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Exploring the Link between Diabetes and Acquired Bisalbuminemia: Case Reports and Literature Review

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Abstract:- Bisalbuminemia, characterised by the division of the albumin fraction on serum protein electrophoresis without an increase in concentration, is a rare protein anomaly that can present as either congenital or acquired. While congenital bisalbuminemia has a genetic basis, acquired bisalbuminemia is often associated with various underlying conditions, including excessive use of beta-lactam antibiotics, pancreatic fistula, and certain monoclonal immunoglobulins.

Recent interest has emerged regarding the potential relationship between bisalbuminemia and diabetes mellitus. This study aims to explore the role of diabetes in acquired bisalbuminemia through the presentation of two cases and a review of relevant literature.

Case 1 describes a 68-year-old female with recurrent pneumorespiratory infections, leading to the discovery of bisalbuminemia and subsequent diagnosis of diabetes mellitus. Case 2 involves a 71-year-old patient presenting with worsening lower back pain and bisalbuminemia, ultimately leading to a diagnosis of diabetes mellitus.

Discussion highlights the significance of diabetes as a potential contributing factor to acquired bisalbuminemia, as suggested by previous case reports and prospective studies. While further research with larger cohorts is needed to confirm these findings, the inclusion of diabetes biological workup in bisalbuminemia cases may aid in early detection and management.

In conclusion, this study underscores the potential association between uncontrolled diabetes and acquired bisalbuminemia, suggesting the importance of assessing for diabetes in such cases to improve diagnostic approaches for this rare condition.

I. INTRODUCTION

Bisalbuminemia is an uncommon protein abnormality distinguished by the division of the albumin fraction in serum protein electrophoresis, without a rise in its levels(1). It can occur as either congenital or acquired, with the latter frequently connected to different underlying conditions(2). While congenital bisalbuminemia has a genetic basis, acquired bisalbuminemia is often associated with a range of factors, including excessive use of beta-lactam antibiotics, pancreatic fistula, and the interaction of specific monoclonal immunoglobulins(3).

In recent years, there has been growing interest in investigating the potential association between bisalbuminemia and diabetes mellitus(4–6). While diabetes has been implicated as a possible contributing factor in previous case reports, a comprehensive understanding of this relationship remains elusive. Therefore, this study aims to explore the role of diabetes in acquired bisalbuminemia through the presentation of two cases and a discussion of relevant literature.

II. CASE REPORTS

➢ *Case 1*

A 68-year-old female patient, with no significant medical history including no previous diagnosis of GERD, asthma, rhino-sinusitis, HIV, immunodeficiency, or tobacco use, presented with recurrent pneumorespiratory infections. The patient experienced more than four episodes of cough, fever, and purulent expectoration, which had been managed with antibiotics and steroids. Upon clinical examination, there were no signs of oedema in the lower extremities, and the patient's body mass index was within the normal range at 31, with no other discernible pathological findings.

Given the recurrent nature of the respiratory infections, a comprehensive diagnostic workup was initiated, including plasma protein electrophoresis. The results revealed a normal hemogram, suggesting no overt abnormalities in blood cell counts or morphology. Further biological workup revealed a normal renal profile, with creatinine levels at 80 µmol/L, uric acid levels at 160 µmol/L, and urea levels at 6 mmol/L. The serological workup yielded negative results for HIV, hepatitis, and syphilis, ruling out these infectious etiologies as contributing factors to the recurrent pneumorespiratory infections.

The serum protein electrophoresis revealed a bisalbuminemia (Figure 1;A), characterised by a bifid peak of albumin. Following the results of the serum protein electrophoresis (EPP), we conducted a thorough re-evaluation of the patient's medical history through an

