CASE REPORT

Extended Spectrum Beta Lactamase producing Cephalosporin resistant *Salmonella* Typhi, reported from Rawalpindi, Pakistan

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Abstract

Typhoid is endemic in many parts of southeast Asia. Due to the resistance of the organism to first line of antibiotics (ampicillin, chloramphenicol, cotrimoxazole) as well as to fluoroquinolones, third generation cephalosporins have been in use for the empiric treatment of typhoid for years. However an increasing incidence of Salmonella Typhi is being reported sporadically from various regions. We report a case of typhoid due to Salmonella Typhi which was non-responsive to treatment with a cephalosporin, was found to be multidrug resistant and resistant to ciprofloxacin and third generation cephalosporin as well. The patient was finally treated successfully with intravenous administration of a carbapenem.

Keywords: Typhoid fever, Salmonella Typhi, cephalosporin, carbapenem.

Introduction

Typhoid fever is a common and serious infectious disease endemic in many parts of Southeast Asia.[1] The disease is associated with high rates of morbidity and mortality and requires appropriate antimicrobial therapy for successful clinical outcomes. Rising drug resistance is becoming a major issue in the treatment of enteric fever. Consequent to the emergence of multidrug resistance and resistance to quinolones, cephalosporins became the forefront for the treatment of typhoid.[2] However, an evidence of rising MICs to cephalosporins and production of Extended Spectrum Beta lactamases (ESBLs) by Salmonella enteric serovar Typhi is emerging. Resistance to cephalosporins occurs due to the production of extended spectrum Beta lactamases (ESBLs) by the organisms and have been detected in various organisms of the family Enterobacteriacae. The genes for the production of ESBLs are carried on plasmids or transposons and may be transferred to other members of the family, hence making them resistant to cephalosporins. This is an extremely alarming situation as the dissemination of these resistant organisms will further limit the therapeutic options for treating typhoid.

We report a case of typhoid due to Salmonella enteric serovar Typhi which was resistant to all the first line antibiotics as well as fluoroquinolones and third generation cephalosporin. Hence the patient had to be treated with meropenem, a carbapenem drug which is not usually recommended for the treatment of typhoid fever.

Case Report

A previously healthy 17 years old male presented to the hospital with 14 days history of continuous, high grade fever with rigors and chills, headache and fatigue. There was no history of diarrhoea or constipation. At the time of admission, he was febrile with temperature 39°C, looked unwell and was found mildly dehydrated. On examination, abdomen was tender and spleen was palpable 3 cm below the left costal margin. On auscultation, he had bradycardia (heart rate 56 beats/min) and bowel sounds were present. Blood examination showed Haemoglobin of 8.7 g/dl, total leukocyte count was $3.3X10^9$/L and C-reactive protein was positive. The LFTs and serological markers for acute viral hepatitis were normal. Urinalysis and stool examination revealed no abnormality. Ultrasound of abdomen showed an enlarged spleen with a few enlarged mesenteric lymph nodes. His past history was unremarkable. He was provisionally diagnosed as a case of typhoid. Blood and stool were collected for culture and the patient was put on injection ceftriaxone 2gram intravenous stat and then continued as 1gram IV twice daily. The patient was discharged on request with advice to continue treatment in out patient department. Meanwhile blood culture revealed the growth of multidrug resistant (ampicillin, cotrimoxazole, chloramphenicol) Salmonella Typhi which was also resistant to ciprofloxacin, azithromycin, aztreonam, gentamicin and ceftriaxone, was an ESBL producer and sensitive only to meropenem. The patient was recalled who was still having fever despite treatment. Physical examination at the time of readmission revealed a body temperature of >39°C and pulse rate of 120/minute.

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Abdomen was diffusely tender with increased bowel sounds. Keeping in view the sensitivity report the patient was put on Injectable Meropenem 1 gram 8 hourly. He continued to have high grade fever (>39ºC) for 3 days and then remained febrile for only one day with temperature <39ºC.His general condition became better and his appetite improved. Repeat blood and stool culture were negative. Keeping in view the high resistance of the isolate Injection Meropenem was continued for 7 more days.

The patient was discharged from the hospital 10 days after admission when he had fully recovered, was afebrile and was feeling well.

Discussion

With the emergence of resistance to ampicillin, cotrimoxazole and chloramphenicol, ciprofloxacin became the drug of choice for treating typhoid. However, a rising resistance to ciprofloxacin reported from various regions lead to decreased use of fluoroquinolones as empiric treatment of typhoid. The option left was to use either azithromycin or a third generation cephalosporin. The isolate from our patient was resistant to both of these antimicrobials as well. Resistance to 3rd generation cephalosporins has also been reported from other countries. Sarika Jain et al[1] carried out a study on 344 strains of Salmonella and resistance to 3rd generation cephalosporin was observed in 7(2%) strains of Salmonella Typhi. A single cephalosporin resistant ESBL (and transferable among Enterobacteriacae) producing Salmonella Typhi was isolated from Japan in 2010.[3] First ESBL producing Salmonella Typhi from Bangladesh was reported in 2012[4] and has also been reported from Phillipines.[5] Yvonne et al[6] reported a cephalosporin resistant, ESBL producing Salmonella Typhi from the blood of an Iraqi woman in Germany. Amna et al., carried out a study in Faisalabad, Pakistan, on 30 isolates of Salmonella Typhi and found an emerging resistance to cephalosporins, however, no ESBL producing strain was detected.[7] In a recent study carried out in Bangladesh, twenty four Salmonella Typhi isolates from stool culture of typhoid patients were resistant to ceftriaxone.[8]

The spread of ESBL producing strains of Salmonella Typhi conferring resistance to broad spectrum cephalosporins is worrisome as their spread may seriously limit therapeutic options for treating typhoid. The high resistance to first line antimicrobials, fluoroquinolones and resistance to third generation cephalosporins will leave us with no option but to resort to carbapenems and tigycyclines for empiric treatment of typhoid. This in turn can have serious implications for empiric antimicrobial therapy in a country where typhoid is endemic.

References

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