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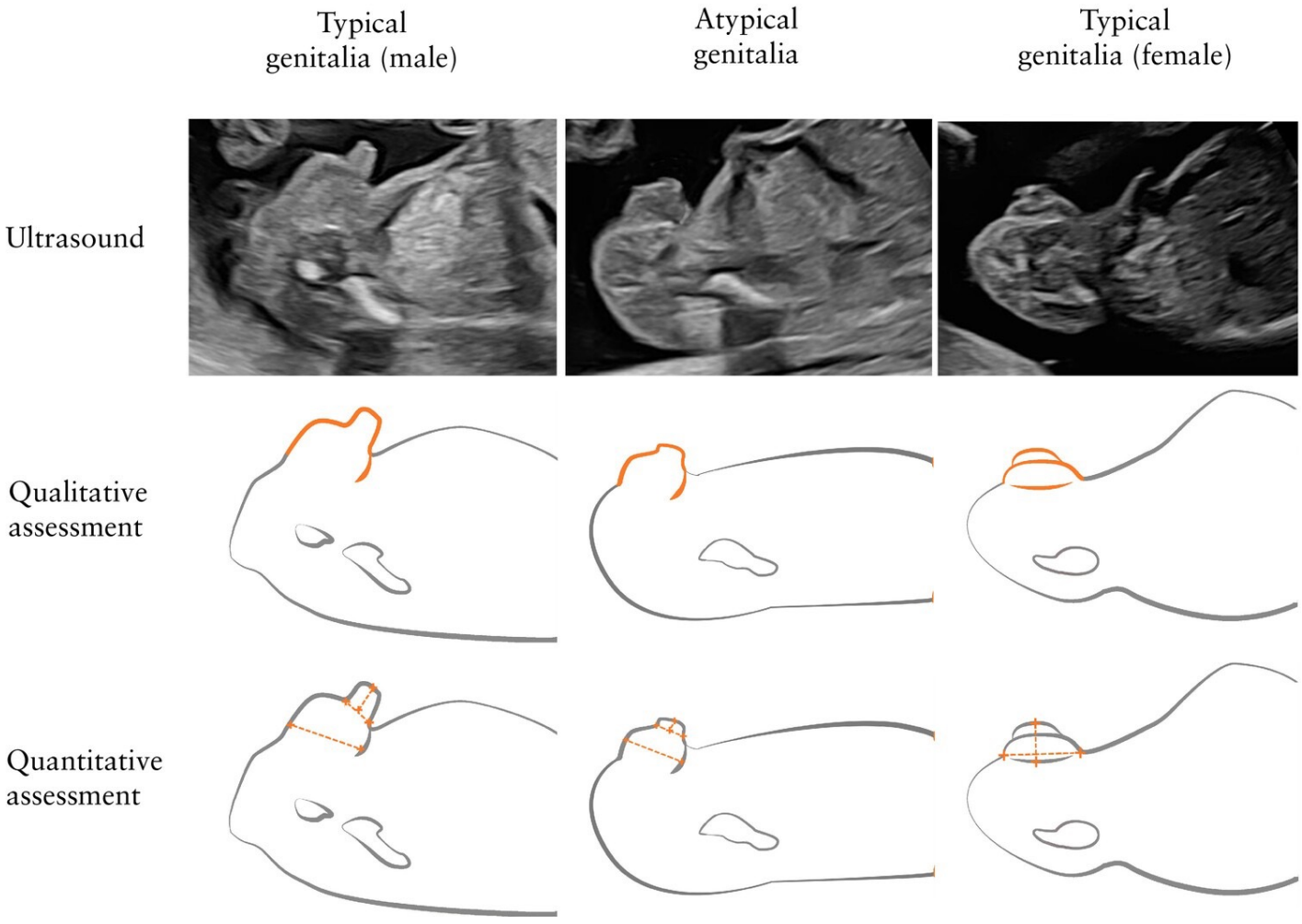


A CLINICAL CASE OF AMBIGUOUS GENITALIA IN A NEWBORN

Abstract:

Introduction: Ambiguous genitalia, also called atypical genitalia, is a rare condition where a child is born with outer genitals that do not look either male or female. Lack of production of certain hormones can cause the embryo to develop with a female body type, regardless of genetic sex.

Methodology: A 20-day-old baby came in OPD with persistent vomiting and dehydration. She had hypernatremia, hypokalemia, and cardiac arrhythmia. Genital examination showed ambiguous genitalia. Karyotyping report XY genotype. With conservative management, she recovered and went home but returned back in an emergency within a few days in poor condition. There was severe depletion of serum potassium level and persistent arrhythmia, for which the baby was transferred to NICU and put on a ventilator. The baby finally died due to persistent arrhythmia.

Result: on first admission, the baby had hypokalemia (2.6 mmol/L), hypernatremia (168 mEq/L), moderate dehydration, and metabolic acidosis (pH 7.31, bicarbonate 18 mmol/L). The baby was managed conservatively and discharged. On the 2nd admission, the baby had poor general condition, persistent metabolic acidosis (pH 7.28 and bicarbonate 12 mmol/L), and persistent hypokalemia.

