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BRIEF COMMUNICATION

Open Neural Tube Defect in a Fetus with MURCS Association: Value Addition of Fetal Autopsy in Counseling

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Introduction

In prenatal medicine, MURCS association (MUllerian, Renal, Cervicothoracic Somite abnormalities) is a less well-known polymalformative condition than VATER or VACTERL (Vertebral, Anal, Cardiac, Tracheo-Esophageal, Renal, Limb defects). The literature on fetal diagnosis of MURCS association is scarce and thus the awareness is low among prenatal diagnosticians. This is principally due to the difficulty in identifying the lead pathology in this condition—Mullerian—by prenatal ultrasound. However, correct identification of this polymalformative condition is important since the recurrence risk is quite low similar to VATER/VACTERL. We describe the prenatal ultrasound findings, autopsy findings and discuss the implications of these, in the prenatal diagnosis and counseling.

Case Report

A 31 year old primigravida at 19 weeks 5 days of gestation presented as a case of Arnold Chiari malformation for a second opinion. Detailed fetal evaluation using real time B mode 2D and 3D ultrasonography (Voluson S8 C 1-5 and RAB 2-6, Wipro GE healthcare) revealed a singleton gestation corresponding to 19 weeks 5 days showing classical features of Arnold Chiari malformation: postero-inferior herniation of vermis, obliteration of cisterna magna, bilateral ventriculomegaly, lemon shaped skull, and a large open neural tube defect over the lumbar region. Extended imaging of the fetus further identified the following: unilateral renal agenesis on the right side and segmentation defect of the vertebral column at cervico-thoracic junction (C8/T1) and thoracolumbar junction (T12/L1). Figure 1 shows the prenatal ultrasound findings.

The parents were counseled at length about the expected perinatal and postnatal outcome with emphasis on the neuromotor, neurosensory and autonomic neurological outcomes secondary to the open neural tube defect. However, the usual counseling on the recurrence risk for open neural tube defect (i.e., a risk increment by tenfold and reduction of recurrence by folate prophylaxis) was appropriately not advised. The parents were motivated to subject the fetus for autopsy if they elected for termination. The presence of vertebral, renal and spinal abnormalities was thought to be in favour of a cluster polyformative condition such as VATER and hence genetic evaluation was not offered considering the cost-yield balance.

Subsequently the pregnancy was terminated and fetal autopsy was performed. A fetogram confirmed the presence of hemivertebrae at C7 and T11–T12 with associated scoliosis. The fetus was female. External examination was unremarkable except for the fetal back that showed a large defect with exposed neural placode (Fig. 2). Internal examination confirmed unilateral (right side) absence of right kidney and right ureter. In addition, the right fallopian tube and the right half of uterus was absent (Fig. 3). Pathological examination of vagina could not be performed due to technical difficulties.

The final diagnosis after autopsy was that of MURCS association with additional finding of open neural tube defect.

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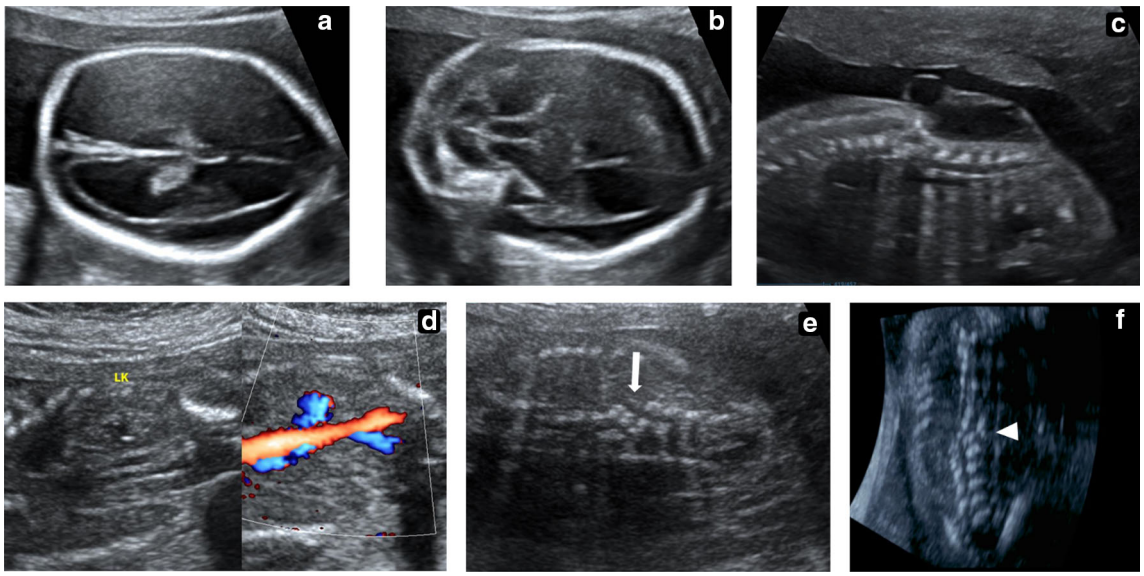

