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Case Report Open Access

The Use of Azithromycin in Pediatric Typhoid Fever without Complication: A Case Report

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ABSTRACT

Typhoid fever is an infection caused by the bacterium *Salmonella typhi*. The prevalence is still high among emerging countries, such as Indonesia. There are limited options for the treatment of typhoid fever in children and more so is complicated by the emergence of antimicrobial resistance. The use of azithromycin has evolved as an important drug in the treatment of typhoid.

A male, aged 7 years and 2 months, was admitted to our hospital with remittent fever 4 days prior. The patient also presented with a period of cough since 2 days, and constipation, with full consciousness. The child had basic immunization completed for his age. He had a history of frequent consumption of street food. The diagnosis of typhoid fever was confirmed by serologic testing of positive 8 IgM Salmonella. Initially, the patient was treated with intravenous antibiotics of ceftriaxone for 8 days but shoed no clinical improvement, then the treatment was changed to intravenous azithromycin for 4 days and his condition improved greatly. The patient showed a better response with the use of azithromycin.

The management of typhoid fever remains challenging up to this day with variations in treatment response. From this case, we can conclude that azithromycin in some patients may show better improvement in the management of typhoid fever in pediatric patients. Although, ceftriaxone and other third-generation cephalosporins are still highly effective against *Salmonella typhi*.

Keywords: Typhoid fever; salmonella typhi; enteric fever; azithromycin

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Introduction

Salmonella enterica serovar typhi is the agent causing typhoid fever predominantly in the developing world and is still associated with mortality and morbidity rates in the pediatric population. It is transmitted by water contamination and through unhygienic food ingestion. In Indonesia, it is estimated 800-100.000 people are with typhoid fever all year round. The prevalence is 91% among 3-19 group of age.[1,2,3] Treatment of choice is with antibiotics. Chloramphenicol was first used in around 1948 by Woodward, but in the 1970s, Salmonella became resistant. In 1980 and 1990, *Salmonella* became resistant to ampicillin and cotrimoxsazole. This trend of multiple-drug resistance for the strain *Salmonella typhi* in recent years has made treatment for typhoid more complicated. Azithromycin has been proven in vitro to have a role in enteric pathogen elimination including *Salmonella spp*, excellent penetration into most tissues, and achievement of concentration in macrophages and neutrophils that are > 100-fold higher than concentration in serum.[4,5,6]

Here, we report a case of a boy of 7 years and 6 months with typhoid fever without complication that was treated with azithromycin.

Case

A boy aged 7 years and months was admitted to W hospital emergency room with an infrequent fever 4 days before admission, the fever was relieved with antipyretic, the fever mostly felt at night. The patient also presented with infrequent cough 2 days, nausea, and has not defecated for the past 4 days. The appetite was rather good.

Figure 1. Picture of the patient

In physical examination, the patient showed full consciousness, a fever of 38.7C and tachypnea of 42 times per minute, other vital signs were normal. Hyperemic pharynx and audible rales on both lungs with no wheezing. Laboratory work revealed a normal Hemoglobin level of 13.7 g/dl, leukocyte of 5,100/mm^3, and platelet of 170,000/mm^3. The liver, and kidney functions were normal. The chest x-ray revealed pneumonia dextra.

