A Case of Cloacal Anomaly Associated with Complications Leading to the Death of a New born: Lessons Learnt through Forensic Autopsy for Better Health Care

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Abstract
Neonatal autopsy is a developing field in Sri Lanka. It needs human expertise as well as infra-structure with basic and advanced facilities in imaging, serology, genetics, biochemistry etc. Sir Lanka has relatively low neonatal mortality rates compared to other South Asian countries. Cloaca anomaly is a rare pathological condition almost always affecting female infants due to abnormal development of cloaca during the embryonic period. This is basically due to disordered development of endodermal – incorporation of allantois into the hindgut, formation of mesodermal urorectal septum and rupture of the cloacal membrane during the 4th and 7th week of gestation. Sometimes it is associated with disordered development of metanephros, mesonephric duct and paramesonephric duct from which the upper portion of the urinary tract including kidney, ureteric bud and female genital tract develop including fallopian tubes, uterus and upper two-thirds of the vagina. Isolated abnormal development of cloaca is compatible with life and it may be amenable to surgery, though such surgery may invariably involve multiple steps. On the other hand, the outcome is poor when it is associated with other anomalies elsewhere in the body. This case elaborates the death of a female neonate within two hours of birth with a cloacal anomaly complicated by multiple other anomalies of kidney, ureter and lung. It emphasizes the limitations of antenatal investigations in delineating all anatomical and pathological conditions and the need for a meticulous neonatal autopsy to compensate the limitations of antenatal diagnostic techniques.

Keywords: Cloacal anomaly, perinatal death, neonatal autopsy, oligohydramnios, renal agenesis, lung hypoplasia

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Introduction

Cloaca anomaly is a rare pathological condition almost always affecting female infants due to abnormal development of cloaca during the embryonic period after five weeks of gestation.[1,2] Cloacal malformation is a condition in which there is a single opening for the genital, urinary and gastrointestinal tracts.[2] The Prevalence of this deviation has been generally quoted in the collected works as 1:50000.[3] In the UK, it is 2.8 cases per 100000 live births.[4] No accurate data are available regarding the incidence of cloacal anomalies in Sri Lanka at present. Variations from this isolated anomaly are common due to associated disordered development of metanephros, mesonephric duct and paramesonephric duct from which the upper portion of the urinary tract including kidney, ureteric bud and female genital tract develop including fallopian tubes, uterus and the upper two-thirds of the vagina. Sometimes, this incidence is misdiagnosed as fistulae including ureto-vaginal fistula, recto-vaginal fistula or recto-uterine fistula. Therefore, proper diagnosis is important for its management by multidisciplinary team including neonatologist, paediatrician, radiologist and paediatric/neonatal surgeon as well as for maintaining accurate medical statistics of the country. Pure isolated abnormal development of cloaca is compatible with life and it may be amenable to surgery, though such surgery may invariably involve multiple steps. On the other hand, the outcome is poor when it is associated with other anomalies elsewhere in the body.

Case report

A 33-year-old mother delivered a baby whose death was confirmed within two hours. The antenatal history of the mother was uneventful until term. Near to term, at 38 weeks of gestation, an ultrasound

