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A Female Infant Who Had both Complete VACTERL Association and MURCS Association: Report of a Case

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Abstract
A 41-day-old female infant with VACTERL association was transferred to the pediatric intensive care unit of our hospital. She had been delivered at 36 weeks gestation by spontaneous vaginal delivery and weighed 2340 g. Esophageal atresia type A with long gap, anal atresia, cardiac anomaly (atrial septal defect and patent ductus arteriosus), thoracic vertebral dysplasia, left renal agenesis, and minor anomalies (left-side facial nerve palsy, left-side difficulty in hearing, and the absence of the right thenar) had been diagnosed by various examinations. She was transferred to our hospital to receive treatment for heart failure due to a cardiac anomaly. We recognized vaginal atresia during a radical operation for anal atresia (rectovestibular fistula) at 8 months of age. Furthermore, magnetic resonance imaging (MRI) revealed agenesis of the uterus. MURCS association includes Mullerian duct aplasia or hypoplasia, renal aplasia, and cervicothoracic somite dysplasia. This is the first case of complete VACTERL association combined with MURCS association.

Key words VACTERL association · MURCS association

Introduction

VACTERL association[1] is a nonrandom association of several congenital anomalies, including vertebral anomaly, anal atresia, cardiac anomaly, tracheoesophageal fistula, renal aplasia, and limb defects. However, VACTERL association is rarely combined with genital anomalies, and vertebral malformations tend to be located more often in the caudal region. Duncan et al.[2] described the concept of MURCS association in 1979. MURCS association includes Mullerian duct aplasia or hypoplasia, renal aplasia, and cervicothoracic somite dysplasia. MURCS association is more infrequent than VACTERL association. We herein report the first known patient to have complete VACTERL association with MURCS association.

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Case Report

A 41-day-old female infant with VACTERL association was transferred to the neonatal intensive care unit (NICU) of our hospital. A fetal ultrasound examination revealed polyhydroamnion and no intestinal dilation, and the fetus was therefore suspected to have esophageal atresia. The infant was delivered at 36 weeks gestation by spontaneous vaginal delivery at a local hospital. The infant had Apgar scores of 6 and 5 at 1 min and 5 min, respectively, and weighed 2340 g. A gastrostomy and transverse colostomy were performed on the fourth day of life. Various examinations revealed esophageal atresia, gross type A with long gap (Fig. 1), anal atresia (rectovestibular fistula), cardiac anomaly [atrial septal defect (ASD) and patent ductus arteriosus (PDA)], thoracic vertebral dysplasia, and left renal agenesis, and the patient was diagnosed as having VACTERL association. She also had left-side facial nerve palsy, left-side difficulty in hearing, and an absence of the right thenar. Heart failure gradually became apparent due to massive shunting caused by PDA and ASD. She was transferred to the NICU of our hospital at 41 days of age for further treatment. A cardiac surgeon at our hospital performed PDA ligation and pulmonary artery (PA) banding at 43 days of age. At 8 months of age, she underwent radical surgery (posterior sagittal anorectoplasty) for rectovestibular fistula. During this surgery, we recognized vaginal atresia (Fig. 2). Magnetic resonance imaging (MRI) confirmed that she had agenesis of the uterus

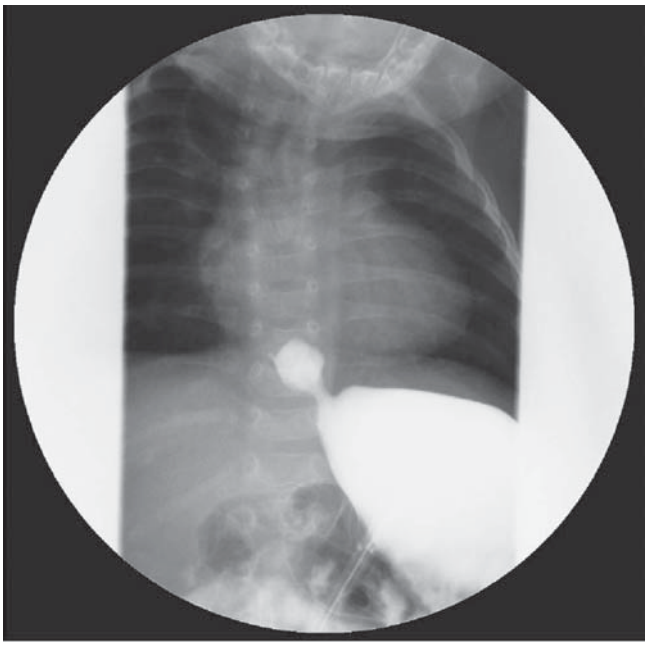

Fig. 1. A radiograph obtained at 3 months of age at our hospital shows a dilated proximal esophageal pouch with air in the upper-right-side thoracic and distal esophagus. Long gap esophageal atresia type A was revealed. A thoracic second and third vertebral anomaly was demonstrated

