CASE REPORT

Congenital analbuminaemia: A case report

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Abstract

Congenital analbuminaemia (CAA) is a rare autosomal recessive disorder in which affected individuals have absent or extremely low levels of serum albumin. Adults with this condition are mostly asymptomatic. To the best of our knowledge this is the first case of congenital analbuminaemia reported in Pakistan. While being treated for acute respiratory tract infection, a very low albumin level was incidentally detected. This lead to further investigations and eventually the diagnosis was made. The complication of hyperlipidaemia associated with this disease was present in our patient. However, with subsequent treatment by intravenous albumin infusion, the serum albumin level and hyperlipidaemia improved. In this case report, we highlight the importance of diagnosing and treating this condition in adults at an early stage. This prevents complications that have been known to occur in this disease which include hypercholesterolaemia, hyperlipidaemia and recurrent respiratory tract infections. Rarely, it may be complicated by hypercoagulability and osteoporosis.

Keywords: Congenital analbuminemia, hypercoagulability, respiratory infection, ALB.

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Introduction

Congenital Analbuminaemia is an inherited autosomal recessive disorder with an incidence of one in 1,000,000 live births. Serum albumin concentration may range from less than 1 g/L up to 10 g/L.[1] Individuals with this disease have very low levels or complete absence of serum albumin. It is caused by mutation in ALB gene and so far twenty-five variations within the ALB gene have been discovered.[2] The most common symptoms and signs present are lethargy, hypotension and oedema, while abnormal blood tests include hypercholesterolaemia and hyperlipidaemia.[3] This disease is not severe in adult analbuminaemic individuals due to the rise in other serum proteins as a compensatory mechanism.[1] The diagnosis is based on protein electrophoresis and is confirmed by ALB gene mutation analysis. Clinically, only about 90 cases have been reported worldwide. We report the first case from Pakistan of congenital analbuminaemia.

Case Report

A twenty one years old Pakistani boy presented to the emergency department of the National hospital and medical center Lahore in May, 2019 with the complaint of fever and shortness of breath for past two days. He was hospitalised and started treatment for acute respiratory tract infection based on the clinical signs and symptoms. His systemic examination was unremarkable and he had normal dietary habits. His family history revealed healthy and non-consanguineous parents and his developmental milestones were normal. His siblings were healthy too. He had a history of recurrent respiratory tract infections since childhood.

Clinical examination showed obesity with the weight of 113 kg, height of 5.5 feet and body mass index of 42 kg/m^2, normal vital signs, pulse of 88 beats per minute, regular, blood pressure of 110/80 mmHg and temperature of 98 degrees Fahrenheit. He had peculiar lower limb lipodystrophy (Figure 1). Abdominal examination revealed

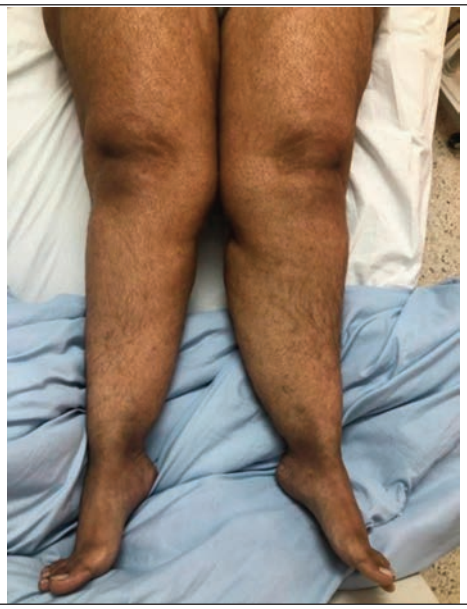

Figure-1: Peculiar lower limb lipodystrophy seen in the patient.

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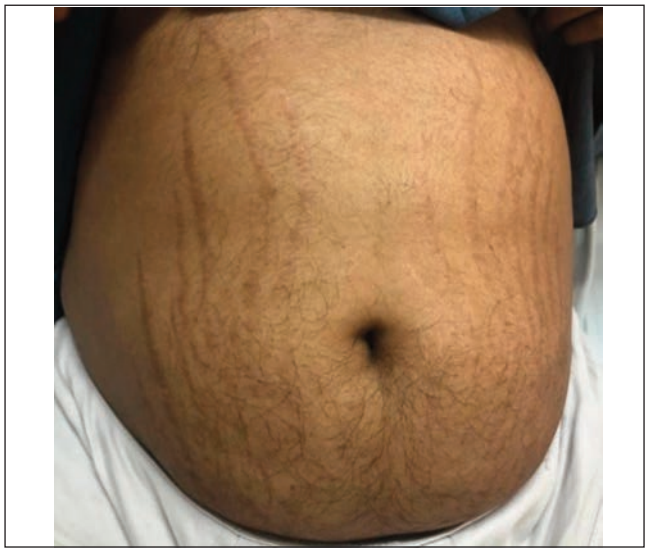

Figure-2: Abdominal striae: an additional finding seen in the patient.

bulky abdomen with central umbilicus, striae present (Figure 2), there were no visible veins or pulsations and there was no tenderness or visceromegaly. Respiratory system findings were consistent with respiratory tract infection. There was no corneal arcus or other signs of dyslipidaemia present and rest of the examination was unremarkable.

