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Case Report

VACTERL Association in an 18 Year Old Teenager with Covid-19 like Symptoms and Multiple Neurologic Features

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Abstract

VACTERL association is the occurrence of three or more birth anomalies that affect different body organs. Although it is commonly diagnosed at infancy, it may also be first recognised in adulthood. We present an 18 year old female with four birth anomalies (imperforate anus, scoliosis, Tetralogy of Fallot and unilateral renal agenesis) who had Covid-19 like symptoms and multiple neurologic features that were associated with loss of consciousness and later quadriplegia. This case highlights the likelihood of VACTERL association being diagnosed for the first time in adulthood and the need for a high index of suspicion to look for other anomalies once one defect is observed.

Keywords: VACTERL association; anomalies; body organs; Covid-19.

Abbreviations: VACTERL: Vertebral Anomalies (V), anal atresia (A), cardiac malformations (C), Tracheosophageal fistula (TE), renal dysplasia (R) and limb abnormalities (L); Covid-19: Corona Virus Disease 2019; SPO2: Oxygen Saturation; RTPCR: Reverse Transcriptase Polymerase Chain Reaction; CNS: Central Nervous System; TOF: Tetralogy Of Fallot; ASD: Atrial Septal Defect; VSD: Ventricular Septal Defect.

Introduction

VACTERL association is a non-random association of multiple birth defects that affects two or more body organs [1, 2]. VACTERL is defined by the concurrence of at least three of the following component features: vertebral anomalies (V), anal atresia (A), cardiac malformations (C), Tracheoesophageal fistula (TE), renal dysplasia (R) and limb abnormalities (L) [3]. These defects may be obvious at birth (e.g. anal atresia, tracheoesophageal atresia, radial defects) or recognised later in life (e.g cardiac, vertebral, and renal malformations). The combination of the malformation varies from one to another and an affected individual may not have all the 6 anomalies [4]. The cause of VACTERL association remains unclear and found to occur as a sporadic entity and the risk of recurrence among family member is low [3]. VACTERL association may be underdiagnosed especially in children with fewer problems, but the prevalence has been estimated at 1:10000 to 1:40000 live births [5, 6]. There is no reported ethnic or geographic association. There is a paucity of information regarding VACTERL association related issues and outcome in the adulthood. Most of the clinical and research works done so far has been in the paediatric age group. Also, there is paucity of report on case of VACTERL association in Nigeria. Hence the need to report a case of VACTERL association in an18-year-old lady who was found to have multi-organ anomalies on presentation with febrile illness and breathlessness that was associated with multiple neurological features (coma, later quadriplegia, subcortical ischaemic infarcts, multifocal meningeal inflammation and left cerebellar infarct).

Patient and Observation

We report a case of an 18-year-old female student who presented to the Emergency department of Federal Medical Centre Yenagoa, Bayelsa State, Nigeria during COVID-19 pandemic with a history of fever and breathlessness of 2 days duration and loss of consciousness of 12 hours duration, and was admitted as a suspected case of COVID-19

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pneumonia. The fever was high grade, intermittent, relieved by analgesics and tepid sponging. She did not have headaches, neck pain, stiffness, photophobia, vomiting or seizure, and no history of trauma to the head, cough, orthopnea, paroxysmal nocturnal dyspnea or hemoptysis. There was however a history of episodes of effort intolerance which occurred quite often over the past 4 years. No symptom suggestive of urinary tract infection.

She had a corrective surgery for imperforate anus as an infant and was noticed to have lateral curvature of the spine since the age of 2. She attained menarche at 16 years. She is the 4th Child of a family of 7 and no family member with any form of congenital anomaly. On Examination, she was in respiratory distress with respiratory rate of 60cpm, Sp02 of 43%, axillary temperature of 38◦C, pale, anicteric, dehydrated, and no dependent edema. She was comatose with Glasgow Coma score of 3, no obvious cranial nerve deficit and the pupils were equal and reacted to light sluggishly. There was no sign of meningeal irritation. The tone was normal across all joints. She had transmitted breath sound in all lung fields. Her blood pressure was 90/70mmHg with pulse rate of 150 beats per minute. The first and second heart sounds were present with a precordial pan-systolic murmur loudest at the left parasternal edge and an ejection systolic murmur over the pulmonary area.

