

A Case of Lipoid Congenital Adrenal Hyperplasia Presenting with Cholestasis

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Abstract

Background: Lipoid congenital adrenal hyperplasia, is the rarest and usually the most severe form of adrenal steroidogenic defect, which may present as infantile cholestasis.

Case Presentation: Here we present a 45 days old infant who came to our attention with cholestasis and severe intractable vomiting and electrolyte disturbances. Evaluation resulted in diagnosis of congenital adrenal hyperplasia. Hydrocortisone and fludrocortisone improved the symptoms including jaundice and vomiting. Hyponatremia and hyperkalemia also resolved with above mentioned treatment.

Conclusion: Congenital adrenal hyperplasia as one of the causes of neonatal cholestasis should be kept in mind, whenever there are also electrolyte abnormalities.

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Introduction

Neonatal cholestasis is defined as prolonged conjugated hyperbilirubinemia that occurs in the newborn period. It results from diminished bile flow and/or excretion, which can be caused by a number of disorders. Neonatal cholestasis affects approximately one in 2500 births [1,2]. The evaluation of neonatal cholestasis may appear complicated because of the large number of

potential diagnoses, the similar clinical presentations of a variety of conditions and the non specificity of diagnostic tests.

However, reduction of bile secretion into bile canaliculi with similar mechanism to hypocortisolism in idiopathic hypopituitarism and congenital lipoid adrenal hyperplasia (CAH) can result in cholestasis.

CAH is characterized by deficiency of all adrenal and gonadal steroid hormones, increased

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adrenocorticotropin hormone (ACTH) secretion, and marked adrenal hyperplasia with progressive accumulation of cholesterol esters. It is transmitted as an autosomal recessive trait [3,4].

Although CAH occasionally presents later in infancy, patients with severe form of congenital lipid hyperplasia who have typically severe adrenal insufficiency present very soon after birth, with vomiting, diarrhea, volume depletion, hyponatremia and hyperkalemia. Male infants usually have female external genitalia due to lack of testicular androgen production, but female infants are normally developed at birth [5,6].

Case Presentation

A 45 days old infant with female appearing genitalia was admitted because of recurrent vomiting, poor feeding and cholestasis. It was a product of consanguineous parents with birth weight of 3300 grams. Problems started from third day of life with recurrent vomiting and poor intake which led to poor weight gain.

Intermittent clay colored stool was reported by parents, with changing to completely acholic type a few days before admission. No similar presentation or family history of other features of liver or endocrine disease was reported. On Physical examination length measured 50 cm (<5th percentile), weight 3000 g (<5th percentile), and head circumference 36.5 cm (5-10th percentile). She had a weak pulse, with a heart rate of about 130 beats per minute. Blood pressure was 50/40 mmHg at admission. She had pallor and decreased

subcutaneous fat and ill appearance with severe dehydration. Patient's sclerae and skin were obviously jaundiced. External genitalia seemed normal female type. The patient was admitted to PICU and blood drawn for necessary laboratory tests. Initial resuscitation including; rehydration therapy and correction of blood glucose and electrolyte abnormalities started. Broad spectrum antibiotic also was administered due to patient's ill appearance.

Sepsis workups including blood culture and urine culture were performed, which later results showed both negative. Considering cholestasis presentation, other investigation including tyrosine level, laboratory assessment for metabolic disorders including serum and urine amino acid chromatography, urinary organic acid profile and NH₃ and lactate levels were evaluated with all in normal range but serum alpha1 antitrypsin concentration was mildly increased. The markers for hepatitis and TORCH infections were also negative.

The laboratory tests were as follows: serum sodium 102 meq/lit and serum K⁺ level 9 meq/lit. Total and direct bilirubin was 13.9 mg/dl and 5.4 mg/dl retrospectively. Erythrocyte sedimentation rate was 7. Thyroid function test was normal and serum glucose level by either glucose oxidase or orthotoluidine method were lower than normal but with no significant difference. Other laboratory findings are shown in Table 1. Buccal smear was negative for Barr body. Abdominal sonography showed both adrenals hypertrophic but otherwise normal. Pelvic sonography revealed the testicles in the inguinal canal; moreover, a uterus was not detected in pelvis. Ophthalmic funduscopy in view of corioretinitis, cataract was not conclusive; chromosome study showed 46XY pattern.

