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Case Report *Volume 6 Issue 1*

A Rare Case of Arterial Tortuosity Syndrome with Multisystem Manifestations

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Abstract

Arterial tortuosity syndrome (ATS) is an exceptionally rare autosomal recessive genetic disorder characterised by the elongation and tortuosity of arteries, often leading to aneurysms, dissections, or stenosis. Additional associations include connective tissue abnormalities affecting multiple systems. The congenital connective tissue disorder is associated with mutations in the SLC2A10 gene, resulting in the deficiency of the vital protein GLUT10. This case report details a 25-day-old male with ATS, showcasing distinctive facial features, musculoskeletal anomalies, and cardiovascular complications. Imaging studies, including chest X-ray and CT aortogram, revealed tortuosity and elongation of major arteries. Further cardiac assessment identified restrictive ventricular septal defect and a tortuous aortic arch with aneurysmal branches. The discussion emphasizes the potential morbidity and mortality associated with ATS, emphasizing the importance of early diagnosis through specialized tests and genetic analysis. The case underscores the need for antenatal imaging modalities to enhance diagnostic accuracy and facilitate timely management. The conclusion advocates for comprehensive diagnostic approaches, encompassing imaging and genetic testing, to confirm ATS and initiate timely symptomatic treatment. Emphasis is placed on the crucial role of genetic counselling and psychosocial support for affected individuals and their families.

Keywords: Arterial Tortuosity Syndrome; Elongation and Tortuosity of Arteries; Aneurysms; SLC2A10 Gene Mutation; GLUT 10 Deficiency; Hernia; Distinctive Facial Features; Musculoskeletal Anomalies; Ventricular Septal Defect; Medium Sized Arteries

Abbreviations

ATS: Arterial Tortuosity Syndrome; CTEV: Congenital Talipes Equinovarus; CNS: Central Nervous System; CRT: Capillary Refilling Time; CT: Computed Tomography; LRTI: Lower Respiratory Tract Infection; DAMA: Discharge Against Medical Advice; ATS: Arterial Tortuosity Syndrome; DHA: Dehydroascorbic Acid; TIFFA: Targeted Imaging for Fetal Anomalies.

Introduction

Aortic tortuosity and elongation of the medium-sized arteries are hallmarks of ATS, an autosomal recessive connective tissue disease resulting from biallelic mutations in the SLC2A10 gene. GLUT10 inactivation brought on by

SLC2A10 mutations results in abnormal collagen and/or elastin synthesis [1].

The Vascular symptoms of Arterial Tortuosity Syndrome (ATS) include focal stenosis of aortic and/or pulmonary segments, as well as widespread elongation and tortuosity of the aorta and mid-sized arteries. Non vascular features of ATS include signs of generalized connective tissue disorder, such as soft or doughy hyperextensible skin, joint hypermobility, inguinal hernia, and diaphragmatic hernia. Skeletal anomalies like pectus excavatum or carinatum, arachnodactyly, scoliosis, knee/elbow contractures, and camptodactyly are common. The primary cause of illness and death is the cardiovascular system, which is also more susceptible to aneurysm formation at any age [2].

