***Case Report***

**MULTIPLE DRUG RESISTANCE TYPHOID FEVER (MDRTF)**

Sabeeha Kausar

Faculty of pharmacy, university of Sargodha

**ABSTRACT**

 A 20 year old girl was examined suffering from high fever from one week and abdominal pain for few days. The patient had suffered from typhoid fever last year. Ultra sonogram of abdominal, hematology-cell analysis, serology (Widal test), and urine analysis and blood culture was performed for accurate diagnosis. Ultra sonogram shows multiple organ infection by salmonella typhi. Hematological analysis shows the elevated level of t- lymphocytes and anemia. In widely test, patient serum was agglutinated with the bacterial antigen i.e. lipopolysacharide and flagellar proteins. The typhoid test was positive for IgG. The patient was diagnosed with typhoid fever. Patient possesses multi drug resistance and the rational treatment was with ceftriaxone for one week and patient recovered.

**KEY WORDS**

 MDRTF (multiple drug resistance typhoid fever), poor hygienic conditions, salmonella typhi, IgG (immunoglobulin G), RES (reticul o endothelial system), rational use of antibiotics and prevention of typhoid fever.

**CORRESPONDING AUTHOR** Sabeeha Kausar, Faculty of Pharmacy, University of Sargodha, Sargodha, Pakistan. Email; sabeehakausar86@gmail.com; Cell no; 03026842464

 **INTRODUCTION**

 Typhoid fever remains serious health threat principally due to poor health measures e.g. sewage disposal, chlorination of water supply and other safety measures. It is considered as global health problem with over 21.6 million cases and 250,000 deaths annually (1-2). The typhoid fever is caused by facultative Gram –ve rod, *salmonella typhi*. (3) The organism is transmitted through oral fecal route and habitat is human colon only. Thus disease is often associated with poor sanitation and hygiene (4). The organism infects the cell of reticul o-endothelial system especially in the liver and spleen. Endotoxin in the cell wall causes fever. Capsule (Vi antigen) is virulence factor (5). Chronic carrier state is established in gallbladder. The organism excreted in the bile results in oral fecal spread to others. Serological tests are suggested as rapid diagnostic test instead of blood culture. Most commonly used are widal and typhidot test. While treating the typhoid multiple drug resistance is considered against first line flouroquinolones and ampicillins and the effective treatment is by third generation cephalosporin e.g. ceftriaxone. Two vaccines are in common use; one injectable vaccine contains purified Vi polysaccharide capsule as the immunogen and other orally used contain live attenuated S. typhi as immunogen.(6)

**CASE REPORT**

 A 20 year-old girl admitted with a one-week history of intermittent high-grade fever (>100°F ), malaise, nausea, and abdominal pain. The physical examination revealed discomfort in the right upper quadrant and lower abdomen. Ultra sonogram of the abdomen revealed hepatomegaly (12 cm) and gall bladder, bile ducts, pancreas and kidney were found normal. No other abnormalities were detected. Spleen size was enlarged at 9 cm. Overall results revealed mild hepatosplenomegaly. Hematological analysis show the anemia(Hb level 10 mg/dL) and lymphocytes were slightly elevated at 52.3%. Widal testing revealed the patient’s serum was agglutinated with the lipopolysaccharide TO (1:200) and flagellar TH (1:100) and antigen of serotype *S.* Typhi was present. Typhidot test was positive for IgG. The urine analysis report exhibited pus cells 3-4; occasional RBC; epithelial cells 2-3; bile salt and bile pigment were negative; and bacterial cells absent. Blood cultures were negative with no history of antimicrobial therapy in the previous seven days.

 The first line therapy was started before the test reports by penicillin i.e. ampicillin (25 mg thrice a day orally) and chloramphenicol (125 mg four time a day orally) along with paracetamol after every four hours till the axillary temperature remain below 100°F and pantoprazole plus ranitidine in two separate doses. This therapy was maintained till the reports clear the diagnosis. But the therapy was not much effective as patient showed multi drug resistance. After two days physician prescribe Quinolone i.e. ciprofloxacin(250 mg thrice a day orally) along the paracetamol and pantoprazole plus ranitidine in same doses for seven days.After the seven days, same test were carried out and results were a bit different. *S. typhi* was grown in blood culture. Salmonella did not grow on urine and stool cultures. In antibiotic susceptibility testing of the isolated strain, there was resistance to ciprofloxacin, chloramphenicol and co-trimoxazole and slight resistance to ceftriaxone.The physician prescribe third generation cephalosporin i.e. ceftriaxone (500 mg twice a day orally) for seven days. Repeated Gruber-Widal test revealed that TO antibodies increased to 1:800 and TH antibodies to 1:200 one week later.

 After a week, after clinical examination, the results were negative and physical symptoms also disappeared and no relapse occur during the follow up.

**DISCUSSION**

Typhoid fever is an emerging health problem in developing countries specifically in Asia with the 5 to 20 % mortality rate(7). WHO statistics estimate 22 million cases with approximately 200000 deaths(8). Multiple drug resistance is emerging problem in the treatment of typhoid fever. The patient complete case study is described in the start. Generally symptoms appear in the typhoid are fever, nausea, headache, abdominal pain, hepatomegaly, spleenomegaly , anemia etc. same symptoms are mentioned in the *Tatli et al*(9). The therapy given to the patient was penicillins (ampicillin and chloramphenicol). To reduce other complication pantoprazole (proton pump inhibitor) plus ranitidine (histamine receptor antagonist) was used. Paracetamol (analgesic and antipyretic) was also administered to reduce the axillary temperature. But the patient do not show effective recovery as the S. typhi strain is developing resistance to the penicillins. Other antibiotics such quinolones (ciprofloxacin) was administered but the the test reports results were not satisfactory. The final therapy was by third generation cephalosporin (ceftriaxone). After a week the patient recovered and the organism was completely eradicated and no relapse occurred. The treatment of patient was based on the previous treatment of typhoid cases in the corresponding medical complex. Ceftriaxone is the rational therapy in multi drug resistant patients*. Acharya et al(10)* reported intravenous doses of ceftriaxone 75mg/kg once daily in children for five days, with clinical cure defervescence with out complications or relapse, and no further treatment was required. Tatli et al(11) also observed in their case study same results for ceftriaxone.

 **CONCLUSION**

 Multidrug resistance is emerging problem in treatment of typhoid fever. Ceftriaxone is well tolerated drug but is expensive. Ofloxacin is used alternatively which is cheap and have comparable therapeutic effect. Rational use of antibiotics is necessary for the complete treatment and elimination of organism with minimal complications. The choice of drug and the duration of therapy depend on several factors such as the clinical severity of the case, the patient’s condition, and drug resistance, as well as the physician’s experience and available resources. The increasing antibiotic resistance of *S. typhi* is a concern. The treatment of typhoid fever with third-generation cephalosporins, such as ceftriaxone is associated with higher cure rates.

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**RECOMMENDATIONS**

**1-**As S. typhai is transmitted from contaminated water and poor sewerage disposal, highly effective measures should be taken to avoid this disease. Public health awareness schemes should be conducted.

2-Although effective vaccines are available for typhoid fever but the plans for large scale vaccination programs s

Should be highly managed in infants and children.

3-As the S.typhi is developing resistance against first line antibiotics, therapy should be done with care for quick recovery. 4-Rational use of antibiotics should be insured to reduce the extent of complications and resistance.

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