

# Neonatal Case of Mckusick-Kaufman Syndrome Difficulty of Diagnosis and Management

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## Abstract

McKusick-Kaufman syndrome (MKKS) is a rare autosomal recessive disorder. We report the case of McKusick-Kaufman syndrome in a term female neonate. Antenatal ultrasound found a large cystic abdominal mass corresponding to hydrometrocolpos with bilateral hydronephrosis. This finding was confirmed after birth and its association to polydactyly permitted us to give the diagnosis of MKKS. Exploratory laparotomy revealed vaginal atresia and suspected the association to Hirschprung disease.

MKKS is difficult to diagnose antenatally and complementary explorations should be done after birth to establish a definitive diagnosis.

**Keywords:** McKusick-Kaufman syndrome; Neonate; Hydronephrosis; Polydactyly; Vaginal atresia; Laparotomy; Ultrasound

## Introduction

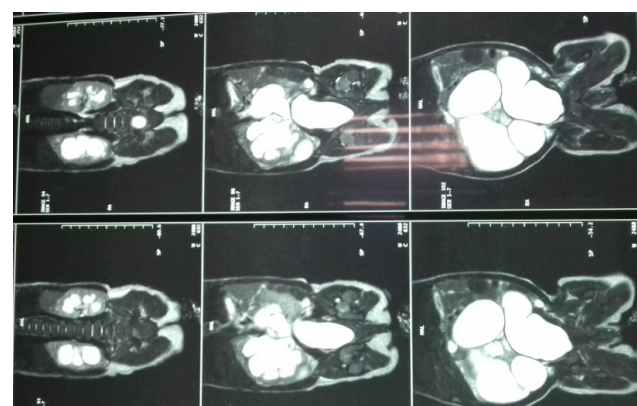
Hydrometrocolpos is caused by the accumulation of mucous secretions in the vagina and uterus due to congenital tract obstruction, such as vaginal atresia or imperforate hymen [1]. It can be seen in different syndromes such as McKusick-Kaufman syndrome (MKKS) and Bardet-Biedl syndrome (BBS). MKKS is a rare autosomal recessive disorder. We report the case of a female neonate with hydrometrocolpos, bilateral hydronephrosis and post-axial polydactyly.

## Case Report

We report the case of Alaa, a female neonate born at 37 week's gestation (WG) to a 31 year old mother, 2nd gravida 2nd para with previous history of medical interruption of pregnancy of a male fetus at 22 WG with hexadactyly and enlarged bilateral polycystic kidneys, the diagnosis of Bardet-Biedl syndrome (BBS) was highly suspected by foetopathology examination. At 34 WG, an ultrasound evaluation revealed large cystic abdominal mass as well as bilateral hydronephrosis

Alaa was born after spontaneous labour by vaginal delivery and required neonatal resuscitation for Apgar score of 3 and 5, respectively at 3 and 5 min. Postnatal examination revealed a birth weight of 3700 g, a head circumference of 32 cm and length of 48 cm. There were facial features of trisomy 21. Alaa had respiratory distress that needed nasal Continuous Positive Airway Pressure (n CPAP). Abdominal examination revealed a large midline cystic mass. There was bilateral postaxial polydactyly with brachydactyly of the upper extremities. Abdominal ultrasonography showed a large cystic pelvic mass measuring 10 × 8 × 8 cm situated between the bladder and the rectum, corresponding to a hydrometrocolpos. Both kidneys were enlarged measuring 40 × 25 mm with bilateral hydronephrosis and thinned renal parenchyma measuring 8 × 10 mm. Transverse and left colon were moderately enlarged. These findings were confirmed by abdomino-pelvic tomodensitometry (Figures 1-3). Initial laboratory exams revealed a Creatinine level of 100 µmol/l at 24 h of life. Alaa was transferred to a pediatric surgical unit. Peroperative gynecologic examination showed the presence of a single orifice similar to the urinary meatus and the absence of vaginal orifice. In order to release the

pressure from the urinary tract, about 150 ml of an opalescent fluid was aspirated from the enlarged uterus. Culture of this fluid was negative. A Petzer probe was inserted into the uterus to release the pressure. Renal function improved after release of the compression secondary to the distended uterus, but enteral feeding was not tolerated with abdominal distension. The neonate then had an exploratory laparotomy that



