Case Report

Aberrant Abdominal Umbilical Arteries in VACTERL – Association: A First Case Report

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A 38-week-gestational age male neonatal death from a 27-year-old-mother was reported. The autopsy found multiple congenital anomalies such as scoliosis of thoracic spine with 13 pairs of ribs, anal atresia, bilateral renal agenesis, and club feet. These anomalies were diagnosed VACTERL – association that must include at least three out of six principal anomalies of previously mentioned, e.g., (1) V – vertebral defects, (2) A - anal atresia, (3) C – cardiac anomalies, (4) TE – tracheo-esophageal fistula, (5) R – renal anomalies, and (6) L – limb abnormalities. In addition, other anomalies were also observed in this case, i.e., cryptorchidism both sides, jejunal diverticulum, and aberrant abdominal umbilical arteries.

Keywords: *VACTERL – association, VATER – association, Congenital anomalies, Vertebral defects, Anal atresia, Cardiac anomalies, Tracheo-esophageal fistula, Renal anomalies, Limb abnormalities, Cryptorchidism, Jejunal diverticulum, Aberrant abdominal umbilical arteries*

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VACTERL association is a sporadic non-random co-occurrence of a group of congenital malformations that expresses at least three of the following core components[1,2], vertebral defects (V), anal atresia (A), cardiac anomalies (C), tracheo-esophageal fistula (TE), renal anomalies (R) and limb abnormalities (L). Other congenital anomalies may also be present such as inguinal hernia, gonadal anomalies, small intestinal malformation, etc.[3]. In the present study, a case of neonatal death from VACTERL associated with cryptorchidism, jejunal diverticulum, and aberrant abdominal umbilical arteries was reported. From previous literature review, aberrant abdominal umbilical arteries have never occurred together with VACTERL association.

Case Report

A 38-week-gestational age, male neonate died 4 hours after delivery from a 27-year-old mother. The body measured 2300 grams in weight and crown-heel length was 46 centimeters (cm). The head, chest, and abdominal circumferences were 31, 30, and 24 cm, respectively. The length of attached umbilical cord was 3.5 cm long and 0.6 cm in diameter. External examination revealed prominence of both infraorbital creases, bilateral cryptochidism and club feet. A lipofibroma nodule about 1 cm in diameter was found at midline of the back just above coccyx. The anus was imperforated. Internal examination revealed athelectasis of both lungs but no abnormality was detected within the trachea, bronchi and esophagus. Agenesis of both kidneys, ureters and renal arteries were noted. Umbilical arteries originated from the upper and middle part of abdominal aorta instead of both internal iliac arteries. In addition, there was a true diverticulum (1.5 cm in length and 0.5 cm in diameter) at distal part of jejunum. Furthermore, dilated blind pouch of rectum was found, measured 10 cm. in length and maximum to 4 cm in diameter with meconium content. The right testis was found in the lower right part of the abdominal cavity while the left testis was found in the left side of pelvic cavity. Whole body postmortem radiographs revealed right sided thoracic scoliosis, supernumerary thoracic spine and ribs (13 pairs of ribs), and absence of third to fifth lumbar spines and sacrum. The left pelvic bone was quite smaller than the right side. Brain, thymus gland, thyroid gland, heart, liver, spleen, adrenal glands, pancreas, penis, and umbilical cord were grossly unremarkable. Microscopic examination showed no

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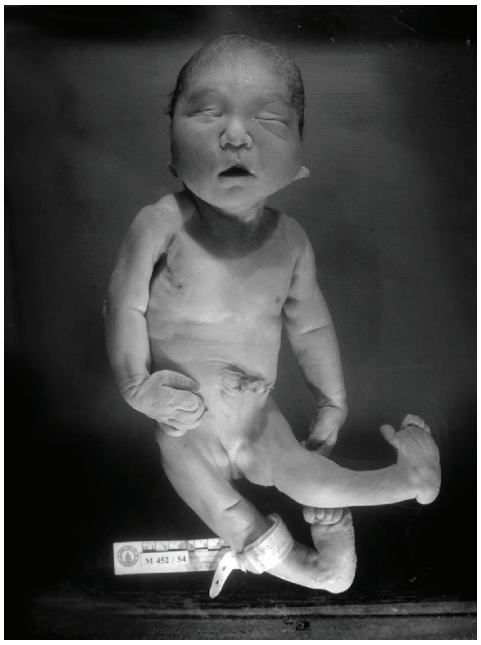

Fig. 1 External examination revealed deformity of pelvis and lower extremities with club feet

