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Hypospadias in Neonates: Associated Renal and Extra-Renal Anomalies Identified Through Routine Ultrasound Screening in a Tertiary NICU

Sulaiman A. Almunaifi, Aymen H. El Emmawie, Mohd U Tak, Mohammed A. Bayoumi, Mohamed H A Hassan

Neonatal Intensive Care Unit, Neonatology Department, General Ahmadi Hospital, Kuwait Oil Company (KOC), Ahmadi, Kuwait

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ABSTRACT

Background: Hypospadias is one of the most prevalent genital birth abnormalities in males,it is second to undescended testis. There is some evidence that hypospadias coexists with other urinary system abnormalities.

Aim: This case series aimed to describe renal and extra-renal anomalies detected by routine ultrasound screening among neonates with hypospadias.

Methods: Retrospective case series including five neonates diagnosed with hypospadias in our unit over a two-year period, abdominal and pelvi-renal ultrasound was requested to exclude associated renal anomalies in addition to cranial ultrasound and Echocardiogram to exclude extra renal association.

Results: Three out of our five neonates showed renal anomalies. One patient had left renal agenesis and the other 2 patients had different grades of hydronephrosis.These findings were consistent with previous reports describing an association between hypospadias and renal/urogenital anomalies.

Conclusion: Hypospadias may be an early clinical marker of underlying renal or extra-renal anomalies. Additionally, hypospadias should not be undervalued as a urethral opening malformation because it could be the first sign of more serious urogenital or extra-renal abnormalities....

Keywords: Neonates, hypospadias, associated urogenital anomalies, extra renal anomalies, abdominal ultrasound.

INTRODUCTION

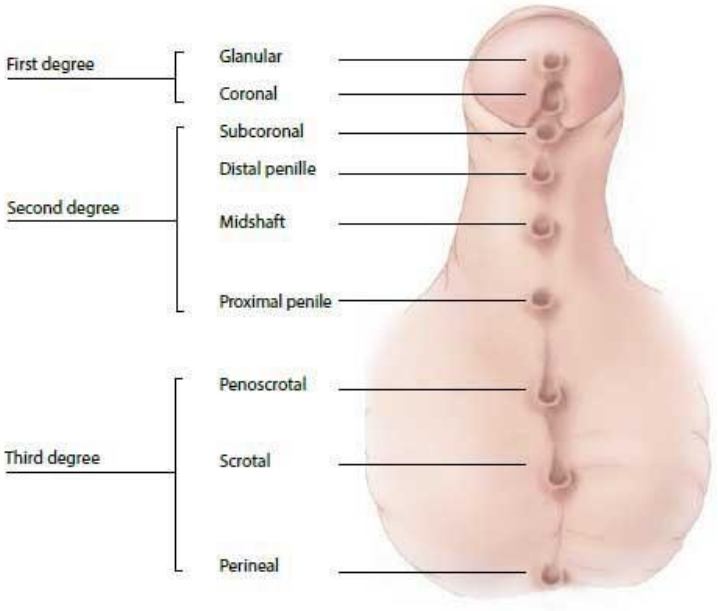
Congenital anomalies of the kidneys and urinary tracts (CAKUT) are disorders that arise during embryonic development and produce a wide range of abnormalities in the kidneys and outflow pathways, including the ureters, the bladder and the urethra. The prevalence is estimated to be between 4 to 60 per 10,000 births (depending on the registry)with the variation resulting from difference in sample sizes, diagnosing techniques and ethnic differences among studies [1].

If the kidneys do not mature in severe cases of CAKUT, the fetus will not survive. However, in less severe situations, the newborn may survive with both outflow tract and renal pathology. Other cases may not be identified until maturity [2].

The development of the kidneys and outflow systems during pregnancy is influenced by environmental factors and genetic defects since nephrogenesis lasts until 36th week gestation with renal genesis beginning at third week gestation. The abnormal development of the kidneys and outflow tracts have been associated with numerous genes and mutations that have been found in CAKUT patients [2].