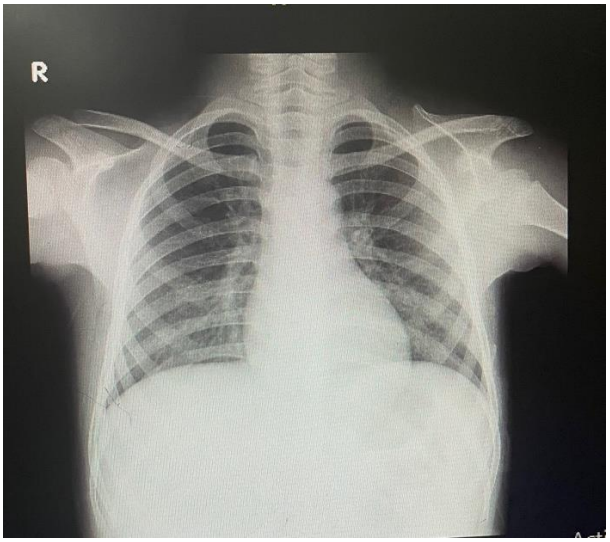

Figure 2. The chest x-ray of the patient with an impression of pneumonia dextra

The patient was initially treated for pneumonia and was given intravenous antibiotics of ceftriaxone and gentamicin, however, after 7 days of treatment, the clinical symptoms of pneumonia were relieved but the fever was still persistent accompanied by nausea and constipation. We further tracked the cause of the fever and found that the Tubex test was positive 8. The patient then was treated as typhoid fever and was given azithromycin intravenous for 4 days continued with oral azithromycin. The fever, and nausea were relieved, the patient had defecated, so the patient was then discharged.

Discussion

Our patient initially presented with a fever for 4 days, accompanied with cough, nausea, and constipation as the marked symptoms. Due to Covid situation in our hospital, the patient was suggested to have a chest x-ray examination and the result was pneumonia dextra. We initially treated this patient as having pneumonia for the reasons, this patient had fever, cough, and shortness of breath. The treatment was started with intravenous antibiotics of ampicillin and gentamicin. The cough, shortness of breath were relieved but the fever was still ongoing, so we tracked for possible typhoid fever causing the persistent fever.

Typhoid fever caused by an invasive pathogen of *Salmonella typhi* from contaminated feces, food,

and water. *S.typhi* is a negative gram bacteria, has flagella, no capsule, and not forming anaerob facultative spores. It has antigen somatic O, flagel antigen H, and envelope antigen K. S.typhi invade the body from the mouth and into the gastric mucosa in terminal ileum, in the peyeric patch, S.typhi crosses the epithelial barrier and enter the mesenteric lymphnodes and into the bloodstream via lymphatic channel. This is called primary bacteremia. The bacteria that is already in the bloodstream then replicated at the macrophages, and can be released again into the bloodstream causing secondary bacteremia. This condition marked the end of incubation period and will end up in clinical signs and symptoms of typhoid. The clinical signs of typhoid fever in most cases is called step-ladder temperature. Initiated with insidious symptoms, then got higher and peak at the first week. Many parents reported that the fever is higher at night, and it can be accompanied with decrease of consciousness. Prodromal signs are malaise and anorexia. Other signs and symptoms are dominantly gastrointestinal tract which include stomachache, constipation, diarrhea. Several parents also reported cough and pain when swallowing in their children[7,8,9,10]

The test for serologic testing tubex was positive 8 which was deemed as strong positive. The IgM for *Salmonella* can be detected in the blood for 3 months after infection. The gold standard for Salmonella diagnosis, is still through isolation from culture. However, this is quite challenging as it requires a longer time for the result and the condition of the patient may deteriorate before the result is out.

Based on the latest recommendation from Ikatan Dokter Anak Indonesia (IDAI), the antibiotic used for the first line is chloramphenicol, amoxicillin, and cotrimoxsazole. The second line is ceftriaxone and cefixime, indicated for multi-drug resistant strains of *S.typhi*. However, WHO South East Asian Region (SEARO) recommends the use of azithromycin or third-generation cephalosporin for enteric fever case caused by *S.typhi* in the Southeast Asia region. Azithromycin is from the macrolide group of antibiotics, and has a broad spectrum, that works to inhibit protein synthesize and lower the formation of biofilm. This antibiotic is of bacteriostatic. Azithromycin is an antimicrobial agent from the macrolide group given orally that is stable in acidic environment. Due to its wide antibacterial spectrum for *Streptococcus pneumonia*, *Moraxella catarrhalis*, and atypical pathogen, Azithromycin has widely been used for infectious disease therapy in children and is considered one of the most prescribed antibiotic in children. It also has better accumulation in the phagocytes, hence, better distribution to the source of infection. Up to this day, there is no report of resistance *S.typhi* to azithromycin.[11,12,13,14] The typhoid vaccine is considered an efficient tool to prevent typhoid fever. In March 2018, WHO recommended the use of typhoid conjugate vaccines in endemic countries, in 2019, Pakistan has become the first country in the world to introduce the WHO-recommended typhoid vaccine to its routine immunization program.[15] In Indonesia however, typhoid vaccine has now been introduced and is considered safe to be delivered to

children from the age of 2 years.

