

Autoimmune vasculitis in a child following tetralogy of Fallot repair in Uganda

Abstract

Introduction: Tetralogy of Fallot is one of the conotruncal abnormalities and is the most common cyanotic heart disease worldwide. Conotruncal abnormalities have been closely associated with 22q.11 deletion syndrome. Children with 22q.11 deletion syndrome often have thymic hypoplasia, hypocalcaemia and have an increased susceptibility to viral, fungal and bacterial infections due to poor T-cell production. Autoimmune vasculitis has not been well documented among individuals with Tetralogy of Fallot (TOF) though a few reports exist in association with 22q.11.2 deletion syndrome.

Case summary: We report a case of an 11 year old child post TOF repair who presented to the Uganda Heart Institute with persistent high grade fevers, abdominal pain, mucosal bleeds and hypocalcaemia, hypokalemia, hypomagnesaemia, thrombocytopenia and elevated acute phase reactants-leukocytosis (17.9x10³), neutrophil count 16x10³(89%), elevated C-reactive protein (80mg/l) and elevated immunological tests (C-ANCA, 18U/ml). She improved on intravenous methyl prednisolone.

Conclusion: Children with Tetralogy of Fallot can still manifest with complications such as autoimmune disorders and severe infections given the association with 22q.11 deletion syndrome. Screening for autoimmune abnormalities and electrolytes especially calcium improves on their outcome. We were not able to perform the FISH analysis (for Fluorescent in Situ Hybridization) to confirm the diagnosis of 22q.11.2 deletion syndrome in KT.

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Background

Tetralogy of Fallot is the most common cyanotic congenital heart disease worldwide.¹ Among other conotruncal abnormalities, 13-16% of Tetralogy of Fallot individuals are reported to have 22q11.2 deletion syndrome which is characterized by thymic hypoplasia, endocrine abnormalities and hypocalcaemia.² Individuals with micro deletion 22q11.2 deletion syndrome are prone to auto immune disorders. Defects in thymic development predispose them to impaired immune function especially T cell deficiency.³ However autoimmune vasculitis has not been well documented in children with Tetralogy of Fallot. We report on an eleven-year-old child post Tetralogy of Fallot repair who presented with persistent fevers and an over whelming infection.

The case report

KT

11-year-old girl had Tetralogy of Fallot (TOF) repair 8years prior to developing the reported illness. She was referred to Uganda Heart Institute from a peripheral clinic with a history of fever and back ache which had been treated as a urinary tract infection with cefalexin then ceftriaxone with no improvement. Four days later, she developed a petichae like rash which was involving the palms and sole of the feet. She also developed bloody diarrhea approximately 9motions in 24hours and abdominal pain. Her previous medical history indicated good health after the TOF repair until a year prior to admission when she developed an acute abdomen which mimicked appendicitis, a skin rash and persistent fevers. She is the last born in the family. Her elder sister suffered a congenital heart disease (ventricular septal defect) that closed spontaneously and her niece had double outlet right ventricle.

Clinical examination

Revealed a sick child with a fever 39°C petichae on palms and soles of the feet Oral thrush and bleeds in the mouth she also had blisters on the lower limbs with secondary infection. She was hypoxic with an oxygen saturation of 86% on room air. Cardiovascular exam revealed, BP 88/56mmHg, grade 3/6 ejection systolic murmur in the left upper sternal area. Abdominal examination revealed had generalized tenderness, no palpable organs. Mentation was good, muscle tone, bulk and power was normal (on admission).

Baseline laboratory results

upon admission; Full haemogram showed leukocytosis, WBC 17.9x10³, with differential neutrophil count 16x10³(89%), Hemoglobin 12.3g/dl, thrombocytopenia 93x10³ and highly elevated C-reactive protein (CRP) of 80mg/l (NR<6mg/l). The peripheral film revealed macro platelets, left shift and no schistocytes. Electrolytes were deranged (Figure 1).

Hypocalcaemia

1.6(2.1-2.5)mEq/L, Hypokalemia 2.6mmol/L and hypomagnesaemia 0.6mEq/L and the coagulogram;PT/APTT were normal. Blood culture did not grow any organisms; urine analysis revealed yeast cells and cultured>10⁵ Candida albicans.

Cardiac echo

Showed an intact VSD patch with no residual shunt Good LV systolic function Moderate pulmonary artery conduit stenosis, peak gradient 44mmHg, free pulmonary regurgitation no vegetations

or thrombi were seen. Fevers escalated despite broad spectrum antibiotics (Piperacillin/Tazobactam), Cefotaxime and Vancomycin.

