

Successful Treatment of Acute Enteric Myocarditis with IVIG Infusion: An Unusual Complication of Enteric Fever.

Rajkumar Kundavaram¹, Harish Kadiri¹, Priya Gogia^{1,✉}, Amber Kumar¹, Mahesh Maheshwari¹, Shikha Malik¹

¹Department of Pediatrics, All India Institute of Medical Sciences, Bhopal.

Abstract

Myocarditis, the inflammation of myocardium can be caused by a variety of etiological agents with clinical manifestations ranging from asymptomatic to cardiogenic shock. Enteric fever is a very common illness in children and can have a wide range of complications both enteric and non-enteric. The reported incidence of myocarditis in enteric fever ranges from about 1-5%. Paediatricians must be aware of the rare complications that might make the diagnosis challenging. We present one such case of a 6-year-old boy who came to us with a history of fever, diarrhoea and hypotension. On initial evaluation, the child was in cardiogenic shock and was started on IV antibiotics and inotropes. Laboratory evaluation confirmed enteric fever, and Electrocardiogram and echocardiography revealed myocarditis with dilated cardiomyopathy. The child did not improve with initial supportive care. Administration of IVIG resulted in a dramatic improvement in LVEF. The child is now thriving well with normal cardiac function.

Keywords

Myocarditis, enteric fever, IVIG, cardiogenic shock

Introduction

Myocarditis is inflammation of the myocardium caused by a wide range of etiological agents both infectious and non-infectious. The true incidence is unknown and the different clinical presentations range from asymptomatic to cardiogenic shock which result in uncertainty about the diagnosis¹. Myocarditis has been shown to be the third leading cause of death among young, athletes². The leading cause is viruses, especially Coxsackie and Adeno-viruses and a large no of cases are immune mediated. Myocarditis due to bacterial infections is quite rare. Enteric fever is a common febrile illness in children caused by *Salmonella typhi*, a gram negative bacteria that primarily cause diarrheal illness in humans by ingestion of contaminated food products, especially poultry and eggs. The clinical presentation varies depend on the organ system involved and pose challenge to the treating physician. Enteric fever complicated by

myocarditis is a rare phenomenon in the modern era with widespread availability of diagnostics and antimicrobial drugs. We report a child with enteric myocarditis who was successfully treated with Intra venous Immunoglobulins.

Case details

6-year male child was referred to our institute with features of congestive cardiac failure. On probing history, the child had fever on and off for the past 2 weeks associated with loose stools, pain in the abdomen and vomiting. He has been admitted to some other hospital for the same and received oral antibiotics with supportive care. The child was referred to our institute due to deterioration of clinical and hemodynamic parameters. On initial

Corresponding Author

Dr Priya Gogia

Assistant professor, Department of Pediatrics, All India Institute of Medical Sciences, Bhopal.
Email: gogiapriya09@gmail.com

How to cite:

Kundavaram R, Kadiri H, Gogia P, et al, Successful Treatment of Acute Enteric Myocarditis with IVIG Infusion: An Unusual Complication of Enteric Fever. *Future Health* 2023; 1(1):100-103.
Submitted: 18 June 2023
Accepted: 16 July 2023

evaluation, the child had tachycardia (PR 141/min, gallop rhythm), tachypnea (RR 30/min), Hypotension (BP 81/49 mm Hg), CRT- 2 sec and SpO2 98% on Oxygen support by prongs at two lit/min. Chest auscultation revealed bilateral basal crept, and abdomen examination revealed hepatomegaly. The initial impression was sepsis with shock. The hemodynamic parameters worsened after IV normal saline bolus, so the probability of cardiogenic shock was considered.

Congenital heart disease, dilated cardiomyopathy, myocarditis, and cardiac arrhythmias were considered differentials. The child had no history suggestive of congenital heart disease like failure to thrive, feeding difficulties, and suck rest suck cycle. There was also no history of rash or bleeding manifestations, sore throat, cough or respiratory distress and also no history of joint pains. So we considered myocarditis as the cause of cardiogenic shock, with probable aetiology being viral or bacterial.