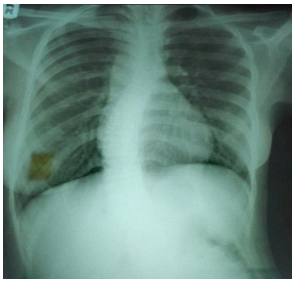

Figure 1: CXR film that equally shows scoliosis of the thoracic vertebrae.

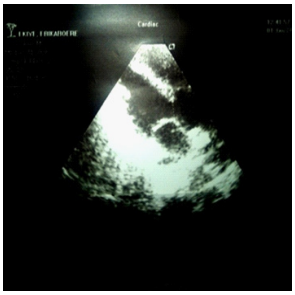

Figure 2: Echo image showing the ventricular septal defect (VSD).

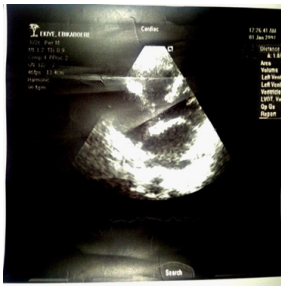

Figure 3: Echo showing the ventricular septal defect (VSD) and overriding aorta.

Investigation results included a full blood count which revealed a hemoglobin of 7.4g/dl, white cell count of 22,200 cells per cubic millimeter and predominantly neutrophilia (83%). The erythrocyte sedimentation rate was 40. The blood film revealed hypochromasia, anisocytosis, neutrophil band forms and neutrophilic leukocytosis. The electrolytes at presentation revealed bicarbonate (19mmol/l), Urea (19.6mmol/l), and Creatinine (202µmol/l), while the other parameters were within normal values. A repeat of the electrolytes a week later showed normal values. COVID-19 RTPCR test was negative and Chest radiograph revealed marked scoliosis of the thoracolumbar spines with crowded right posterior ribs (**Figure 1**). Echocardiography revealed normal left ventricular geometry, normal left ventricular systolic function (EF is 58%), normal left ventricular diastolic function, membranous ventricular septal defects, overriding aorta with moderate aortic regurgitation, increased pulmonary flow gradient (pulmonary stenosis) and moderate tricuspid regurgitation with no vegetation noted (**Figures 2&3**). Abdominal ultrasound revealed absent right kidney and obstructive uropathy of the left kidney. Her brain MRI showed subcortical ischemic infarcts, multifocal meningeal inflammation and left cerebellar ischemic infarct (**Figure 4&5**).

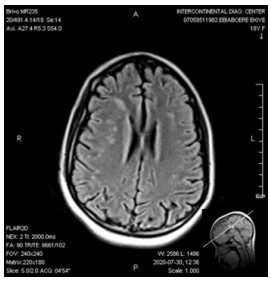

Figure 4: FLAIR image showing multiple hyper-intense lesions in the subcortical white matter with enhanced meninges.

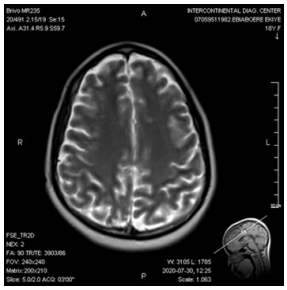

Figure 5: T2 image showing multiple hyper-intense lesions in the subcortical white matter with enhanced meninges.

A diagnosis of VACTERL association with septicemia and a possible septic embolic phenomenon was made. She received high flow intranasal oxygen and was transfused with three units of packed cells. Parenteral antibiotics (Vancomycin 1g 12 hourly, ceftriaxone/sulbactam 3g 12hourly, Ampicillin 2g 6 hourly, Metronidazole 500mg 8 hourly) were administered as well as injection dexamethasone 8mg 8hourly and subcutaneous enoxaparin 40mg 12 hourly. She regained full consciousness 2 weeks into admission, but was noticed to be quadriplegic. Physiotherapy was commenced, and she has made a significant recovery of the motor function of her limbs.

