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Case Report

McKusick-Kaufman Syndrome in an Iraqi Neonate

Nabeeha Najatee Akram[1], Shaymaa Khalid Abdulqader[2], Wassan Nori[3], Mustafa Ali Kassim Kassim[4], Alexandru Cosmin Pantazi[4*]

1 Department of Pediatrics, College of Medicine, Mustansiriyah University Baghdad, Baghdad, Iraq
2 Department of Radiology, Al-Kindy College of Medicine, University of Baghdad, Baghdad, Iraq
3 Department of Obstetrics and Gynecology, College of Medicine, Mustansiriyah University, Baghdad, Iraq
4 General Medicine, Faculty of Medicine, "Ovidius" University of Constanta, Constanta, Romania

* Corresponding author's email: pantazi.cosmin@365.univ-ovidius.ro

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ABSTRACT

McKusick-Kaufman (MKS) syndrome is a rare, autosomal recessive disorder determined by a genetic mutation in the MKKS gene on chromosome 20. MKS commonly manifests with three primary components: Polydactyly, congenital heart defects, and genital and urogenital abnormalities. Most reported cases are of Amish descent, with only one Arabic documented case. We present a case of a genetic mutation of MKKS gene in an Iraqi female neonate who presented with repeated non-projectile non-bilious vomiting and abdominal distension. The examination showed a post-axial polydactyly in the hands and feet, an ejection systolic murmur, and an abdominal mass. Perineal examination revealed no vaginal orifice. Diagnosing MKS may necessitate a comprehensive approach due to its rarity and diversity in manifestation. Ruling out Bardet-Biedl syndrome, which shares MKS features, was difficult due to genetic test unavailability; for that patient was kept on follow-up. A high suspicion index, early diagnosis, and customized treatment strategies are essential to address each case's distinct symptoms and requirements, frequently using a multidisciplinary medical team to prevent complications.

Introduction

McKusick-Kaufman syndrome (MKS) is a rare, autosomal recessive disorder, determined by genetic mutation in the MKKS gene on chromosome 20, characterized by a triad of hydrometrocolpos (HMC) in females, post-axial polydactyly, and congenital heart disease (1–3), while in males the main documented genital anomalies are hypospadias, cryptorchidism, and chordee (1). MKS was first described by McKusick in 1964, who reported an inherited form of hydrometrocolpos and polydactyly in a family of Amish descent.

Later, in 1971, Kaufman discovered the presence of congenital cardiac disease, further elucidating the syndrome (2). Since that time, more than 100 cases have been described, most reported cases were in the Amish population. A single previous report of MKS was reported in an Arabic female patient 20 years ago (2).

The clinical diagnosis of MKS relies on a classical diagnostic triad, after excluding other overlapping syndromes, especially Bardet-Biedl syndrome (BBS)(4). MKS diagnosis is suspected in the neonatal period by the clinical evidence of hydrometrocolpos and post-axial polydactyly. However, confirming the diagnosis is often delayed until the age-dependent symptoms of BBS are excluded, which occur around the age of 5 years (5). This makes the documented prevalence of the disorder questionable, as some cases are labeled as MKS at a very young age before the age-dependent features of BBS can be excluded (6). Molecular diagnosis of MKS can be established by finding biallelic pathogenic variants in MKS identified by molecular genetic testing (7) as the locus for MKS syndrome has been mapped to 20p12, close to the jagged1 gene (3).

Although there is a degree of clinical overlap between MKS and BBT syndromes, it is important to note that there are also distinct characteristics that may be used to separate them. BBS is a multifaceted condition that encompasses a broader spectrum of characteristics beyond the commonly shared triad components observed in MKS (4). The other BBS traits encompass retinal degeneration, which has the potential to progress to visual impairment, obesity, compromised cognitive function, and several other endocrine irregularities (4).

There are no published clinical guidelines for the management of patients with MKS, which made the treatment of this disorder tailored to the signs and symptoms expressed by the patients. The therapeutic management begins with surgical repair of the obstructive lesion causing HMC and drainage of the accumulated fluid (8). Treatment for polydactyly and congenital heart defects and other anomalies follow the standards (1).

We present a female newborn with hydrometrocolpos (resulting from vaginal atresia), post-axial polydactyly, and congenital heart disease (atrial septal defect) in an Iraqi neonate diagnosed with McKusick-Kaufman syndrome

Case report

A female neonate born to non-consanguineous marriage at 39 weeks of gestation presented to the emergency room (ER) on the 3rd day of life with repeated non-projectile non-bilious vomiting and abdominal distension since birth. There was no bowel motion since birth and low urine output.

