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Omphalocele, Exstrophy of Bladder, Imperforate Anus and Spinal Defect Complex on an Aterm Baby

Ni Kadek Wiwik Agustini[1], I Wayan Dharma Artana[2], Kadek Deddy Ariyanta[3]

[1]Udayana University, Medical Faculty,
Department of Child Health, Sanglah Hospital, Denpasar, Indonesia
wiwik.agustini.suryanatha[at]gmail.com

[2]Udayana University, Medical Faculty,
Department of Child Health, Sanglah Hospital, Denpasar, Indonesia
dharma.artana[at]yahoo.com

[3]Udayana University, Medical Faculty,
Department of Pediatric Surgery, Sanglah Hospital, Denpasar, Indonesia
deddyariyanta[at]yahoo.com

Abstract: ***Omphalocele, exstrophy of bladder/cloaca, imperforate anus, and spinal defects (OEIS complex) is an extremely rare congenital anomaly with varied clinical presentation. The exact aetiology is unknown but genetic associations have also been hypothesized. It results from defective blastogenesis leading to improrer closure of anterior abdominal wall and defective development of cloacae and urogenital septum. We reported a zero-day old baby presented with omphalocele, exstropy of bladder, imperforata anus, ambiguous genitalia and spinal defect. Laboratory examination showed normal result. Radiological imaging showed an exstrophy of bladder, gastroschizis and hemivertebrae CV Th 10, 11, 12. The patient underwent laparotomy, adhesiolisis, bladder closure, caecum tubularization and colostomy. The patology anatomy examination result from intrabladder specimen revealed unidentified specific organ. He showed improvement and discharged after 26th days of hospitalisation. The patient was planned to undergo sex chromosome examination to determine the sex of the patient. The OEIS complex can be diagnosed based on the clinical manifestation of omphalocele, exstrophy bladder or cloacal, imperforate anus and spinal anomalies. Fetal ultrasound and fetal MRI on 2nd trimester of pregnancy are critical diagnostic. Fetal tomographic ultrasound imaging (TUI) also can be used. The prognosis of OEIS complex depends on the severity of the anomalies, the prevalence of infection and bowel anomalies.***

Keywords: OEIS complex, diagnosis, outcome

1. Introduction

Omphalocele, exstrophy of bladder/cloaca, imperforate anus, and spinal defects (OEIS complex) is an extremely rare congenital anomaly with varied clinical presentation [1], [2]. The incidence of OEIS complex has been reported to range between 1/200, 000 to 400, 000 of live births [1], [2].

The exact aetiology was unknown. It is sporadic, but genetic associations have also been hypothesized that results from defective blastogenesis leading to improrer closure of anterior abdominal wall and defective development of cloacae and urogenital septum [2], [3]. There were reports of recurrence in siblings and concurrent occurrence in monozygotic twins [1], [3].

The diagnosis of OEIS complex refers to the combined occurrence of omphalocele, exstrophy of bladder or cloacal, imperforate anus and spinal defects. Diagnosis of OEIS complex can be made on 2nd trimester of pregnancy. Fetal ultrasound and fetal MRI are critical in the diagnosis of OEIS complex; in addition, fetal tomographic ultrasound imaging (TUI) also can be used.

The prognosis of OEIS complex depends on the severity of the anomalies, which may be life threatening, due to the prevalence of infection and bowel anomalies [3], [4]. Surgical procedures include closure of omphalocele, separation of ileocecal connection from the exstrophied bladder plate, and reapproximation of an end colostomy with preservation of all bowels [3], [5]. The success of these procedures cannot guarantee a good quality of life. Due to the poor prognosis, early prenatal diagnosis of OEIS complex is required to give parents the option to terminate the pregnancy; it is also helpful to plan the appropriate perinatal management if the parents want to keep the pregnancy [6].

2. Case Report

A zero-day old patient, ambiguous genetalia, was referred from B Hopital to Emergency room (ER) S Hospital with diagnosis multiple congenital malformation. The multiple congenital malformation consisted of a mass on the abdomen, no anus, ambiguous genetalia, and mass on the lower back of the patient. Meconium was leaked from the mass on the abdomen of the patient. The patient was active, no temperature instability nor shortness of breath.

