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Case Series

VACTERL Association; The Hidden Iceberg. Case Series and Article Review

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Abstract

Background and Aims: VACTERL association is a rare condition. Its prevalence reported 1 in 20,000 births. According to Solomon., *et al*. the mostly used classification and accepted by researchers and clinicians. It's characterised by the presence of one the following criteria: (i) 3 or more major component features of VACTERL association or (ii) 2 major component features together with an affected 1st degree relative or (iii) 2 major component features together with another anomaly. No evidence of genetic or phenotypic predistortion has been reported.

Methods: This case series reports retrospectively; clinical presentations, management and outcomes of five patients diagnosed with VACTERL association in tertiary referral centre serving country with small population. We discussed related anomalies, health burdens and reviewed recent updated research studies.

Results: Five patients presented in the case series are boys. Three presented with triad of VACTERL component features, one had a tetrad, and one had a pentad. The most common VACTERL component in the reported cases, was cardiac, renal and vertebral anomalies since 4 of the 5 patients had one of these anomalies, whilst the least prevalent was limb anomalies since only one of the patients exhibited this. Imperforate anus was the most common form of anal anomaly, seen in two patients. None noted antenatally and all five have been screened for all features postnatally.

Conclusion: With high index of suspicion, we would recommend screening for all different component features of VACTERL association once there is clinical evidence of congenital anomaly to avoid potential morbidity and mortality.

Keywords: *VACTERL Association; Vertebral Defects (VD); Anal Atresia (AA); Tracheoesophageal Fistula (TEF)*

Introduction

VATER association was first described in 1973 as the non-random co-occurrence of the following congenital anomalies - Vertebral Defects (VD), Anal Atresia (AA), Tracheoesophageal Fistula (TEF) with or without Oesophageal Atresia (OA), Radial and Renal Dysplasia (RD) [1,2]. Cardiac Defects (CD) and Limb Abnormalities (LA) were later included, and the condition was termed VACTERL association [3,10,11]. Patients are considered to have the VACTERL association when three or more organ systems are involved [4] without evidence of an alternative genetic or phenotypic diagnosis [5-7].

In 2011 Solomon., *et al.* [8] proposed that VACTERL association patients should have 1 of the following 3 criteria: (i) 3 or more major component features of VACTERL association (ii) 2 major component features together with an effected 1st degree relative (iii) 2 major component features of VACTERL together with another anomaly [8]. The 1st criterion of Solomon., *et al*. is mostly used and accepted by

researchers and clinicians. According to Kallen., *et al*. [9] VACTERL association patients can be divided into 2 groups - an upper group which have cardiac anomalies and a lower group which have renal anomalies [9].

In this case series we report the clinical characteristics, management and outcomes of all patients diagnosed with VACTERL association in Mater Dei Hospital, Malta and discuss their anomalies in relation with other research studies over the last decade.

Case Series

Patient 1

A boy, born at 37 weeks gestation via normal vaginal delivery to Asian nonconsanguineous parents. He was transferred to NICU at 10 hours of age in view of cyanotic episodes and desaturations. He was monitored and initially did not require any ventilatory support. Upon examination, the neonate had an imperforate anus with a small subcutaneous fistula, running anterior to the anus towards base of scrotum with meconium staining. He had bilateral small hydrocoeles and both testes were in the scrotum. He had a sacral dimple which did not have any overlying hair. The rest of the neonatal examination was normal although he developed cyanotic spells during and immediately after feeds.

A nasogastric tube (NG) was placed, patient kept nil by mouth (NBM) and a urinary catheter was inserted. A chest and abdominal X-ray were performed as well as a renal ultrasound (US) and echocardiogram to screen for associated anomalies. Echocardiogram revealed a patent foramen oval (PFO) and mild flow acceleration right pulmonary artery (RPA) stenosis. Renal US reported normal findings, however, chest and abdominal X-ray, shown a hypoplastic right 1st rib (Figure 1). He did not have any limb anomalies.

