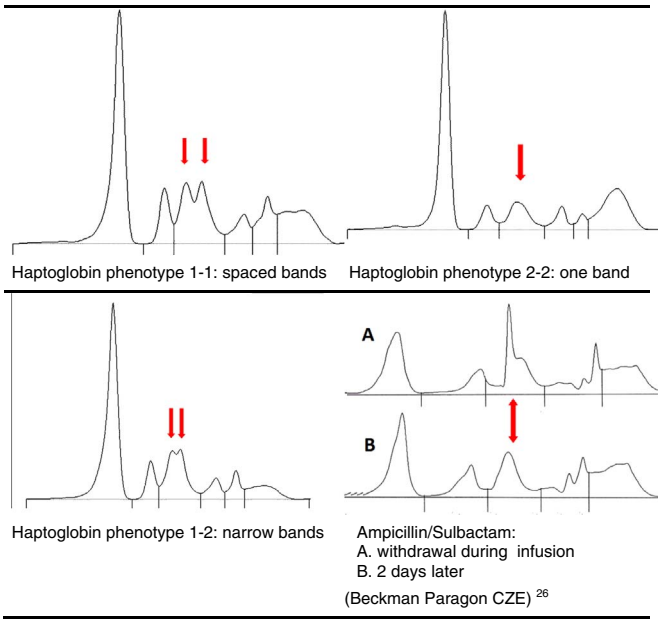

Fig. 6. Irregularities in the alpha-2-globulin fraction.

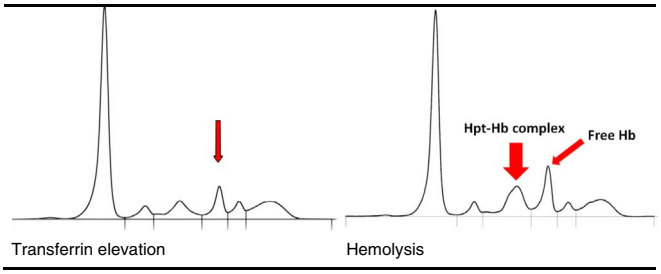

Fig. 7. Irregularities in the beta-1- (and alpha-2-) globulin fraction.

3.2.2. Alpha-2-fraction

Haptoglobin binds free hemoglobin and inhibits its oxidative activity. Hemolysis releases free hemoglobin which is bound by haptoglobin. The haptoglobin-hemoglobin complex will be subsequently removed by the reticuloendothelial system. Haptoglobin has been found in all mammals and is produced mostly by hepatic cells. Any inflammatory process (infection, extreme stress, burns, major crush injury, allergy, etc.) may increase the level of haptoglobin, because it is an acute phase protein [34].

Alpha-2-macroglobulin is the major component of the alpha-2-fraction and produced by the liver. It increases in nephrotic syndrome, which causes the urinary loss of lower molecular weight proteins, including albumin (molecular weight 67 kDa) and IgG (150 kDa), while the large sized alpha-2-macroglobulin (725 kDa) hardly passes through the glomerular filter. Alpha-2-macroglobulin can than reach serum levels equal to or greater then those of albumin in order to maintain oncotic pressure [35].

Decreases: Haptoglobin can decrease to an undetectable level in intravascular hemolysis [34,37]. Aberrant non-functional forms of alpha-2-macroglobulin have also been reported [38].

Increases: Seen with acute phase response and nephrotic syndrome.

Irregularities (Fig. 6): In vitro hemolysis profoundly increases the alpha-2-fraction [39] and irregularities may appear in the cathodic part because of the haptoglobin-hemoglobin-complex (Fig. 7) [19,23]. Other causes are haptoglobin-phenotypic variants which are usually of no pathological significance, haptoglobin acute phase elevations (malignancy, Hodgkin's lymphoma, colitis ulcerosa), alpha-2-macroglobulin increase in nephrotic syndrome and exogenous substances, for instance antibiotics or radiopaque agents [16,36]. In contrast to agarose

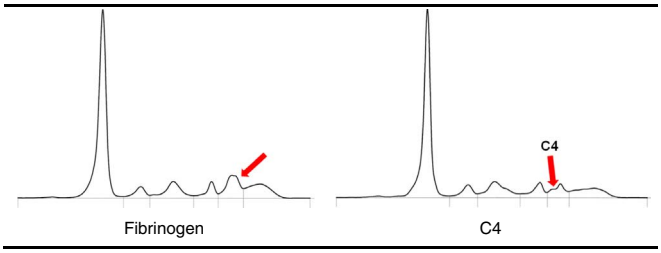

Fig. 8. Irregularities in the beta-2-globulin fraction.