Fig. 1 **a** Lemon sign with ventriculomegaly; **b** banana sign of cerebellar herniation; **c** myelomeningocele; **d** left kidney visualised, right kidney absent; **e**, **f** thoracolumbar hemivertebrae causing scoliosis

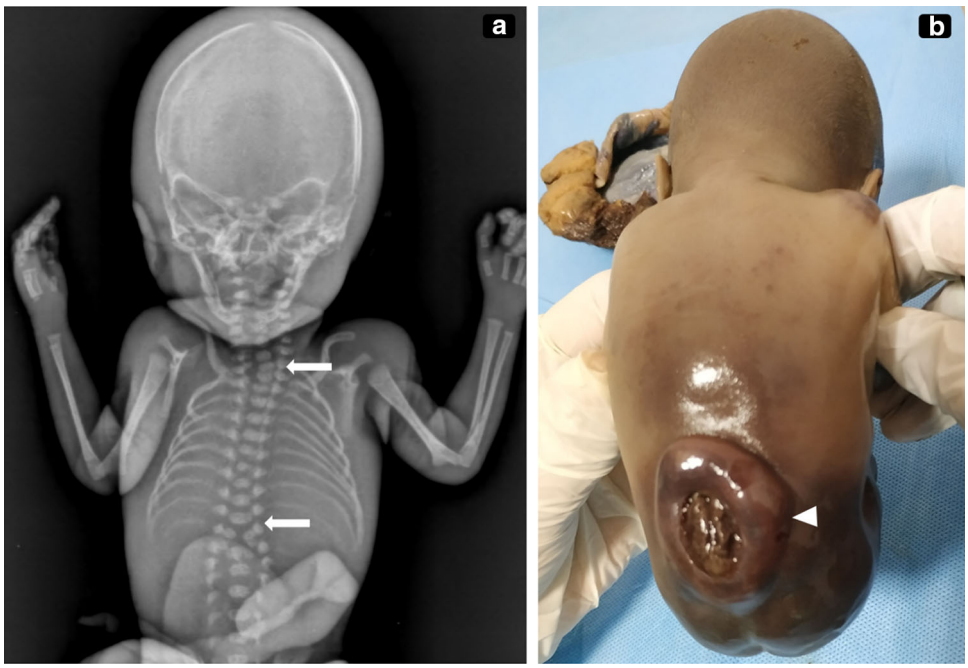

Fig. 2 **a** Fetogram showing multiple hemivertebrae (solid white arrows) at cervical and thoracic levels. **b** Gross specimen showing large lumbar myelomeningocele (arrowhead)

Discussion

The findings of this case study showcase the value addition provided by fetal autopsy in arriving at a complete diagnosis.

MURCS association is a polymalformative condition consisting of a cluster of abnormalities of the Mullerian system, Renal system and the somites of cervicothoracic region, typically vertebral body defects. The exact aetiology is unclear with no hard evidence to point to a genetic or teratogenic cause. The MURCS association has been predominantly reported in the paediatric and the young adults age group typically following investigation for a gynaecological presentation.

The constellation of defects was first identified and reported by Duncan et al. [1]. The authors hypothesise that the close spatial relation of the blastemas of the cervicothoracic somites, arm buds, and pronephric ducts at the fourth week of embryonic development might explain this non-random cluster of abnormalities. Most of the cases