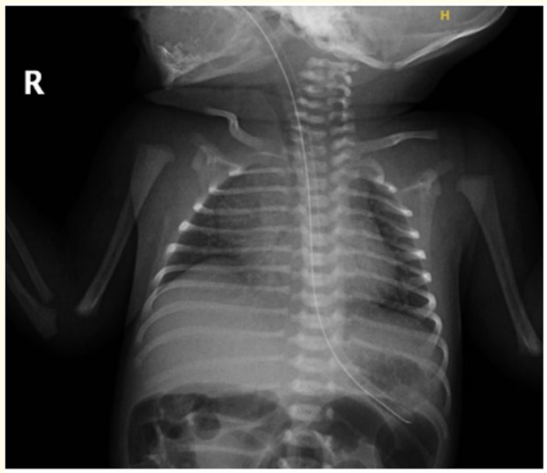

Figure 1: *Chest X-ray. Hypoplastic right first rib.*

At 24 hours, after discussion with parents, the neonate underwent a rigid bronchoscopy, examination under anaesthesia (EUA) of anus, Pena stimulation and posterior sagittal anorectoplasty (PSARP). Bronchoscopy revealed a possible H type trachea-oesophageal fistula just above the carina which was however inconclusive and was later excluded after a tube oesophagogram.

Post-operative period was uneventful, and tube enteral feeding commenced a day later. Further investigations in the form of sacral US and micturating cystourethrogram (MCUG) were performed in the early post operative period. The US excluded the presence of spina bifida or tethered cord. MCUG showed a small blind ending bladder diverticulum but no signs of vesico-ureteric reflux (VUR) (Figure 2).

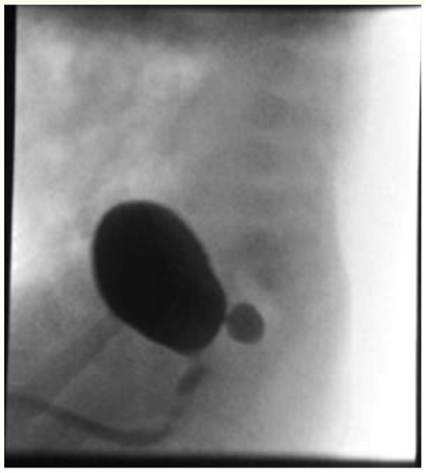

Figure 2: *Micturating cystourethrogram - There is a small blind ending diverticulum arising from left postero-inferior aspect of urinary bladder.*

The tube oesophagogram done at day 6 post operatively excluded a tracheoesophageal fistula but accidentally identified that the proximal small bowel and duodeno-jejunal flexure were placed on the right of the midline, in keeping with malrotation of the midgut (Figure 3). The neonate was again starved, and the parents consented for an explorative laparotomy and Ladd's procedure on day 6 of life. EUA of the anus confirmed a patent anus and a healing anoplasty.

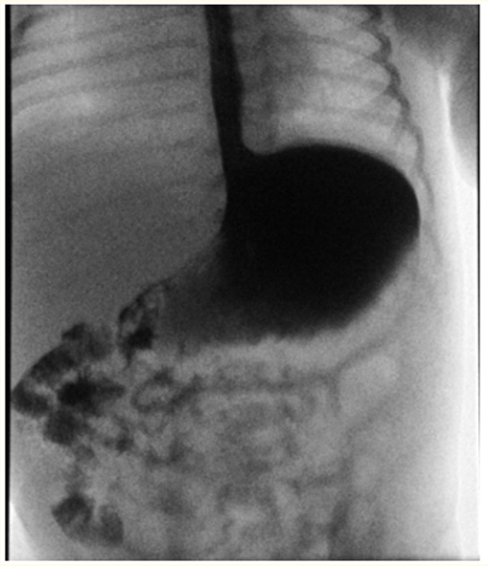

Figure 3: *Tube oesophagogram. Proximal small bowel and duodeno-jejunal flexure lie to the right of the midline in keeping with malrotation.*

Post-operatively, the neonate recovered well at NICU. He was started on TPN and the NGT was kept on free drainage. The neonate was started on oral feeds 4 days post operatively and the total parenteral nutrition (TPN) was weaned off. Serial anal dilatations were started 14 days post PSARP. After the patient was discharged, serial anal dilatations were performed by the parents for the following months and the neonate was closely monitored on regular outpatient visits.

At 11 months of age, a diagnostic cystoscopy was performed. This confirmed the presence of a right sided bladder diverticulum and normal ureteric orifices were identified. DMSA showed no renal scarring but revealed that the right kidney was smaller than the left one, with uptake of 41% on the right and 59% on the left. The renal system is being monitored with serial renal US.

In his last clinic visit at 3 years of age, the child was growing optimally along the 30th growth centile. His last US Kidneys showed a difference of only 2 mm between the left and the right kidneys with normal bilateral antero-posterior diameter of the renal pelvises (APPDs). He opens bowels daily but when he develops occasional bouts of constipation controlled with macrogol sachets.

Patient 2

A boy, born at 40+6 weeks gestation, via ventose delivery due to foetal distress, to nonconsanguineous Spanish parents. Physical examination revealed intermittent tachypnoea and thick upper airway secretions requiring suctioning. The neonate was transferred to NICU and intubated 90 minutes after birth due to desaturations and cyanotic episodes with saturations down to 75%.