Patient was born aterm and spontaneously, assisted by midwife at B Hospital. Patient was vigorous, with birth weight was 2300 grams, body length was 46 cm, and head circumference 31 cm.

Mother was 38 years old, and it was her 6th pregnancy. Mother visited midwife for antenatal care every month. There was no history of ultrasonography. There were histories of abortion on the 1st and 2nd pregnancy (on the first trimester of pregnancy), with history of prematurity

on the 3rd until 5th pregnancy then the children had grown up without any disability. Mother only consumed multivitamins during pregnancy given by the midwife routinely. There was no history of fever, premature rupture of membrane, chorioamnionitis, fatal distress, greenish amniotic fluid, vaginal discharge, nor urinary tract infection. There was no history of same congenital malformation in the family.

On the date of admission, the physical examination showed the patient was active, with good tones and reflexes. Vital sign showed the heart rate was 150 beats/minutes, respiration rate was 48 times/minutes, temperature 36 ^{0}C. General examination showed the head circumference was normal, the face was not dismorfic, no icteric nor anemic on the conjungtiva with positive reflect on both pupil. Nose, ear, throat and mouth were normal. There was no retraction with normal heart sound. The breath sound was normal, the abdomen looked distended with mass consist of omphalocele and exstropy of bladder and cloaca with meconium leaked from it. The patient also had atresia ani, ambiguous genetalia and spina bifida. The extremities were normal and warm with capillary refill time less than 2 second. **(Figure 1)**

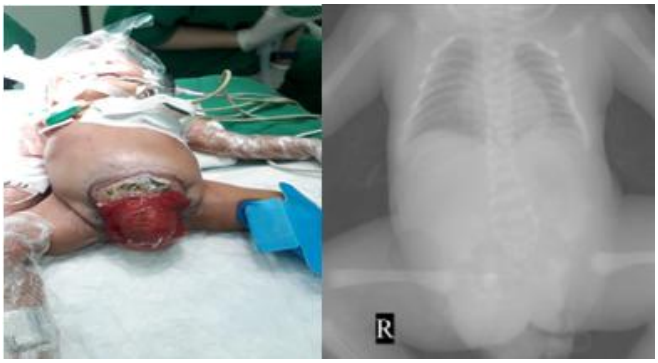

Figure 1 & 2: The patient clinical presentation and patient's babygram

Figure 3: The clinical presentation after surgery

Laboratory findings showed leucocyte 22.94 103/µL, neutrophyl 55.44%, neutrophyl absolute 12.72 103/µL, lymphocyte 31.86 %, lymphocyte absolute 7.31 103/µL, hemoglobin 21.4 g/dL, hematocryte 64.34%, thrombocyte 280.4 103/µL, and procalcitonin 0.85 ng/ml. The renal function test, liver function test, electrolyte and physiology homeostatic were within normal limit. The babygram revealed cardiopulmonary was within normal limit with gastroschizis and hemivertebrae CV Th 10, 11, 12 **(figure 2).** Based on the clinical and adjunctive examination the patient was diagnosed with aterm infant, low birth weight (2300 grams), appropriate for gestational age, OEIS complex (omphalocele, extrophy of the bladder, imperforate anus, spina defect).

The patient was treated in neonatal intensive care unit (NICU) with incubator. Patient was fasted and given total parenteral nutrition. Eleven days after admitted the patient underwent laparotomy, adhenosiolisis, bladder closure, tubularisasi caecum and colostomy **(figure 3).** After the operation, patient was continued fasted and given total parenteral nutrition. Enteral nutrition was started after the patient was stable and increased gradually. The patient also given antibiotics, analgetic, and used stent ureter. The specimen intrabladder was transferred for patology anatomy examination with result the specific organ cannot be identified.

During the hospitalization patients showed improvement and patient was discharged after 26th days of hospitalization. The patient was planned to undergo sex chromosome examination to determine the sex of the patient.