examination revealed oligohydramnios, with an echogenic pattern suggestive of dilated bowel loops and cystic pelvic mass with fluid measuring the size of 9cm x 9.5cm with the imperforated anus. The bladder was not seen separately and the right kidney was not visualized due to cystic mass. The baby was delivered at a tertiary care hospital as planned by the obstetric team and the baby did not cry immediately after birth, though the tone and colour were normal. The heart was beating at a reduced rate. The baby was pronounced dead after two hours of resuscitation in the neonatal intensive care unit. Post mortem MRI was not done due to technical constraints. Birth weight was 2850g. A complete meticulous autopsy revealed gross abdominal distension, bilateral club foot, imperforated anus and single common opening between labia majora of genitalia. Unilateral agenesis of the right kidney, left hydro-ureter and pelvi-calyceal dilation of the left kidney were evident. Large bowel loops were grossly dilated, terminal part (hindgut) was narrowed before being incorporated within the wall of the uterus opening into the uterine cavity. (Figure 1, 2, 3, 4) The urinary bladder and the uterus were coalesced into a single mass, (figure 1) but separated by a common wall (development of uro-vaginal septum). The uterus and the vagina were distended severely and filled with meconium and thick turbid fluid. (figure 02) The urethra opened into the upper part of the vagina. Dilatation of the pelvi-calyceal system with normal glomerulus and tubules of the left kidney was evident according to histology. Histology of the wall of the cloacal mass revealed large bowel epithelium (figure 5) and glands shared with altered structure and epithelium due to ongoing pathological process. (figure 6) Both lungs were not expanded, multiple bullae were present on the surface of both lungs. (figure 7) Histology of the lung revealed bilateral pulmonary hypoplasia. (figure 8)

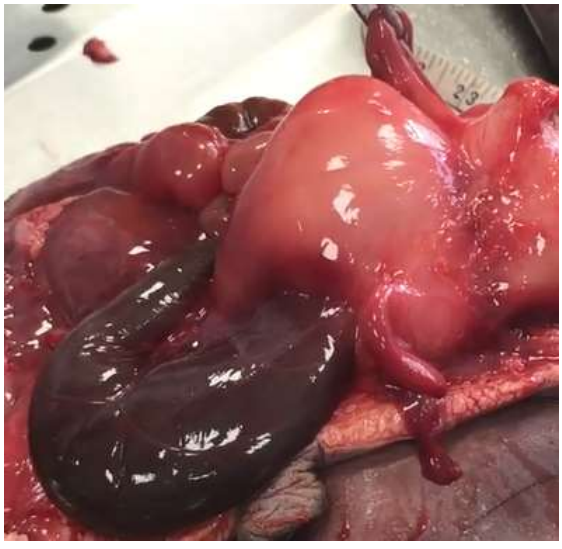

Figure 01: Bladder (blue arrow), uterus (black arrow) and the terminal part of the grossly dilated hindgut (green arrow) as a part of anomalies

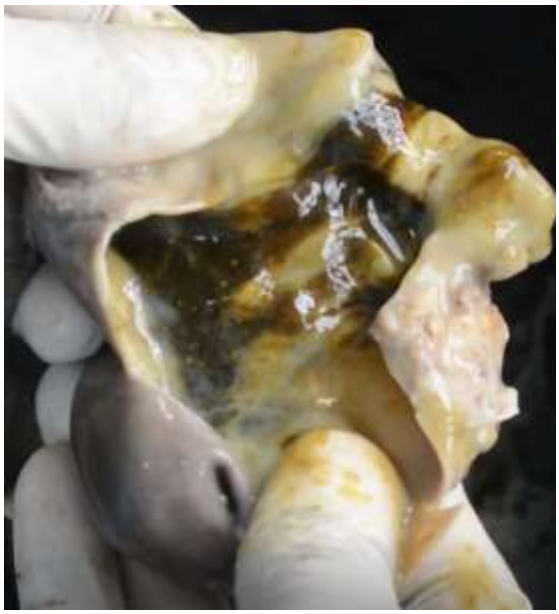

Figure 02: Uterus is distended with full of dark green meconium and turbid thick fluid (formalin-fixed dissection)

Figure 03: Cut open uterus with the fusion of bilateral mullarian duct (Blue arrow) and opening of hindgut (red arrow)

