

# Neonatal Meningitis Together With 11-Beta Hydroxylase Enzyme Deficiency: A Case Report

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## Citation

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## Abstract

Congenital adrenal hyperplasia is a disease which results in autosomal recessive transition with deficiency of the necessary enzymes for cortisole synthesis from cholesterol. The most frequently deficient enzyme is 21-hydroxylase and the second most common is 11-beta hydroxylase. A deficiency of 11-beta hydroxylase is seen in 5 -8% of congenital adrenal hyperplasia cases. An increase in androgyny develops depending on the clinical findings. Neonatal meningitis is an important central nervous system infection because of morbidity and mortality. Of all age groups, meningitis is most commonly seen in neonates. This study presents the case of a 20-day old baby who presented at our emergency department with neonatal sepsis and meningitis, then on physical examination was seen to have ambiguous genitalia and investigative tests resulted in a diagnosis of 11-beta hydroxylase deficiency.

## INTRODUCTION

Congenital adrenal hyperplasia develops as a result of the deficiency of the necessary enzymes for the synthesis of cortisole from cholesterol. A deficiency of 11-beta hydroxylase, cortisole and corticosteroids in the zona fasciculata layer of the adrenal gland results in an accumulation of cortisole primary matter (1). Of all congenital adrenal hyperplasia cases, 5-8 % show a deficiency of 11-beta hydroxylase enzyme (1). In Turkey this rate is known to be 13.5 -16% (2). Clinical findings of virilisation and hypertension are seen and autosomal recessive transition (1,2).

This study presents a case initially diagnosed as meningitis but following physical examination at the clinic and investigative test results, resulted in a diagnosis of 11-beta hydroxylase deficiency.

## CASE

A 20-day old infant was brought to the Paediatric Emergency Unit of Harran University Medical Faculty with complaints of high temperature, non-feeding and changes in consciousness. From the patient history it was established that the birth had been a normal vaginal birth in hospital and the complaints had started 5 days previously. The findings of the first examination in the emergency department gave an initial diagnosis of sepsis and meningitis and the infant was admitted to the neonatal intensive care unit. The mother and

father were first cousins and physical development was normal. The general condition was average with consciousness tending towards drowsiness, temperature 39 °C, pulse 140/min, respiration 30/min, blood pressure: 80/40 mmHg. The neonatal reflexes were weak, the fontanel swollen and signs of opisthotonus. Genital examination revealed a hypertrophic clitoris and labia joined at the midline (Prader Grade III) (Figure 1, Figure 2). Other system examination results were normal.

Tests carried out at 20 days: White Blood Cell 34000 cells/mm<sup>3</sup>, CRP 10 mg/dl, Sodium 151mg/dl, Potassium 4 mg/dl, Calcium 10 mg/dl, Urea 305, Creatinine 1.6 mg/dl, DHEA-S 60 mg/dl (N:4-68 mg/dl), 17-OH Progesteron 183 ng/ml (N:0.1-0.5 ng/ml), Androstenedione 35 ng/ml (N:0.1-0.5), 11-Deoxycortisole 80 ng/ml (< 8 ng/ml), Cortisole 22 (N:4-25) ng/ml, free testosterone 704 (N:241-827) ng/dl. Lumbar puncture in the Thoma lam method determined 10 x 10 cells/mm<sup>3</sup> in all areas ( Cerebrospinal fluid dispersal 60% fragmented, 40% Lymphocyte) Cerebrospinal fluid biochemistry; Glucose:10 mg/dl, synchronous blood sugar 70 mg/dl, chloride 100 mg/dl, protein 150 mg/dl. The internal genital structures of ovaries, uterus and vagina were evaluated by Batın Ultrasonography. Chromosomes type 46 XX were seen. From these findings the case was diagnosed as meningitis, 11-beta hydroxylase enzyme deficiency and prerenal insufficiency. Appropriate antibiotherapy and fluid treatment was started. Klonazepam

treated was added due to the continuation of opisthotonus. An appropriate dosage of oral hydrocortisol treatment was started. A control lumbar puncture was done after treatment. There were no cells in the cerebrospinal fluid. CSF values were normal. Antibiotic treatment of Cefotaxime with Amikacin was given 14 days.