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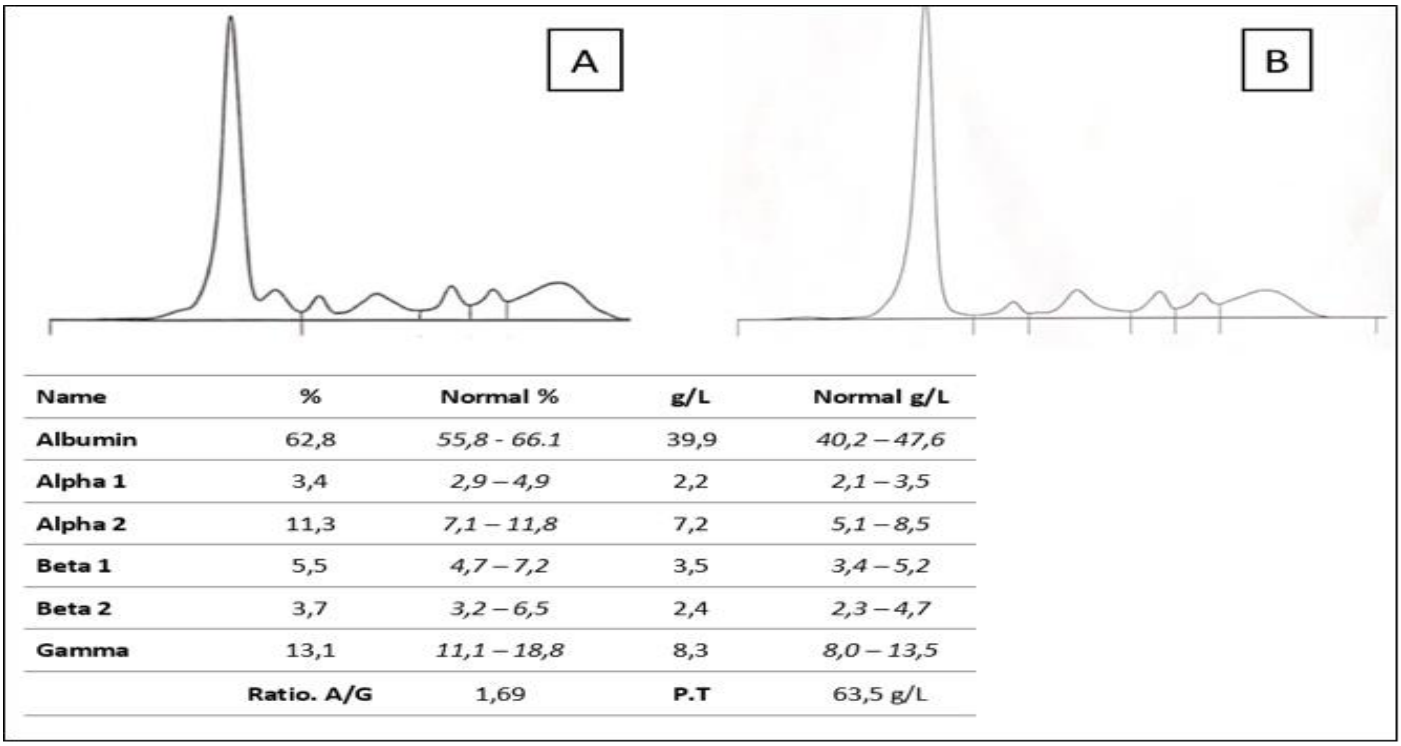
interview, focusing particularly on the use of beta-lactam antibiotics and gastrointestinal symptoms such as abdominal pain, itching, and jaundice. The patient reported negative findings for all these inquiries.

Subsequently, a comprehensive biological assessment was conducted, consisting of a lipid profile, liver function tests, total protein levels, fasting blood glucose, and glycated hemoglobin (HbA1c). The results revealed an HbA1c of 15%, fasting blood glucose of 3g/dl, and hypoproteinemia. A urinalysis strip test later indicated ketonuria at 3 crosses and proteinuria at 2 crosses. A diagnosis of diabetes mellitus was established, and the patient was referred to endocrinology for diabetes management and treatment of her acidosis. After three months, a follow-up serum protein electrophoresis (EPP) showed regression, with the previously widened albumin band having disappeared (Figure 1;B).

➢ *Case 2*

A 71-year-old patient, with no significant medical history, presented with a worsening of longstanding lower back pain five months prior to consultation, with transient improvement of symptoms with NSAIDs and physiotherapy, as well as recurrent rhinopharyngitis. Over the past month, there has been a marked increase in lower back pain, weight loss, fatigue, loss of appetite, and frequent domestic falls.

Clinical examination revealed no notable abnormalities, including no neurological deficit and no edema of the lower extremities. ENT examination revealed no abnormalities.



Name	%	Normal %	g/L	Normal g/L
Albumin	62,8	55,8 - 66.1	39,9	40,2 – 47,6
Alpha 1	3,4	2,9 – 4,9	2,2	2,1 – 3,5
Alpha 2	11,3	7,1 – 11,8	7,2	5,1 – 8,5
Beta 1	5,5	4,7 – 7,2	3,5	3,4 – 5,2
Beta 2	3,7	3,2 – 6,5	2,4	2,3 – 4,7
Gamma	13,1	11,1 – 18,8	8,3	8,0 – 13,5
	Ratio. A/G	1,69	P.T	63,5 g/L

Fig 1: Patient One's Serum Protein Electrophoresis

- Electrophoretic profile showing a bifid peak of albumin.
- Regression of the bisalbuminemia after achieving diabetes equilibrium.

