The McKusick-Kaufman syndrome: report of a case with some associations

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McKusick-Kaufman syndrome (MKS) is a rare autosomal recessive condition consisting of congenital hydrometrocolpos, polydactyly and congenital heart defect. We present a female stillborn, the product of non-consanguineous parents, who presented postaxial polydactyly on both feet, micrognathia and marked abdominal distension. Postmortem examination revealed bicornuated cystic uterus and intestinal malrotation. She also had flat left kidney and left hydroureter due to compression by the cystic mass.

Key words: congenital hydrometrocolpos, bicornuated uterus, polydactyly, vaginal atresia, hydroureter, malrotation, abdominal cyst.

The McKusick-Kaufman syndrome (MKS) consists of congenital hydrometrocolpos with polydactyly and congenital heart malformation[1,2]. Hydormetrocolpos was found second to vaginal atresia and bilateral postaxial hexadactyly in an offspring of first-cousin parents by Dungy et al.[3] It is an autosomal recessively inherited condition of different ethnic backgrounds[4,5]. Other abnormalities reported in affected cases include several in other organs, especially the genitourinary system[6,8]. We report a new case of MKS syndrome with bicornuated uterus and intestinal malrotation.

Case Report

The patient was born to a 33-year-old G3, P1 woman and a 35-year-old father, both of Turkish descent. There was no consanguinity and other family history was not contributory. There was no prenatal care and the pregnancy was complicated at 33 weeks of gestation, when the mother presented with vaginal bleeding. No fetal heart beat could be heard and fetal ultrasonography revealed polydactyly, abdominal cyst, pes equinovarus deformity and possibly oligohydramnios. The gynecologist induced the delivery.

The birth weight was 2700 g (52% of the term, compatible with 35th gestational week). External examination showed CH (Crown-Heel), CR (Crown-Rump) and foot lengths as 40 cm, 30 cm, and 6 cm respectively (all compatible with 31-34 gestational weeks). There was postaxial polydactyly on both feet and marked abdominal distension with petechia around the umbilicus (Fig. 1a). Micrognathia and facial appearance were characteristic for Potter facies due to

Fig. 1a. Marked abdominal distension with petechia around umbilicus and polydactyly of the feet.

oligohydramnios sequences (Fig. 1b). There were overriding skull bones and scalp edema. The external genitalia was normal female but with a questionable short vagina.

Postmortem examination: Internal examination revealed a midline cyst measuring 6x4x3 cm (Fig. 2). The cyst was located just beneath the branching point of the aorta, between the two iliac arteries. There was a dilated bicornuated uterus with a blind vaginal orifice. Other findings included malrotation of the intestines, flattened left kidney and left hydroureter due mechanical compression by the mass, and a normal bladder. No other abnormalities were detected and the heart was normal.

Histopathological study of the cyst wall revealed endometrial epithelium, stroma and myometrium.

Fig. 1b. Micrognathia and characteristic facial appearance due to oligohydramnios.

Fig. 2. The cyst measuring 6x4x3 cm in the midline.

Discussion

Sexual differentiation of the reproductive pathway begins early in the fetal period (35 mm embryo, 8 ½ postfertilization week) under the influence of the gonadal hormones. Arising as coelomic invaginations in the metanephros, the paramesonephric ducts grow caudally to form uterine tubes. Afterwards they approach each other and begin to fuse before reaching the urogenital sinus. The fusion is usually complete by 10 weeks and the cavities (uterus and vagina) become a single genital canal caudally. Incomplete fusion leads to many anomalies, e.g. septate uterus. At the end of the first trimester, the developing vagina becomes occludde by a cellular mass termed vaginal plate. The cells of the vaginal plate desquamate during the second trimester and the established vaginal lumen slides down along the urethra to its separate opening into the vestibule. The hymen is the partition that persists between sinovaginal bulbs and the urogenital sinus. A failure of the canalization leads to vaginal atresia, septa or stenosis. Vaginal atresia and/or imperforate hymen results in an accumulation of fluid within the reproductive organs, namely hydro(metro)colpos[9].