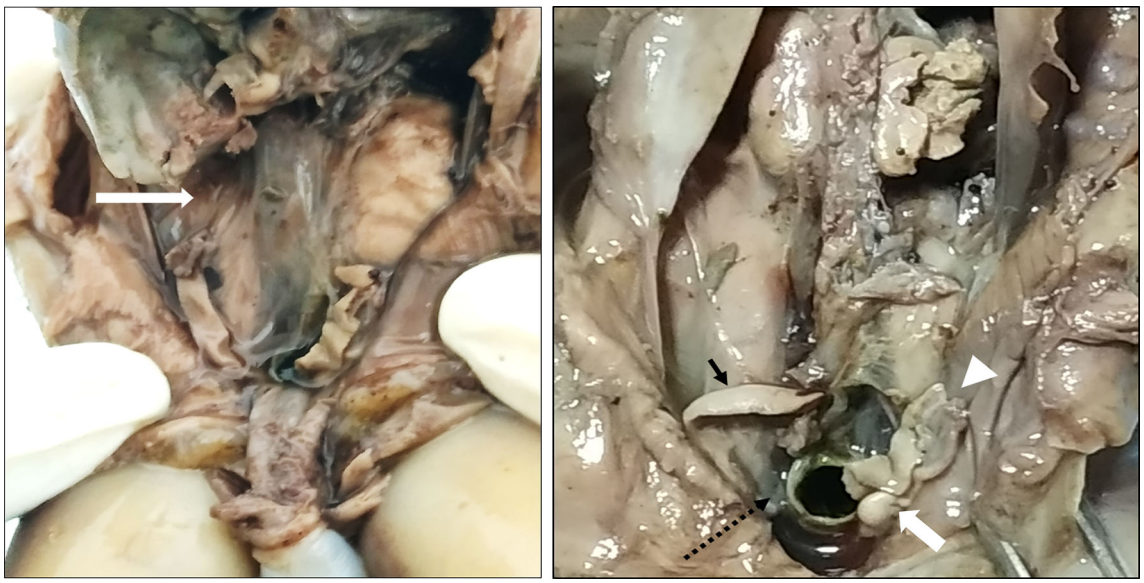

Fig. 3 Left panel showing empty right renal fossa (white solid arrow); right panel showing presence of left hemiuterus (white solid arrow), left fallopian tube and ovary (white arrowhead), Absence of right hemiuterus and fallopian tube (black dotted arrow) and presence of right ovary (black arrow)

reported in the literature are sporadic. Anecdotal reports of familial clustering [2] and chromosomal abnormalities [3] are also present. This has led to the assumption that the condition is a polytopic field defect of multiple possible aetiologies.

It is also important to note that many of the so-called MURCS association reported in the literature as variants of the Mayer–Rokitansky–Kuster–Hauser (MRKH) syndrome cannot be considered as true MURCS association since the presence of all three components is required to make such a diagnosis and to distinguish it from the more common MRKH syndrome. Table 1 presents a selected review of the literature on MURCS association conforming to the strict triad [1–9].

To our knowledge, there are only a few case reports of fetal diagnosis of MURCS with open neural tube defect [4, 5]. The direct implication of the final diagnosis on the case management is in the counseling: MURCS syndrome is a sporadic disorder in the vast majority and the parents were thus reassured regarding the very low risk of recurrence. Although ONTD was present in this fetus, the standard tenfold increase in recurrence and folate mediated risk reduction is not applicable in this case. This is because the recurrence risk in ONTD depends on the aetiology rather than the defect per se.

Isolated ONTD are assumed to be of multifactorial aetiology and have a tenfold higher risk of recurrence. This increased recurrence risk is also amenable to reduction by prophylactic preconceptional folate intake. The same does not hold true for ONTD that occurs as part of syndromes such as Meckel - Gruber or MURCS. While, Meckel - Gruber syndrome, which is autosomal recessive has a 25% risk of recurrence, the recurrence risk of MURCS cannot be accurately predicted at present, as its genetic aetiology still remains largely elusive.

In conclusion, a diagnosis of MURCS association should be strongly considered in a female fetus in the presence of vertebral segmentation defects and renal

Table 1 Review of reports conforming to the classic triad

S. no	References	No of cases	Prenatal/ Postnatal	Mullerian	Renal	Vertebra	Others
1	Duncan et al. [1]	30	Postnatal	Aplasia/ hypoplasia	Renal agenesis and/or ectopy	Anomalous vertebrae, C5-T1	Short stature, ribs and upper extremity malformations, Sprengel deformity, deafness
2	Greene et al. [2]	1	Postnatal	Agenesis	Unilateral renal agenesis	Incomplete C6 vertebra Fusion of T2–3 vertebrae	Rib anomalies, cerebellar cyst, cortical heterotopia, unilateral cleft lip, heterotaxy
3	Mahajan et al. [6]	7	Postnatal	Agenesis	Unilteral renal agenesis	Cervical vertebral fusion abnormality	
4	Fernandez et al. [7]	1	Prenatal	Agenesis	Unilateral renal agenesis	Hemivertebra, single	Dilated urinary bladder, absent urethra, patent urachus, cord cyst
5	Balasubramanian et al. [8]	1	Postnatal	Agenesis	Unilateral renal agenesis	Spinal defect at C5,C6,T9,T10	15 pairs of ribs, hamartomatous lipomatosis
6	Dabkowska et al. [3]	1	Postnatal	Agenesis	Unilateral renal agenesis	Klippel—Feil deformity	Arnold Chiari malformation type 1, cubitus valgus
7	Morao et al. [9]	1	Postnatal	Absent vagina, Hemiuterus	MCDK	Sacral agenesis	Anorectal malformation
8	Lin et al. [4]	1	Prenatal	Absent uterus	Bilateral agenesis	Fused T2,T3 andT4, 11 pairs of ribs	Occipital encephalocele, bilateral Sprengel deformity, right radial hypoplasia and absent thumb
9	Suri et al. [5]	1	Prenatal	Absent uterus, vagina	Right renal agenesis	Cervicothoracic vertebral abnormality, Hemivertebra	Occipital encephalocele, soft palate cleft, short webbed neck
10	Present case	1	Prenatal	Hemiuterus	Unilateral renal agenesis	Hemivertebra, multiple	Open neural tube defect (meningomyelocele)

MCDK multicystic dysplastic kidney

abnormalities, especially in the absence of other components of VACTERL association.

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