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Unraveling the Diagnostic Implications of Elevated Prealbumin Levels in Lithium-Induced Hypothyroidism: A Case Report

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Abstract:- Prealbumin, a multifunctional protein synthesized primarily in the liver, serves as a critical biomarker in clinical practice, offering insights into nutritional status and prognostic outcomes. While its precise physiological role remains incompletely understood, prealbumin is known to facilitate hormone transport, particularly of thyroxine, and contribute to neuroprotection. Clinically, prealbumin levels are sensitive indicators of recent changes in protein intake and absorption, making them invaluable in guiding therapeutic interventions. Alterations in prealbumin levels have been associated with various medical conditions, including chronic kidney disease, liver disease, and cancer, emphasizing its prognostic significance across diverse clinical contexts. we report a case of a 42-year-old male with bipolar disorder managed on lithium therapy, presenting with depressive symptoms and unexpected hyperprealbuminemia. Subsequent investigation revealed primary hypothyroidism secondary to lithium intoxication, highlighting the intricate relationship between lithium therapy, prealbumin levels, and thyroid dysfunction. We discuss the mechanisms and clinical implications of lithium-induced hypothyroidism, emphasizing the importance of considering thyroid function in patients with elevated prealbumin levels. This case underscores the necessity for vigilant monitoring and timely intervention to optimize patient outcomes in cases of lithium-induced thyroid dysfunction. Continued research is crucial for elucidating the complex interactions between prealbumin, lithium therapy, and thyroid function, enhancing our understanding and management of these metabolic disturbances.

Keywords:- *Elevated Prealbumin; Lithium-Induced Hypothyroidism; Biomarkers; Clinical Implications.*

I. INTRODUCTION

Prealbumin, a multifunctional protein synthesized primarily in the liver[1], serves as a biomarker in clinical practice, offering insights into both nutritional status and prognostic outcomes. While its exact physiological role remains incompletely understood, prealbumin is known to facilitate hormone transport, particularly of thyroxine, and contribute to neuroprotection[2]. Clinically, prealbumin levels are sensitive indicators of recent changes in protein intake and absorption, making them invaluable in assessing nutritional status and guiding therapeutic intervention[3] Moreover, alterations in prealbumin levels have been associated with various medical conditions, including chronic kidney disease, liver disease, and cancer, highlighting its prognostic significance across diverse clinical contexts[4–6].

In this context, we present a case report elucidating the diagnostic implications of elevated prealbumin levels in the setting of lithium-induced hypothyroidism.

II. CASE REPORT

We present the case of a 42-year-old male patient with a history of bipolar disorder since the age of 22, managed on a daily regimen of 600 mg of lithium, maintaining a lithium level of 1 nM/L. For the past 4 months, the patient has been experiencing depressive mood, accompanied by anxiety symptoms, anorexia, and a weight loss of 10 kg. Despite treatment with fluoxetine at a dosage of 20 mg per day prescribed by his psychiatrist, there has been no significant improvement in his symptoms.

The patient presented for consultation with signs of malnutrition and dehydration. Upon questioning, he reported a significant decrease in appetite over the past 4 weeks, with no fever or signs of infectious syndrome, palpitations, diarrhea, or vomiting.

On clinical examination, the patient presented with irritability and asthenia, along with a depressive mood. His body mass index was 22, indicating weight loss exceeding 10% (from 80 kg to 78 kg). No icterus or lower limb edema was observed. Urine dipstick test results were negative. Abdominal palpation and rectal examination yielded no abnormalities. Cardiopulmonary auscultation revealed no abnormal findings.

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Considering this clinical presentation, a thorough biological assessment was conducted, including a complete blood count, which did not reveal any signs of anemia. Additionally, an extensive ionogram returned within normal limits, with a lithium level within the therapeutic range at 1 nM/L. Furthermore, serum protein electrophoresis identified a profile with a prealbumin peak.