Following undescended testis, hypospadias is the second most prevalent congenital defect in boys [3]. The urethral opening is shifted down the ventral side of the penis as a result of inadequate closure of the penile tissues during development. [4]. Based on the preoperative meatal position, hypopadias are typically categorized as anterior, penile, or posterior. The most popular categorization, Duckett's classification defines about 70% of hypospadias as mild to moderate because they are glanular or distally located on the penis, whereas the remaining hypospadias are more severe and complex [5].

Patients with hypospadias are more likely to develop associated anomalies, according to numerous publications to date. These fall into three categories: extra-urinary, genital, and urinary tract abnormalities. The last category includes changes to the cardiothoracic and craniofacial tissues. [6]..



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Cases presentation:

Through the duration of 2 years starting from November 2023 to November 2025 our unit had 5 patients of hypospadias summarized in (Table 2) and the details of the patients are as follows:

Case 1: Term baby with an examination showing a mild form of glanular hypospadias, there were no associated anomalies or dysmorphic features, his abdominal ultrasound (US) showed a prominent Pelvicalyceal system while the cranial ultrasound was reported normal and Echocardiogram showed Patent Foramen Ovale (PFO). A sacral ultrasound was due to the presence of an atypical sacral dimple and the US showed Subdural lipoma.

Case 2: Late preterm 36 weeks Gestational Age (GA), had a coronal form of hypospadias, without dysmorphic features or associated anomalies, Abdominal US showed left renal agenesis, in addition to Right sided grade 1 pelvicalyceal system dilatation. A cranial US Shows peri-ventricular flare (PVF) normal while Echocardiogram showed PFO.

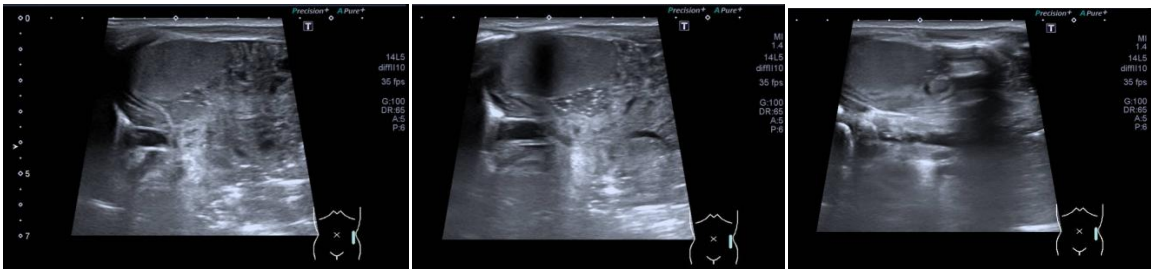

Fig1A: Case 2 Left kidney agenesis

Fig 1B: Case 2 dilated right kidney PCS

Case 3: Was a term baby with the Glanular form of hypospadias, there was no associated anomalies or dysmorphic features, his abdominal and cranial US were unremarkable and the Echocardiogram showed PFO with a small closing Patent Ductus Arteriousus (PDA).

Case 4: Was a term baby with Glanular hypospadias, no associated Dysmorphic features, Abdominal US showed right grade

III & left grade I hydronephrosis, cranial US was normal while the Echocardiogram showed PFO with a small closing PDA.

Case 5: Was a term baby with coronal hypospadias, no associated Dysmorphic features, Abdominal US was completely normal, cranial US was normal while the Echocardiogram showed PFO.

	GA	Type of hypospadias	Abdominal US	Cranial US	Echo	Associated Anomalies
Case 1	Term	Glanular	Prominent PCS	NAD	PFO	Subdural lipoma betweenL2 and L4
Case 2	36 weeks	Coronal	left kidney Agenesis/ Right grade I PCS dilatation	PVF	PFO	
Case 3	Term	Glanular	NAD	NAD	PFO / small closing PDA	
Case 4	term	Glanular	right grade III & left grade I hydronephrosis	NAD	PFO / small closing PDA	
Case 5	Term	Coronal	NAD	Nad	PFO	

Discussion:

The literature indicates that newborns with hypospadias have patterns of co-oexisting with other abnormalities. Other urogenital problems, such as kidney and urinary bladder disorders, which are thought to develop in the same area as these male genital abnormalities, were found in several of the top pairings. Opitz initially defined developmental field defects as abnormalities that appear as a result of disruptions in the embryo's complex structure development [7]. The etiologies of faults in the same developmental area are unknown, although they are probably interconnected and complicated [8]. These structures are believed to be connected in a "spatial, temporal, and hierarchal manner" [9].