3. Discussion

Most cases of OEIS complex occur spontaneously, but there are reports of recurring case in siblings and concurrent occurrence in monozygotic twins, suggesting a genetic contribution to the pathogenesis of OEIS complex [11] Several associations have been suggested:

a. Teratogenic exposition: OEIS complex has been shown to be associated with prenatal exposure to diazepam, diphenylhydantoin [3]- [7]
b. Genetic factors: possibly associated trisomies 13, 18 and 21, triple X syndrome. [3], [7], [8]- [11]
c. Single defects in blastogenesis and mutations in Homeobox genes (such as HLXB9), mutations in mitochondrial 12S rRNA, 3q12.2-q13.2 deletion, and 9q34.1-qter deletion [7], [11] Lee et al describe a case of OEIS complex in monozygotic twins. This concordance of monozygotic twins for the defects may support the theory that early malformation complexes as OEIS and monozygotic twinning are manifestations of the same discordance of early blastogenesis [7]
d. Multiple pregnancies: higher incidence of OEIS in monozygotic twins suggests a possible genetic contribution to the occurrence of this multisystem defect [2], [7].
e. Sporadic familiar occurrence: the most frequently etiology [7].
f. Failure of cloacalseptation: resulting in a common cloaca [7].
g. Breakdown of the cloacal membrane: resulting in exstrophy and omphalocele [7].
h. Incomplete vertebral fusion: resulting in open neural defect (Spina bifida) [7].

OEIS complex also associated with Opitz G/BBB syndrome, Goltz syndrome, oculoauriculovertebral syndrome, and frontonasal dysplasia. Significantly increased maternal serum alphafetoprotein (MSAFP) has been reported associated with OEIS complex. The high MSAFP is related to abdominal wall defects and open spina bifida identified in the OEIS complex [3], [11]. In this case**,** the etiology of OEIS complex was unclear. History of abortus on the 1st and 2nd mother pregnancy might be related to genetic factors, although the etiology of the abortus were also unclear.

The pathophysiology of OEIS complex is still being studied. OEIS is considered to be a defect in blastogenesis, beginning in the first four weeks of human development. According to different authors, OEIS has probably an heterogeneous etiology and may result from a single localized defect in early caudal mesoderm and it is thought to lead to one of three defects, failure of cloacal septation resulting in a common cloaca, breakdown of cloacal membrane resulting in omphalocele and exstrophy or incomplete vertebral fusion resulting in open neural defects [4]. The development of the cloacal membrane occurs between days 5 and 42 of gestation, some author said approximately at 29 days of development [3], [4]. The cloacal membrane is composed of ectodermal and endodermal layers. It covers the region from the umbilicus to tail portion of the embryo at the 4-mm stage. In the 8-mm stage, the primitive streak mesoderm invades the membrane to form the lower abdominal wall. During the 8 to 16 mm stage, the urorectal septum grows to divide a single cloacal chamber into the anterior urogenital system and the posterior alimentary system. In cloacal exstrophy, the persistent cloacal membrane produces a wedge effect that impedes the migration of the mesoderm streak to form the anterior abdominal wall. The persistent cloacal membrane is thought to be unstable and will rupture. If it ruptures before the division of the cloacal chamber by the urogenital septum, cloacal exstrophy occurs. If it ruptures after the formation of urogenital septum, the result will be exstrophy of the bladder. The coexistence of cloacal exstrophy and spinal dysraphism may be explained by a single insult in the embryonic tail in early pregnancy [3], [5].

The diagnosis of OEIS complex refers to the combined occurrence of omphalocele, exstrophy bladder or exstrophy cloacal, imperforate anus and spinal anomalies [1]. OEIS complex involves abnormalities of almost everybody system and shows variability from case to case. Gastrointestinal malformations are found in almost all cases. The most prominent defect is a blind-ending colon with imperforate anus. Other anomalies include duplication of the colon, intestinal malrotation, atresia, short gut, and situs inversus [3], [5]. Ambiguous genitalia are common in OEIS. In females, the most common genitalia anomaly is dysraphism in almost 100% case [3], [4]. Abnormalities of the external genitalia almost always occur, with either total absence of genital structures or various degrees of ambiguity [2], [11]. Common spinal abnormalities include hemivertebrae, tethered cords, and lipomyelocystoceles, extra vertebrae, and absent vertebrae [3], [6]. Terminal myelocystoceles constitute approximately 5% of skin-covered lumbosacral spina bifida, an arachnoid-lined meningocele that is in continuity with the spinal subarachnoid space, and a low-lying, hydromyelic spinal cord that traverses the meningocele and then expands into a large terminal cyst that does not communicate with the subarachnoid space [2], [6]. Limb anomalies may be secondary to defects of the spinal cord. Arthrogryposis (condition of severe limb contractures), talipes, syndactyly, and thumb hypoplasia have all been documented in patients with this condition [3], [4]. It has been identified that talipes in association with OEIS complex is closely related to a tethered cord, whereas other lower extremity anomalies are more frequently associated with spina bifida. Although central nervous system anomalies are not very common, Chiari malformation and hydrocephalus may be present in patients with open spinal defects [3], [4]. Most of the case showed the brain structur was normal and have normal intelligence [2].

