A rare co-existence of two autosomal recessive conditions: Congenital adrenal hyperplasia due to 21-hydroxylase deficiency (*CYP21A2* mutation) with Beta thalassemia major

Aniqa Aslam[1], Sommayya Aftab[1,2], Tahir Shaheen[1], Muhammad Nadeem Anjum[3], Anjum Saeed[3], Huma Arshad Cheema[3]

[1]Department of Paediatric Endocrinology and Diabetes, The Children's Hospital & The Institute of Child Health, Lahore.
[2]Consultant Paediatric Endocrinologist and Diabetologist, Hameed Latif Hospital, Lahore
[3]Department of Paediatric Gastroenterology and hepatology, The Children's Hospital & The Institute of Child Health, Lahore.

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INTRODUCTION

- 21-hydroxylase deficiency is the most common cause of congenital adrenal hyperplasia (CAH). It is an autosomal recessive condition due to *CYP21A2* mutation leading to 21-hydroxylase enzyme deficiency in adrenal gland which leads to decrease synthesis of cortisol and aldosterone and increased synthesis of androgens as shown in figure 1.

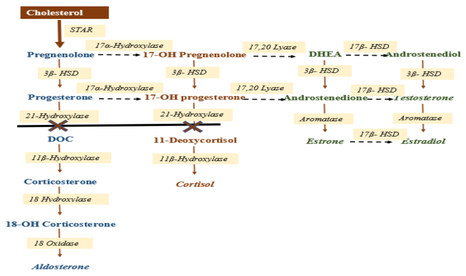


Figure-1. Showing Pathophysiology of CAH due to of 21-hydroxylase deficiency

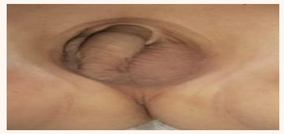
- Beta thalassemia is an autosomal recessive condition caused by defective beta-globin chain synthesis and accumulation of unbound alpha globin chains leading to ineffective erythropoiesis.
- We are reporting a case with rare co-existence of CAH due to 21-hydroxylase deficiency with beta thalassemia major.

CASE SUMMARY

Initial Presentation

- A 20-day old neonate presented with complaints of failure to thrive and repeated vomiting. He was born to consanguineous parents with two more sibling (one sibling known to have thalassemia major). There was no history of infant's death, ambiguous genitalia and CAH in family.
- On examination baby was severely dehydrated with normal male like genitalia (bilateral testis palpable in scrotum) as shown in figure 2.

Figure-2 Showing abnormal male like genitalia



Initial workup & Diagnosis

- Initial investigations revealed severe hyponatremia, hyperkalemia, metabolic acidosis with raised 17-OH progesterone (table-1), all suggestive toward salt looser CAH.

Table-1 showing initial investigations

Investigations	Results
Sodium	128
Potassium	8.8 mmol/L
17-OH Progesterone	>320 ng/L

Genetic Analysis

- It was later confirmed by genetic testing that he is having CAH (21-hydroxylase deficiency) due to homozygous pathogenic CYP21A2 variant c.955C>T p.(Gln319*).

Initial Management

- After initial stabilization with IV hydrocortisone, he was started on long term hydrocortisone (20mg/m2/day in 3 divided doses) and (fludrocortisone 0.1 mg/ day) along with education regarding sick day management
- At 11 months of age, he presented with marked pallor and hepatosplenomegaly. Full blood count showed Hb of 5.6 g/dl with reticulocytes count of 2.8 % and peripheral smear showing anisocytosis and poikilocytosis.
- Hb electrophoresis done suggestive of beta thalassemia major as shown in table-2

Table-2 Showing Hb Electrophoresis

Hb Electrophoresis	Result
HbA1	14.6 %
HbA2	4.9 %
HbF	80.5 %

- He received a transfusion and was started on folic acid supplementation with proper follow up for need of repeated transfusions and chelation

DISCUSSION

- This is very rare coexistence of two different autosomal recessive conditions.
- Literature review just reveal only one such case reported in India in 2012 by Yewale etal.

CONCLUSION

- We are reporting a very unusual co-existence of two different autosomal recessive conditions: 21-hydroxylase deficiency and Beta thalassemia Major.
- It might be due to increased penetrance of Thalassemia major and CAH (21-hydroxylase deficiency) in our population with increasing trend of consanguineous marriage.

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CONTACT INFORMATION

Aniqa Aslam
Aniqaslam2812@gmail.com
Post-graduate Trainee
The Children's Hospital & The institute of Child Health, Lahore