NG tube was passed. However, chest X-ray (CXR) revealed coiled NG in the upper oesophagus (Figure 4) and a stomach air bubble was visible, indicative of oesophageal atresia (OA) with tracheoesophageal fistula (TEF). The findings were discussed with the parents, and they were consented for surgery. Preoperatively the neonate was optimised by inserting a replogle tube in the proximal oesophageal stump, which was placed on continuous suctioning. An echocardiogram carried out in the first 24 hours of life revealed a patent ductus arteriosus which was normal for age and a 55 mm atrial septal defect (ASD). On first day of age the neonate underwent diagnostic bronchoscopy, where OA type C (according to the Gross classification of OA) was identified with TEF. Thoracotomy, primary anastomosis of the OA, ligation and division of the fistula were performed. A trans-anastomotic tube was inserted intraoperatively and kept *in situ*.

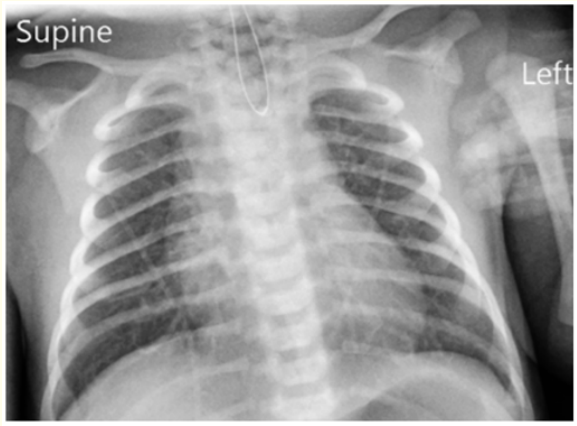

Figure 4: *Chest X-ray. Coiled NGT in the upper oesophagus.*

Post operatively the neonate was transferred to NICU and kept sedated, which were eventually weaned off prior to extubating on day five post operatively. The neonate was given TPN and lipids via umbilical venous catheter. At 1 week post operatively a tube oesophagogram

was performed which confirmed no anastomotic leak after which enteral feeding was started. He had some difficulty with establishing oral feeding but improved gradually and established expressed breast milk via bottle then direct breast feeding later.

Renal US showed mild left hydronephrosis. Subsequent micturating cysto-urethrogram (MCUG) showed a grade 4 left sided VUR but no evidence of posterior urethral valves (PUV) (Figure 5). In view of this the neonate was started on prophylactic antibiotics. An US of the spine revealed no cord tethering and no signs of spina bifida. This infant did not have any vertebral or limb abnormalities.

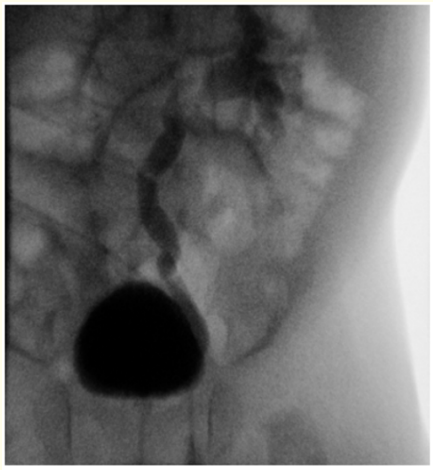

Figure 5: *Micturating cysto-urethrogram (MCUG). Grade 4 left sided vesico-ureteric reflux but no evidence of PUV.*

This infant was lost for follow up as his parents emigrated back to Spain. In his last clinic visit at 4 months of age, the infant was growing optimally. His last US kidneys showed no renal pelvis dilatations and no hydronephrosis.

Patient 3

A boy, born at 35^{+5} weeks gestation via emergency lower segment caesarean section (LSCS) due to deceleration on cardiotocography (CTG) monitor. The father had neurofibromatosis type 1. The infant's parents are nonconsanguineous Caucasian parents. The pregnancy was complicated with the mother developing gestational diabetes. The infant was born without respiratory effort and required 2 sets of inflation breaths with good response. He was transferred to NICU at 30 minutes of life in view of persistent tachypnoea with an oxygen requirement. He was immediately started on high flow nasal canula, maintenance fluids and antibiotics via an umbilical venous catheter (UVC). He was given Vitamin K and started on phototherapy later due to persistent hyperbilirubinemia and thrombocytopenia.

