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Research Article

Bisalbuminemia: Insights into its Clinical Manifestations, Diagnostic Complexities, and Relevance in Modern Medicine

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Abstract— Bisalbuminemia, also known as alloalbuminemia, is a rare hematologic disorder characterized by the presence of two distinct serum albumin fractions in the blood. This condition is typically benign and asymptomatic, but its discovery can be puzzling for clinicians due to its rarity and often incidental nature. The occurrence of bisalbuminemia can be hereditary or acquired, with the hereditary form being passed down in an autosomal dominant fashion, while the acquired form is linked to liver disease, kidney disease, or drug exposure. The condition is most commonly identified during routine serum protein electrophoresis (SPE) testing, when an unusual albumin pattern is observed.
In this report, we present a case of a patient diagnosed with bisalbuminemia. We discuss the clinical presentation, diagnostic challenges, and management strategies, emphasizing the importance of considering rare hematologic conditions in patients presenting with unexplained hypoalbuminemia and abnormal serum protein electrophoresis results. This case underscores the need for awareness of such conditions among clinicians and laboratory personnel to avoid unnecessary testing and misdiagnoses.

Keywords— Bisalbumenia, hematologic disorder, hypoalbuminemia, serum protein electrophoresis

1. Introduction

Bisalbuminemia is an uncommon hematologic condition marked by the presence of two separate serum albumin fractions, which can present diagnostic challenges for clinicians. While generally benign and asymptomatic, its rarity often makes diagnosis challenging for clinicians, particularly as it is frequently discovered incidentally. The disorder can be either hereditary or acquired, with hereditary bisalbuminemia inherited in an autosomal dominant manner. Acquired forms are associated with underlying conditions such as liver or kidney disease or exposure to certain medications.

The condition is most commonly detected during routine serum protein electrophoresis (SPE), where an abnormal albumin pattern draws attention. Although it usually does not cause symptoms, bisalbuminemia may be associated with unexplained hypoalbuminemia in some patients.

We report a case of bisalbumenia in a patient presenting with hypoalbuminemia and atypical serum protein electrophoresis findings, highlighting the clinical manifestations, diagnostic workup,. [1, 2,3].

2. Methods

2.1 Sample Collection and Preparation

Serum samples were collected from patients following standard venipuncture procedures. Blood was drawn into serum separator tubes and allowed to clot at room temperature for 30 minutes. After centrifugation at 3000 rpm for 10 minutes, the serum was separated and stored at -20°C until further analysis.

Serum protein electrophoresis (SPE) was performed using the Sebia Minicap system, a fully automated capillary electrophoresis platform designed for high-resolution protein separation. The Minicap system operates by applying a high-voltage electric field to separate serum proteins based on their charge and size. The process utilizes capillary tubes filled with an alkaline buffer to achieve rapid and accurate separation of serum proteins, including albumin.

Sample was loaded on to the disk on the Sebia Minicap system with standard buffers . Proteins migrated through the capillary based on their electrophoretic mobility. Albumin, being the most negatively charged protein, migrated fastest toward the anode.

Detection: Proteins were detected via UV absorbance at 214 nm, and a protein profile was generated with the characteristic peaks representing the different protein fractions: albumin, α1-globulins, α2-globulins, β-globulins, and γ-globulins.

2.2 Analysis and Interpretation

The electrophoretic patterns were analyzed using Sebia's proprietary software, Phoresis, which provides quantification and graphical visualization of the protein fractions. Bisalbuminemia was identified by the presence of two distinct albumin peaks or a broadened albumin band, deviating from the usual single albumin peak observed in normal SPE profiles.

2.3 Quality Control

To ensure reliability, normal and abnormal control sera were run at the start of each day and after every 20 samples. Calibration of the Minicap system was performed according to the manufacturer's protocols, and the buffer systems were replenished regularly to maintain the consistency of electrophoretic conditions.

2.4 Data Analysis

Quantitative analysis of the albumin fractions was performed by measuring the area under each peak corresponding to albumin. The presence of bisalbuminemia was confirmed by observing two distinct albumin bands. Further analysis of the globulin fractions was performed to rule out other conditions that might affect protein electrophoresis patterns, such as monoclonal gammopathies.

2.5 Confirmation of Diagnosis

Patients with suspected bisalbuminemia based on abnormal SPE patterns underwent repeat testing for verification. Additional laboratory tests, including liver and kidney function tests, were performed to assess potential underlying causes in acquired cases.