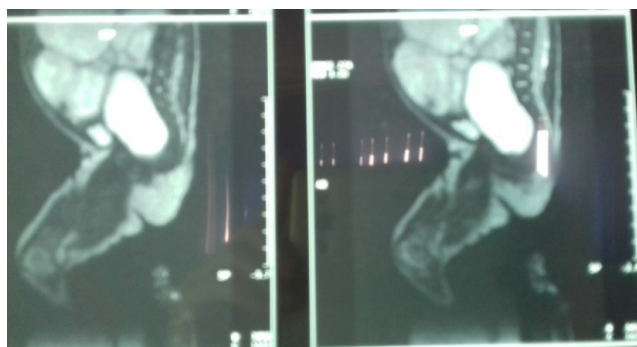
**Figure 1:** Frontal view of the lower abdomen. Large cystic pelvic mass measuring 10 × 8 × 8 cm situated between the bladder and the rectum, corresponding to a hydrometrocolpos. Both kidneys were enlarged measuring 40 × 25 mm with bilateral hydronephrosis and thinned renal parenchyma measuring 8 × 10 mm. Transverse and left colon were moderately enlarged.

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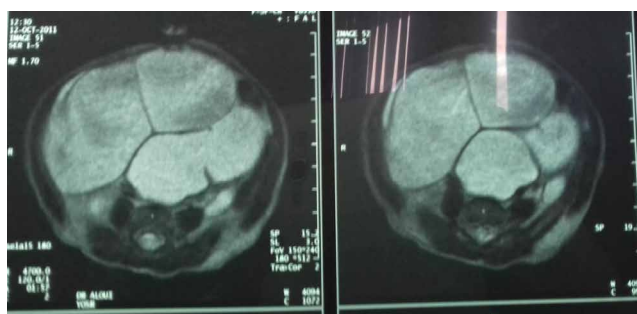
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**Figure 2:** Sagittal view of the lower abdomen.



**Figure 3:** Transversal view of lower abdomen.

revealed a disparity of calibre between a small rectum and an enlarged sigmoide, transverse and left colon. Hirschprung disease was suspected and rectal biopsy confirmed this diagnosis. Right transverse colostomy was performed. Alaa died 5 days later of septic shock.

## Discussion

McKusick-Kaufman syndrome (MKKS) (OMIM 236700) is a rare autosomal recessive inherited syndrome that was first described by McKusick in 1964 [2] in the Old Order Amish population, where it affects an estimated 1/10000 people [1,3,4]. This disease affects the development of the hands and feet, heart and reproductive system. It is characterized by a combination of three cardinal signs: postaxial polydactyly, heart defects and genital abnormalities [1,5]. Hydrometrocolpos presents in 80-95% of affected females and results either from vaginal atresia or imperforate hymen. Congenital heart defects seen in 10-20% of reported cases, includes atrioventricular canal, ventricular septal defect and hypoplastic left heart [1,6].

These signs overlap with another autosomal recessive inherited syndrome, called Bardet- Biedl syndrome (BBS). BBS (OMIM 209900) associates obesity, retinitis pigmentosa, postaxial polydactyly, mental retardation, developmental delay, cognitive impairment and renal and urogenital anomalies [2,7]. Because some of these features are not seen at birth, it can be difficult to tell apart of these two syndromes in infant and early childhood. Sonmez et al. recommended that all cases of MKKS should be re-evaluated for retinitis pigmentosa and other signs of BBS in the teenage years [8].