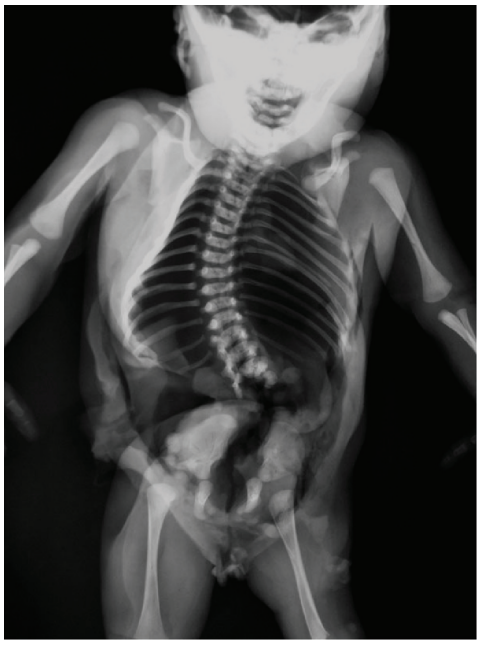

Fig. 2 Radiograph revealed thoracic scoliosis, supernumerary thoracic spine and ribs (13 pairs) and absence of third to fifth lumbar spines and sacrum

specific pathological features except athelectasis of both lungs.

Discussion

The sporadic, non-random co-occurrence of a group of congenital malformations that derived from the embryonic mesoderm consisting of vertebral defects (V), anal atresia (A), tracheo-esophageal fistula with esophageal atresia (TE) and radial dysplasia (R) was first named "VATER association" in 1972[4]. Later other three principal abnormalities were included, *i.e.*, cardiac anomalies (C), renal anomalies (R), and limb abnormalities (L), therefore was renamed to be "VACTERL association"[5,6]. The diagnostic criteria of VACTERL association require a finding of at least three of these core congenital anomalies[1,2,7]. The incidence of VACTERL – association is approximately 1 in 10,000 to 1 in 40,000 live-born infants[1]. It is more common in male[2,8]. The anomalies occur during embryogenesis[7,9], which involves various congenital malformations as described below[1,2,6-8].

V – vertebral defects frequently occur together with rib anomalies with prevalence of approximately 60 to 80%. The abnormalities in this group show segmentation defects or abnormal spinal curvature. In a case with segmentation defect, the expression reveals hemivertebrae, butterfly vertebrae, wedge vertebrae, dysplastic, hypoplastic, supernumerary or absent vertebrae, and dysgenesis or agenesis sacrum, etc.[3]. In a case with abnormal spinal

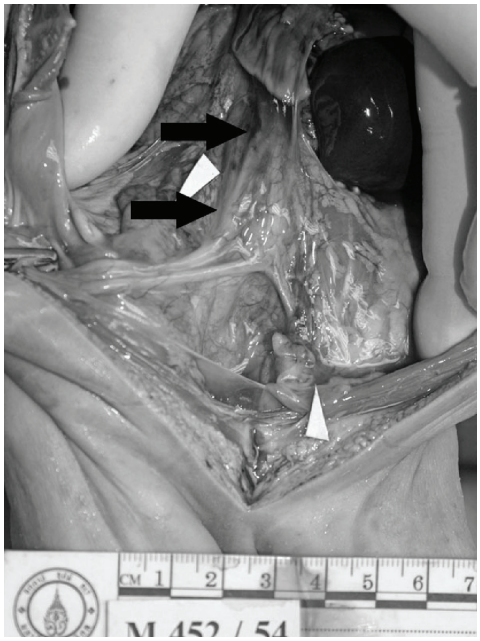

Fig. 3 Umbilical arteries originated from upper and middle part of abdominal aorta

curvature, the expression reveals scoliosis, kyphosis, or lordosis. Scoliosis detection may be the first sign of VACTERL association[10]. The rib anomalies, *i.e.*, fused, supernumerary, hypoplastic or bifid ribs may be found.

A – anal atresia or imperforate anus occurs with frequency of approximately 55 to 90%. It may occur together with fistula between genitourinary tract or perineum[3].

C – cardiac anomalies occur with frequency of approximately 40 to 80%. The abnormalities that frequently occur are ventricular septal defects, atrial septal defects, and Tetralogy of Fallot while the less frequent abnormalities are truncus arteriosus and transposition of the great vessels[7].

TE – tracheo-esophageal fistula occurs with frequency of approximately 50 to 80% and may appear together with esophageal atresia.

R – renal anomalies are found in approximately 50 to 80%. The abnormality appears with wide range of severity and type, *e.g.*, agenesis, hypoplastic or dysplastic kidneys, horseshoe kidney, ectopic kidney, multicystic kidney, ureteropelvic junction obstruction, and hydronephrosis. Other anomalies are duplicated collecting system, urethral constriction, hydroureter, and hypoplastic renal artery[3].