On examination after resuscitation, the infant was tachypnoeic with intercostal and subcostal recessions, left sided torticollis, a shortened deformed left upper limb with an absent left thumb and an elongated right thumb. He also had imperforate anus with meconium passing through the urethra. Both testicles were in the scrotum with a small left hydrocoele and a reducible right inguinal hernia.

Skeletal survey showed vertebral segmentation anomalies with thoracic butterfly vertebrae. There was associated scoliosis of the C6-T4 vertebrae, left fused ribs, an absent left radius, a bowed left ulna, left thumb deficiency and a right triphalangeal thumb. It also showed an underdeveloped left lung when compared to his right one (Figure 6 and 7). Abdominal and spine US showed normal looking kidneys bilaterally. The distal colon and rectum were distended with meconium and the urinary bladder was empty and displaced anterolaterally. All other intra-abdominal organs were normal. The conus and cauda equina were normal with no cord tethering and no evidence of spina bifida.

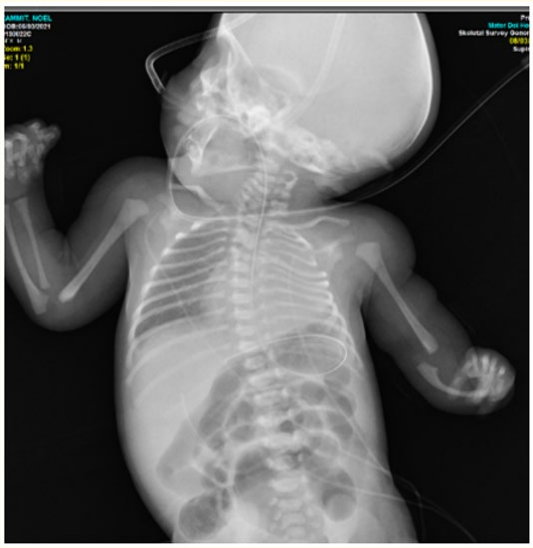

Figure 6: *Skeletal Survey. Absent left radius. Bowed left ulna. Normal right ulna and radius. Normal clavicles, humeri and scapulae. Deformity of left-sided ribs noted. Vertebral segmentation anomalies of C6-T4 with associated scoliosis. Underdeveloped left lung as compared to right lung.*

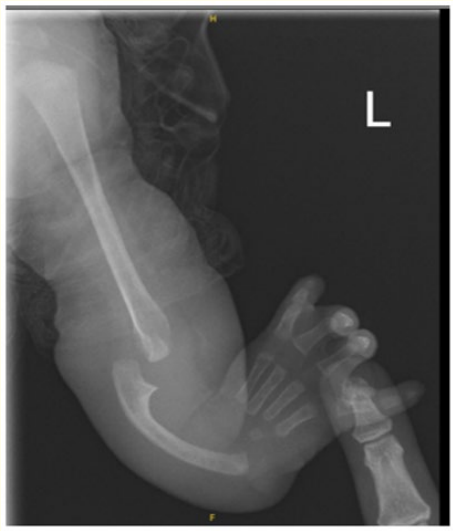

Figure 7: *Left arm X-ray. Absent left radius. Bowed left ulna. Abnormalities of the metacarpal bones. Hand held open by mother's finger.*

Echocardiogram at birth showed global hypertrophy with no outlet obstruction. He also had a 5mm ASD with left to right shunt. Cranial US reported mild periventricular flaring.

At 2 days of age, parents were consented for surgery and the neonate underwent a refunctioning loop colostomy and insertion of a right internal jugular vein line to replace the UVC.

Post operatively he was kept nil by mouth and continued IV antibiotics for 7 days after which he was commenced on uroprophylaxis. The NGT was kept on free drainage. TPN was started then enteral feeds via NGT followed 2 days later and were fully established by day 8 post operatively. The TPN was eventually weaned off and NGT removed. Tube oesophagogram excluded a tracheoesophageal fistula (TEF) and further imaging of the renal tract was normal other than the recto-bulbar fistula. Stoma nurses ensued stoma care and was taught to parents.

The infant was discharged home at 1 month of age on uroprophylaxis and regular oral sodium supplementation to replace stoma losses. The infant was followed up closely as an outpatient by the neonatologist, orthopaedic and paediatric surgeons, geneticist and physiotherapy.

MCUG at 6 weeks of age confirmed a fistula between the blind ending distal rectum and the bulbar urethra (Figure 8). At 3 months calorific supplementation was required to evert failure to thrive. At 5 months the infant was admitted with bronchiolitis which resolved with no complications. At 11 months of age the infant underwent a laparoscopic assisted anorectoplasty with ligation and excision of the recto-bulbar fistula after which he was transferred to NICU for intensive monitoring.