A comprehensive biological and radiological evaluation was performed, including standard dorsolumbar radiography, which showed no lytic lesions or signs of bone demineralization. The biological assessment revealed anemia with hemoglobin levels at 11 g/dl, without evidence of inflammatory syndrome, and a normal renal profile.

Due to clinical suspicion of multiple myeloma, serum protein electrophoresis (EPP) was performed, revealing a biphasic peak of albumin without a monoclonal spike (Figure 2, A).

Given the bisalbuminemia, additional investigations including lipid profile, liver function tests, HbA1c, and fasting blood glucose were conducted, showing an HbA1c of 17% and fasting blood glucose of 5g/dl. A urinalysis strip test indicated ketonuria at 4 crosses, glycosuria at 3 crosses, and proteinuria at 3 crosses.

A diagnosis of diabetes mellitus was established, and the patient was referred to endocrinology for diabetes management and treatment of her acidosis. After three months, a follow-up serum protein electrophoresis (EPP) showed regression, with the previously widened albumin band having disappeared (Figure 2, B).

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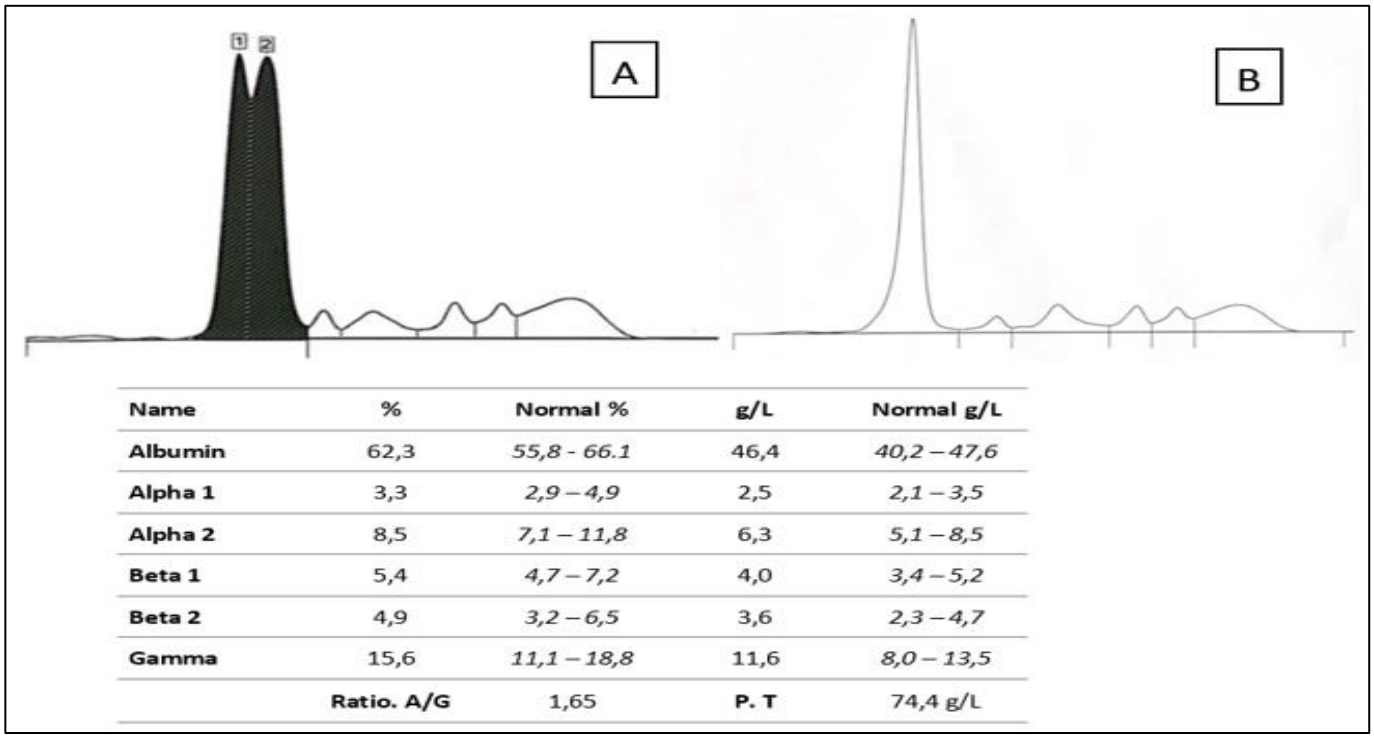