Hydro(metro)colpos was first reported in the mid 19th century, and towards the middle of the 20th century, efforts were aimed at classification according to the underlying anomaly. Vaginal atresia is seen rarely and is usually associated with other anomalies of the genitourinary tract such as fistulas[6], or is associated with Robinow's syndrome[10]. In the presented case, uterus septus bicollis was associated with mid-vaginal atresia.

Development of limbs occurs between the 5th and 8th gestational weeks. Although development and even contraction of the heart begin earlier,

development of valves and septa of the heart occurs when hand and foot plates form and finger and toe rays become visible[8]. Therefore, one can expect to see limb abnormalities together with heart and urogenital system malformations.

Hydrometrocolpos associated with polydactyly and congenital heart diseases are the cardinal feature of the MKS[1-4]. Kaufman et al.[4] noticed that postaxial polydactyly and/or congenital heart disease may sometimes be associated with hydrometrocolpos. Interestingly, in the kindred reported by McKusick et al.[1], one of the girls had hydrometrocolpos with polydactyly, while another girl in the same family had only congenital heart disease without hydrometrocolpos. Other reported associated anomalies are congenital heart diseases such as patent ductus arteriosus, ventricular septal defect, single atrium; urinary tract anomalies such as micropenis, glandular hypospadias, undescended testis, hydronephrosis, hydroureters, displaced urethral meatus, polycystic kidneys; Mullerian duct anomalies such as duplications of uterus or vagina; anorectal anomalies such as rectovaginal fistula, anal atresia; intestinal malrotation and Hirschsprung's disease; skeletal abnormalities such as syndactyly, cervical ribs, vertebral anomalies, retinal dystrophy; and pituitary diysplasia[5-8,9]. Non-immune hydrops in a MKS case has been also reported[10]. Intestinal malrotation and left hydroureter were present in our case. The fetal abnormalities resulting from hydrometrocolpos make it possible to diagnose MKS prenatally in female patients[5]. On the other hnand, in male patients who have an affected female relative, polydactyly is the only clue for diagnosis most of the time, although hypospadias, undescended testes or small penis may be associated[5,13].

The MKS is inherited as an autosomal recessive trait and parental consanguinity has been reported in all case when there are multiple affected siblings in the family[7]. Recently, using two pedigrees from the original work of McKusick et al. in the Old Order Amish population, short tandem repeat polymorphism screening showed homozygosity in 20p12 between D20S162 and D20S894. This region includes several genes including the jageed[1] gene. However, sequencing of the jagged1 gene in two unrelated individuals with MKS has not revealed any disease-causing mutations[14]. Therefore, other gene products may be involved in the pathogenesis of MKS in non-Amish populations, and sporadic cases, such as the one presented here, may attract the attention of research workers dealing with gene mapping. Indeed, a recent analysis in an Amish and a sporadic, non-Amish case revealed a frame shift mutation predicting premature protein truncation, and this protein showed structural similarity to the chaperonin family of pyroteins[15].

On the other hand, there are a few other syndromes with hydrometrocolpos associated with polydactyly, namely, Bardet-Biedl syndrome (BBS), Pallister-Hall syndrome, Ellis-van Creveld syndrome and orofaciodigital syndrome, type IV[16-17]. And recent data has revealed a significant overlap between MKS and BBS, in view of a series of patients having vaginal atresia and postaxial polydactyly in infancy and later developing obesity and retinal dystrophy[16].

In children with polydactyly and cystic masses in the lower abdomen, hydrometrocolpos should be considered and prenatal and postnatal ultrasound should be performed[18-19]. Hydrometrocolpos with polydactyly may easily lead to the diagnosis of MKS, but this should be done with caution in infancy. Systematic ophthalmological and neurodevelopmental follow-up should be established in order not to underdiagnose BBS[16].

Furthermore, Rosen and Bocian[12] reported a case of McKusick-Kaufman syndrome, but this case also had non-immune hydrops. A large pelvic mass was prenatally mistakenly attributed as due to inferior vena cava compression and lymphatic obstruction.