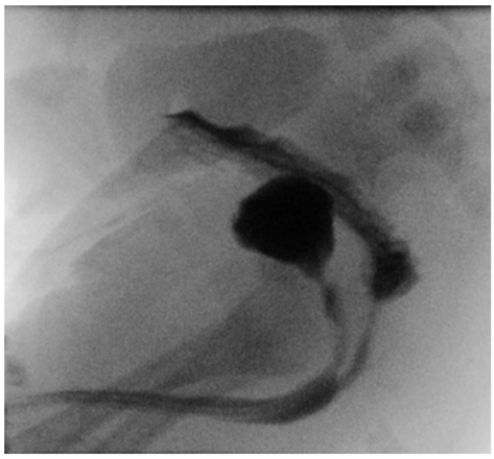

Figure 8: *MCUG. A fistula between the blind ending distal rectum and the proximal bulbar urethra.*

Post operatively the infant was kept intubated and ventilated. Unfortunately, he developed respiratory deterioration, lost his airway and required CPR. Despite a successful resuscitation, he continued to deteriorate over the next 2 days. An EEG performed 2 days later showed an isoelectric picture in keeping with profound encephalopathy. Parents decided care withdrawal, the infant was then extubated and passed away.

This infant had all the VACTERL association anomalies except for OA and TEF.

Patient 4

A boy, born via LSCS as the pregnancy was complicated with polyhydramnios and the mother developing gestational diabetes. At birth the neonate was transferred to NICU due to desaturations and choking episodes. A CXR identified a coiled NGT in a blind ending oesophagus

in keeping with OA. At day 1 of life the TEF and OA was repaired. At day 7 of life, he underwent repair of a Type A interrupted aortic arch (according to the Celoria-Patton classification of interrupted aortic arch), ventricular septal defect (VSD) and ASD. Postoperatively, He developed recurrent bronchiolitis, wheezing episodes and aspiration pneumonias. At 2.5 months, an oesophageal stricture was identified on video fluoroscopy in the middle 1/3 of the oesophagus and subsequently dilated. At 18 months of age, he underwent left ventricular outflow tract obstruction relief and augmentation of the ascending aorta with delayed sternal closure 2 days later, due to progressive significant left ventricular outflow tract obstruction (LVOTO) and aortic arch obstruction.

He developed severe gastro oesophageal reflux disorder (GORD), the child had failure to thrive and was started on naso-jejunal feeds. In view of his GORD, he underwent a Nissen fundoplication at 1 year 9 months. He was followed up closely with video fluoroscopy and at 4.5 years of age he underwent OGD and dilatation of oesophageal stricture. At 7 years of age the child had recurrence of subaortic stenosis for which he underwent resection of the stenotic segment and aortoplasty of the ascending aorta. At 8.5 years of age, he underwent OGD and balloon dilatation of a fibrous oesophageal stricture in the upper third of the oesophagus. The OGD and dilatation was repeated 4 weeks later with good effect.

Apart from his cardiac issues the child also had scoliosis of the lumbar spine which did not require operative correction and is being followed up by the orthopaedic team annually. He did not have anorectal, kidney or limb anomalies.

Patient 5

A boy, born at 36 weeks gestation by normal vaginal delivery following a pregnancy complicated by polyhydramnios. At birth he required resuscitation following apnea and profound cyanosis.

On examination after resuscitation the infant was tachypnoeic with intercostal and subcostal recessions. His abdomen was soft and not distended. There were no upper limb or lower limb structural anomalies. The infant's back appeared normal and his anus was patent.

He was transferred to NICU at 25 minutes of life and was immediately intubated and NGT was impossible to pass and a CXR identified a coiled NGT in a blind ending oesophagus in keeping with oesophageal atresia. A replogle tube was passed into oesophagus following this diagnosis. The infant was taken to theatre and underwent ligation of the distal tracheoesophageal fistula and insertion of gastrostomy. A concern was raised of the possibility of an anomalous azygous vein distribution taking most of the venous drainage of the lower body. A femoral venous line was also inserted. At day 7 of life, the infant underwent a second thoracotomy with repair of the OA with primary anastomosis. Post operatively patchy consolidation of the right lung was noted in keeping with an aspiration pneumonia which was treated with antibiotics. The patient was weaned off ventilation onto BIPAP and eventually nasal prongs. This was complicated with right sided phrenic nerve palsy which resolved spontaneously after chest physiotherapy.