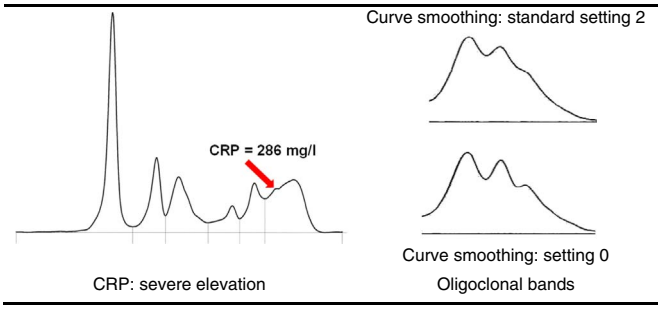

Fig. 9. Irregularities in the gamma-globulin fraction: CRP elevation (left) effect of curve smoothing (right).

Table 1
Possible causes of pseudo monoclonal gradients.

Phenotypic variants of physiological proteins:
● Albumin
● Alpha1-antitrypsin
● Haptoglobin
Significant, pathological elevation of single proteins:
● Alpha-1-acid glycoprotein (orosomucoid)
● Haptoglobin
● Hemopexin
● CRP
● Lysozyme
● IgG 4
Sample condition:
● Hemolysis
● Icterus
● Plasma
● Age, storage conditions
● (Lipemia)
Exogenous components (pre-analytical errors):
● All substances absorbing at 200 nm
– Radio opaque agents
– Antibiotics
– Plasma expander
– Therapeutic monoclonal antibodies

electrophoresis, lipoproteins do not contribute to alpha- and beta-fractions in sebia capillary electrophoresis.

Monoclonals: Monoclonal proteins in this area have been reported, but are rare [40–43].

3.3. Beta fraction

Capillary electrophoresis allows the separation of two beta fractions, which improves detection of monoclonal proteins [7]. This is the second most frequent location for monoclonal proteins, but other proteins are physiologically present. Monoclonal proteins are prone to alter the fraction shape (asymmetry) or cause an unusual elevation of a fraction (comigration). It is advisable to check any sample with a high beta-1- or beta-2-band with immunofixation, because this will detect a hidden, underlying monoclonal component, even in the absence of any obvious visual abnormality.

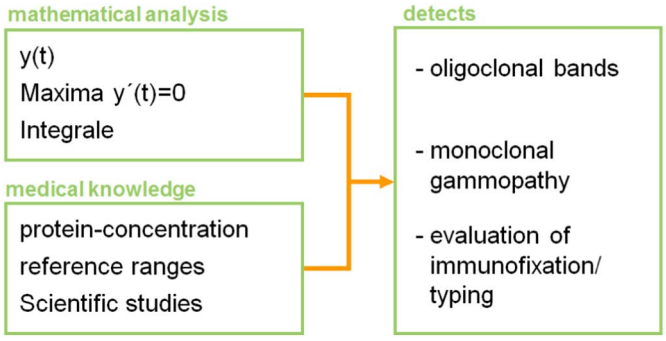

Fig. 10. Objectives of software use. The final output combines mathematical curve analysis with texts from a knowledge database to interpret typical patterns.

3.3.1. Beta-1-fraction

Decreases: Can be caused by genetic atransferrinemia or iron overload that leads to transferrin decrease.

Increases (Fig. 7): Seen with iron deficiency or hemolysis with free hemoglobin [44].

Irregularities: Hemopexin caused by malignancy or inflammation [45–47]. Exogenous substances, for instance the pre-analytic application of antibiotics or radiopaque agents [16,36].

Monoclonals: Monoclonal proteins in this area are often of the IgA or free light chain type.

3.3.2. Beta-2-fraction

Decreases: They are seen with autoimmune disease (active SLE) and membranoproliferative glomerulonephritis which cause complement consumption. Stored samples are subject to in vitro complement degradation.

Increases: Present with IgA increase or an acute phase reaction. A sample with a beta-2 fraction exceeding the beta-1 fraction should be checked by immunofixation for a monoclonal gammopathy.

Irregularities (Fig. 8): Patients under heparin therapy or dialysis occasionally produce blood samples that do not fully clot. Fibrinogen is present in plasma but absent in serum samples. These conditions can cause a visible fibrinogen band between the beta and gamma-globulin region which can mimic presence of a monoclonal protein. Other irregularities are caused by complement [18], stored sample degradation or exogenous substances, for instance the pre-analytic treatment with antibiotics or radiopaque agents [16,48].

Monoclonals: Monoclonal proteins in this area are frequently of the IgA or free light chain type.

3.3.2.1. Beta-gamma Interzone. **Increases**: IgA monoclonal proteins typically migrate here. A strong polyclonal increase often leads to confluence of the beta-2- and gamma band, called beta-gamma bridging or beta-gamma fusion. This is seen accompanying alcoholism, cirrhosis, respiratory infection, skin disease or rheumatoid arthritis.

Irregularities: One case with an extremely elevated CA 19-9 concentration has been reported [49].

