

ไซรีโนมีเลีย (กลุ่มอาการเงือก) ร่วมกับภาวะไตสองข้างไม่พัฒนาและหลอดเลือดแดงสายสะดือเส้นเดียว: รายงานผู้ป่วยจากผลการชันสูตรและข้อมูลด้านคัพภวิทยา

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บทคัดย่อ

ไซรีโนมีเลีย หรือ กลุ่มอาการเงือก เป็นความผิดปกติแต่กำเนิดที่พบได้ยากและมักเสียชีวิต โดยมีลักษณะสำคัญคือ การเชื่อมติดกันของขาตอนล่างร่วมกับความผิดปกติของอวัยวะภายในหลายระบบ กลไกการเกิดโรคยังไม่ชัดเจน โดยมีสมมติฐานสำคัญ เช่น ความผิดปกติของการพัฒนาหลอดเลือด และความบกพร่องของการสร้าง mesoderm ส่วนหาง รายงานนี้เป็นทารกเพศหญิงครบกำหนด (อายุครรภ์ 37+1 สัปดาห์) จากมารดาอายุ 21 ปี การตรวจอัลตราซาวนด์ก่อนคลอดพบภาวะทารกโตช้าในครรภ์ น้ำคร่ำน้อย และไม่พบไตทั้งสองข้าง ภายหลังคลอดพบลักษณะขาเชื่อมติดกัน ไม่มีรูทวารหนัก ไม่มีอวัยวะเพศภายนอก และใบหน้าผิดปกติแบบพอดเตอร์ ร่วมกับพบหลอดเลือดสายสะดือสองเส้น ทารกเสียชีวิตภายในสองชั่วโมงหลังคลอด การชันสูตรศพยืนยันการไม่มีไตทั้งสองข้าง ปอดเจริญไม่เต็มที่ ไม่มีระบบทางเดินปัสสาวะ และความผิดปกติหลายประการของรูปร่าง การตรวจกรพบการเจริญช้า และสายสะดือมีเส้นเลือดแดงเพียงเส้นเดียว ขณะที่การตรวจทางจุลพยาธิวิทยาของปอดพบความไม่สมวัยเมื่อเทียบกับอายุครรภ์ รายงานนี้สะท้อนถึงลักษณะของไซรีโนมีเลียที่สัมพันธ์กับกลุ่มอาการพอดเตอร์ และเน้นย้ำบทบาทของการชันสูตรศพในการอธิบายความหลากหลายของความผิดปกติ สนับสนุนสมมติฐานทางคัพภวิทยา และเป็นประโยชน์ต่อการให้คำปรึกษาก่อนตั้งครรภ์

คำสำคัญ: ไซรีโนมีเลีย; กลุ่มอาการเงือก; ภาวะไตไม่พัฒนา; หลอดเลือดแดงสายสะดือเส้นเดียว; ภาวะเกิดต่อเนืองพอดเตอร์

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Sirenomelia (Mermaid syndrome) with bilateral renal agenesis and a single umbilical artery: An autopsy case report with embryological insights

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Abstract

Sirenomelia, also known as mermaid syndrome, is a rare and typically lethal congenital anomaly characterized by the fusion of the lower extremities and multiple visceral malformations. Its pathogenesis remains debated, with proposed mechanisms including abnormal vascular development (vitelline artery steal) and defective caudal mesoderm formation (defective blastogenesis). We describe a full-term female fetus (gestational age of 37+1 weeks) born to a 21-year-old primigravida, in whom prenatal ultrasonography revealed growth restriction, anhydramnios, and bilateral renal agenesis. At delivery, the neonate showed fused lower limbs, imperforate anus, absent external genitalia, dysmorphic facial features consistent with Potter's facies, and a two-vessel umbilical cord, and died two hours after birth. Autopsy confirmed bilateral renal agenesis, pulmonary hypoplasia, an absent urinary tract, and multiple dysmorphic features. Placental examination revealed delayed villous maturation with a single umbilical artery, and histology revealed lung immaturity inconsistent with gestational age. This case illustrates the classical presentation of sirenomelia associated with the Potter sequence and underscores the role of autopsy in clarifying its anomaly spectrum, supporting embryological hypotheses, and guiding prenatal counseling.