Complete Blood counts and renal and Liver function tests were normal. Workup for malaria and dengue was negative, Urine routine microscopy was normal, and blood and urine cultures were sterile. Serological workup for scrub typhus was negative, COVID-19 RT-PCR was also negative. WIDAL titres were significantly high (O titre - 1:480), and Typhidot-IgM was also

positive. Although both these tests are not specific for the diagnosis of enteric fever, a provisional diagnosis of clinical enteric fever was made. However, salmonella couldn't be isolated from stool or blood. Chest X-ray was suggestive of cardiomegaly. The child had rhythm abnormalities with 12 lead electrocardiograms showing low voltage complexes and ST-T changes. Troponin I and T levels were normal, but Pro-BNP levels were elevated. Echocardiography revealed Dilated Cardiomyopathy with a low Left Ventricular Ejection Fraction (35%). Thus, a provisional diagnosis of enteric fever with myocarditis and dilated cardiomyopathy was made.

Treatment:

Injectable 3rd generation cephalosporin was started along with dobutamine infusion. 24 hours after dobutamine infusion, cardiac function did not show improvement, so milrinone was added. Amiodarone was started because of frequent premature ventricular contractions and intermittent tachycardia episodes after a paediatric cardiologist consultation. As the ST-T changes were persistent and CCF was not resolving, IV Immunoglobulins were given @2g/kg over two days, with which a dramatic response in LVEF was seen. Inotrope support tapered off and stopped gradually. The child is discharged from our intensive care unit after eight days in stable condition.



Figure 1: 12 lead ECG showing significant ST-T changes (ST elevation in V3, V4, tall and broad T waves in lead II) with frequent PVC

The child was followed up in our Paediatric cardiology clinic seven days after discharge, and the repeat Echocardiogram showed near normal LVEF and Pro-BNP levels. No rhythm abnormalities were noted in the electrocardiogram.

Discussion:

Enteric fever is caused by *Salmonella typhi*, a gram-negative gut pathogen with an incubation period of about 14-21 days³. It is transmitted by feco-oral route, affecting the areas with poor hygiene. The estimated global burden is about 12 million illnesses and 128,000 deaths on a yearly basis⁴. With the widespread availability of antibiotics, mortality due to typhoid has dropped to only 1%. The clinical presentation is varied, affecting almost any organ system in the body, making it diagnostically challenging. Most of the complications occur in the third week of illness if proper antibiotic therapy is not initiated, resulting in perforation of the ileum more commonly as well as other extra-intestinal complications. These include pulmonary, rheumatological, central nervous system, and hepatobiliary problems. The reported incidence of cardiovascular complications in literature is around 1%-5%, including myocarditis, pericarditis and arteritis⁵.

Myocarditis is seen rarely in typhoid, and only a few cases have been reported so far, the first one dating back as long as late 19th century. It may present like myocardial ischemia or can be asymptomatic during its course and then cause sudden nonspecific hemodynamic deterioration. As the symptoms are highly nonspecific, it can be easily missed in the absence of a high index of clinical suspicion. Acute myocarditis presents like a nonspecific illness with gradual progressive hemodynamic alterations ending up as dilatation and impaired contractility of the ventricles⁶. Another variety fulminant myocarditis, presents with rapid and progressive hemodynamic deterioration but will show dramatic improvement in ventricular function on initiating treatment. Echocardiography can differentiate between the two conditions. Patients with fulminant myocarditis have near normal left ventricular diastolic dimensions but increased septal thickness at presentation, while those with acute myocarditis had increased diastolic dimensions but normal septal thickness².

The exact pathological mechanisms leading to myocarditis in enteric fever are still unclear. Still, it has been postulated that the pathogenesis depends on the amount of inoculum size, virulence, immune-host response, history of previous exposure, and local protective factors⁷. Myocardial damage might be secondary to the involvement of the endocardium or due to the direct bacterial invasion from bacteremia. Sepsis-induced myocardial depression and

subsequent remodelling may also play an important role.

Echocardiography will detect impaired ventricular function and diagnosis of myocarditis, even in the subclinical presentations. The findings may include LV dilation, changes in LV geometry like the development of a more spheroid shape and wall motion abnormalities⁶. The systolic dysfunction is generally global. Tissue Doppler Imaging can be abnormal, but data on this is limited. Mild mitral regurgitation and tricuspid regurgitation could be seen. ECG show nonspecific changes like low voltage complexes, ST T segment, and T wave changes⁸. Cardiac MRI can confirm the diagnosis of myocarditis; however, sensitivity is variable, time-dependent and the abnormalities are nonspecific⁹. Most of the cardiac centres use The Lake-Louise Criteria to diagnose clinically suspected myocarditis. However, the gold standard is endomyocardial biopsy, and the diagnosis of myocarditis is based on the Dallas Criteria but not routinely performed due to the risks involved and the availability of non-invasive methods to diagnose¹⁰. We did not get a Cardiac MRI in our patient due to the high risk of mobilising sick children on inotrope support.