Although the majority of the literature focuses on older infants and children, our study focused on the neonatal age group. Our goal is to begin investigations early to raise awareness of the significance of looking into this age group, particularly since we discovered that three out of our five babies had some type of congenital malformation.

Since all of the newborns in our study were diagnosed at a tertiary neonatal facility from birth, we refer to this late presentation in other studies as being caused by a variety of causes, such as socioeconomic issues or challenges in accessing regional hospitals that handle these health issues.

Since all of our patients had glanular, and coronal hypospadias, family incidence seems to be more common for anterior and middle forms than for posterior varieties.

The literature shows varying percentages of hereditary patterns and the existence of family history, for instance. Hypospadias is equally passed down the maternal and paternal lines of the family, with a sibling of a male affected boy having a 9–17% chance of developing the condition [10]. Another study indicates an estimated heritability of 57–77%.

Jasim et al. [11] found that only 4 out of 66 boys (6.1%) with hypospadias had a positive family history [11,12], which is consistent with other research from Tanzania [13] and Nigeria. They also found that hypospadias is linked to familial clustering, affecting first-, second-, or third-degree relatives in 6.1% of cases. Out of the five cases in our series , only one patient had a positive family history.

In ***Jasim et al.,*** The proximal form was seen in a small percentage of boys, but the penile, subcoronal, coronal, and glanular kinds were more common (66.67%) among various cases of hypospadias [11]. which was with consistent with our findings since all of our patients had coronal and distal glanular types.

The combination of renal problems and hypospadias may also suggest congenital anomalies of the kidneys and urinary tract (CAKUT), which includes renal agenesis and cystic kidney defects, as well as hypospadias and other urogenital malformations [1,14]. Genetic mutations affecting multifunctional transcription factors and other proteins that interfere with intermediate mesoderm and endoderm development are the cause of CAKUT, which result in numerous urogenital system defects. [15].

According to Katherine L. Ludorf et al., who reported that 23.33% of the top 30 combinations between hypospadias and associated anomalies had either renal agenesis, renal dysgenesis, or cystic kidney disease, three of our five cases had the following renal defects: one baby had renal agenesis with hydronephrosis affecting the other formed kidney, and the other

two cases had different stages of isolated hydronephrosis [9].

One study found that hypospadias especially affected 13.0% of male newborns with VACTERL [16]. Nevertheless, these flaws are not always regarded as defining characteristics of VACTERL [16]. Although the exact developmental relationship between hypospadias and certain craniofacial and neurodevelopmental problems is unknown, there have been some reports of an increased frequency of these defects in children with hypospadias [17,18,19].

However, none of our study cases was syndromic; the cranial ultrasound revealed no abnormalities other than periventricular flare, which is not a congenital anomaly, and there was no obvious dysmorphism or other concomitant anomalies that might be classified under certain syndromes.

Studies investigating individual birth problems co-occurring with hypospadias revealed that congenital cardiac disorders were present in over half of the top outcomes 17/30 combinations [20]. Congenital heart problems may be caused by mutations in a number of genes that are involved in the development of structural kidney and related defects (such as urinary tract anomalies), according to a recent animal models[21].

Other than Patent Ductus arteriosus (PDA) and Patent Foramen Ovale (PFO), which spontaneously closed and are regarded as typical findings in early infancy, all of our individuals had ECHO without significant cardiac defects.

Conclusion: Hypospadias may be an early clinical marker of underlying renal or extra-renal anomalies.Additionally, hypospadias should not be undervalued as an urethral opening malformation because it could be the first sign of more serious urogenital or extra-renal abnormalities.

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