Figure 04: Hindgut is narrowed and incorporated within the wall of the uterus

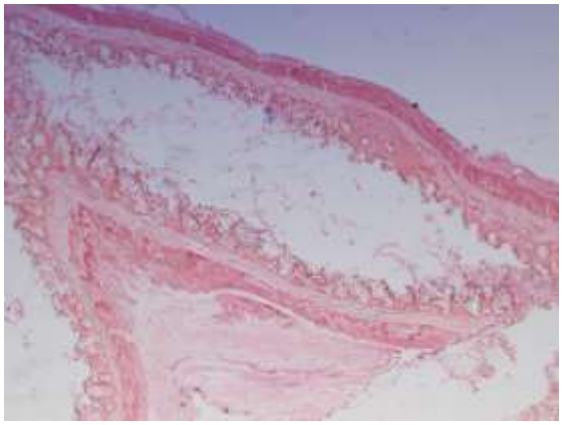

Figure 05: Histology shows part of the hindgut incorporated into the wall of the uterus

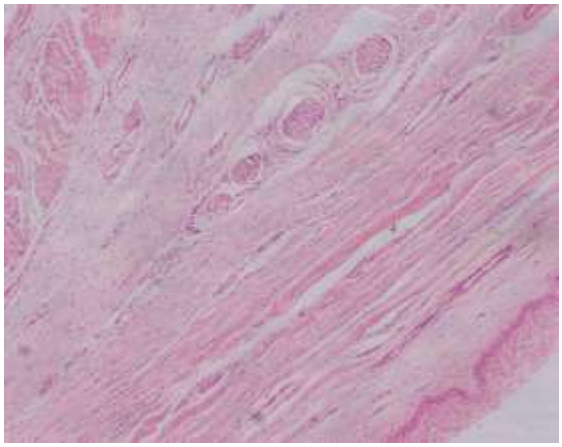

Figure 06: Histology of wall of the mass with stratified squamous epithelium indicates chronic irritation

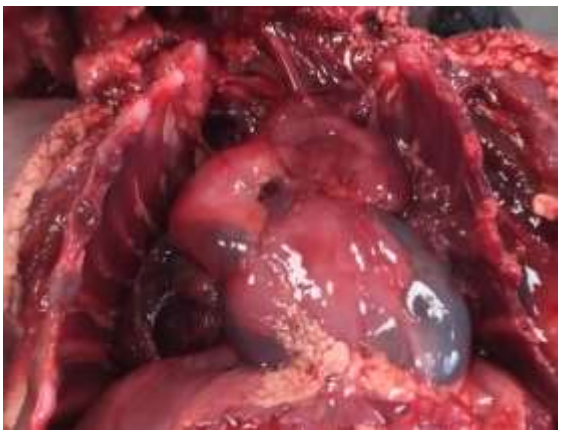

Figure 07: Non-expansion of bilateral lungs with multiple bullae on surface

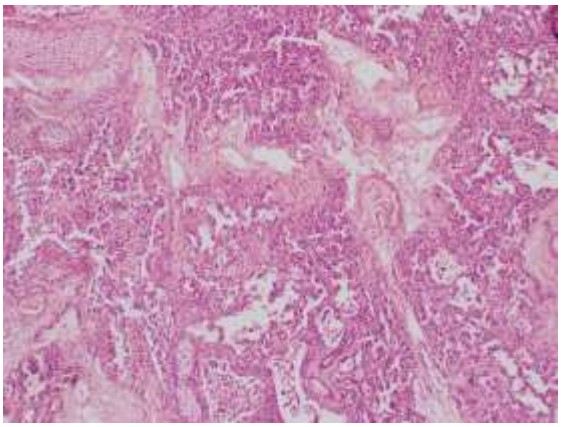

Figure 08: Lung histology revealed that hypoplasia with saccular phase, no increasing acquisition of alveoli

Discussion

Cloaca is a sac-like structure where the terminal part of the developing hindgut drains its excreta and the mesonephric duct excretes urine. Additionally, the proximal part of allantois is also connected to the cloaca while the distal part of allantois opens to the exterior through the umbilicus in early gestational age. Cloaca is separated into primitive urogenital sinus anteriorly and anorectal canal posteriorly by the uro-rectal septum during the gestational age of 4 to7 weeks.[5] Then, the urogenital sinus forms the bladder and urethra in front of the recto-anal canal.[6] Failure of the development in the cloaca forms different types of cloacal anomalies as reported in our case which include imperforated anus, terminal part of bowel merging through the wall of the uterus and opening of the urethra into the upper part of the vagina.