Case Report

A 25-day old male baby, first born to a non-consanguineous parent, full term, born by normal vaginal delivery, baby had an APGAR score of 9-10, cried after tactile stimulation. The baby was admitted in NICU for 2 days in view of respiratory distress. The baby had a right foot mild CTEV (Ponseti technique used for treatment) and fracture of right clavicle, treated accordingly. He was then discharged to be reviewed after 1 month. At 15 Days of life the baby presented with swelling over the left inguinal region, insidious in onset, initially peanut in size, gradually progressive and increasing in size. Immunization was not administered at birth. Family history of non-consanguineous marriage; history also includes a sudden death of a child at age of 2 years in a third degree maternal relative. Nutritional History showed Direct Breastfeeding. Anthropometry showed, baby weight of 3.37 kgs, length of 53cms, hip circumference of 37.5cms, chests circumference of 33.5cms. Objective examination revealed micrognathia, retrognathia, hypotonia, Right Congenital Talipes Equinovarus (CTEV), Pectus Excavatum (Figure 1) receding jaw, no preauricular tags, normal oral cavity, sacral dimple and tuft of hair present, bilateral femoral pulse palpable, bilateral testicular noted. Systemic examination revealed- normal S1 with loud P2, grade 3/6 Pan systolic murmur in the left parasternal area; Equal Bilateral chest movements, Conducted Sounds heard; Soft, non-distended Abdomen, left sided inguinal swelling +; CNS s/o good cry, tone and activity. General examination revealed no pallor/ icterus/ cyanosis/ clubbing/ lymphadenopathy/ neck glands). Vital signs showed Pulse rate of 142 beats per minute; Respiratory rate of 46 cycles per minute; showed variations in Saturation- right upper limb(97%) right lower limb(95%) left upper limb(100%) left lower limb(96%); Temperature of 98.7F; Capillary Refilling Time (CRT) less than 3 seconds; Blood Pressure revealed that the lower limbs had significantly lower blood pressure (100/60) as compared to upper limbs (120/60) with Radio-femoral delay.

Figure 1: (A) Pectus excavatum, (B) Right Congenital Talipes Equinovarus (CTEV) is noted and (C) Distinctive features such as beaked nose, droopy cheeks, large ears, micrognathia and retrognathia are noted.

Provisional Diagnosis: Cervical Arch with Coarctation of Aorta

Management and Outcome: Laboratory investigations such as, complete urinary examination showed pale yellow coloured acidic urine with pH of 7, which was negative for blood/ ketones/ bile pigments/ bile salts/ nitrite, with 2-3 pus cells (slightly above normal), 1-3 epithelial cells and no RBC deposits/ casts/ crystals. Serum Creatinine of 0.18mg/dL (low, consistent with neonatal values as normal range is between 0.2-0.4 mg/dL). Serum Glucose of 130 mg/dL. Serum Sodium of 135 mmol/L (slightly below normal). Serum Potassium of 4.8 mmol/L. Serum Chloride of 100 mmol/L. Serum Calcium of 10.1mg/dL. Liver function Test showed Serum Total Bilirubin of 1.61 mg/dL (slightly elevated), Direct Conjugated Bilirubin of 0.45 mg/dL (slightly elevated), Unconjugated Bilirubin of 1.2 mg/dL, Serum Albumin of 3.0gdL (slightly below normal). Clotting time of 9 min. Bleeding time of 2.30 min. Prothrombin Time Test of 11.4 seconds. INR of 0.81 seconds (slightly below normal). Activated Partial Thromboplastin Time of 31.9 seconds.

Imaging was done, in which Ultrasound Spine showed no abnormality. Ultrasound Neurosonogram showed no abnormality. Ultrasound shows evidence of Herniation of bowel loops through a 7 mm defect in the left inguinal region suggestive of Left Inguinal Hernia. Chest radiography showed widened mediastinum and prominent aortopulmonary window, fracture of Right Clavicle (Figure 2). Cardiac investigations were done in which Electrocardiography showed normal sinus rhythm, normal axis with left ventricular hypertrophy. Detailed cardiac evaluation by transthoracic Echocardiography was done, which was suggestive of Restrictive Perimembranous Ventricular Septal Defect restricted by Right Coronary Cusp Prolapse causing mild

Aortic Regurgitation; Tortuous Aortic Arch with aneurysmal Arch branches with right descending aorta, the descending aortic doppler study showed pulsatile Rows with no diastolic tailing.