Conclusion: With all the above findings, we can conclude that the baby was suffering from congenital adrenal hyperplasia, probably due to 17 alpha-hydroxylase deficiency.

Keywords:

ambiguous genitalia, karyotyping, congenital adrenal hyperplasia

Introduction: Ambiguous genitalia, also called atypical genitalia, is a rare condition where a child is born with outer genitals that do not look either male or female. They may have features of both sexes or not be fully developed. The characteristics of the child's genitals may not match their internal sex organs or their genetic sex. [1]

Sex determination and sex differentiation can be divided into chromosomal sex or karyotype (46 XX, 46 XY, or variants), gonadal sex (presence of a testis or ovary), and phenotypic sex (external genitalia and internal structures). [1]

The human embryo is bipotential, with genetic sex determined at conception. The male and female reproductive organs and genitals both come from the same tissue in the fetus. Male differentiation requires specific molecular and biochemical stimuli

at particular times. Female differentiation occurs in the absence of male-determinant genes. [2] Ambiguous genitalia can develop if the process that causes this fetal tissue to become "male" or "female" is disrupted. The physical appearance of people with this condition can vary widely. Rarely, the physical appearance may be fully developed as the opposite of the genetic sex. For example, a genetic male may have developed the appearance of a female. [2]

The common disorders of sexual development are Klinefelter Syndrome (47XXY), Turner Syndrome (45X), Mixed gonadal dysgenesis, Congenital adrenal hyperplasia (CAH), Androgen insensitivity syndrome and Cryptorchidism [3]

Lack of production of certain hormones can cause the embryo to develop with a female body type, regardless of genetic sex. Androgen insensitivity syndrome is such a condition where even if the body makes the hormones needed to develop into a physical male, the body does not respond typically to those hormones. This may produce female characteristics, even though the genetic sex is male. [3]

Here we presented a case of a newborn with ambiguous genitalia

The case: A 20-day-old female (previously diagnosed at the time of birth as per the birth certificate) patient came to the emergency room with complaints of intermittent vomiting for 3 days. On examination, the baby was moderately dehydrated, irritable, and semiconscious. The mother gives a history of premature birth delivered by SVD at 28 weeks. His birth weight was 1.7 kg. The baby was kept in the NICU for the first 72 hours, where he was treated with fluid, oxygen, and phototherapy (for 1 day) for physiological jaundice. No history of sepsis or antibiotic estimation had been seen according to the previous treatment record. The baby, along with the mother, was discharged on Day 5 of life. The mother also complained of a history of mild respiratory distress, which gradually aggravated for the last 6 to 7 days, for which she took the baby to a local health centre, where she was treated with a bronchodilator, fluid, expressed milk, nebulisation, and antibiotics. For the last 3 days, because of intractable vomiting and altered sensorium, the baby had been referred to the emergency department of the College of Medicine and Sagore Dutta Hospital.

Materials and methods: The baby was admitted to the neonatal intensive care unit. On admission, she had severe respiratory distress with RR 84/m, chest retraction, and mild cyanosis was present. Heart rate was 142/m, BP was 70/40 mmHg, and the baby

was irritable but lethargic, with moderate dehydration. Pallor and jaundice were absent. The baby was primarily treated with fluid, oxygen, and nebulisation. A blood sample was collected at the admission. Blood reports showed a normal hemogram, hypernatremia, hypokalemia, routine liver function tests, and thyroid function test reports.

The arterial blood gas report at 12 hours of admission showed metabolic acidosis with normal sodium and persistent hypokalemia. The baby was then put on Na-bicarbonate to combat metabolic acidosis and potassium chloride injection for hypokalemia.

With 4 days of supportive treatment of hypokalemia, the baby stabilised, respiratory distress improved, and electrolyte imbalance corrected.

However, in the systemic examination, the baby had persistent tachycardia. Genital examination showed an enlarged clitoris/penis.

The chest X-ray and ECG were normal; echocardiography was within normal limits. Then, the paediatrician suggested karyotyping, in which 46XY was found.

After 8 days of homestay, the baby was again hospitalized for persistent respiratory distress. On admission, the baby was diagnosed again to have hypernatremia, hypokalemia, and metabolic acidosis. The baby was shifted to the NICU for better management and was put on mechanical ventilation. Gradually, the baby's condition became poor with persistent acidosis, and after 5 days of hospital stay, the baby died.