L – limb abnormalities are found in approximately 40 to 70% in babies. The abnormality of upper extremities reveal the following, *e.g.*, dysplasia, hypoplasia, agenesis or aplasia of radius, hypoplasia of ulna, clubbed hand, or thumb anomalies. For thumb anomalies, it may express in polydactyly, syndactyly, absent, malformed, or dislocated thumb. The abnormality of lower extremities reveal clubbed feet[3]; syndactyly of toes, absence of phalange, metatarsal bone, tibia and fibula, hypoplasia of tibia, fibula, and ischial bone.

In addition, other non-VACTERL defects that occur together with VACTERL association were reported. Single umbilical artery, one of non-VACTERL with prevalence of approximately 30%[11], is considered to be the first clue to diagnosis[12,13]. Other non-VACTERL, *i.e.*, genital defects and abnormality of respiratory tract are found with approximately 23% in both groups[11]. Genital defects include cryptorchidism, scrotal atrophy, micropenis, vaginal atresia, anomalies of uterus, ovarian agenesis, etc. while hypoplastic or agenesis of lung is observed in respiratory tract anomaly. Ear defects, cleft lip, cleft palate, inguinal hernia, duodenal atresia, Meckel's diverticulum, malrotation of small intestine, heterotopic pancreas, hypoplastic adrenals, etc.[3] may be found.

Prenatal imaging such as ultrasound[7,13-15], echocardiogram, or magnetic resonance will assist antenatal diagnosis of single umbilical artery that has been accepted to be the first clue to diagnosis. Moreover, these techniques can detect polyhydramnios and a lack of a gastric bubble due to tracheo-esophageal fistula, dilated colon due to imperforate anus, and other abnormalities in vertebral, heart, kidneys, and limbs.

The etiology and pathogenesis of VACTERL association have still been poorly known. Some authors reported that it frequently occurs in diabetic mothers[7] or mothers who received teratogenic agents, *e.g.*, adriamycin[9], cholesterol-lowering statin[1,7], lead[1], estrogen, or progesterone during first trimester of pregnancy[1,3]. In addition, some reports indicated that the cause of VACTERL association may be from genetics, *e.g.*, mutation of Gli or HOXD13 genes[16] that render the defect of zonic hedgehog pathway signaling during embryogenesis[1,7-9,17].

From autopsy investigation in the present study, the findings are compatible with VACTERL association because more than three core component features were detected, *i.e.*, (V) thoracic scoliosis, supernumerary thoracic spine and ribs (13 pairs of ribs) and third to fifth lumbar spines and sacral agenesis, (A) anal atresia, (R) bilateral renal agenesis, and (L) congenital club feet. Furthermore, non-VACTERL type defects were also detected in the present case, *i.e.*, cryptorchidism, true jejunal diverticulum and both umbilical arteries originated from upper and middle part of abdominal aorta instead of right and left internal iliac arteries as seen in normal babies.

Both cryptorchidism and diverticulum have been found as non-VACTERL type defects in previous literatures. However, aberrant abdominal umbilical arteries have never been found together with VACTERL association but there have been reports in several cases of caudal regression syndrome[18].

Conclusion

A 38-week-gestational age, male neonate still alive for four hours after delivery was reported in the present study. He was diagnosed as VACTERL association from more than three core components of congenital malformation, (V) vertebral defects expressed scoliosis of thoracic spine, supernumerary ribs and thoracic spine, and third to fifth lumbar spines and sacral agenesis, (A) anal atresia or imperforate anus, (R) bilateral renal agenesis, and (L) limb

abnormalities expressed club feet. Other abnormalities found were cryptorchidism, jejunal diverticulum, and aberrant abdominal umbilical arteries.