Diagnosis of OEIS complex can be made prenataly. Fetal ultrasound and fetal MRI are critical in the diagnosis of OEIS complex, and the findings are reliable. In addition, fetal tomographic ultrasound imaging (TUI) may represent a useful adjunct to conventional two dimensional ultrasound in the prenatal diagnosis [2], [8], [11]. In cases where imaging criteria for diagnosis of lower abdominal wall defects are difficult to discern, color Doppler helps confirm the diagnosis of exstrophy bladder and its differentiation from omphalocele [1]. Diagnosis of OEIS complex in early pregnancy is extremely difficult. USG is the imaging modality of choice to diagnose OEIS Complex in the 2nd trimester [3], [7]. Girz et al first reported the first-trimester sonographic diagnosis of OEIS complex [11], [16]. Chen et al used fetal tomographic ultrasound imaging (TUI) and MRI for the prenatal diagnosis of OEIS complex in a fetus at 20 gestational weeks and suggested that fetal TUI and MRI are useful adjuncts to conventional two-dimensional ultrasound in the prenatal diagnosis of OEIS complex [11-18].

Austin et al described major criteria for the prenatal diagnosis of OEIS, it consists of nonvisualization of the fetal bladder, infraumbilical abdominal wall defect, omphalocele, myelomeningocele) and minor criteria (lower extremities malformations, renal anomalies, ascites, widened pubic arches, narrow thorax, hydrocephalus, single umbilical artery). [2], [3], [6], [11]. Nevertheless, nowadays, the prenatal diagnosis of OEIS is possible by the identification of:

a. A midline infra-umbilical defect with an irregular mass: in the inferior abdominal wall or cystic anterior wall structure (persistent cloacal membrane) or with omphalocele. [7], [12]
b. Absence of the bladder between the two umbilical arteries [7].
c. Lumbo-sacral myelomeningocele. Common spinal defect include hemivertebrae, sacral anomalies and either tethered cord and meningocystocele. Kallen et all wrote that the spinal defect may occur more cranially and are not restricted to the lumbosacral region [7], [8].

d. Anomalies of the inferior limbs are possible but club feet, limb duplication or amputations are generally not seen with OEIS [7], [8], [10].
e. Wide pubic arch is classically present with symphysis pubis diastasis and congenital hip dislocation [7]
f. Single umbilical artery: It is a frequent associated sign [2], [4], [7], [11].
g. Genital anomalies. Classically, the sex determination is often not possible. Other uro-genital anomalies are possible, including genital duplication [7].
h. Anal atresia [7].
i. Omphalocele. Majority of authors consider OEIS as a distinct syndrome, but there is a discussion if the exstrophy of the bladder sequence, exstrophy of the cloaca sequence or urorectal septum malformation sequence should be referred to distinct clinical entitities [7].
j. Associated Anomalies: Different anomalies can be associated with OEIS complex:

1. Cardiac anomalies: cardiac defects have been described with exstrophy of the cloaca alone as atrial and ventricular defect [2], [4], [7].

2. Renal anomalies including renal agenesis, duplicate collecting system, hydronephrosis, and a pelvic kidney have also been described [2], [4], [7].

3. Increased nuchal translucency. The most likely cause of increased nuchal translucency is probably vascular or hemodynamic, but the mechanism remains unclear. [2], [4], [7], [11]- [18]

4. Conclusion

The OEIS complex can be diagnosed based on the clinical manifestation of omphalocele, exstrophy of bladder or cloacal, imperforate anus and spinal anomalies. Fetal ultrasound and fetal MRI on 2nd trimester of pregnancy are critical diagnostic, fetal TUI also can be used. The prognosis of OEIS complex depends on the severity of the anomalies, the prevalence of infection and bowel anomalies

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