The gene for MKKS is mapped to chromosome 20p12 and encodes a protein with similarity to members of the chaperonin family [9,10]. In 2000, the MKKS gene was identified in one Old Order Amish family and one non-Amish patient with the MKKS phenotype [2,9]. This

gene was shown to map to the BBS 6 locus, one of the loci previously identified for BBS families. Schaefer and al demonstrated in 2011 that molecular diagnosis revealed genetic heterogeneity for the overlapping MKKS and BBS phenotypes. They have concluded that the association hydrometrocolpos with polydactyly may be, in a Non-Amish population, a priority indicator for BBS diagnosis as opposed to MKKS that is a much rarer diagnosis. Therefore, patients and their family may benefit from BBS molecular testing for prognosis, follow-up and genetic counseling [2]. Molecular genetic testing of MKKS was not done in our patient, as it is indicated for individuals with an MKK phenotype older than age five years in whom other clinical features of BBS have been excluded [11]. Another disorder in which hydrometrocolpos occurs with post-axial polydactyly is Ellis-Van Creveld (EVC) syndrome (OMIM 225500). In EVC syndrome, the cardinal phenotypic features are chondrodysplasia with acromelic growth retardation, polydactyly, ectodermal dysplasia with dystrophy of nails and congenital heart disease [11].

This syndrome is difficult to diagnose prenatally [12]. Farrel et al. described prenatal diagnosis of MKKS by ultrasonography and recurrence of abdominal distension due to peritoneal cysts. They suggested that retrograde flow of secretions from the uterus may be a factor in the abdominal distention of hydrometrocolpos [13].

Hydrometrocolpos, present in 80-95% of affected females, is caused by the accumulation of cervical secretions from maternal estrogen stimulation. It results either from vaginal atresia or the presence of a transverse vaginal membrane, or imperforate hymen. Congenital heart defects seen in 10-20% of reported cases, includes atrioventricular canal, ventricular septal defect and hypoplastic left heart [1,6]. In our case echocardiography was normal. Slavotinek and Biesecker reviewed the most common associated features in 49 individuals with MKK phenotype, 75% were diagnosed at birth and 98% by the age of 6 months. The most common feature were hydrometrocolpos (95%), then hydronephrosis (63%), vaginal agenesis (59%); hands were affected in only 29% of cases [11]. The diagnosis of MKKS in males is based on genital malformations (most commonly hypospadias, cryptorchidism); post-axial polydactyly and congenital heart disease [11].

Some evaluations are recommended, following initial diagnosis of MKKS, in order to establish the extent of disease. These evaluations include pelvic ultrasound examination to detect genitourinary malformations, skeletal radiographs to detect osseous polydactyly and syndactyly, echocardiogram to detect congenital heart defects [11].

Congenital vaginal atresia is a rare obstructive anomaly of the female genital tract with a reported incidence at term babies of 0.014 to 1% [14-17]. Individual surgical approaches should be considered to repair this genital anomaly, depending on the anatomical conditions. Various vaginoplasty techniques are available. The surgical method should be chosen based on the patient and the type of anomaly, such as McIndoe technique which is the most popular and preferred technique [14,18,19]. A new technique developed by Vecchietti combines surgical and conservative methods and involves epithelialization from the outer skin layer [14,20].

This disease needs multidisciplinary management and long term support. Ciccone et al. proposed project Leonardo. This project demonstrated the feasibility of incorporating care managers (specially trained nurses) into the health care system. Care managers worked directly with individual patients, helping them to make lifestyle changes, monitoring their conditions and providing the necessary information and advice to promote patient empowerment, enhance

self-management skills and achieve better compliance with care recommendations [21].

## Conclusion

MKKS is a rare syndrome. Its symptoms are similar to those in BBS. The diagnosis is difficult. Continued surveillance is recommended and could later establish the diagnosis of BBS. Management is mainly surgical.

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