Keywords: Sirenomelia; mermaid syndrome; renal agenesis; single umbilical artery; potter sequence

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Introduction

Sirenomelia, also known as mermaid syndrome, is a rare congenital anomaly with an estimated incidence of 0.8 to 4.2 per 100,000 pregnancies^{1,2}. It manifests with different degrees of fusion of the lower extremities, most often accompanied by bilateral renal agenesis, absent urinary tract, imperforate anus, and genital agenesis³. The prognosis is poor, largely due to renal agenesis and pulmonary hypoplasia, which are incompatible with neonatal survival⁴.

The pathogenesis of sirenomelia remains controversial, with two main hypotheses. The vascular steal hypothesis states that an aberrant vitelline artery diverts blood flow from the caudal embryo, leading to hypoperfusion and abnormal development of lower body structures^{5,6}. Alternatively, the defective caudal mesoderm hypothesis suggests that primary developmental failure in the caudal region during early embryogenesis is the causative mechanism^{7,8}. Both processes may contribute, with vascular disruption serving as the final pathway.

Potter sequence, which results from severe oligohydramnios due to renal agenesis or urinary tract obstruction, is characterized by pulmonary hypoplasia and distinctive craniofacial features (“Potter facies”), including low-set ears, a flattened nose, and microstomia⁹. This sequence is commonly associated with bilateral renal agenesis and frequently overlaps with sirenomelia.

Maternal diabetes is the most consistently reported risk factor⁹, although associations

with maternal age extremes, tobacco and cocaine exposure, hyperthermia, and teratogenic environmental factors have also been described¹⁰. Prenatal ultrasonography can facilitate diagnosis, but detection may be limited in cases of severe oligohydramnios.

Due to its rarity and phenotypic heterogeneity, each case provides valuable insights into clinical recognition, embryological mechanisms, and parental counseling. Here, we report a case of sirenomelia with bilateral renal agenesis, Potter’s sequence, and a single umbilical artery, confirmed by complete autopsy and placental examination, and discuss its implications in light of current pathogenetic concepts.

Case report

A 21-year-old primigravida with no underlying illness attended regular antenatal care beginning at a gestational age (GA) of 7+3 weeks. She reported cigarette smoking until six weeks of gestation but denied alcohol or illicit drug use during pregnancy. Routine serological tests were unremarkable (blood group A Rh-positive, hemoglobin 13.4 g/dL, venereal disease research laboratory (VDRL) non-reactive, HIV and HBsAg negative). Ultrasound revealed severe fetal growth restriction (<10th percentile), anhydramnios, dolichocephaly, bilateral renal agenesis, absent bladder, and a suspected single umbilical artery. This case report was approved by The Human Research Ethics Committee of Thammasat University (Medicine) (MTU-EC-PA-0-106/67). Written informed consent was

obtained from the patient for the use and publication of anonymized clinical data.

An elective cesarean section was performed for breech presentation. A female infant weighing 1,620 g (below the 3rd percentile) was delivered. The newborn exhibited striking malformations, including complete fusion of the lower extremities (Figure 1a), rudimentary polydactyly of the right hand (Figure 1b), dysmorphic facial features consistent with Potter's facies (Figure 1c),

absent external genitalia (Figure 1d), and an imperforate anus (Figure 1e). The umbilical cord contained one artery and vein (Figure 1f). Despite admission to the neonatal intensive care unit (NICU) for palliative care, the infant survived for only two hours. Postmortem plain radiography (babygram) demonstrated fusion of the lower extremities, a single femur, two tibiae, and absent fibulae, consistent with sirenomelia type V (Stocker and Heifetz classification)¹¹ (Figure 2).



Figure 1 External morphology of the neonate. a) gross photograph showing fused lower extremities, b) lateral view with polydactyly of the right hand, c) dysmorphic facial features consistent with Potter facies, including low-set ears, downward-curved nose, slit-like mouth, and prominent infraorbital folds, d) the absent of external genitalia, e) imperforate anus, and f) single umbilical artery at the fetal site

