

Unusual Case of 20year Male-Resistant Typhoid Fever

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Abstract:- A very common infectious disease but still emerging as extensive resistant known as resistant typhoid fever, caused by gram negative *Salmonella enterica* serovar Typhi (S.Typhi). This bacteria invades human cells by evading host defence system with the help of virulence plasmids and clustered genes called as salmonella pathogenicity islands (SPIs). These factors help bacteria to bind with plasmid mediated antimicrobial resistance gene and enable bacterium to become resistant strain or extensively resistant. After usage of multiple drugs for enteric fever made us to introduce tetracycline as last resort drug.

I. INTRODUCTION

➤ Background

As enteric fever presents as non-specific febrile illness, heightened clinical awareness and appropriate test are critical to identify cases. *Salmonella enterica* serotype Typhi, Para typhi A, Para typhi A B and Para typhi C causes potentially severe and occasionally life threatening bacteremic illness referred as typhoid fever and paratyphoid fever collectively called as enteric fever.

Estimated 11-21 million cases of typhoid fever and 5 million cases of paratyphoid fever occurs worldwide every year causing deaths of 1,35,000- 2,30,000. In South Asian countries, now a days *Salmonella typhi* had developed extensively resistant strains which becomes troublesome for physician community. XDR strains of *S. typhi* recently emerged from Pakistan showed resistance to most of the first line anti-biotics including cephalosporin and become significant public health threat due to limited treatment option. We report one such case of 20 year old male presenting to our General Medicine department of KLE, Hospital Belagavi.

II. CASE REPORT

A 20Year old male from Karnataka without any comorbidities, no habits, not on any regular medication presented with complaints of fever associated with chills since 7 days which was not associated with bodyache, rash, no burning micturition, no retro-orbital pain. He had also cough but without expectoration since 2 days of presentation. He also received oral and injectable anti-biotics for 6 days outside this hospital.

On presentation to this hospital, the patient had high grade fever of 103degree farrenheit with chills, restlessness. On examination his blood pressure was 90/60 mmHg, pulse rate was 108 bpm, with mild right hypochondriac tenderness.

On 1st day started on injectable anti-biotic meropenem keeping in mind that he had already received broad spectrum antibiotics like doxycycline and azithromycin.

On 2nd day of presentation, he developed loose stools and vomiting which was relieved on medication after which he developed fever and cough with expectoration. so empirically started on levofloxacin. Chest X-ray was within normal limit, AFB for sputum analysis was negative and gram showed positive cocci in chains.



Fig 1 Chest X-ray PA view (within normal limit)

On 3rd, he had again fever which was associated with severe chills and on per-abdominal examination he developed mild splenomegaly so we started empirically on artesunate and stopped meropenem and levofloxacin but peripheral smear came to be negative for malarial parasite.

On 4th day, his blood culture came to be positive for *salmonella enterica* serotype Typhi sensitivity shown below

HI-TECH LABORATORY

Patient Name :	IP / OP No :
Ordered Loc : Private Room Bed No: CB05	Gender : Male
Accession No : 23219712	Age : 20 Y
Consultant : JAYAPRAKASH APPAIGOL	Vch_No : 1003938
Class : Private - Private	Sample Collected : 09/06/2023 06:57PM
Current Loc : GROUND FLOOR (1220) Private Room CB05	Sample Received : 09/06/2023 8:04 pm

Salmonella enterica serotype Typhi

Amox/K Clav	<=8/4	S
Cefotaxime	<=2	S
Colistin	<=2	S
Cefepime	<=8	R*
Ertapenem	<=2	S
Imipenem	<=4	S
Meropenem	<=1	S
Meropenem	64	R*
Piperacillin	64	R*
Tetracycline	<=4	S
Ampicillin	<=8	R*

Ceftazidime	4	ESBL
Cefazolin	<=8	R*
Ciprofloxacin	>2	R
Cefuroxime	>16	R*
Fosfomycin	<=32	S
Levofloxacin	>4	R
Moxifloxacin	>1	R
Pip/Tazo	<=16	S
Trimeth/Sulfa	<=2/38	S
Tigecycline	<=1	S

Note : S - Sensitive (++++), R - Resistant, I - Intermediate (++)

Group A : primary drugs for the specific organism group

Group B : to be used in case patient allergy - intolerance or failure to respond to an antimicrobial agent in group A.