3.4. Gamma fraction

This is the most common area for monoclonals. The immunoglobulins are generally the only proteins present. However, any substance absorbing at 200 nm will be picked up on capillary electrophoresis.

3.4.1. Decrease (hypogammaglobulinemia)

Hypogammaglobinemia predicts reduced serum immunoglobulins (mainly IgG) with a relatively high positive predictive value of 93% and a negative predictive value of 84% [50]. Usually only a substantial decrease of IgG1, the main IgG constituent, is regularly recognized by a

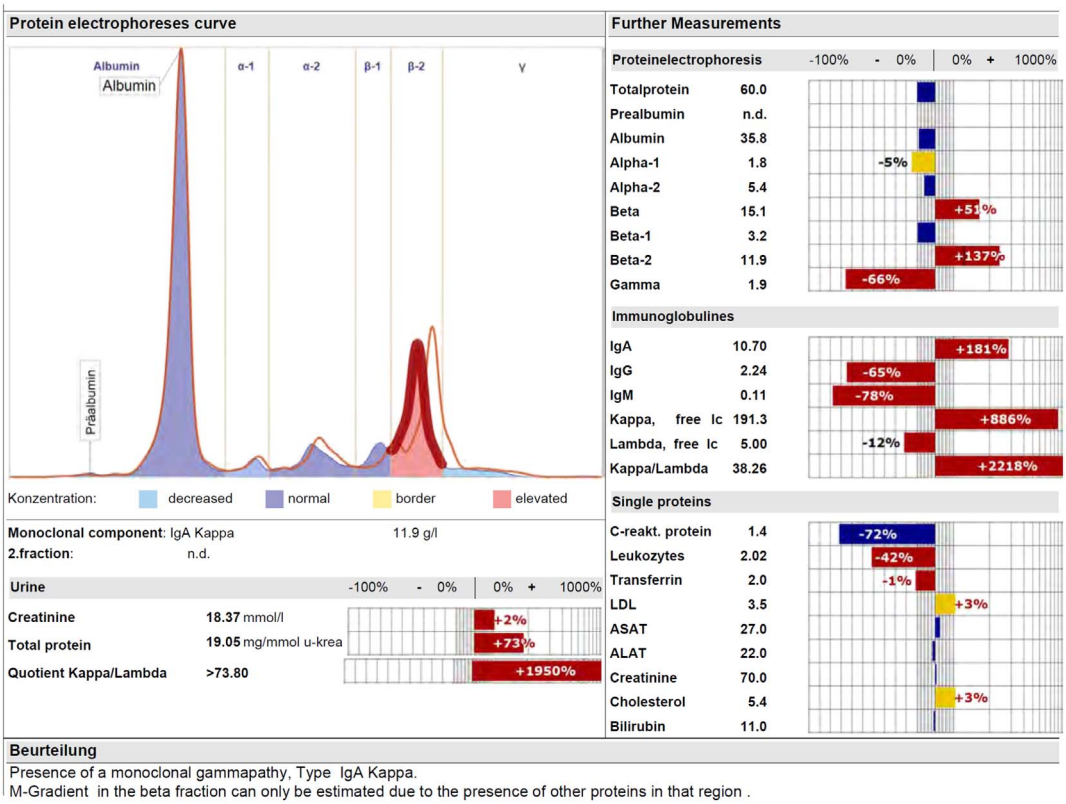

Fig. 11. Graphical representation of electrophoresis and associated analytes.

low total IgG [51,52]. It is seen in common variable immunodeficiency (CVID); a decreased antibody production in response to antigenic challenge which is often associated with hematologic and autoimmune disorders and recurrent pyogenic infections. Genetic causes include X-linked agammaglobulinemia or IgA deficiency that occurs with a frequency of 1:500 in the population and is associated in 20% with IgG 2 subclass deficiency [19]. It can also occur idiopathically or secondary to a large number of other diseases [53].

8–35% of patients with a monoclonal gammopathy of unknown significance (MGUS) have reduced uninvolved polyclonal immunoglobulins (immunoparesis) [54]. This is especially common with light chain myeloma. Consequently, in absence of a discernible M-spike as the only criterion for reflexive testing in SPE-negative patients, "*the immunofixation positive rate and sensitivity in hypo-gammaglobulinemia were 12.2% and 15.6% respectively, compared to 6.4% and 77.1% in normo-gammaglobulinemia*" [50].

3.4.2. Increase (polyclonal elevation)

A polyclonal "swell like" gamma elevation indicates an excess of immunoglobulins, i.e. hypergammaglobulinemia. Polyclonal gammopathies can occur with any reactive or inflammatory process, and they are usually associated with nonmalignant conditions. The most common causes are severe infection, acute late stage inflammation (acute hepatitis, pyelonephritis, interstitial nephritis), chronic inflammation, chronic infectious disease (chronically persistent hepatitis), autoimmune disease (collagenosis, rheumatoid arthritis, systemic lupus erythematosus, other connective tissue disease or lymphoma) [18,19].