In conclusion, we presented a new McKusick-Kaufman syndrome form Turkey, which was characterized by congenital hydrometrocolpos, bicornuated cystic uterus, intestinal malrotation, and bilateral postaxial polydactyly.

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REFERENCES

1. McKusick VA, Bauer RL, Koop CE, et al. Hydrometrocolpos as a simply inherited malformation. JAMA 1964; 189: 813-816.
2. McKusick VA, Weilbaecher RG, Gragg GW. Recessive inheritance of congenital malformation. JAMA 1968; 204. 113-118.
3. Dungy CI, Aptekar RG, Cann HM. Hereditary hydrometrocolpos with polydactyly in infancy. Pediatrics 1971; 47: 138-141.

4. Kaufman RL, Hartmann AF, McAlister WH. Family studies in congenital heart disease II: a syndrome of hydrometrocolpos, postaxial polydactyly and congenital heart disease. Birth Defects Orig Art Ser 1972; 8: 85-87.
5. Chitayat D, Hahm SY, Marion RW, et al. Further delineation of the McKusick-Kaufman hydrometrocolpos-polydactyly syndrome. Am J Dis Child 1987; 141: 1133-1136.
6. Tran ATB, Arensman RM, Falterman KW. Diagnosis and management of hydrometrocolpos syndromes. Am J Dis Child 1987;141: 632-634.
7. Cantani A, Tacconi ML, Benincori N, Picarazzi A, Cecoli D, Gausin S. Rare syndromes. The Kaufman-McKusick syndrome. A review of the 44 cases reported in the literature. Ann Genet 1987; 30: 70-74.
8. Robinow M, Shaw A. The McKusick-Kaufman syndrome: recessively inherited vaginal atresia, hydrometrocolpos, uterovaginal duplications, anorectal anomalies, postaxial polydactyly, and congenital heart disease. J Pediatr 1979; 94: 776-778.
9. Larsen WJ. Human Embryology (2nd ed) New York. Churchill Livingston; 1997, 261-309.
10. Balcı S, Beksaç S, Haliloğlu M, Ercis M, Eryılmaz M. Robinow syndrome, vaginal atresia, hematocolpos and extra middle finger. Am J Med Genet 1998; 79: 27-29.
11. Davenport M, Taitz LS, Dickson JA. The Kaufman-McKusick syndrome: another association. J Pediatr Surg 1989; 24: 1192-1194.
12. Rosen RK, Bocian ME. Hydrops fetalis in the McKusick-Kaufman syndrome: a case report. Am J Obstet Gynecol 1991;165: 102-103.
13. Kumar D, Primhak RA, Kumar A. Variable phenotype in Kaufman-McKusick syndrome: report of an inbred Muslim family and review of the literature (Abstract). Clin Dysmorphol 1998; 7: 163-170.
14. Stone DL, Agarwala R, Schaffer AA, et al. Genetic and physical mapping of the McKusick-Kaufman syndrome. Hum Mol Genet 1998; 7: 475-481.
15. Stone DL,Slavotinek A, Bouffard GG, et al. Mutation of a gene encoding a putative chaperonin causes McKusick-Kaufman syndrome. Nat Genet 2000; 25: 79-82.
16. David A, Bitoun P, Lacombe D, et al. Hydrometrocolpos and polydactyly: a common neonatal presentation of Bardet-Biedl and McKusick-Kaufman syndromes.J Med Genet 1999; 36: 599-603.
17. Yapar EG, Ekici E, Aydoğdu T, Şenses E, Gökmen O. Diagnostic problems in a case with mucometrocolpos, polydactyly, congenital heart disease, and skeletal dysplasia. Am J Med Genet 1996; 66: 343-346.
18. Farell SA, Davidson RG, De Maria, et al. Abdominal distention in Kaufman-McKusick syndrome. Am J Med Genet 1986; 25: 205-210.
19. Schaap C, de Die-Smulders CE, Kuijten RH, Fryns JP. McKusick-Kaufman syndrome: the diagnostic challenge of abdominal distension in the neonatal period. Eur J Pediatr 1992; 151: 583-585.