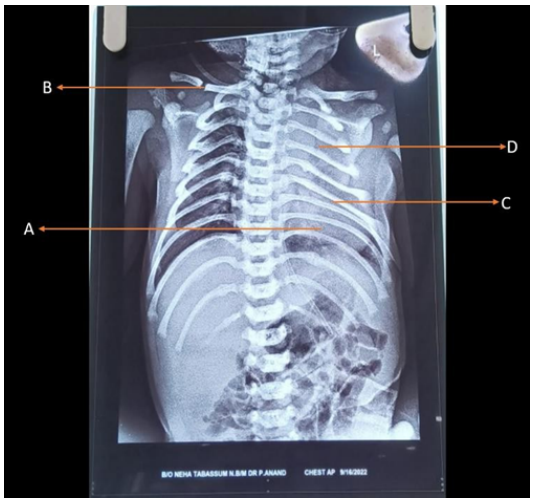

Figure 2: Chest Xray (AP view) - rotated Film-
A: Cardiomegaly noted with widening of the subcarinal angles.
B: Fracture of right clavicle is noted.
C: Crowding of ribs is seen.
D: Consolidation is seen in the left lung

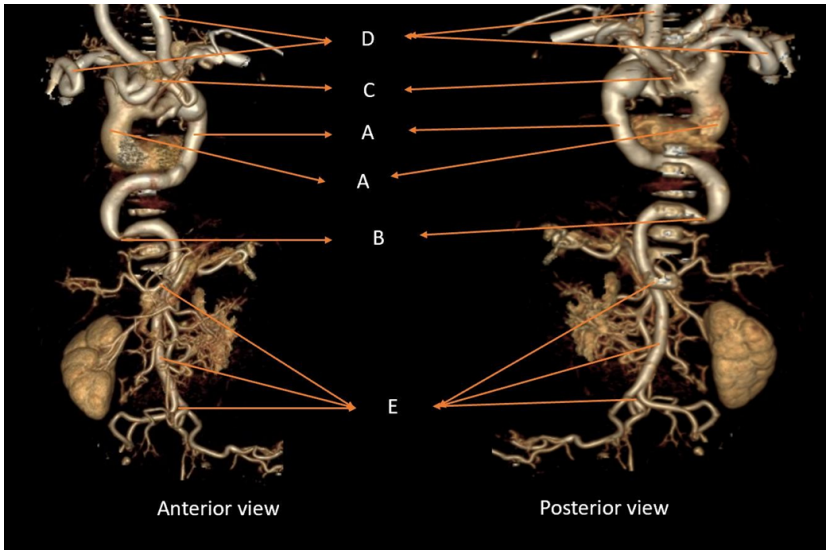

Figure 3: CT Aortogram-
A: Gross elongation and tortuosity of ascending aorta, arch of aorta and descending thoracic aorta is visible. Meandering aorta is noted upto the chest wall.
B: Mild kinking at the level of fourth rib of posterior chest wall. At the areas of kinks, significant luminal narrowing is noted.
C: Tortuosity of origins of great arteries and their branches leading to cluster of vessels is noted suggestive of cluster of vessels sign.
D: Gross elongation and tortuosity of the brachiocephalic trunk, right common carotid artery, right subclavian artery, left common carotid artery and left subclavian artery is noted.
E: Tortuosity and elongation of abdominal aorta, common iliac arteries, celiac trunk.
F: No aneurysm, ectasia, dissection, dilatation or thrombosis is noted.

On further evaluation, computed tomography (CT) Aortogram showed gross elongation and tortuosity of Ascending Aorta, Arch of Aorta and Descending Thoracic Aorta (mild kinking at the level of 4th rib of posterior chest wall. These findings were consistent with Arterial Tortuous Syndrome, though no evidence of aneurysm, dissection or thrombosis was noted (Figure 3).

The patient was provided with attentive care including warmth, oxygen therapy, and proper hydration at two-thirds of the maintenance Ruid volume. Initially, conservative treatments such as intravenous antibiotics, nebulizations, and physiotherapy were administered for Broncho-Pneumonia (LRTI). However, further investigation through a CT aortogram uncovered multiple narrowed segments of the aorta, leading to the consideration of Balloon Angioplasty. The patient attenders were also recommended to undergo genetic testing to confirm ATS. Unfortunately, the patient's caregivers opted for discharge against medical advice (DAMA), and subsequently, the patient was lost to follow-up.