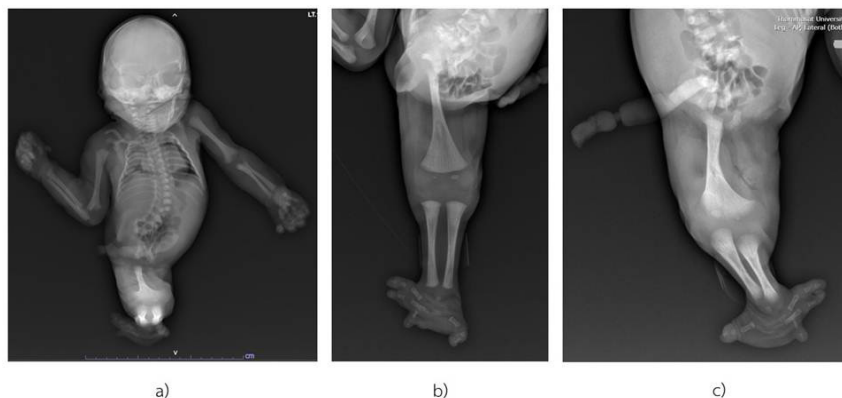


Figure 2 Postmortem plain radiograph (babygram). a) babygram anteroposterior, b) leg anterior, and c) leg posterior

Autopsy Findings: External examination confirmed fused lower limbs. Internally, bilateral renal agenesis and absence of the urinary bladder were observed (Figure 3a). The lungs were hypoplastic (14.4 g), and the heart

and great vessels were structurally normal. The placenta weighed 316 g (3rd-5th percentile) with a two-vessel cord (Figure 3b) and no infarction or inflammation was observed.

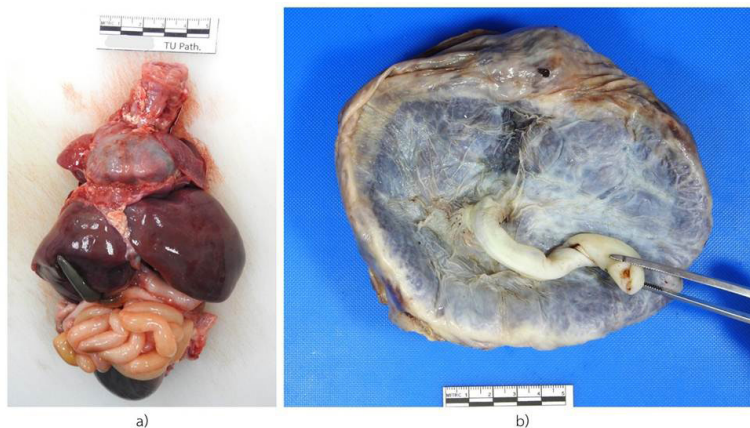


Figure 3 Internal autopsy and placental findings. a) thoracoabdominal dissection demonstrating hypoplastic lungs, bilateral renal agenesis, and an absent urinary bladder and b) placenta with central insertion of a two-vessel cord

Histology: Microscopy of the lungs showed saccular-stage immaturity inappropriate for gestational age, confirming the pulmonary hypoplasia (Figure 4a). Placental sections revealed delayed villous maturation with

reduced syncytial knots and a two-vessel cord (Figure 4b) without evidence of chorioamnionitis or infarction. Other organs showed autolytic changes without any specific pathology.

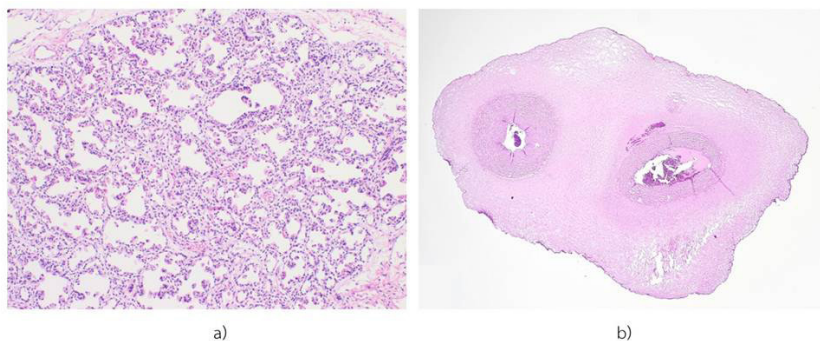


Figure 4 Histological features. a) lung tissue showing saccular-stage immaturity inappropriate for gestational age (H&E, x100) and b) single umbilical artery and vein (H&E, x2)

Discussions

Sirenomelia has striking congenital anomalies, with fusion of the lower extremities serving as its hallmark feature. Most cases of sirenomelia demonstrate lower limb fusion with reduction anomalies, such as absent fibulae or hypoplastic feet³. In contrast, our case exhibited rudimentary polydactyly, which is a rare finding in sirenomelia. This unusual feature suggests phenotypic overlap with other limb patterning disorders and underscores the heterogeneity of caudal morphogenetic disruption, where both reduction and duplication anomalies may coexist¹².