Results:

Table 1: Investigations done on the 1st-time admission as follows:

Parameters	Method	Value	Unit	Reference range
Bilirubin (Total)	Photometry	1.6	mg/dL	
Bilirubin (direct)	Photometry	0.6	mg/dL	
Urea	Photometry	12.5	mg/dL	
Creatinine	Photometry	0.82	mg/dL	
Sodium	Indirect ISE	168	mEq/L	135-145
Potassium	Indirect ISE	2.6	mmol/L	3.6-5.2
Random blood sugar	Photometry	52	mg/dL	
Hemoglobin	Photometry	14.9	g/dL	11.5-15.5
Total leukocyte count	DC detection method	8600	*10^3/µL	5 - 13

Differential count	DC detection method	N: 42%, L:52%, M:3%, E:2%, B: 1%	%	N-40-60%, L-20-40%, M-2-5%, E-1-4%, B-0-0.9%
ESR	Westergren method	18	mm/hr	3-13
Platelet	Microscopy	260*10^3	*10^3/µL	170-450*10^3
CRP	Immunoturbidimetry	19	Mg/dl	<10

Abbreviation: RBC – Red Blood Corpuscles, WBC—White blood corpuscle N – Neutrophil L-Lymphocyte, E-Eosinophil, B-Basophil, M – Monocyte, PCV-Packed cell volume

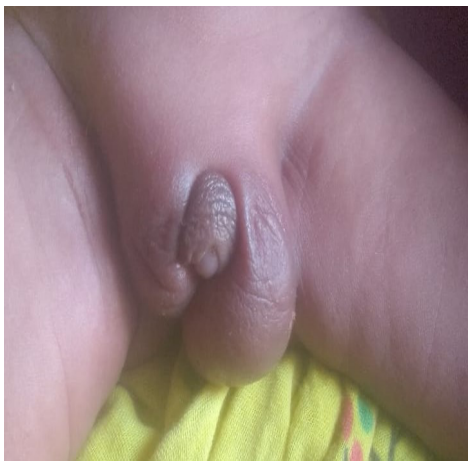
Table 2: ABG report on 1st admission

Parameter	Value	Unit	Reference range
pH	7.31		7.35-7.45
pCO2	46	mmHg	35-45
pO2	78	mmHg	75-100
HCO3	18	Mmol/L	22-26
BE	-4	Mmol/L	±2

Abbreviation: BE: Base Excess

Table 3: ABG report on 2nd admission

Parameter	Value	Unit	Reference range
pH	7.28		7.35-7.45
pCO2	48	mmHg	35-45
pO2	74	mmHg	75-100
HCO3	12	Mmol/L	22-26
BE	-10	Mmol/L	±2



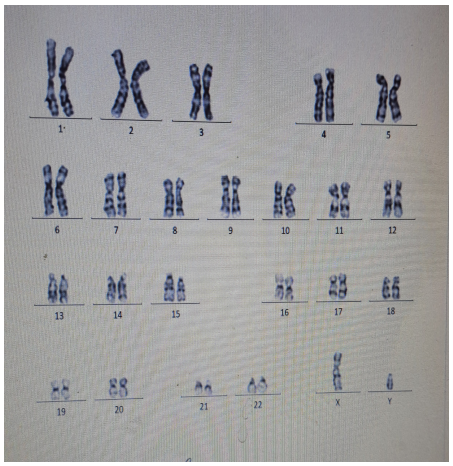


Fig 1: External genitalia and the karyotyping profile of the baby

Discussion:

17-alpha-hydroxylase deficiency (17OHD) is a rare autosomal recessive disorder caused by mutations in the *CYP17A1* gene, which occurs in 1 in 50,000 live births and only 1% of congenital adrenal hyperplasia (CAH). [4] There is a decrease in cortisol, androgen, and estrogen production with a subsequent increase in adrenocortico-trophic hormone (ACTH) and gonadotropin levels. [5] High ACTH levels contribute to increased production and accumulation of 17-deoxycorticosteroids, especially deoxy-corticosterone. Excessive levels of mineralocorticoids lead to volume expansion, hypertension, hypokalemia, and high, regular, or suppressed aldosterone, with oligo/amenorrhea in females and pseudo-hermaphroditism in males. [6]

Androgen and estrogen production is also affected because 17-hydroxylase/17 in the gonads plays an important role in sexual maturity throughout fetal life and puberty. [7] This results in ambiguous or female external genitalia in affected male individuals and absent or delayed pubertal development in female patients. [8]

In the present case, the newborn baby presented with hypernatremia, hypokalaemia, and ambiguous genitalia. The baby was dehydrated during hospitalization. During the course of treatment, there was persistent hypokalemia, hypernatremia, metabolic acidosis, and arrhythmia.

The karyotyping profile of the baby shows the presence of the Y chromosome (genotypically male). But the external genitalia is poorly developed (a small-sized penis resembling a clitoris).

In 17-OHD, there may be salt and water wasting and hypokalemia, where in the present case we got the presence of hypokalemia and dehydration. But in our case, the baby had hypernatremia, maybe due to excessive vomiting and dehydration.

The cardiovascular defect in the present case can be explained by the possibility of arrhythmia and sudden cardiac arrest in congenital adrenal hyperplasia as per the study of Agarwal S et al. in 2005. [9]

Persistent hypokalemia and arrhythmia, which is a well-established complication in congenital adrenal hyperplasia, have also been found in our case, and the baby died due to cardiac arrest with persistent arrhythmia.

Conclusion: With all the above findings, we can conclude that the baby was suffering from congenital adrenal hyperplasia, probably due to 17 alpha-hydroxylase deficiency.

Limitation: Due to a lack of time and resources, we could not perform the assay of hormones like ACTH, and CRH, and enzymes like 17 alpha-hydroxylase directly

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