Discussion

The relatively rare autosomal recessive connective tissue disease known as arterial tortuosity syndrome (ATS) is characterized by extensive arterial involvement, large and middle-sized artery elongation, tortuosity, and aneurysms. This disorder has been linked to SLC2A10 mutations. The glucose transporter GLUT10 is encoded by this gene [3]. GLUT10 is a member of the SLC2A transporter family; GLUT10 promotes the absorption of dehydroascorbic acid (DHA), D-glucose, D-galactose, and 2-deoxy-D-glucose [4]. A redundant vascular pathway during initial arteriogenesis, an imbalance between arterial lengthening and the corresponding development of surrounding anatomic structures during childhood and adolescence, or an additional stimulus to arterial elongation during adulthood are all potential causes of vascular elongation [5]. Just 106 people have been found to have ATS that has been genetically verified, making it an exceptionally rare condition [6].

Patients exhibit signs of connective tissue, such as hyperextensible skin, hernias, cutix laxa, and distinctive facial features. Micrognathia, an extended face, a high palate, a beaked nose, and downward-slanting palpebral fissures are characteristic facial traits [3,7]. We observe comparable distinctive facial traits in our case study as well.

Compromised vascular integrity in the arterial vascular beds, disordered connective tissues covering blood vessels and even non-vascular structures throughout the body are among the pathophysiological characteristics of ATS. These factors result in the vessel wall and other connective tissue becoming more flexible and weaker [8].

In the absence of a specific mutation of the SLC2A10 gene, a diagnosis of severe arterial tortuosity (as opposed to ATS) can be made on the basis of the clinical presentation and angiographic presence of multiple tortuosities, stenoses, and aneurysms. However, whole-exome sequencing is recommended to reach a definitive diagnosis of rare genetic conditions characterized by high genetic heterogeneity and phenotypic overlap [9].

The patient's family history includes the sudden cardiac death of a 2-year-old third-degree relative on the maternal side. This event was not evaluated and remained undiagnosed. However, in the light of the recent case, it is possible that the previous incident could have been a severe form of arterial tortuosity syndrome, given its autosomal recessive inheritance pattern. This suggests that the sudden cardiac death might be attributed to a severe form of ATS. In order to potentially avert possibly fatal complications connected to the abnormal vasculature, it is imperative that patients with arterial tortuosity syndrome have a high index of suspicion and have prompt diagnostic work-up. For all patients with connective tissue disease—including those with arterial tortuosity syndrome—echocardiographic screening is advised, and all patients are required to have routine follow-up. Some patients may benefit from surgical intervention with early identification; aortic root replacement for aortic aneurysms and/ or pulmonary artery reconstruction have produced positive short-term clinical and hemodynamic results [10]. Individuals with ATS benefit from frequent cardiovascular follow-up including yearly MRA or CT scans with 3D reconstruction from the head to the pelvis beginning at birth or at the time of diagnosis. Additionally an echocardiogram every three months until the age of five years. Blood pressure should be monitored at each appointment [2].

Conclusion

Antenatal imaging modalities, including Targeted Imaging For Fetal Anomalies (TIFFA) and fetal echocardiography, if conducted, could have furnished significantly enhanced diagnostic data, thereby facilitating more effective management of the neonate both pre and postnatally.

Considering the case report above, early diagnosis, Imaging, 2D Echo, and Molecular Genetic testing would support the confirmation of the illness and prompt symptomatic treatment.

Lesson Learnt

Importance of Early Diagnosis and Intervention

While the prognosis for ATS is typically unfavourable, prompt

diagnosis and intervention results in improved clinical and symptomatic outcome for the patient.

Need for Antenatal Imaging

Antenatal imaging methods like Targeted Imaging for Fetal Anomalies (TIFFA) and fetal echocardiography play a crucial role in the early identification of ATS, ensuring appropriate treatment strategies.

Supportive Care and Genetic Counselling

This highlights how crucial it is to give patients and their families' thorough care and help dealing with both the medical side and the emotional challenges of living with a rare genetic disorder like ATS.

Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series

Patient Consent

Written informed consent was obtained from a legal representative guardian for patient information to be published in this case report.

Declaration of Conflict of Interest

The authors declared no potential contracts of interest with respect to the research, authorship, and/or publication of this case report.

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