3. Results and Discussion

A 56-year-old male presented to the outpatient clinic with complaints of generalized weakness, fatigue, and peripheral edema for the past three months. Physical examination revealed bilateral lower limb pitting edema with no evidence of hepatosplenomegaly or lymphadenopathy. Laboratory investigations showed serum albumin level: 3.87 g/dL and normal liver and renal function tests. Serum protein electrophoresis demonstrated two distinct albumin peaks, consistent with bisalbumenia. Further evaluation, including autoimmune serology and imaging studies, did not reveal any underlying systemic disorders or liver pathology.

The diagnosis of bisalbumenia was established based on the presence of two distinct serum albumin fractions detected by serum protein electrophoresis. Differential diagnosis included monoclonal gammopathies, familial dysalbuminemic hyperthyroxinemia, and other rare protein abnormalities, which were ruled out through additional laboratory and imaging studies.(Figure 1). Free light chain assay revealed normal kappa/lambda ratio (Table 1).:

Bisalbuminemia is an infrequent hematologic disorder defined by the presence of two distinct serum albumin fractions, often identified incidentally through serum protein electrophoresis (SPE).This condition can be either hereditary, passed in an autosomal dominant pattern, or acquired due to liver or kidney diseases, drug exposure, or other underlying medical conditions. Despite its rarity, bisalbuminemia is typically benign and asymptomatic, though it may sometimes present with clinical signs of hypoalbuminemia such as edema, fatigue, or signs of protein loss. The discovery of this condition often prompts further investigation due to the unusual presence of dual albumin peaks on SPE, which can complicate the interpretation of results and the differential diagnosis process.

Patients with bisalbuminemia frequently present with hypoalbuminemia or abnormal serum protein electrophoresis patterns, making diagnosis challenging. The identification of this condition requires a high index of suspicion and careful interpretation of laboratory findings to differentiate bisalbuminemia from other conditions that may cause abnormal albumin fractions, such as nephrotic syndrome, liver dysfunction, or monoclonal gammopathies.

The diagnostic process involves repeat testing using advanced techniques like capillary electrophoresis, which offers greater resolution than traditional gel electrophoresis. In some cases, genetic testing may be necessary to confirm hereditary bisalbuminemia, especially when a family history of the condition is present.

Management strategies for bisalbuminemia are typically supportive, as the condition is often asymptomatic and does not require aggressive treatment. Symptomatic relief may be provided for patients with hypoalbuminemia-related symptoms, such as diuretics for edema. Underlying conditions, if present, should be treated to mitigate potential exacerbations of hypoalbuminemia. For patients with acquired bisalbuminemia, addressing the primary disease or discontinuing the causative drug can lead to normalization of the albumin profile. Regular follow-up is advised to monitor disease progression and assess treatment response, especially in patients with underlying systemic illnesses that may impact albumin levels.

In summary, bisalbuminemia is a rare but clinically significant condition that can pose diagnostic challenges due to its atypical presentation and association with abnormal serum protein electrophoresis patterns. A careful approach to diagnosis and management, with a focus on ruling out other causes of abnormal albumin fractions and providing appropriate supportive care, is essential in optimizing patient outcomes [4,5].

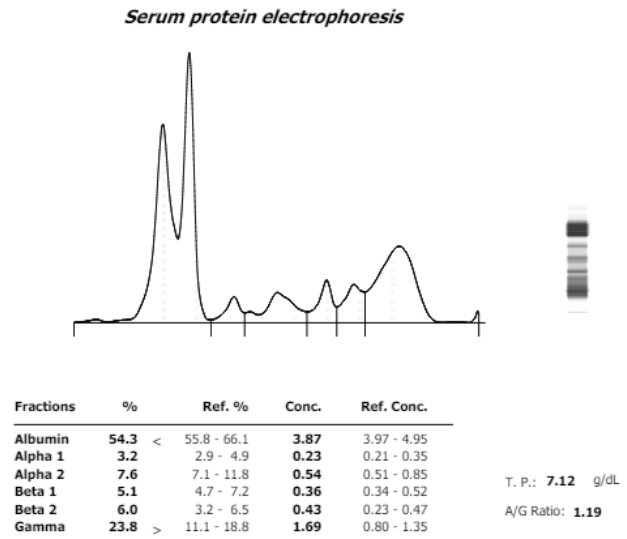

Figure 1 . Electrophoregram demonstrating the serum protein profile of the patient diagnosed with bisalbuminemia. The electrophoretic separation reveals the presence of two distinct albumin fractions indicated by arrows. The albumin fractions appear separated from the gamma globulin region, highlighting the characteristic abnormality associated with bisalbuminemia.. Additionally, the presence of other serum proteins such as alpha-1 antitrypsin, alpha-2 macroglobulin, and immunoglobulins can be observed in their respective regions.