The newborn was vaginally delivered by a midwife at home. The mother received inadequate pre

natal care and did not have a prenatal ultrasound. The family history was negative for congenital disorders. The mother was G4 P3 A1; the abortion resulted from severe abdominal trauma.

On clinical examination, a newborn with weight of (3.5 kg) and length of (51cm) both are normal for her age, normal facial profile, and post-axial polydactyly in hands and feet. The chest exam was not significant apart from ejection systolic murmur with the fixed splitting of second heart sound in the left upper sternal border with no radiation. Abdominal examination reveals distension with a lower mid-line abdominal mass (Figure 1A). Perineal examination revealed no vaginal opening but normal anal and urethral orifices (Figure 1B).

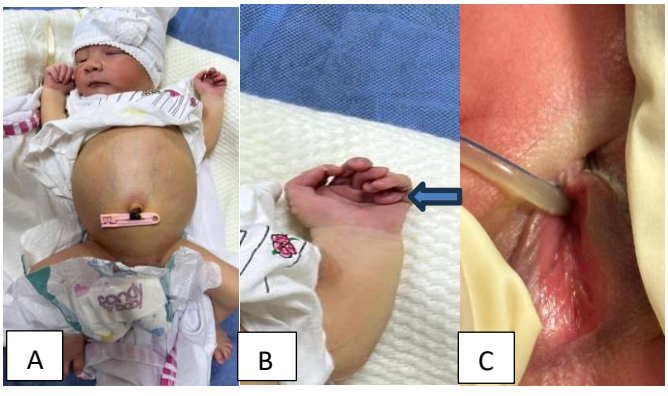

Figure 1: The patient's picture showing A: abdominal distension from the pelvic mass B: postaxial polydactyly in hand (blue arrow). C: absent vaginal orifice.

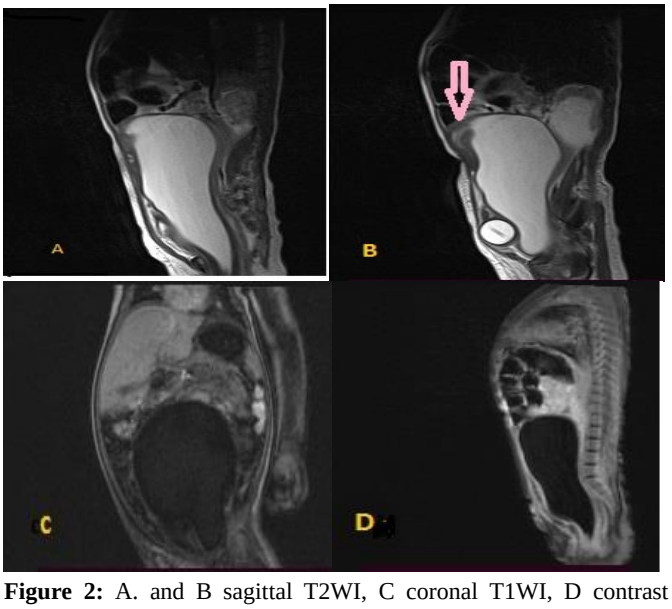

Figure 2: A. and B sagittal T2WI, C coronal T1WI, D contrast enhances sagittal T1 WI images showing that the vagina is massively distended measured (33x80x110 mm) and filled with fluid SI displaying hypointense in T1WI and hyperintense in T2 WI. The uterus (pink arrow) is superiorly and anteriorly displaced by the distended fluid-filled vagina. The urinary bladder is compressed and displaced anteriorly.

Abdominal ultrasound revealed a well-defined, thick wall cystic suprapubic lesion (82 x 41mm) filled with thick turbid fluid. Both kidneys were normally positioned but enlarged with bilateral severe pelvicalyceal system (PCS) dilatation (33 mm) on the right and (30 mm) on the left. Echocardiography showed moderate size atrial septum defect (ASD) secondum (7.8 mm) with a left to right blood flow. Abdominal MRI revealed a massively distended vagina (33 x 80

x 110 mm) filled with fluid, with an anteriorly displaced normal-size uterus, compressing the bladder (Figure 2), and bilateral moderate-severe dilatation in PCS with dilated tortious ureters (Figure 3). Surgery was done on day 4 of life. A cruciate incision was made to create a vaginal orifice, a huge amount of milky fluid was drained, and vaginoplasty was performed.