CT Thorax with revealed a prominent azygos vein but no abnormalities in the azygos venous circulation. The infant was also identified to have vertebral segmentation anomalies with 13 pairs of ribs are bilaterally. A hypoplastic right half of the 9th vertebra resulting in minor scoliosis. Abnormal lordosis at the LI and L2 level. Fused LI and L2 vertebrae fusion. Free floating right 11th rib. Fusion of the right transverse process of the right 9th rib to the right 8th rib US Abdomen and spine revealed an uncomplicated horseshoe kidney and spinal cord tethering. An echocardiogram performed revealed excluded cardiac anomalies. The infant's developed conjugated hyperbilirubinemia requiring phototherapy from days 5 to 9 of life. The infant was discharged home from NICU after oral feeds were established.

The child underwent OGD and dilatation of oesophageal stricture at age of 4 but has otherwise remained well. Genetic studies via array comparative genomic hybridization revealed a deletion of 320 - 550 kb band on 18q 22.1. He continues to be followed up with regular US of his renal tract for his horseshoe kidney which has remained stable. This patient had 4 the VACTERL association anomalies namely: vertebral, TEF with OA and RA.

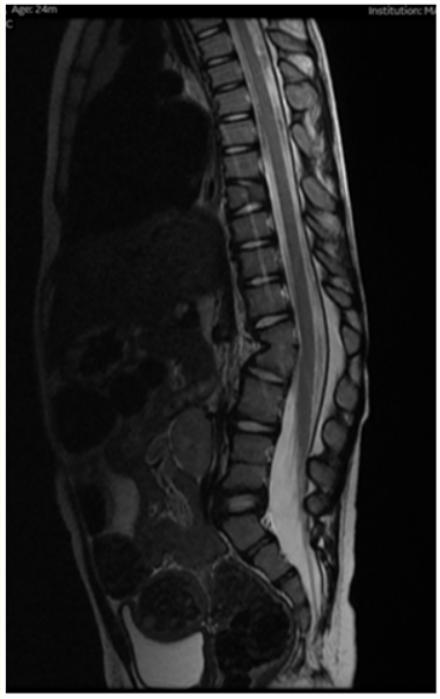

Figure 9: *MRI spine taken at 2 years of age - The spinal cord is tethered, terminating at the level of L4. There is hemivertebra at the T9 level, fusion of the L1 and L2 vertebrae with a mild focal kyphosis at this level. Well as fusion of the L4 and L5 vertebrae.*

Discussion

The VACTERL association anomalies of each patient are summarised in table 1. The five patients presented in this review were all males, 46 XY. From these patients, three had a triad of VACTERL component features, one had a tetrad and one had a pentad of component features. Van de Putte., *et al*. [12] in their EUROCAT population-based study comprising 397 VACTERL association patients reported that 49% had a triad, 15% had a tetrad, 4% had a pentad of component features; whilst only one patient had the full spectrum of features [12]. The most commonly observed VACTERL component in the reported cases, was cardiac, renal and vertebral anomalies since 4 of the 5 patients had one of these anomalies, whilst the least prevalent was limb anomalies since only one of the patients exhibited this. The different component features and their frequencies of the reported VACTERL association patients are shown in table 1.

Solomon., *et al*. [8] reported component features in decreasing order of frequency as being CVRATL [8]. They also observed that each component feature was present in at least 50% of the patients except for limb anomalies which was present in less than 50% of patients. In the reported cases, the frequencies of component features in decreasing order are CVRTAL. This is order is very similar to that of Solomon., *et al*. [8] - CVRATL. Similarly in our case series all component features are seen in at least 50% of the patients except for limb anomalies. In contrast, the frequency of component features in decreasing order as reported by Rittler., *et al*. [13] was AVTRLC whilst that of Oral., *et al*. [14] was VATRLC.

In the reported cases, the most common cardiac anomaly was ASD seen in four patients whilst the most common form of anal atresia was imperforate anus seen in two patients. With regards to vertebral and renal anomalies there was no predominant anomaly seen in the reported patients.

Incidence and aetiology

According to the EUROCAT (European Surveillance of Congenital Anomalies) Database the prevalence of VACTERL association was 1 in 20,000 births between 2012 and 2016 [12]. VACTERL association is not known to be more prevalent in a particular area of the world or ethnic community [5]. However, some studies claim that VACTERL association is more common in the male sex [8,15-17]. This may be attributed to X-linked inheritance, sex-influenced expression and imprinting defect mechanisms, even though the aetiology of VACTERL association is heterogenous and unknown [8,15-17].

