

Case Report

# Female pseudohermaphroditism in a prenatally diagnosed cloacal malformation with hydronephrosis, dilated bladder, hydrometrocolpos, and oligohydramnios

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## Abstract

**Objective:** To present female pseudohermaphroditism in a prenatally diagnosed cloacal malformation.

**Case report:** A 29-year-old, primigravid woman referred for counseling at 17 weeks of gestation because of oligohydramnios and an intra-abdominal cyst in the fetus. The woman was not exposed to any virilizing agent during this pregnancy. She did not undergo any assisted reproductive technology for this pregnancy. Level II ultrasound showed a singleton with fetal biometry equivalent to 16 weeks, oligohydramnios, hydrometrocolpos, dilated bladder, and bilateral hydronephrosis. A diagnosis of cloacal malformation was made. The parents elected to terminate the pregnancy at 18 weeks of gestation. A 196-g fetus was delivered with a distended abdomen, a phallus-like structure, a small perineal opening below the phallus-like structure, and an imperforate anus. At birth, the fetus was misdiagnosed as a male with an imperforate anus and a perineal fistula. Cytogenetic analysis of the cord blood revealed a karyotype of 46,XX. Array comparative genomic hybridization analysis of the fetal tissues revealed no genomic imbalance. The phallus-like structure was an enlarged clitoris and contained accessory phallic urethra.

**Conclusion:** Prenatal diagnosis of cloacal malformation with ambiguous genitalia should be paid attention to avoid misdiagnosis of a male with an imperforate anus and a perineal fistula. Cytogenetic analysis is helpful to determine the sex under such circumstances.

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**Keywords:** cloacal malformation; clitoris; female pseudohermaphroditism; prenatal diagnosis

## Introduction

Cloacal malformation, persistent cloaca, or cloacal dysgenesis sequence has an incidence of 1 in 50,000 births and

has been seen exclusively in females when the urethra, vagina and rectum fail to develop separately and drain into the perineum through a common channel [1,2]. Cloacal malformation can be classified into the urethral type and the vaginal type [3]. In the urethral type of cloacal malformation, the perineal opening is continuous with the urethra, whereas in the vaginal type of cloacal malformation, the perineal opening is continuous with the vagina but not the urethra [3]. Persistent cloaca

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accounts for 10% of all anorectal malformations in females [4]. In birds and reptiles, persistent cloaca is normal. However, in humans, the cloaca is a transient structure and should be divided by 6 weeks of gestation and result in a urogenital sinus anteriorly and a hindgut posteriorly [2].

With the advent of fetal ultrasound and magnetic resonance imaging, congenital cloacal anomalies can be prenatally diagnosed [5–20]. Ambiguous genitalia presenting as a phallus-like structure may be associated with cloacal malformation. Here, we present the case of a female fetus with a prenatally detected cloacal malformation, a phallus-like structure (enlarged clitoris), a single perineal orifice, and an imperforate anus. The fetus presented ambiguous genitalia and was misdiagnosed as a male at birth.

### Case report

A 29-year-old, primigravid woman was referred for counseling at 17 weeks of gestation because of oligohydramnios and an intra-abdominal cyst in the fetus. Her husband was 31 years old. The woman and her husband were healthy and non-consanguineous, and there was no family history of congenital anomaly. The woman was not exposed to any virilizing agent during this pregnancy. She did not undergo any assisted reproductive technology for this pregnancy. Level II ultrasound showed a singleton with fetal biometry equivalent to 16 weeks, oligohydramnios, hydrometrocolpos, dilated bladder, and bilateral hydronephrosis (Fig. 1). A diagnosis of cloacal malformation was made. The parents elected to terminate the pregnancy at 18 weeks of gestation. A 196-g fetus was delivered with a distended abdomen, a phallus-like structure, a small perineal opening below the phallus-like structure, and an imperforate anus (Fig. 2). At birth, the fetus was misdiagnosed as a male with an imperforate anus and a perineal fistula. Cytogenetic analysis of the cord blood revealed a karyotype of 46,XX. Array comparative genomic hybridization analysis of the fetal tissues revealed no genomic imbalance. The phallus-like structure was an enlarged clitoris and contained accessory phallic urethra.