The limitation of this case is the limited number of patients treated with Azithromycin, therefore, this study can't yet be used as the guideline therapy for typhoid fever in pediatric cases.

Conclusion

A case of typhoid fever without complication that was treated with azithromycin from a boy aged 7 years and 6 months is reported. The patient was initially treated with ceftriaxone for 7 days but showed no clinical improvement in the duration of a fever. The diagnosis of typhoid was based on history taking, physical examination, and laboratory support. After treatment with azithromycin for 6 days, the patient's condition improved greatly. This report may help in providing additional information regarding the treatment of typhoid.

Conflicts of Interest

There is no conflict of interest

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References

1. Kadir S, et al. Salmonella Hepatitis in Children: A Update. Dhaka, Pakistan: Northern International Medical College Journal. 2019.
2. Ahmad S. Assessment of Liver Function Tests in Children with Typhoid Fever: A Hospital Based Study. Nepal: Journal of Nepal Medical College. 2019
3. Parry MC, Hien TT, Dougan G et al.Typhoid Fever. The new England journal of medicine. 2002: 347(22); 1770-82.
4. Rao KN, Pratusha R, Acharya A. Azithromycin and ceftriaxone in uncomplicated typhoid fever in paediatric patients: a prospective comparative and randomized open labelled trail. Int J Contemp Pediatr 2020;7:2316-20
5. Effa EE and Bukirwa H. Azithromycin for treating uncomplicated typhoid and paratyphoid fever (enteric fever). The Cochrane library. 2008. 1-38
6. Abramowics M, Zuccoti G, editors: Handbook of antimicrobial drugs: drugs for bacterial infections. The Medical Letter, ed 20, New Rochelle, NY 2015.
7. Hadinegoro, Sri Rezeki, et al. Demam Tifoid dalam Buku Ajar Infeksi dan Penyakit Tropis edisi Keempat. Jakarta: Badan Penerbit Ikatan Dokter Anak Indonesia. 2016.
8. Kliegman, Robert, et al. Typhoid Fever in Children. Philadelphia. 2016: Nelson Textbook of Pediatrics 20th Editiom.
9. Suwatro S, et al. Laboratory Parameters for Predicting Salmonella Bacteremia: a Prospective Cohort Study. Jakarta, Indonesia: SAGE pub journal. 2016
10. Karoli R, Fatima J, Chandara A, Singh G. Salmonella hepatitis: An uncommon complication of a common

disease. J Fam Med Primary Care 2012;1:160-2.
11. Zmora N, Shrestha S, Neuberger A, Paran Y, Tamrakar R, Shrestha A, et al. (2018) Open label comparative trial of mono versus dual antibiotic therapy for Typhoid Fever in adults. PLoS Negl Trop Dis 12(4): e0006380. https://doi/org/10.1371/journal.pntd.0006380
12. Sumit Raim Umesh Shukla, Arti Kapil, Suhsila Dahiya, Priyanka Sharma, Cefriaxone treatment failure in two cases of Enteric Fever caused by CTX-M15 positive Salmonella Typhi and its gastrointestinal carriage, Indian Journal of Medical Microbiology, 2022, https://doi.org/10.1016/j.ijmmb.2022.04.001
13. Craig WA, Andes DR. In vivo activities of ceftazolone, a new cephalosporin, with and without tazobactam against Pseudomonas aeruginosa and Enterbacteriaceae, including strains with extended spectrum B-lactamses, in the thighs of neutropenic mice. Antimicrob Agents Chemother. 2013;57:1577-1582.
14. Antolis Y, Rampengan T, Wilar R, Homenta Rampengan N. Azithromycin vs. chloramphenicol for uncomplicated typhoid fever in children. Vol. 53, Original Artice Paediatr Indones.
15. Ullah I, Khan K, Mehmood Q, Malik M, Ahmed A, Munir U. Irrational use of azithromycin in typhoid endemic areas: A challenge on multidrug-resistant typhoid treatment. Vol. 1, Review Article, Trends in Infection and Global Health 2021