Cloacal anomalies may be associated with other anomalies such as vertebral, spinal cord, renal, ureteric, cardiac, tracheal and oesophageal anomalies and ambiguous genitalia. This case is associated with unilateral agenesis of the right kidney and ureter, left hydro-ureter and moderate hydronephrosis of the left kidney. Distension of

uterus and vagina caused by the accumulation of meconium (figure 1and 2), secretions of uterus and urine may be the reason for obstruction of the lower urinary tract (urethra) which indirectly causes the bladder distension above the pelvic cavity (figure 1), hydro-ureter and hydronephrosis of the right kidney. Absence of the right kidney, impaired left renal functions due to hydronephrosis and lower urinary tract obstruction were likely to cause oligohydramnios as demonstrated by the antenatal ultra sound scan. Volume and contents of Amniotic fluid around the foetus is important for the development and maturation of lungs regardless of the aetiology. Severe and persistent oligohydramnios is a well-established aetiological factor for the hypoplasia of both lungs.[7] Adequate amniotic fluid is a need for the development of limbs which allows the free movement of limbs in-utero preventing contractures.[8] Persistently inadequate fluid fails to prevent the mechanical pressure on the developing limbs and as such, causes bilateral contracture deformity of feet commonly known as 'Talipes' as was evident in this case.

In utero, the placenta is the major foeto-maternal organ which takes over the function of foetal lungs such as the delivery of oxygen and removal of carbon dioxide from the foetal circulation. At the time of delivery, the first breath of the neonate induces the lungs to expand to commence its physiological function. Inadequate development of lungs (figure 7 and 8) causes neonatal distress and early death within a short period after delivery as demonstrated in this case. Usually, isolated cloacal anomalies are compatible with life, but indirect complications due to persistent cloaca and other associated anomalies precipitate intra uterine death or an early neonatal death as has happened in this case with renal and pulmonary anomalies.

Even though the antenatal ultrasound scan has detected dilated bowel loops, imperforated anus and cystic pelvic mass with fluid measuring 9cm x 9.5cm, it has failed to demonstrate the detailed anatomy of the cloaca and the absence of the right kidney due to the masking effect of the abdominal mass. MRI scan is very sensitive in diagnosing detailed anatomy which had not been performed in this case. This case highlights the role of autopsy as the gold-standard in diagnosing the detailed pathology in similar cases. In this case, the autopsy has added additional findings in neonatal pathology compared to the findings recovered through antenatal investigations and radiology. Therefore, it is highly recommended that an autopsy be done in all possible cases of perinatal death even though the cause of death is known and natural as was the matter in this case. This may help to improve the academic understanding of neonatal pathology of rare conditions as well as alleviate doubts of the parents regarding the possible medical mismanagement and negligence. It also will give a better I sight in the planning of their future pregnancies.

Due to the limitations of the facilities of tertiary advancement in in-utero foetal medicine and surgery, not only in Sri Lanka but also in many other countries in the world, certain categories of neonatal deaths are not preventable. Release of lower urinary tract obstruction is likely to reverse the hydroureter and hydronephrosis and produce adequate amniotic fluid with the induction of development of the mature lung. Detecting the accurate pathology and documentation of accurate statistics by competent paediatric pathologists at the autopsy with adequate pre-autopsy radiological investigations in this context may improve this field in future. Zamir et al reported that hydronephrosis and hydroureter have gradually subsided postoperatively in nine patients (foetuses) after drainage of hydrocolpos with cloacal anomalies.[9]

A comprehensive search of the literature using MEDLINE and PubMed by a plastic surgical team in Poland [10,11] suggested that in case of lung immaturity, the urinary bladder can be decompressed with one of the following methods: transcutaneous application of vesical catheter under ultrasound supervision[12], vesicostomy via open method[13] or the use of catheter reinforced with metal mesh.[14] Sri Lanka as a leading nation with overall low foetal and infant death rates among the South Asian countries, development of the field of foetal medicine and surgery is important for further reduction in preventable neonatal deaths as in the developed world. Detecting the accurate pathology and documentation of accurate statistics by a competent autopsy pathologist, in this context will invariably improve this field in future.