Name	%	Normal %	g/L	Normal g/L
Albumin	62,3	55,8 - 66.1	46,4	40,2 – 47,6
Alpha 1	3,3	2,9 – 4,9	2,5	2,1 – 3,5
Alpha 2	8,5	7,1 – 11,8	6,3	5,1 – 8,5
Beta 1	5,4	4,7 – 7,2	4,0	3,4 – 5,2
Beta 2	4,9	3,2 – 6,5	3,6	2,3 – 4,7
Gamma	15,6	11,1 – 18,8	11,6	8,0 – 13,5
	Ratio. A/G	1,65	P. T	74,4 g/L

Fig 2: Patient two's Serum Protein Electrophoresis

- Electrophoretic profile showing a biphasic peak of albumin without a monoclonal spike.
- Regression of the bisalbuminemia after achieving diabetes equilibrium.

III. DISCUSSION

Bisalbuminemia is a rare qualitative protein anomaly characterized by the splitting of the albumin fraction on serum protein electrophoresis, without an increase in its concentration(4,7). It can be either congenital or acquired, depending on whether it is permanent or transient. Congenital bisalbuminemia is hereditary, while acquired bisalbuminemia can occur due to overdosing with beta-lactam antibiotics, pancreatic fistula, or the binding of certain monoclonal immunoglobulins(8).

The first suspicion of diabetes as a potential associated factor with bisalbuminemia arose in 1976, as reported by Vladutiu AO et al.(4) They identified three cases of bisalbuminemia among hospitalized patients. Remarkably, all three patients had diabetes mellitus, with two of them having a family history of diabetes. Importantly, there was no familial history of congenital bisalbuminemia in these cases.

At that time, they suggested that the potential association between bisalbuminemia and diabetes remained unexplained. Nevertheless, they proposed that it would be intriguing to investigate patients with bisalbuminemia and their relatives for diabetes, hinting at the possibility of a connection between the two conditions.

Acquired bisalbuminemia is, by definition, transient, and the electrophoresis profile returns to normal after the treatment of the underlying pathology(9,10). The most well-known causes of this condition are treatment with beta-lactam antibiotics, pancreatic fistula, and chronic nephropathy(11). Table 1 regroups the causes of acquired bisalbuminemia described in the literature(12)

Table 1: Causes of Acquired Bisalbuminemia

Condition	Associated Causes
Treatment with high doses of beta-lactams	Cephalosporins, Penicillin
Pancreatitis	Rupture of pancreatic pseudocysts, Pancreatic fistulas
Monoclonal gammopathies	Multiple myeloma, Benign monoclonal immunoglobulin
Hepatopathies	Autoimmune hepatitis, Hepatic cirrhosis, Adenocarcinoma liver metastases
Hyperamylasemia	
diabetes	
Alzheimer disease	
Chronic renal failure	Nephrotic syndrome with minimal glomerular lesion

Severely uncontrolled diabetes has long been suspected as a potential cause of bisalbuminemia(4–6). In a prospective study conducted in 2018 by Lugat and al.(5), which included 5 patients, it was concluded that increased glycated albumin (GA) levels due to uncontrolled diabetes might indeed be a causative factor for acquired bisalbuminemia. This condition

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was found in 80% of patients with HbA1c levels exceeding 13.0%.

Nevertheless, they suggested that studies with larger samples would be necessary to confirm the implication of diabetes as a cause of bisalbuminemia.

Consequently, while investigating the origin of bisalbuminemia, we believe that including a diabetes biological workup is crucial, despite the rarity of this condition.

IV. CONCLUSION

Our study underscores the potential association between uncontrolled diabetes and acquired bisalbuminemia. While additional research with larger cohorts is necessary to validate our findings, our results suggest that assessing for diabetes may be beneficial in cases of acquired bisalbuminemia. This insight could improve diagnostic approaches for this rare condition.

- *Statement of Ethics*

The patient has provided written consent for the publication of his personal data, including personal images.

- *Disclosure Statement*

The authors declare that there are no conflicts of interest.

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