The discrepancy between the results of the serum protein electrophoresis and the clinical presentation prompted us to investigate the etiology of hyperprealbuminemia in the context of malnutrition. Further inquiry explored the possibility of high-dose corticosteroid or nonsteroidal anti-inflammatory drug intake, as well as underlying adrenal pathology, but no supportive evidence was found. Additional investigation through thyroid hormone level measurement revealed primary hypothyroidism, with a TSH level of 8 mUI/L and a borderline low T4; thyroid antibodies were negative. Cervical ultrasound did not reveal nodules or goiter.

We concluded the diagnosis of subclinical drug-induced hypothyroidism due to lithium intake. The patient was treated with levothyroxine, resulting in clinical improvement and regression of the prealbumin peak following euthyroidism achievement.

III. DISCUSSION

Prealbumin, a protein primarily synthesized in the liver but also found in the choroid plexus and retinal pigment epithelium, is released into the bloodstream, cerebrospinal fluid (CSF), and eyes[1, 2, 7]. While its exact physiological role remains incompletely understood, prealbumin is known to transport thyroxine and retinol-binding protein bound to retinol[8, 9] Moreover, it contributes to neuroprotection and facilitates neurite outgrowth following injury, indicating its multifaceted involvement in hormone transport and neural health support[2].

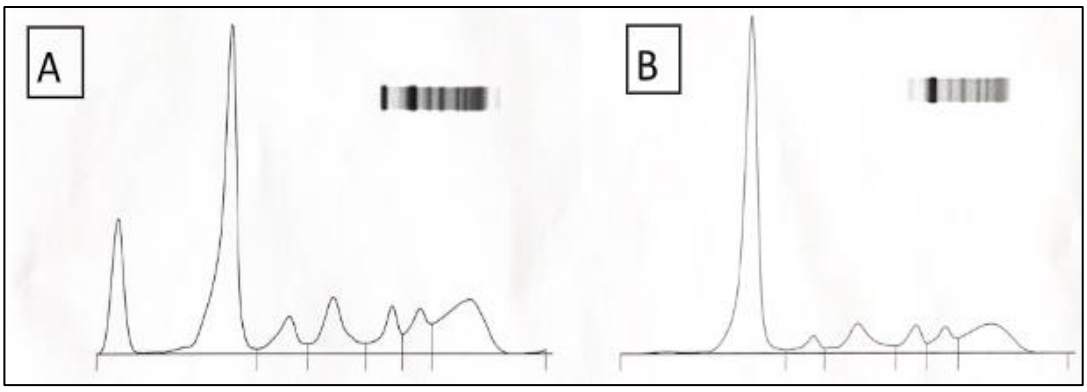

Fig 1:A: Electrophoretic Profile Indicative of an Inflammatory Syndrome with a Prealbumin Peak. B: Normal Electrophoretic Profile of the Control after Achieving Biological Euthyroidism.

Prealbumin is extensively utilized as a biomarker in clinical practice, offering valuable insights into both nutritional status and prognostic outcomes across a spectrum of medical conditions[10–13]. Its sensitivity to recent changes in protein intake and absorption makes it particularly adept at assessing nutritional status. Low prealbumin levels have been linked to elevated mortality rates, prolonged hospital stays, and increased complication rates. Furthermore, prealbumin levels serve as predictive indicators in conditions such as chronic kidney disease, liver disease, and cancer. Tracking alterations in prealbumin levels over time enables clinicians to evaluate the efficacy of nutritional interventions and determine overall patient prognosis[14].

Physiologically, prealbumin levels are influenced by factors such as age, with newborns having lower levels that gradually increase until puberty and then slightly decrease after the age of 50. Gender differences are also noted, with males generally exhibiting higher levels than females during early adulthood. During pregnancy, prealbumin synthesis decreases slightly due to increased estrogen levels[15].