The aetiology for persistent cloacal anomalies/uro-rectal septum malformation sequences remains unknown. Risk factor analysis identified statistically significant positive associations with reported maternal use of any fertility medication or an assisted reproductive technology procedure, pre-pregnancy obesity and peri-conceptional exposure to x-rays.[15] This baby had unilateral agenesis of the right kidney, single ureter and unusual opening of hindgut within the uterus in addition to cloacal anomalies suggesting that these conditions may have different etiologies when compared with cases with isolated cloacal anomalies.

Mutational analyses of UPIIIA, SHH, EFNB2 and HNF1β in the persistent cloaca and associated kidney malformations were not done in this case due to lack of technical facilities.[16] Karyotyping for associated syndromes such as Down and other forms

of trisomy were not done due to delay in separating living tissue such as blood, because nucleated leukocytes are commonly used in Sri Lanka for karyotype studies in selected centres. These genetic/molecular studies may be important for accurate diagnosis and counselling of parents to plan future pregnancies, but these studies are not commonly practised in Sri Lanka. Parents are retrospectively advised to follow genetic counselling with a clinical geneticist for the planning future pregnancies.

"Surveillance of foeto-infant deaths involves the ongoing, systematic collection, analysis, and interpretation of data related to foeto-infant deaths, essential to the planning, implementation and evaluation of public health practice, closely integrated with the dissemination of these data to those who need to know and linked to prevention and control of such deaths".[17] In Sri Lanka, all perinatal deaths (>22 weeks POG or > 500g weight up to 7 days after birth) of both government and private hospitals should be notified to the head of the institute by the medical officer confirming the death (at the obstetric or paediatric unit) using the Perinatal Death Documentation Format (P-1) within 24 hours. This format includes columns U, V, W, X, Y1, Y2 and details related to time and causes of the perinatal death. Therefore, the accuracy of certifying the death with antenatal data without autopsy is questionable and gives inaccurate statistics to the National Foeto-Infant Mortality Surveillance Mechanism conducted by the Ministry of Health with the collaboration of the Family Health Bureau (FHB), as the national nodal point.

Theoretically, judicial and pathological autopsy in all perinatal deaths will overcome these issues, but it is practically impossible due to various reasons such as inadequate experts in this field, lack of radiological, histological and other basic and ancillary investigations except in teaching and general hospitals. Even though these basic facilities are available in hospitals, they may not be readily available in the context of autopsy practice in Sri Lanka. The multi-cultural and religious background of Sri Lanka is a limiting factor in autopsy especially in the context of consent for pathological autopsy.

Finally, the development of any medical field including Perinatal and Paediatric Pathology, Perinatal Medicine and Perinatal Surgery is not possible without the enormous support of financial, technical, administrative and political stake-holders of the country.[18] This case should be an eye-opener for the health care policy makers of a country to pay renowned interest in the infrastructure development of medicolegal services of the country.

Conclusions

Cloacal anomaly affects female infants due to abnormal embryonic development. Antenatal diagnosis of this abnormality is difficult. When associated with other anomalies it may prove to be incompatible with life and as such with the limitations and difficulty of antenatal diagnosis, conducting a careful and detailed autopsy with pre-autopsy radiology to detect details of pathological anomalies for accurate medical statistics, counselling of parents and development of perinatal health care sector becomes imperative.

Disclosure statement

Conflicts of interest: The authors declare that they have no conflicts of interest.

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