### Discussion

The present case prenatally manifested oligohydramnios, bilateral hydronephrosis, dilated bladder, and hydrometrocolpos. Warne et al [1] found that the main prenatal ultrasound findings of cloacal malformation are a cystic pelvic mass, bilateral hydronephrosis, and lack of visualized bladder, and suggested that cloacal malformation should be considered prenatally in any female fetus with bilateral hydronephrosis, a poorly visualized bladder, and a cystic lesion. Taipale et al [21] found cloacal anomaly simulating megacystis in the first trimester, and suggested that detection of megacystis in the first trimester should include a differential diagnosis of cloacal malformation. Hayashi et al [5] suggested that the main prenatal ultrasound finding of cloacal malformation is a hypo-echoic and separated retrovesical mass located in the fetal abdomen. Correct prenatal diagnosis of cloacal malformation

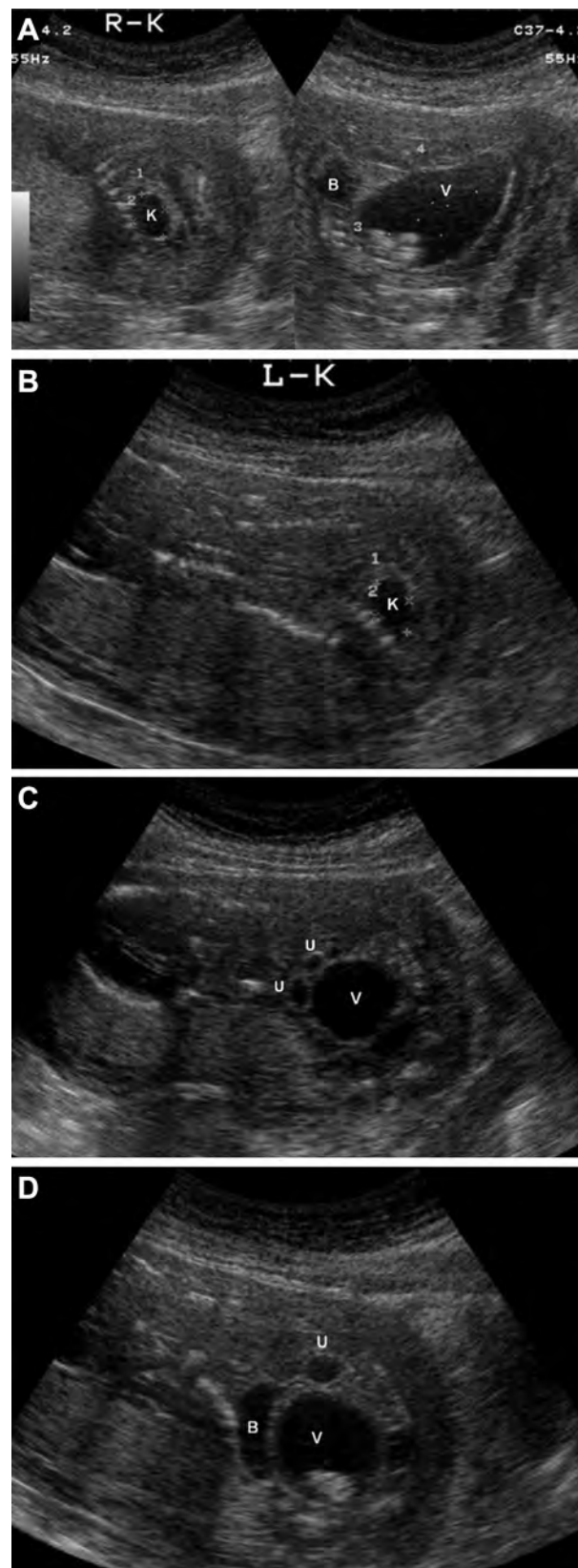


Fig. 1. Prenatal ultrasound at 17 weeks of gestation shows (A) right hydro-nephrosis (R–K), dilated bladder (B) and hydrocolpos (V), (B) left hydro-nephrosis (L–K), (C) hydrometrocolpos, and (D) dilated bladder (B), uterus (u) and vagina (v).

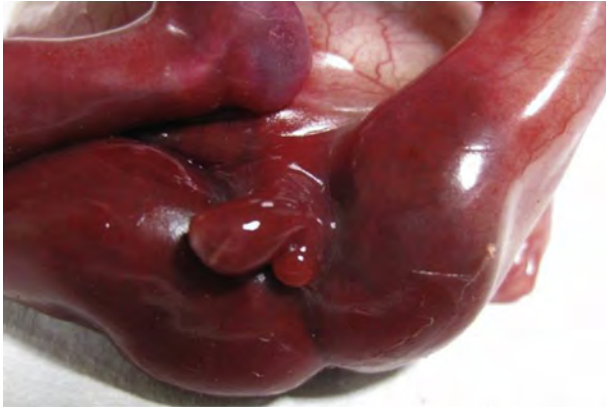


Fig. 2. A phallus-like structure with urethral meatus, a perineal opening below the phallus-like structure and an imperforate anus.