Although there may be some inheritance of individual component anomalies, this occurs rarely [18]. Sonic hedgehog pathway gene mutations may be involved in the development of VACTERL association [8]. Environmental factors which are related to the development of VACTERL association include maternal diabetes and in utero exposure to statins, doxorubicin, oestrogen, progesterone or lead toxicity [8].

VACTERL association component features

Vertebral anomalies (VA)

From the reported cases, four had vertebral anomalies namely: scoliosis, hypoplastic ribs, fused ribs and butterfly vertebrae. Vertebral anomalies are often seen with rib anomalies. Vertebral anomalies occur approximately in 60 - 80% of VACTERL association patients [8,13,19-22]. They include hemivertebrae, butterfly vertebrae and wedge vertebrae, which occur due to vertebral fusion anomalies, absent or supernumerary vertebrae and associated scoliosis [21,23]. Patients with anorectal malformations may have associated dysplastic sacral vertebrae, however, whether the latter should be included as a component feature for the diagnosis of VACTERL association, is debatable [21,23,24]. According to the degree of severity of vertebral anomalies the patients may require surgical correction.

Anal atresia (AA)

From the reported cases, two patients had imperforate anus with one having an associated recto-bulbar fistula. Both were treated initially with a defunctioning loop colostomy in the first few days of life, followed by an open/laparoscopically assisted PSARP procedure at a later date. The frequency of anorectal anomalies in VACTERL association patients is 55 - 90% [8,13,19,21]. These anorectal anomalies may include: ectopic anus, absence, atresia and stenosis of the rectum or anus with associated rectovaginal, rectovesical and recto bulbar fistulas [12]. Anal anomalies are usually diagnosed and treated in the immediate postnatal period in contrast to other VACTERL association anomalies, such as renal anomalies, which may initially go undiagnosed until further workup [5].

Cardiac defects (CD)

Four of the five reported cases had cardiac anomalies; all had ASD and one also had a VSD and a Type A interrupted aortic arch, the latter requiring multiple surgeries for correction in the neonatal period. Cardiac anomalies are common in VACTERL association patients and occur approximately in 40 - 80% of patients [8,13,21]. Anomalies range from severe structural malformations inconsistent with life or requiring multiple surgeries, to minor defects [8,21,25]. These include congenital malformations of the cardiac chambers, cardiac septa, great arteries (including PDA) and cardiac valves [12].

Tracheoesophageal fistula (TEF)

This may occur with or without OA. It is seen in 50-80% of VACTERL association patients [8,13,19,21]. Three of our patients had TEF with associated OA requiring immediate surgical intervention with ligation of the distal fistula and primary anastomosis of the OA. Patients with TEF with OA usually present early and can also be diagnosed in the prenatal period with polyhydramnios or absence of the gastric bubble [12]. They typically present with choking and cyanotic episodes postnatally and can be diagnosed on CXR with a coiled NG tube in the oesophagus after an attempt at passing an NGT [12,26]. Continued monitoring is required throughout life to detect complications such as recurrence of the TEF, GORD and oesophageal strictures [25].

Renal anomalies (RA)

Renal defects are reported in 50 - 80% of VACTERL association patients [8,13,20,21]. Cunningham., *et al.* [27] reported: VUR with an associated structural defect as the most common renal anomaly in 27% of their VACTERL association patients; unilateral renal agenesis in 24%, dysplastic/multicyclic kidneys in 18% and duplex kidneys in 18%. Renal anomalies can be divided into structural defects such as renal agenesis, horseshoe kidneys and polycystic kidneys and non-structural anomalies such as VUR [27]. Diagnosis of renal anomalies is more challenging than other component features of VACTERL association, unless specific imaging studies are performed [5]. Four of the five reported cases had renal anomalies namely VUR, horseshoe kidney, bladder diverticulum and a recto-bulbar fistula. Late diagnosis of renal anomalies may lead to complications such as hypertension and renal dysfunction sometimes necessitating renal transplant [25]. Due to the high incidence of VUR in VACTERL association patients, Cunningham., *et al.* recommend a screening renal US as part of initial workup of patients with suspected VACTERL association [27]. If on renal US abnormalities such as hydronephrosis or renal scarring is identified, further imaging with MCUG and other imaging studies are implicated [27].

Limb anomalies (LA)

Limb anomalies are the least common of all the VACTERL association component features reported in 40 - 50% of patients [8,13,19,28]. Common limb anomalies include: radial or ulnar anomalies and other reduction defects of the upper limb such as thumb aplasia or hypoplasia and polydactyly [5,12]. The only patient from our reported cases who had limb anomalies had an absent left radius, with a bowed left ulna, left thumb deficiency and a right triphalangeal thumb.