The treatment of enteric myocarditis and associated cardiomyopathy is the same as other variants of myocarditis. Supportive care and timely initiation of appropriate antibiotics and inotropes will improve clinical outcomes. However, our child didn't improve with this measure. Some studies showed the beneficial use of dexamethasone on adults, but the data on paediatric patients is sparse¹¹. Yinig Li et.al concluded in a meta-analysis that IVIG might improve LVEF and survival in children with myocarditis^{11,12}. Another meta-analysis by Xin Huang et al. concluded that IVIG therapy for acute myocarditis in children and adults is associated with improved recovery of LVEF¹¹. We administered IVIG (2g/kg), and the repeat echocardiogram after 48 hours showed improved LVEF.

Conclusions:

In developing countries like India, rare complications of a common illness like enteric fever can pose a diagnostic challenge for paediatricians. Myocarditis and cardiomyopathy, though rare can occur in enteric fever, even in immunocompetent cases. These cases can be fatal if not diagnosed and treated early. We suggest that Electrocardiography be part of the regular assessment of enteric fever. Non-invasive modalities like echocardiography and cardiac MRI should be employed for diagnosis. Treatment with IVIG can improve Ejection Fraction and reduce the overall duration of hospital stay. These patients should also be

under close follow up till ventricular function is fully recovered.

References:

1. Putschogl A, Auerbach S. Diagnosis, Evaluation, and Treatment of Myocarditis in Children. *Pediatr Clin North Am.* 2020;67:855–74.
2. Ammirati E, Veronese G, Bottiroli M, Wang DW, Cipriani M, Garascia A, et al. Update on acute myocarditis. *Trends Cardiovasc Med.* 2021;31:370–9.
3. Childs L, Gupta S. Salmonella enteritidis induced myocarditis in a 16-year-old girl. *BMJ Case Rep.* 2012;2012:bcr2012007628.
4. Stanaway JD, Reiner RC, Blacker BF, Goldberg EM, Khalil IA, Troeger CE, et al. The global burden of typhoid and paratyphoid fevers: a systematic analysis for the Global Burden of Disease Study 2017. *The Lancet Infectious Diseases.* 2019;19:369–81.
5. Marchello CS, Birkhold M, Crump JA. Complications and mortality of typhoid fever: A global systematic review and meta-analysis. *Journal of Infection.* 2020;81:902–10.
6. Elseify MY, Alsharkawy AA, Al-Fahham MM, ElHady MM. Assessment of lateral mitral, septal and tricuspid myocardial performance indices by tissue Doppler imaging in asthmatic children. *Clin Respir J.* 2018;12:2676–82.
7. Majid A, Bin Waqar SH, Rehan A, Kumar S. From Gut to Heart: Havoc in a Young Patient with Typhoid-associated Cardiomyopathy. *Cureus.* 2019;11:e5049.
8. Kaushal M, Tolani P, Kumar N, Chopda A. Ventricular bigeminy in enteric fever. *Natl Med J India.* 2019;32:216–7.
9. Sanchez Tijmes F, Thavendiranathan P, Udell JA, Seidman MA, Hanneman K. Cardiac MRI Assessment of Nonischemic Myocardial Inflammation: State of the Art Review and Update on Myocarditis Associated with COVID-19 Vaccination. *Radiology: Cardiothoracic Imaging.* 2021;3:e210252.
10. Ammirati E, Buono A, Moroni F, Gigli L, Power JR, Ciabatti M, et al. State-of-the-Art of Endomyocardial Biopsy on Acute Myocarditis and Chronic Inflammatory Cardiomyopathy. *Curr Cardiol Rep.* 2022;24:597–609.
11. Huang X, Sun Y, Su G, Li Y, Shuai X. Intravenous Immunoglobulin Therapy for Acute Myocarditis in Children and Adults. *Int Heart J.* 2019;60:359–65.
12. Li Y, Yu Y, Chen S, Liao Y, Du J. Corticosteroids and Intravenous Immunoglobulin in Pediatric Myocarditis: A Meta-Analysis. *Front Pediatr.* 2019;7:342.