Discussion

The patient presented in this paper had four congenital anomalies, including imperforate anus, tetralogy of Fallot (TOF), unilateral renal

agenesis, and scoliosis. On presentation, she had features suggestive of CNS infection, which responded to a cocktail of antibiotics that covered methicillin resistant staphylococcus aureus (vancomycin,), ampicillin, and cephalosporin and after regaining of consciousness, was found to have quadriplegia. Hence, we think this is a case of VACTERL association that is complicated by septic embolic phenomenon. The combination of the anomalies varies from one affected individual to another, less than 1% of VACTERL associated patients have all the six anomalies [4]. Vertebral anomaly is the most common defect observed among VACTERL associations and has been reported in approximately 60 to 95% of the cases [2, 5]. Scoliosis may be one of the first clinical signs of vertebral anomaly in a suspected case of VACTERL association [7] as seen with our reported case.

Tracheoesophageal or anal defects are usually noted at birth with subsequent surgery intervention in the first days of life, while other malformations are most times seen later in life as an incidental finding [6]. As in this case, she was found to have imperforate anus at birth, which was surgically corrected at infant, scoliosis was observed at the age of 2, while the cardiac defects and unilateral renal agenesis are recent findings in the course of this recent hospital admission. Both tracheaesophageal and anal anomalies have been observed in 62% of cases of VACTERL association [8]. Seventy five percent of these conditions have been reported with cardiac defects and the commonly observed was VSD, ASD, TOF and less common defects are truncus arteriosus, transposition of the great arteries [9, 10]. Our patient has tetralogy of Fallot with moderate aortic and tricuspid regurgitation with a tight stenotic lesion across the pulmonary valve.

Cunningham et al [11] observed that 69% of 48 cases of VACTERL association they studied had a clinical manifestation affecting the renal system. The common renal manifestation was vesico-urethral reflux (27%) followed by unilateral renal agenesis (24%) and then dysplastic multicystic kidneys or duplicated collecting system (18% for each), it was also observed that 88% of patients with structural renal anomaly had an associated anorectal malformation [11]. The index case had right kidney agenesis that was associated with anal imperforation. Occasionally, additional medical emergencies are reported with VACTERL association. Hong and colleague reported a case of Moya Moya disease in a patient with VACTERL who developed seizure at age of [11, 12]. The index case presented with coma, fever, quadriplegia and brain imaging suggestive of brain infarction with meningeal inflammation at the age of 18. Based on the findings on brain imaging and clinical presentation of this patient we can postulate that the presence of cardiac defects seen in VACTERL association may put the patient at risk of septic phenomenon and recurrent lacunar infarct. This may be further explained by the association between reno-vascular and cardiac disease with systemic vasculopathy [12]. Solomon also reported VACTERL association in individuals with facial dysmorphism, pyloric stenosis and hypermobility [13]. Damian et al [14] in 1996 reported a case of VACTERL who had an NP 3243A>G mitochondrial DNA mutation who presented with mitochondrial encephalopathy, lactic acidosis and stroke. Though our patient had quadriplegia and cerebral infarct on brain MRI, we were unable to further investigate her for mitochondrial DNA mutation.

Conclusion

VACTERL association though a rare condition, its true frequency may be difficult to determine as many cases present with one or two anomalies at neonatal period while the other medically significant associated malformations are only noticed incidentally in adulthood. VACTERL association can present with medical complications like brain infarction and septic embolism.It is important to note that in this COVID-19 era, not all patients presenting with COVID-19 like symptoms have COVID-19.

Recommendation

Once one congenital anomaly is observed at birth, other associated anomalies must be evaluated for, as late diagnosis may result in challenges in management which may lead to poorer outcomes later in life.

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