Diagnosis and differential diagnosis

Diagnosing a patient with VACTERL association is difficult since there are several combinations of VACTERL component features which qualify as a diagnosis of VACTERL association. Moreover, there are several different disorders which have component features in common with VACTERL association patients such as Fanconi anaemia, Feingold syndrome, oculo-auriculo-vertebral defect spectrum, Pallister-Hall syndrome, MURCS association [29], CHARGE syndrome [5], Townes-Brocks syndrome and caudal regression syndrome [5]. For this reason genetic assessment plays an essential role to help exclude certain syndromes.

Diagnosis of the different component features of VACTERL association is made clinically [5]. Initial testing of vertebral anomalies can be done with X-ray, US and/or MRI of the spine; anal atresia is usually identified at physical examinations with further imaging such as abdominal US to identify associated genito-urinary defects [5]. Echocardiograms are done as the initial screening test for cardiac malformations, whilst contrast studies are used to confirm TEFs [5]. Renal US is used to screen for renal anomalies followed by an MCUG if needed [5]. Limb defects are detected on physical examination and can be worked up further with X-ray imaging [5].

Vertebral, cardiac, renal and limb anomalies can be identified at antenatal US [30,31]. TEF and ARM are difficult to detect antenatally. TEF may be hinted at by the presence of polyhydramnios and gastric bubble absence at antenatal US; whilst imperforate anus may be seen as a dilated colon at antenatal US [32,33].

Management

Cardiac anomalies, anorectal atresia and TEF which are inconsistent with life, require surgical correction in the immediate postnatal period. Complications of malformations are monitored and treated throughout life. The individual management of our five reported cases is outlined in table 1.

Patient	1	2	3	4	5	Frequency of component features of the reported VACTERL association patients
Gender	Male	Male	Male	Male	Male	
Vertebral anomalies	Hypoplastic right 1st rib	Nil	Vertebral segmentation anomalies with thoracic butterfly vertebrae; scoliosis of the C6-T4 vertebrae, left fused ribs	Scoliosis of the lumbar spine	Multiple vertebral segmentation anomalies	4
Anal Atresia	Imperforate anus with subcutaneous fistula	Nil	Imperforate anus with recto-bulbar fistula	Nil	Nil	2
Cardiac Defects	PFO/ASD	ASD	PFO/ASD	Type A interrupted aortic arch, VSD and ASD	Nil	4
Tracheoesophageal fistula/ Oesophageal atresia	Nil	Type C Oesophageal atresia with distal tracheoesophageal fistula	Nil	Type C Oesophageal atresia with distal tracheoesophageal fistula	Type C Oesophageal atresia with distal tracheoesophageal fistula	3
Renal Anomalies	Bladder Diverticulum	Left hydronephrosis and Grade 4 VUR	Recto-bulbar fistula	Nil	Horseshoe kidney	4
Limb anomalies	Nil	Nil	Absent left radius, a bowed left ulna, left thumb deficiency and a right triphalangeal thumb	Nil	Nil	1
Other	Mid gut Malrotation	Nil	Hyperbilirubinemia requiring phototherapy, right reducible inguinal hernia, left hydrocoele, Underdeveloped left lung	Severe GORD	18q 22.1 deletion	

Surgical Interventions	PSARP; Ladd's procedure for malrotation	TEF ligation. Repair of OA.	Defunctioning loop colostomy and insertion of a right internal jugular vein line; Laparoscopic assisted anorectoplasty with ligation and excision of the recto-bulbar fistula	TEF ligation, OA repair; Repair of Type A interrupted aortic arch, ASD, VSD; eft ventricular outflow tract obstruction relief and augmentation of the ascending aorta; Nissen fundoplication; Multiple OGDs and dilatations of strictures; resection of the stenotic aorta segment and aortoplasty of the ascending aorta	TEF ligation. Repair of OA.	
Number of VACTERL component features for each patient	4	3	5	3	3	CVRATL

Table 1: *VACTERL association anomalies and characteristics of each patient.*

Prognosis

Neonatal mortality of those diagnosed with VACTERL association is as high as 28% [34]. Those who survive typically undergo multiple surgeries throughout their lives, however most will have normal neurocognitive development [14].

Conclusion and Learnt Message

From our experience, we would recommend screening for all the different component features of VACTERL association once there is clinical suspicion of an infant having VACTERL association to avoid potential complications. We also recommend involving parents from day one and to keep them posted as the screening tests reveal new features. This is crucial to relieve the anxiety and clear concerns. Multi-disciplinary team of all health care professionals should have routine meetings to plan the management corrections and repairs in synergetic proactive strategy using the available hospital resources.

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