Table 1. Free light chain assay

Test	Patient Value	Reference Range
Free Light Chain Kappa	74.0 mg/L	3.30-19.40
Free Light Chain Lambda	91.80 mg/L	5.71-26.30
Ratio	0.81 mg/L	0.31-1.56

Table 1. Results of the Free Light Chain Assay in the Patient with Bisalbuminemia. This table summarizes the quantitative measurements of free light chains (FLC) in the serum of the patient diagnosed with bisalbuminemia. The levels of free kappa and lambda light chains are presented alongside the kappa to lambda ratio. The reference ranges for normal serum free light chain levels are provided for comparison. Notably, the data highlight no abnormalities in light chain production, which can aid in the differential diagnosis of plasma cell disorders and other hematologic conditions.

4. Conclusion and Future Scope

This case report underscores the clinical presentation, diagnostic challenges, and management considerations in a patient diagnosed with bisalbuminemia. As a rare hematologic disorder, bisalbuminemia often presents without significant symptoms, leading to its incidental discovery during routine laboratory testing, such as serum protein electrophoresis (SPE). The presence of two distinct albumin fractions on SPE can perplex clinicians, especially when evaluating patients with unexplained hypoalbuminemia.

This underscores the critical need to maintain a heightened level of clinical suspicion when evaluating rare conditions such as bisalbuminemia. Due to its rarity and often subtle presentation, bisalbuminemia may easily be overlooked or mistakenly attributed to more commonly encountered disorders. Accurate recognition and diagnosis require careful interpretation of laboratory findings, particularly during serum protein electrophoresis, where atypical albumin variants may be detected. Misdiagnosis not only delays appropriate management but can also lead to unnecessary investigations or treatments aimed at addressing incorrect assumptions.

One of the key challenges in diagnosing bisalbuminemia lies in differentiating it from other conditions that affect serum protein patterns, such as monoclonal gammopathies, liver disease, nephrotic syndrome, or other systemic illnesses that impact albumin metabolism. A thorough patient history, including familial patterns and drug exposure, combined with advanced diagnostic tools like capillary electrophoresis and mass spectrometry, can help clarify the diagnosis. Genetic testing may also be indicated, especially when hereditary bisalbuminemia is suspected.

Management of bisalbuminemia remains largely supportive, as the condition is generally benign. However, addressing any underlying medical conditions that may contribute to hypoalbuminemia or exacerbation of symptoms is crucial. For patients with acquired bisalbuminemia due to liver or kidney dysfunction or drug exposure, treating the primary cause can help normalize the albumin profile. Regular monitoring is also recommended, as changes in the albumin pattern may reflect disease progression or a response to treatment.

Looking forward, this case emphasizes the need for increased awareness of bisalbuminemia among clinicians and laboratory personnel. Early recognition of this rare disorder can prevent unnecessary diagnostic testing and mismanagement. In addition, further research is warranted to better understand the pathophysiology of bisalbuminemia, particularly in cases where no obvious underlying cause is identified. Investigating the molecular mechanisms responsible for the production of two distinct albumin fractions, both in hereditary and acquired forms, could lead to more precise diagnostic criteria and targeted therapeutic interventions.

Furthermore, while bisalbuminemia is typically benign, understanding its potential long-term implications, especially in patients with comorbid conditions, will be critical in guiding management. Longitudinal studies could provide insight into whether bisalbuminemia has any impact on morbidity or mortality in affected individuals, particularly those with underlying systemic illnesses. Moreover, investigating potential links between bisalbuminemia and other metabolic or hematologic disorders could shed light on previously unknown associations, improving both the diagnostic and therapeutic landscape for patients.

In conclusion, bisalbuminemia, though rare, presents unique challenges in diagnosis and management. Clinicians must be vigilant in considering this condition when faced with unexplained hypoalbuminemia and abnormal SPE patterns.

Enhanced recognition, combined with ongoing research, will aid in optimizing patient care and deepening our understanding of this intriguing hematologic disorder..

Data Availability
None

Conflict of Interest
None

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Authors' Contributions
Dr. Pawan Kumar researched literature and conceived the study and wrote the manuscript. Dr.Pawan Kumar reviewed and edited the manuscript and approved the final version of the manuscript.

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