Table 1: laboratory findings of our patient with congenital lipid adrenal hyperplasia and infantile cholestasis

Lab Tests	Patient	Normal range	Lab Tests	Patient	Normal range
ALT	23	5-40 IU/L	Na	102 meq/lit	135-145 meq/lit
AST	80	10-50 IU/L	K	9 meq/lit	3.5-5 meq/lit
ALP	326	180-1200 IU/L	T. protein	5.3	6.1-7.9 g/L
GCT	123 IU/L	8-90 IU/L	Albumin	4	3.9-5 g/L
Bilirubin total	13.9	0.2-1.3 mg/dL	PT	12	10-12
Bilirubin direct	5.4	<0.3 Mg/dl	INR	1	
Triglycerides	43	40-140	HCT	33.5%	28-42%
Cholesterol	66	120-220	PLT	874 x10 ³ /μL	140-450x10 ³ /μL
Blood glucose	35	60-100mg/dL			

ALK: Alkaline Phosphatase. ALT: Alanine aminotransferase. AST: Aspartate aminotransferase, GGT: Gamma glutamyl transpeptidase

Table 2: Results of laboratory tests of the patient

Lab tests	Patient	Normal range
Cortisol 8AM	1µg/dL	5-23µg/dL
17 hydroxy-progesteron	0.06	<2.5ng/ml
Dehydroepiandrosterone	10 ng/ml↓	<40mcg/dl
Renin	600	
Adrenocorticotropin Hormone	475 ng/L	<۲۰-۱۰۰ ۵۳/۷۵

Severe electrolytes abnormalities guided us to possible diagnosis of CAH, and further evaluation including findings in Table 2 proved this diagnosis. Fludrocortisones and hydrocortisone replacement therapy was instituted and resulted in dramatic improvement. Electrolyte abnormalities and blood sugar was corrected during first week of treatment (Na=130 and K=4.5 Meq/lit). One week later, the total and direct bilirubin declined to 5 and 2.5 mg/dl respectively. After one month, bilirubin levels and all of the liver function tests returned to normal, jaundice disappeared and acholic stools changed to normal pattern. In the following 6 months no history of acholic stool or hypoglycemic attacks were noticed.

On her most recent visit at the age of 15 months, the patient had no obvious problem. Her height was 75 cm (25th percentile), weight 9.5 kg (10-25th percentile) and head circumference 46 cm (25th percentile); her neurodevelopment was appropriate for age.

Discussion

The association between neonatal cholestasis and hypopituitary deficiency is now well recognized [7]. However, only few patients have been described with liver disease and a primary adrenal disorder [8]. Of these, fewer cases had congenital adrenal hyperplasia with aldosterone deficiency. We present a case of neonatal cholestasis in association with adrenal hyperplasia.

The diagnosis of neonatal cholestasis is supported by conjugated hyperbilirubinemia. Considering acholic stools reported by parents, extrahepatic obstruction was ruled out. Routine evaluation including assessment of tyrosinemia, galactosemia, neonatal hepatitis and other

common causes of cholestasis showed absence of known causes of neonatal cholestasis.

Hyperpigmentation and recurrent hypoglycemia, severe electrolytes derangement with low level of cortisol and aldosterone, increased level of ACTH and rennin activity, suggested an adrenal hyperplasia. Congenital lipid adrenal hyperplasia has been proved to be a fatal condition in infancy in two-thirds of reported patients, but some patients survive to go through puberty [9,10].

Lipoid CAH is the most severe and rarest form of salt wasting disease. Affected patients are male hermaphrodites. Patients with congenital lipid adrenal hyperplasia have very low serum cortisol and aldosterone concentrations and very high plasma ACTH concentrations and rennin activity [9,10].

Production of gonadal steroids is also impaired, and serum gonadotropin concentration is high (for age) in children as young as 4.5 years old [10]. Glucocorticoid and mineralocorticoid deficiency has been managed by replacement therapy in a few cases [10]. For reasons that are not clear, serum adrenocorticotrophic hormone (ACTH) concentration and plasma rennin activity may remain elevated during treatment with supra physiologic doses of glucocorticoid and mineralocorticoids [10].

The cause of cholestasis in CAH is not clear yet, but lack of glucocorticoid that may result in decreased bile secretion into the canaliculi have been explained as a possible reason. Since corticosteroids appeared promising to improve bile flow after portoenterostomy and long-term survival, based on initial uncontrolled trials [11], it seems that low level of cortisol may result in decreased bile flow which led to acholic stools in our patient. It is also suggested that cortisol deficiency is the primary disturbance leading to disturbed liver function in infants with hypopituitarism and adrenal insufficiency [8]. This case report supports that concept.

However, it is criticized by other authors [12]. Lacy et al reported a case with neonatal hepatitis and congenital insensitivity to Adrenocorticotropin, and suggested that cortisol deficiency occurring during development, might delay hepatic maturation in the first months of life [13].

A designed study by Lee and Chai, reinforced the overlapping nature of the presenting clinical features of biliary atresia and other etiologies of neonatal cholestasis. As a result of his prospective, descriptive study conducted on 146 infants with neonatal cholestasis, congenital adrenal hyperplasia was diagnosed in only one of 146 patients [14].

Conclusion

To our knowledge there are few reports of CAH as a cause of neonatal cholestasis[15]. Disturbance of the pituitary-adrenal axis, whatever the cause, may occasionally be associated with neonatal cholestasis. Hypoglycemia and electrolytes disturbances in the presence of neonatal cholestasis should be considered for a possible congenital adrenal hyperplasia as a main pathology.

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