References

1. Solomon BD. VACTERL/VATER Association. Orphanet J Rare Dis 2011; 6: 56.
2. Czeizel A, Ludanyi I. VACTERL-association. Acta Morphol Hung 1984; 32: 75-96.
3. Weaver DD, Mapstone CL, Yu PL. The VATER association. Analysis of 46 patients. Am J Dis Child 1986; 140: 225-9.
4. Quan L, Smith DW. The VATER association. Vertebral defects, Anal atresia, T-E fistula with esophageal atresia, Radial and Renal dysplasia: a spectrum of associated defects. J Pediatr 1973; 82: 104-7.
5. Corcoran R, Entwistle GD. Letter: Polycystic ovarian disease and oral contraception. Lancet 1975; 1: 1386-7.
6. Harjai MM, Holla RG, Kale CR. Full spectrum of VACTERL in new born. MJAFI 2008; 64: 84-5.
7. Salati SA, Rabah SM. VACTERL association. Online J Health Allied Scs 2010; 9: 15.
8. Czeizel A, Ludanyi I. An aetiological study of the VACTERL-association. Eur J Pediatr 1985; 144: 331-7.
9. Spilde T, Bhatia A, Ostlie D, Marosky J, Holcomb G 3rd, Snyder C, et al. A role for sonic hedgehog signaling in the pathogenesis of human tracheoesophageal fistula. J Pediatr Surg 2003; 38: 465-8.
10. Raam MS, Pineda-Alvarez DE, Hadley DW, Solomon BD. Long-term outcomes of adults with features of VACTERL association. Eur J Med Genet 2011; 54: 34-41.
11. Bhurtel DR, Losa I. VACTERL (vertebral anomalies, anal atresia or imperforate anus, cardiac anomalies, tracheoesophageal fistula, renal and limb defect) spectrum presenting with portal hypertension: a case report. J Med Case Rep 2010; 4: 128.
12. Murphy-Kaulbeck L, Dodds L, Joseph KS, Van den HM. Single umbilical artery risk factors and pregnancy outcomes. Obstet Gynecol 2010; 116: 843-50.
13. Tongsong T, Wanapirak C, Piyamongkol W, Sudasana J. Prenatal sonographic diagnosis of VATER association. J Clin Ultrasound 1999; 27: 378-84.
14. Tongsong T, Chanprapaph P, Khunamornpong S. Prenatal diagnosis of VACTERL association: a case report. J Med Assoc Thai 2001; 84: 143-8.
15. Gedikbasi A, Yararbas K, Yildirim G, Yildirim D, Arslan O, Gul A, et al. Prenatal diagnosis of VACTERL syndrome and partial caudal regression syndrome: a previously unreported association. J Clin Ultrasound 2009; 37: 464-6.
16. Garcia-Barcelo MM, Wong KK, Lui VC, Yuan ZW, So MT, Ngan ES, et al. Identification of a HOXD13 mutation in a VACTERL patient. Am J Med Genet A 2008; 146A: 3181-5.
17. Kim J, Kim P, Hui CC. The VACTERL association: lessons from the Sonic hedgehog pathway. Clin Genet 2001; 59: 306-15.
18. Duesterhoeft SM, Ernst LM, Siebert JR, Kapur RP. Five cases of caudal regression with an aberrant abdominal umbilical artery: Further support for a caudal regression-sirenomelia spectrum. Am J Med Genet A 2007; 143A: 3175-84.

ความพิการแต่กำเนิดหลายชนิดของโรค VACTERL — association: รายงานการตรวจศพเด็กปริกำเนิด 1 ราย

วิชาญ เปี้ยวนิ่ม, กาญจนา สุจิรชาโต, จิตตา อุดหนุน, อุบล ชูดวง, สมพงษ์ วงค์วิชัย

รายงานการผ่าศพเด็กปริกำเนิดเพศชาย 1 ราย อายุครรภ์ 38 สัปดาห์ คลอดจากมารดาอายุ 27 ปี ผลการตรวจศพพบความพิการแต่กำเนิดหลายชนิด ได้แก่ กระดูกสันหลังคดร่วมกับมีกระดูกซี่โครง 13 คู่ ไม่มีรูทวารหนัก ไม่มีไตทั้งสองข้าง และเท้าปุ้มทั้งสองข้างซึ่งความพิการหลายชนิดดังกล่าวเข้าได้กับโรค VACTERL — association ซึ่งการวินิจฉัยว่าเป็นโรคนี้จะต้องพบความพิการแต่กำเนิดหลักอย่างน้อย 3 ใน 6 ข้อดังนี้ (1) ความพิการของกระดูกสันหลัง (V — vertebral defects) (2) ไม่มีรูทวารหนัก (A — anal atresia) (3) ความพิการของหัวใจ (C — cardiac anomalies) (4) มีรูต่อระหว่างหลอดลมและหลอดอาหาร (TE — tracheo-esophageal fistula) (5) ความพิการของไต (R — renal anomalies) และ (6) ความพิการของแขน/ขา (L — limb abnormalities) นอกจากนี้ยังตรวจพบความผิดปกติอื่น ๆ ร่วมด้วย คือ ลูกอัณฑะไม่ลงถุงทั้งสองข้าง มีกระพุ้งยื่นออกมาจากผนังลำไส้เล็กส่วนปลาย และพบจุดกำเนิดของหลอดเลือดแดงสายสะดืออยู่ผิดตำแหน่งทั้งสองเส้น คือ แยกออกมาจากหลอดเลือดแดงใหญ่บริเวณช่องท้องส่วนต้นและส่วนกลาง (ซึ่งปกติแยกมาจากหลอดเลือดแดงบริเวณโคนขาแต่ละข้าง)