Most affected fetuses have severe visceral malformations, including renal agenesis, absent bladder, and imperforate anus, as demonstrated in the present case report. These anomalies are incompatible with long-term survival, and neonatal mortality is almost universal due to pulmonary hypoplasia secondary to renal agenesis¹.

The presence of the Potter sequence in our case, with pulmonary hypoplasia and characteristic facies (Figure 1c), underscores

the cascade of malformations resulting from bilateral renal agenesis. Potter's sequence arises from prolonged oligohydramnios, leading to pulmonary underdevelopment and compression-related craniofacial changes⁹. Its overlap with sirenomelia highlights the convergence of vascular, mesodermal, and renal developmental defects.

Two pathogenic models have been proposed for sirenomelia. The vascular steal hypothesis suggests that an aberrant vitelline artery diverts blood from the caudal embryo, impairing the development of pelvic and lower limb structures^{5,6}. This theory is supported by the frequent finding of a single umbilical artery, which was also observed in our case (Figure 4b). Alternatively, primary caudal mesodermal deficiency during early embryogenesis may lead to the failure of caudal structure differentiation^{7,8}. This mechanism better explains associated anomalies, such as neural tube defects or vertebral malformations occasionally seen with sirenomelia, and may also account for atypical findings, such as the polydactyly observed in our case (Figure 1b). The current

consensus suggests that both mechanisms may contribute, possibly in complementary ways, with vascular disruption superimposed on a background of mesodermal deficiency. Our findings of a two-vessel cord, bilateral renal agenesis, and severe caudal dysgenesis support this multifactorial hypothesis.

Maternal diabetes has been consistently reported as a predisposing factor^{9,13}, although other associations include maternal age extremes, cocaine use, hyperthermia, and teratogen exposure^{10,14}. Our case is notable for early maternal smoking, which, while not firmly established as a risk factor for sirenomelia, has been implicated in adverse pregnancy outcomes and an increased risk of congenital anomalies. Epidemiological studies suggest that maternal smoking during pregnancy is associated with neural tube defects, limb defects, and orofacial clefts¹⁵. Although a causal relationship with sirenomelia cannot be confirmed, this history underscores the importance of smoking cessation counseling as a preventive strategy in antenatal care.

Prenatal ultrasonography allows for diagnosis, but visualization is often limited by the presence of oligohydramnios. In such circumstances, autopsy remains essential for confirmation, delineation of malformation extent, and counseling. The placental findings in our case, including delayed villous maturation and a two-vessel cord (Figure 4b), provide additional support for the vascular hypothesis.

Additional genetic investigations were not performed. In the present case, severe

structural malformations were detected prenatally, including bilateral renal agenesis and anhydramnios, and the postnatal course was characterized by early neonatal death with a palliative management approach. These factors limited both the feasibility and the potential clinical benefit of further genetic evaluation. Nonetheless, a contributory genetic role cannot be completely excluded, and future studies incorporating molecular analyses may provide further insight into the pathogenesis of this rare condition.

Although rare reports of survival exist, the prognosis is dismal and depends on the presence of at least one functional kidney¹⁶. In the absence of renal function, palliative care is the only option, as illustrated in the present case.

This report underscores the importance of detailed clinicopathologic correlation in rare anomalies such as sirenomelia. The presence of the Potter sequence shows the cascading impact of renal agenesis on fetal development, and autopsy with placental examination yielded valuable embryological insights into its pathogenesis, thereby enhancing the understanding of clinicians and pathologists.

Conclusions

Sirenomelia is a rare and typically fatal anomaly that reflects profound disruption of caudal embryogenesis. This case, characterized by bilateral renal agenesis, pulmonary hypoplasia, a single umbilical artery, and Potter's sequence, reinforces the vascular steal hypothesis while highlighting the interplay between renal

agenesis, oligohydramnios, and pulmonary underdevelopment. Autopsy and placental examination not only confirmed the diagnosis but also provided valuable embryological insights supporting the vascular and mesodermal theories of pathogenesis. While maternal diabetes is an established risk factor, the history of early pregnancy smoking in this case underscores the potential role of modifiable environmental exposures. Although causality cannot be proven, this association reinforces the importance of early antenatal counseling, particularly regarding smoking cessation, as a key preventive strategy for reducing teratogenic risk.

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