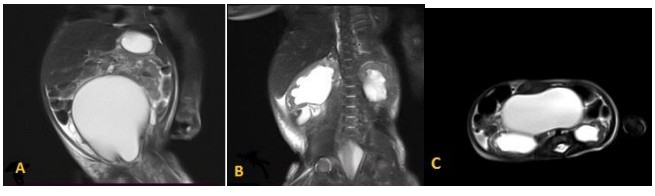

Figure 3: A, B coronal, C axial T2WI images showing that the vagina is a massively distended fluid-filled vagina. B and C show bilaterally severe hydronephrosis and dilated tortuous ureters.

Discussion

McKusick-Kaufman syndrome is rarely reported in Arabic countries, with no previous case documented in Iraq. Only one case was reported earlier in the Arabic population, among Palestinian Bedouin babies, who had the following: Epidemiologically, it was the first case ever reported in an Arabic Bedouin baby at the age of 3 months. The consanguinity marriage was not mentioned in the history. The family history showed an older brother (8 years old) with history of post-axial polydactyly on his 5th Lt hand finger, which was excised shortly following birth; this in contrast to our patients who did not have any family history of polydactyly (2).

We reported an Iraqi female neonate who presented with signs of abdominal mass and gastrointestinal symptoms, vomiting, and absent bowel motions since birth. Physical and imaging examination revealed three clinical features of MKS (hydrocolpos, post-axial polydactyly, and congenital heart disease). Subsequently, the abdominal distension and the mass were drained via cruciate incision and vaginoplasty.

The hydrocolpos has resulted from vaginal atresia that leads to the accumulation of normal secretions under the effect of maternal estrogen. Vaginal atresia is seen in other syndromes like Mayer-Rokitansky-Küster-Hawser, Robinow, and Bardett-Biedl syndrome(9).

Hydrometrocolpos is the most common clinical manifestation of MKS documented in 70% of the affected females. Other studies reported post-axial polydactyly in 60% of cases, and 15% presented with congenital heart disease (5,10,11). Other presentations ranged from hydrops fetalis (12) to malformations involving other systems like renal, respiratory, and gastrointestinal (2,8). So, whenever MKS is suspected, these malformations should be investigated for by the laboratory, radiological, and other diagnostics methods (13).

Prenatal diagnosis is usually suggested by the clinical triad during the second or third-trimester ultrasound (14,15). However, its reliability is questionable as the clinical features of the syndrome may not present prenatally (1) . The early diagnosis of hydrometrocolpos in the affected newborn is vital since the delayed diagnosis may lead to obstructive uropathy and renal failure (16). Moreover, there is the risk of ruptured hydrocolpos, peritonitis, and sepsis leading to death (17,18). Since this sequence of complications can simply be interrupted via the early diagnosis, having a high index of suspicion and increasing pediatricians' awareness about the importance of female newborn genital examination cannot be overstressed (19).

In MKS syndrome, the polydactyly is always reported as post axial type but can affect hands, feet, or both; it may present as a rudimentary skin tag or a complete extra digit (13). Our patient had post-axial polydactyly in both upper and lower extremities.

The presence of congenital cardiac malformation is not consistently observed since a significant number of verified cases have been reported with structurally and functionally normal hearts (20). The etiology of heart problems in MKS remains incompletely elucidated. Scott et al. proposed that a specific allele of the BBS6 gene, known to be mutated in MKS, disrupts a discrete cellular mechanism that plays a role in developing these cardiac abnormalities (21). Heart abnormalities have proven to be a valuable indicator for MKS diagnosis. However, individuals with Bardet-Biedl syndrome have reported heart anomalies with varying rates, as documented in previous studies (22-23).

The dilemma in making a diagnosis of neonate or infant presented with polydactyly -hydrocolpos-congenital heart disease resides in the first place; these features are shared between MKS and BBS and many patients diagnosed as MKS in early life and later turned to be BBS (10,20).

Secondly, the lack of molecular genetic testing for MKS in Iraq adds to the problem. The patient should follow the previous recommendation of the necessity of reevaluation for developing age-dependent features of BBS later in life (10).

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Conflict of Interest

Authors declare no conflict of interest.

Data availability

Data are available upon reasonable request.

ORCID

Nabeeha Akram 0000-0001-8964-8943
Shaymaa Abdulqader 0000-0001-7029-0451
Wassan Nori 0000-0002-8749-2444
Mustafa Kassim 0009-0009-5737-2634
Alexandru Pantazi 0000-0002-7234-2814

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