Pathologically, various conditions can cause significant alterations in prealbumin levels. Increased levels are observed in conditions like renal insufficiency, hypothyroidism, hyperandrogenism, and prolonged corticosteroid therapy. Conversely, a rapid decrease in prealbumin levels is a hallmark of malnutrition, with the severity of the decrease correlating with the extent of nutritional deficiency. Interestingly, in cases of anorexia nervosa, prealbumin levels may appear normal due to the counterbalancing effect of associated hyperandrogenism[2, 7, 16].

In the literature, there have been reported sporadic cases where high doses of prealbumin have been concurrent with hyperthyroidism, although such instances are extremely rare[17].

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Table 1 Provides a Comprehensive Overview of How Prealbumin Levels Vary in Different Situations

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

Table 2: Overview of Prealbumin Levels Variations in Different Physiological And Pathological Conditions.

Category	**Condition**	**Prealbumin Level Variation**
Physiological Variations	**Age**	
	Newborns	0.10 - 0.20 g/L
	Children (up to puberty)	Gradually increases
	Adults (over 50 years)	Slightly decreases in both sexes
	Sex	
	Males (20-40 years)	0.33 ± 0.11 g/L
	Females (20-40 years)	0.27 ± 0.10 g/L
	Pregnancy	
	During pregnancy	Slight decrease due to hypoestrogenism
Pathological Variations	**Increased Prealbumin Levels**	**Decreased Prealbumin Levels**
	Kidney failure Hypothyroidism Hyperandrogenism Endogenous or drug-induced hypercorticism (long-term corticosteroid therapy) High-dose nonsteroidal anti-inflammatory medications (NSAID) Hodgkin's disease	Malnutrition Severe or long-term illness Certain digestive disorders Serious infections Hyperthyroidism Liver disease

In this case, the patient's clinical presentation of malnutrition and dehydration, coupled with an unexpected prealbumin peak, necessitated a thorough investigation into the underlying cause. The absence of signs of infection, gastrointestinal symptoms, or significant physical findings redirected the focus to biochemical and endocrine evaluations.

Lithium, a cornerstone treatment for bipolar disorder, is well-documented for its impact on thyroid function[18, 19]. Chronic lithium therapy can lead to hypothyroidism, a condition characterized by elevated thyroid-stimulating hormone (TSH) levels and low or normal thyroxine (T4) levels[19–21]. Lithium's interference with thyroid function occurs through several mechanisms. Its effects on the thyroid gland encompass various presentations. Goiters, a common early side effect of lithium treatment, are notably more prevalent compared to the general population. Hypothyroidism, affecting a significant percentage of patients, is particularly prominent in individuals with pre-existing thyroid autoimmunity. Conversely, hyperthyroidism, though less frequent, can still occur[22].

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Table 3 Regroups the Mechanisms and Clinical Consequences of Lithium's Effects on the Thyroid Gland.

Mechanism	Clinical manifestations
Inhibition of Thyroid Hormone Synthesis and Release	Lithium decreases the sensitivity of the thyroid gland to TSH, inhibiting the synthesis and release of thyroid hormones.
Impaired Iodine Utilization	Lithium competes with iodine, which is essential for thyroid hormone production, thereby impairing hormone synthesis.
Effects on Thyroid Autoimmunity	Lithium can exacerbate autoimmune thyroid conditions.
Goiters	Four times more frequent than in the general population
Hypothyroidism	8-20% of patients
Hyperthyroidism	5% of cases

IV. CONCLUSION

The elevation of prealbumin levels may serve as a potential indicator for secondary hypothyroidism in the context of lithium intoxication. This finding underscores the intricate relationship between lithium therapy and thyroid function, necessitating thorough assessment and management strategies. Clinicians should remain vigilant in monitoring prealbumin levels, particularly in patients undergoing lithium treatment, as they may provide valuable insights into thyroid dysfunction. Furthermore, this observation highlights the importance of considering thyroid function as part of the differential diagnosis in patients presenting with elevated prealbumin levels, facilitating timely intervention and improved patient outcomes. Continued research and clinical vigilance are essential for enhancing our understanding of this complex interaction and optimizing patient care in cases of lithium-induced thyroid dysfunction.

- *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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