Irregularities of discrete to medium severity can be caused by high concentrations of immunoglobulins; especially IgG 4 in patients with IgG 4 associated autoimmune disease [18,55,56]. Patients on immunosuppressive therapy (cyclosporin, tacrolimus) after stem-cell or renal transplantation sometimes present with two noticeable peaks (IgA, IgG) on a low polyclonal background.(author's personal communication). Differential diagnosis of pseudo-monoclonal gradients should include extreme elevations of CRP [57], older, degraded samples, presence of uremia, rheumatoid factor, circulating immune complexes due to liver cirrhosis, malignancy, cardiac and vascular disease, immunoglobulin-lipid-complex, lysozyme (monocyte-leukemia) [58–61], or exogenous substances, for instance pre-analytic application of antibiotics, radiopaque agents or plasma expander therapy [16,19]. Patients on monoclonal antibody therapy may present with irregularities in capillary electrophoresis; the majority of the monoclonal antibodies are visible in the middle of the gamma-globulin region [62].

3.4.3. Oligoclonal bands

Oligoclonal bands are defined by several, at least two discrete immunoglobulin peaks that migrate closely together during electrophoresis and they appear as narrowly placed peaks on the electrophoretogram. These are most common in the gamma-globulin-region. There is no strict definition. The most common cause is a chronic stimulation of the immune system or immunosuppression. Oligoclonal bands can be underestimated on the Capillarys® due to the smoothing algorithm of the instrument (Fig. 9), which was not present on an earlier and no longer available instrument, the Beckman CZE, which reflects on the discussion between analytical sensitivity and specifity.

3.4.4. Monoclonals

Smaller monoclonal gammopathies can also be transient [5]. In one study, 8.7% of all observed smaller monoclonal gammopathies had no prognostic relevance and were usually associated with infectious diseases [63], especially chronic hepatitis C viral infection [64]. A monoclonal gammopathy is more frequently diagnosed from October to April and a respiratory infection may very well precipitate the diagnosis of a multiple myeloma [65].

There are considerable arguments that these patterns are described as "monoclonal" in low resolution immunofixation and are resolved as "oligoclonal" with the application of higher resolution techniques [17].

3.4.5. CRP elevations

High concentrations of CRP may present as an extragradient in the gamma fraction (Fig. 9) [57,66]. This is a relatively rare condition that was observed only in 1.4% (224 of 15,724 samples) of our own study population. We visually checked 112 samples (CRP between 200 and 300 n = 80, CRP > 300 mg/L, n = 32). 91% showed also an inflammatory pattern, i.e. marked increase of the alpha-1-, alpha-2- or both bands (102/112). These samples presented sometimes with a broad elongated elevation starting at the beta-2-fraction. A visible typical extragradient was rare (CRP between 200 and 300: 19% n = 6/32, CRP > 300 mg/L: 25% n = 20/80). Most of these smaller changes would have been overlooked. This pattern seems to depend additionally upon the immunoglobulin concentration, especially an inflammatory increase of IgM (Table 1).

4. Data visualization

The manual recognition of the changes present in protein electrophoresis is difficult, time-consuming and dependent upon the reviewer. Moreover, protein electrophoresis and other serum and urine laboratory data that supplement each other are frequently requested over a time course and thus presented on different output sheets without any apparent association. We designed software that is in daily use and that combines mathematical curve analysis (Figs. 3, 10) with other relevant laboratory values, uses a medical knowledge base to interpret the data and presents the results on a graphical oriented report form (Fig. 11).

The front page prominently features a colorized electrophoresis curve which accentuates the mathematically identified and manually confirmed monoclonal proteins. Previous curve data is shown as a red line.

These data are automatically complemented with relevant hematological and clinical chemistry values (immunoglobulins, free light chains), provided they have arrived in the laboratory within a 12 hour time period. The values are transformed to percentual multiples of the upper (lower) reference range and colored accordingly. Thus, the constellation of an inconspicuous symmetrical electrophoresis curve with a reduced gamma fraction, diminished immunoglobulins but a relevant increase in free light chains remains distinctively recognizable. The pattern of the increased and decreased electrophoresis fractions is also analyzed and interpreted using entries of a knowledge database.

Up to 6 visits of earlier consultations are summarized on the back page to facilitate patient follow-up. In addition, immunofixation or immunotyping data can be documented and archived online (not shown).

5. Conclusion

Serum protein electrophoresis is a cost-effective, automated method for evaluating the most important proteins and screening for monoclonal proteins. The diagnostic performance characteristic depends decisively on the analytical technique and the quality of the assessment.

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