A significant improvement in the general condition was observed in follow-up. The case was transferred to the plastic surgery clinic for surgical correction. The patient's general condition is good now, the necessary plastic surgery has been done, follow-up is continuing and before discharge from hospital the CSF values were normal.

### Figure 1

Figure 1: External genitalia of case



### Figure 2

Figure 2: Male type external genitalia of case



## DISCUSSION

There is a deficiency of 11-beta hydroxylase in 5-8% of cases of congenital adrenal hyperplasia. The rate seen worldwide is 1/100,000 (3) but this rate is higher in Turkey and the Middle East. The rate of 11-beta hydroxylase enzyme deficiency in Turkey is known to be 15.5 -16% (2). It is an autosomal recessive transition which develops from the lack of 11-beta hydroxylase enzyme in the zona fasciculata layer of the adrenal cortex. The first step in halting the synthesis of cortisol is an accumulation of 11 deoxycortisol and 11 deoxycorticosterone. An effect of the accumulated corticoid deoxycorticosterone is the accumulation of salt which causes hypertension (1). The enzyme is produced from 2 isoenzymes. The isoenzymes CYP11B1 and CYP11B2 play a role in the cortisol synthesis. These isoenzymes are localized in P450 cytochrome in the mitochondrial membrane. The first recognition of an isoenzyme was in 1950 (1,3,4). A deficiency of 11-beta hydroxylase results in the development of a point of mutation in the 8th chromosome (8q22) CYPB1 gene.

The clinical pathology result of non-synthesis of cortisol is an increase in ACTH synthesis. Increased primary substances of cortisol are due to the increase in ACTH. Progesterone, 17-OH progesterone and 11deoxycortisol increase. Androgyn synthesis increases. Clinically, signs of hypertension and virilisation develop. In a study of 26 cases (14 male, 12 female) by Rosler et al in 1982 the 12 females had hypertrophic clitoris, joined labia and developing penile

urethra. Most of the male patients were diagnosed with findings of the early onset of puberty. Hypokalemia was determined in 8 cases (4). Clark et al. presented 2 non-classic cases, one of which was a 6-year old boy with high blood pressure and signs of Tanner 3 precocious puberty, and the other a one-month old girl not showing conjoined labia and with normal arterial pressure (5). In our case no significant finding was seen in the follow-up of blood pressure. The diagnosis was made from the serum 17-OH progesterone, 11-deoxycortisol, 11-deoxycorticosterone and increased androgens. The level of plasma renin and aldosterone was low. A prenatal diagnosis can be made from amniotic fluid or urine 11 deoxycortisol and chorion villus cells and amniocyte DNA analysis. (6).

There is a high rate of mortality and morbidity from neonatal meningitis and this is the age above all others when it is most commonly seen (7). B group streptococci and gram negative bacteria are the most common agents of meningitis in newborns. The distribution of the bacteria responsible for sepsis and meningitis varies from country to country and socio-economic conditions are known to play a role in the etiology. Neonatal meningitis occurs in 0.2 -0.72:1000 live births (7,8,9). There is a higher risk with prematurity, low birth weight, prolonged use of general spectrum antibiotics, total parenteral nutrition and male gender (7,8,9). Neonatal meningitis has a mortality rate varying between 10 -30%. As there are serious outcomes to neonatal meningitis, the treatment regime should be decided by starting with empirical general spectrum antibiotics then continued according to the culture results and complications (7,8,9,10)

With the appropriate antibiotics our case made a significant clinical improvement. No complications were observed during the acute phase. To the best of our knowledge there is no published literature on meningitis and 11-beta

hydroxylase enzyme deficiency together. It was learned from the family that the small birth genitalia grew later. As our case was diagnosed early any negative psychological problems for the future were prevented. In this case report between 11-beta hydroxylase enzyme deficiency with Meningitis not detected any relationship.

In conclusion, the case was given a diagnosis of asymptomatic 11-beta hydroxylase enzyme deficiency and meningitis from physical examination and laboratory results after having been admitted to the neonatal unit. This case is presented due to the rarity of meningitis and 11-beta hydroxylase enzyme deficiency occurring together.

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