Laboratory findings included serum albumin of 0.4 g/dL, serum globulin of 5.2 g/dL, total proteins of 5.6 g/dL. Liver function tests and renal function tests, urinalysis and urinary protein excretion were normal. Serum calcium was 8.2 mg/dL (normal range: 8.6-10.2 mg/dL), serum phosphate was 5.1 mg/dL (normal range: 2.5-4.5 mg/dL), serum parathyroid hormone was 85 pg/ml (normal range: 15.0-68.3 pg/ml) and normal 25-hydroxy vitamin D level of 53.2 ng/mL (optimal range: 30-100 ng/mL). He was treated for acute respiratory tract infection and his condition improved gradually but what was alarming was his asymptomatic extremely low serum albumin levels discovered during his diagnostic workup. This lead us to further search the literature to find out the possible causes of extremely low albumin levels without oedema and underlying renal, hepatic dysfunction or gastrointestinal diseases. We suspected congenital analbuminaemia and therefore further lab workup was done. The protein electrophoresis done after a single albumin infusion, confirmed very low levels of serum albumin concentration and compensatory increase in the levels of other proteins. (Table).

The reduced albumin level of 1.4 g/dL was first noticed three years back. He was given intravenous albumin infusion twice for it, but no proper workup was done. There was no follow-up for years and no treatment was given until this incidentally extremely low albumin level was detected again. His serum lipid profile revealed cholesterol level of 200 mg/dL (desirable range: less than 170), HDL was 38 mg/dL (normal range: more than 40 mg/dL), LDL was 120 mg/dL (normal: less than 100 mg/dL), triglyceride levels were normal 99 mg/dL (normal: less than 150 mg/dL).

Table: Concentration of serum proteins in protein electrophoresis.

	Total %	g/dL	Normal g/dL
Total protein		4.30	6.0-8.5
Albumin	45.0	1.94	3.5-4.7
Alpha 1	3.3	0.14	0.2-0.3
Alpha 2	18.4	0.79	0.4-0.9
Beta	17.4	0.75	0.5-1.0
Gamma	15.9	0.68	0.7-1.5
A/G ratio		0.82	1.1-2.4

He was treated with intravenous albumin infusions (2g/kg), one infusion per week and an improvement in his serum albumin levels and lipid profile was observed on follow-up. He was started on calcium supplements to avoid the development of osteoporosis in the future. Patient's consent has been taken for publishing this case report.

Discussion

Albumin is an important protein that constitutes plasma colloid osmotic pressure, therefore it plays an important role in body fluid distribution. It also binds and transports many substances within the blood.[4]

Congenital analbuminaemia is associated with increased morbidity and mortality during pregnancy and childhood. In adults, compensatory rise in the level of other proteins help them survive.[1] Since analbuminaemia is mostly asymptomatic, it appears in adulthood. However, few patients may present with sequelae such as lower body lipodystrophy, as seen in our patient and major complications such as atherosclerosis, osteoporosis and hyperlipidaemia.

The lipid profile of such patients is deranged showing hypercholesterolaemia and hyperlipidaemia. Elevated serum low-density lipoprotein-cholesterol concentration are also frequently present, as observed in our patient despite having normal dietary habits. In addition, elevated levels of apolipoprotein B, serum high-density lipoprotein-3 and apolipoprotein A-I and A-II levels maybe present as well.[4]

There are different theories suggested by various studies for the underlying mechanism of hyperlipidaemia. One of them demonstrated hepatic origin of the aberrancy. The study proved that albumin deficiency increases the liver production of apolipoprotein B, showing the role of

reduced albumin in lipoprotein metabolism. In addition, the free fatty acids not bound to albumin inhibits lipoprotein lipase, resulting in increased hepatic synthesis of proteins such as Apo A1, Apo B and Apo E along with reduced clearance of triglycerides-rich lipoproteins.[5] Another study conducted on Nagase rats suggests increased extrahepatic synthesis of cholesterol responsible for the hypercholesterolaemia in analbuminaemia. The result showed an increase in HMG co-A reductase protein while its activity remained the same, suggesting post translational regulation of the protein. This proved the underlying mechanism to be extrahepatic. The LDL receptors, HDL receptors and plasma concentration of lecithin cholesterol acyltransferase remained normal, therefore they were not the contributing factors for lipid profile aberrancy.[6] Some studies revealed reversal of abnormal lipid levels in analbuminaemic patients. Waldmann et al. observed that intravenous albumin infusions in analbuminaemic patients resulted in correcting the lipid abnormalities.[7] In another study, Del et al. noticed atorvastatin, a cholesterol lowering drug was associated with decrease in oedema and effective in reducing serum cholesterol level by intravenous albumin infusion. This suggests the possibility that the deficiency of albumin is a contributing factor for hypercholesterolaemia as well as the effect of albumin on lipoprotein metabolism observed in analbuminaemia.[8] On the other hand, it is still uncertain whether analbuminaemia is associated with premature atherosclerosis due the rarity of the condition.

There are other complications associated with congenital analbuminaemia that includes respiratory tract infections, hypercoagulability, osteoporosis and cutaneous angiomata.[9] Recurrent respiratory tract infections and decreased serum calcium levels were observed in the presented case.

Conclusion

Analbuminaemic patients could be asymptomatic but timely screening in suspected patients and appropriate clinical follow-up in this disease is necessary as it is associated with complications such as hypercholesterolaemia, osteoporosis, respiratory tract infections, hypercoagulability, atherosclerosis and obstetrical complications. Although it is benign but there have been conditions reported such as low birth weight, preterm birth, miscarriages, respiratory distress with frequent hospitalisation, and mild developmental abnormalities in few analbuminaemic cases. The presented case confirms the associated conditions of recurrent respiratory tract infections and hypercholesterolaemia.

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Conflict of interest: None.

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