is difficult. Bischoff et al [11] reported correct prenatal diagnosis of cloacal malformation in 6.3% (6/95) of cases. Livingston et al [22] reported correct prenatal diagnosis of persistent cloaca in 6% (3/50) of cases. The common misinterpreted diagnosis includes urinary tract anomalies, dilated bowel, or a cystic pelvic mass. Livingston et al [22] found that 54% (27/50) of cases had associated anomalies. In a review of 95 cases of cloacal malformation with prenatal ultrasound findings, Bischoff et al [11] found the frequencies of ultrasound abnormalities as follows: abdominal/pelvic cystic mass (41.1%), hydronephrosis (37.9%), oligohydramnios (24.2%), distended bowel/bowel obstruction (20%), ascites (15.8%), two-vessel cord (14.7%), dilated bladder (14.7%), dilated ureter (14.7%), polyhydramnios (10.5%), echogenic bowel (8.4%), multicystic kidneys (8.4%), hydrops fetalis (7.4%), hydrocolpos (4.2%), absent kidney (3.2%), abnormal spine (3.2%), and anorectal atresia (3.2%).

The peculiar aspect of the present case was the association of female pseudohermaphroditism with cloacal malformation. The incidence of female pseudohermaphroditism in patients with cloacal malformation is about 7.4% (4/54) [23]. Ambiguous genitalia, penis-like clitoris, and phallic urethra have been documented in the literature of cloacal malformation [23–32]. Broster [24] first described ambiguous external genitalia with a phallus-like clitoris in girls with cloacal or urogenital sinus defects. Cordier et al [25] reported female pseudohermaphroditism associated with cloacal dysgenesis in a pregnancy with severe oligohydramnios, renal dysplasia, a karyotype of 46,XX, female internal genitalia, single umbilical artery, congenital heart defects, and hypoplastic external genitalia of the male type. McMullin and Hutson [26] reported three patients with cloacal malformations, and female pseudohermaphroditism with no endocrinological causes of the phallic enlargement and labial fusion. McMullin and Hutson [26] suggested that masculinization of the external genitalia is secondary to fundamental derangement of urogenital development, and an early anomaly before sexual development may prevent the genitalia from normal androgen-development growth control. Chadha et al [27] reported a 1.5-year-old girl with a urogenital sinus defect, enlarged phallus-like

clitoris, anteriorly located anus, single kidney, and vesicoureteric reflux, and suggested that female pseudohermaphroditism associated with cloacal or urogenital sinus defects is faulty differentiation in the caudal developmental field. Macarthur and Mahomed [28] reported a child with female pseudohermaphroditism, accessory phallic urethra, and posterior cloaca, but no chromosomal, metabolic or adrenal abnormalities. van der Putte [29] studied the penis-like clitoris in three patients with anorectal malformations and showed a fundamental dysgenesis of major structural elements. van der Putte [29] hypothesized that an early error in the formation of cloacal membrane and the adjacent cloaca in embryos between 26 and 29 days postovulation may lead to dysregulation of molecular developmental interactions during the following formation of the genital tubercle. Snyder [30] reported ambiguous genitalia and a high cloacal anomaly in a female co-twin originally thought to be a male. Braga et al [31] reported a newborn presenting with ambiguous genitalia, persistent cloaca, and accessory phallic urethra. The newborn had a karyotype of 46,XX, an enlarged phallic structure (clitoris), bilateral nonpalpable gonads, a single perineal orifice, and a distended abdomen secondary to hydrocolpos. Le Borgne et al [32] reported third-trimester three-dimensional ultrasound diagnosis of a penis-like median genital structure with a urethral meatus in a fetus with a karyotype of 46,XX, cloacal malformation, hydrocolpos, and lack of anal structure. Our case adds to the literature of female pseudohermaphroditism with cloacal malformation.

In summary, we present perinatal imaging findings of female pseudohermaphroditism in a cloacal malformation with an enlarged clitoris, an accessory phallic urethra, a single perineal orifice, and an imperforate anus. Prenatal diagnosis of cloacal malformation with ambiguous genitalia should be paid attention to avoid misdiagnosis of a male with an imperforate anus and a perineal fistula. Cytogenetic analysis is helpful to determine the sex under such circumstances.

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