Day 9 of admission

KT got drowsy but arousable, developed a stiff neck, positive Kernig's sign, Glasgow coma scale 13/15. She later developed generalized tonic seizures, right sided hemiplegic, and loss of speech. Retinal hemorrhages were seen on fundoscopy. The child was treated with intravenous phenytoin though she later developed status epilepticus which was managed by standard protocol and was later incubated. Cerebral spinal fluid (CSF) was relatively normal, protein 10.3, gram stain, no organisms, HSV 1& 2PCR negative, CSF cryptococcal antigen (CRAG) negative MTB-PCR negative. Brain Computed Tomography on two separate occasions was normal, thyroid function tests were normal. The C-ANCA was elevated 18(0-2U/ml), P-ANCA-0.3, normal. With the combined effort of the rheumatologist, pediatrics cardiologists, neurologist and hematologists a diagnosis of autoimmune disease was made basing on the raised C-ANCA. Intravenous methyl prednisolone was given (1mg/kg) and Phenytoin 5mg/kg/day were given followed by prednisolone 30mg once a day to be tapered down. KT improved markedly improved, regained consciousness. The C-reactive protein (CRP) dropped to less than 8mg/l and the electrolytes were normal, the white cell counts 11.6×10^3 , neutrophil count 8.5×10^3 (73%), Hemoglobin 8.7g/dl. We discharged her in good general condition, able to walk and speak. We employed a multi disciplinary approach in the management of KT including the hematologist, neurologist rheumatologist. A year later, she reported two relapses which manifested with low grade fevers and skin lesions which have been treated with short courses of prednisolone (Figure 2).



Figure 1 Lesions in the palms (parental consent and assent were obtained).

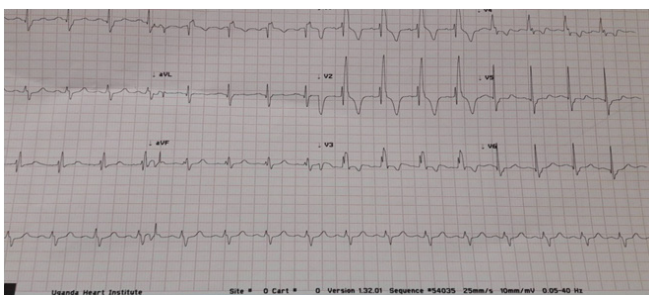


Figure 2 Electrocardiogram showed right axis deviation with right bundle branch block.

Discussion

Autoimmune vasculitis is a rare complication of Tetralogy of Fallot. Studies have reported autoimmune disease associated with 22q11.2 deletion syndrome which is commonly found among individuals with conotruncal abnormalities like Tetralogy of Fallot.² With limited ability to perform genetic studies in our setting, the presentation of KT was similar to that commonly seen among individuals with micro deletion 22q11. Hypocalcaemia is often associated with convulsions⁴ and requires supplementation.⁵ Hematologic abnormalities have been reported among individuals with Tetralogy of Fallot especially coagulation derangement. The sufferers tend to have large dysfunctional platelets.^{6,7} KT had thrombocytopenia and bleeding in the mucous membranes and had large platelets seen on the peripheral film. The thrombocytopenia is often immune related. Patients with Tetralogy of Fallot and Di George syndrome tend to have recurrent infections⁶ just as our patient presented with severe infections including; bacterial infections and fungal infections as evidenced by high neutrophil counts, oral thrush and urine culture for *Candida albicans*. We performed a septic screen including CRP, and blood culture with a possibility of infective endocarditis which is common among children with cyanotic heart disease.⁸

This diagnosis of autoimmune vasculitis was based on elevated CANCA. Other methods for diagnosing autoimmune disorders include the FISH test which is not readily available in our setting. We noted a drastic improvement in the level of consciousness upon commencing intravenous methyl prednisolone which made the diagnosis of autoimmune disorder very likely. In the routine follow up whether before surgery or post operatively, it is recommended to monitor calcium levels, thyroid function tests, complete blood counts and re assess immunologic tests annually.⁴ KT had two sick days in the first year of follow-up in which her C-reactive protein was elevated with an associated leukocytosis. She responded to a 3-day course of oral prednisolone.

Conclusion

Tetralogy of Fallot patients are likely to manifest with challenges in electrolyte regulation especially hypocalcaemia, severe infections and have a high tendencies of autoimmune disorders. Our patient presented with features highly suggestive of deletion 22q11.2 syndrome. Genetic studies would have better informative however these were not available in our setting. A multidisciplinary model is always necessary in the management of these patients.

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None.

Conflict of interest

The author declares no conflict of interest.

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