(Fig. 3). At 12 months of age, ASD patch closure, PA debanding, and reconstruction of the right ventricular outflow tract (RVOT) were performed. Esophageal reconstruction with whole stomach anastomosis to the cervical esophagus was performed at 14 months of age. She experienced acute respiratory failure after reconstruction of the esophagus, and a tracheostomy was therefore performed. She is currently 3 years old and is still using a tracheostomy tube. She currently experiences vomiting several times a week and mosapride citrate is prescribed for gastroesophageal reflux. She recently started to develop seizures and carbamazepine was therefore administered.

Discussion

We herein report a patient with VACTERL association. The patient had a full presentation of anomalies including (1) vertebral defects, (2) imperforate anus, (3) cardiac anomalies, (4) tracheoesophageal fistula, (5) renal defects, and (6) limb defects. VACTERL association was first reported by Corcora et al. in 1975,[1] but only 1.0% of such cases present the full range of anomalies.[3] The present case showed additional anomalies such as Mullerian duct dysplasia/aplasia and anomalies of cervicothoracic somites. These anomalies with unilateral renal agenesis have been recognized as MURCS

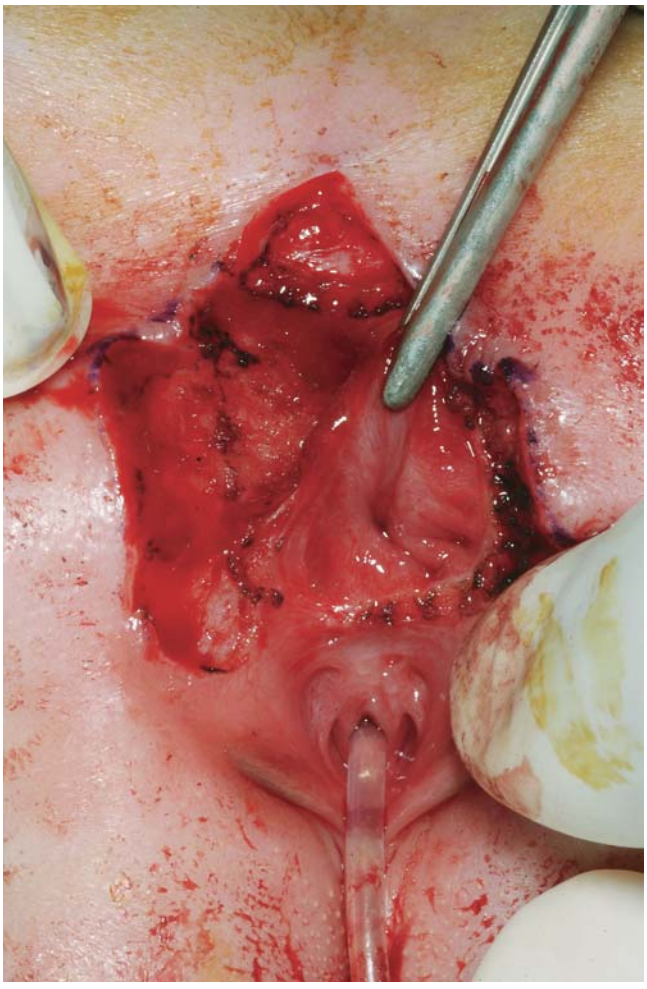

Fig. 2. Vaginal atresia was detected during anorectoplasty at 8 months of age

association and were first reported by Duncan et al. in 1979.[2] MURCS association is rarer than VACTERL association and only approximately 50 cases of MURCS association have been reported to date.[4] The current case represents the second description of a patient with VACTERL association and MURCS association,[5] and the first case of complete VACTERL association combined with complete MURCS association.

VACTERL association and MURCS association have common anomalies such as vertebral defects and renal malformations. There is another combined anomaly named Mayer–Rokitansky–Kuster–Hauser anomaly (MRKHA), whose clinical phenotype overlaps those of VACTERL association and MURCS association. MRKHA is composed of vaginal and uteric abnormalities (Mullerian duct maldevelopment), vertebral anomalies, unilateral renal agenesis, and cardiac defects.[6] Therefore, these three combined malformation diseases may have a common etiology in the early developmental stage. Recently, some quite interesting

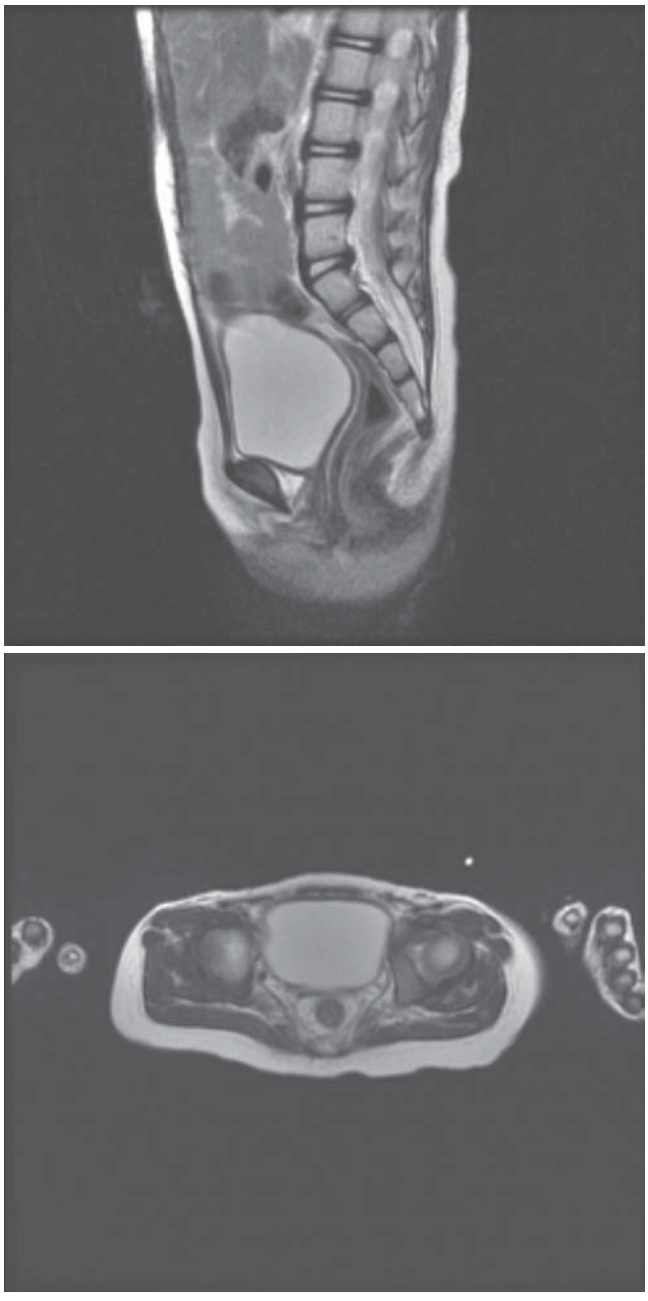

Fig. 3. Magnetic resonance imaging performed after anorectoplasty shows an absent uterus and vagina. *Top panel*, sagittal view; *bottom panel*, cross-sectional view. No uterus or vagina was observed in the space between the bladder and the rectum

and suggestive reports have appeared concerning this issue. Kim et al.[7] reported that VACTERL association-like anomalies were often seen in sonic hedgehog (*Shh*) gene knockout mice. Biason-Lauber et al.[8] found heterozygous mutation of the *Wnt4* gene in a woman with clinical phenotype resembling MRKHA syndrome. The *Shh* gene is a master control gene in early development in humans and it induces the expression of important genes such as *Gli*, *Wnt*, and *BMP-4* genes.[9] This important pathway of early development is very complicated but is well regulated, and dysregulation at some point in the pathway might cause various anomalies related to downstream development. We do not have any data on mutation analyses of these developmental genes, but in the near future the molecular mechanisms regarding the etiology of these similar combined malformation diseases will hopefully be disclosed. Our case had a very rare combination of sequential anomalies and it is useful to further accumulate such cases to elucidate the etiology of these combined anomalies.

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