Group C : Supplemental antimicrobial agents, for treatment of patient allergic to or resistant to primary drugs.

Fig 2 1st Blood Culture Report (on Admission)

According to blood culture report he was started on piperacillin and Tazobactam

On 5th day, he had again developed fever but not associated with chills so we continued same anti-biotic and stopped artesunate.

On 6th day 2nd blood culture came which had shown same organism with same anti-biotic sensitivity pattern. Hence, we continued same antibiotic

HI-TECH LABORATORY

Patient Name : [REDACTED]		IP / OP No [REDACTED]	
Ordered Loc : Private room Bed No: CB05		Gender	: male
Accession No : 23221076		Age	: 20 Y
Consultant : JAYAPRAKASH APPAIGOL		Vch_No	: 176244
Class : Private - Private		Sample Collected : 10/06/2023 10:04PM	
Current Loc : GROUND FLOOR (1220) Private Room CB05		Sample Received : 10/06/2023 10:59 pm	

Salmonella enterica serotype Typhi

Amox/K Clav	>16/8	R
Cefotaxime	>32	R
Ciprofloxacin	>2	R
Ertapenem	<=2	S
Imipenem	<=4	S
Meropenem	<=1	S
Meropenem	64	I
Piperacillin	64	I
Tetracycline	<=4	S
Ampicillin	16	I

Ceftazidime	8	I
Colistin	<=2	S
Cefepime	16	I
Fosfomycin	>32	R
Levofloxacin	>4	R
Moxifloxacin	>1	R
Pip/Tazo	<=16	S
Trimeth/Sulfa	>2/38	R
Tigecycline	<=1	S

Note : S - Sensitive (++++), R - Resistant, I - Intermediate (++)

Group A : primary drugs for the specific organism group

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Group C : Supplemental antimicrobial agents, for treatment of patient allergic to or resistant to primary drugs.

Fig 3 Repeat Blood Culture Report (On Second Spike of Fever)

After 10th day of presentation he had shown recovery with Piperacillin and Tazobactam and discharged on oral Azithromycin. After 3 weeks of discharge he had again fever with chills presented to OPD, we started him on oral tetracycline for 14 days. He remain asymptomatic after 14 days of dose and doing well now.

➤ Investigation

ECG revealed normal sinus tachycardia Total count on admission was 11900 ,platelet was 1.53 lakhs. On 2nd day presentation, his widal, dengue, leptospirosis, weil-felix came negative. Serum Pro-calcitonin was raised (3.23). ANA profile came to be negative. CT abdomen showed multiple abdominal and pelvic lymphadenopathy.

III. DISCUSSION

This case report recalls the importance of early detection of antimicrobial susceptibility of S.Typhi and introduction of appropriate treatment as early as possible.

Table 1 Multidrug Resistant Enteric Fever Treatment Chart (IV-Intravenous, PO-per oral, bid- Twice a Day)

Multidrug-Resistant, Fluoroquinolone-Susceptible	Optimal treatment	Ceftriaxone	2 g/d (IV)	10-14 Days
	Alternative treatment	Azithromycin	1 g/d (PO)	5 Days
		Ciprofloxacin	500 mg bid (PO) or 400 mg q12h (IV)	5-14 Days
Fluoroquinolone resistant	Optimal treatment	Ceftriaxone	2 g/d (IV)	10-14 Days
		Azithromycin	1 g/d (PO)	5 Days
Ceftriaxone resistant	Optimal treatment	Meropenem	1 g q8h (IV)	10-14 Days
		Azithromycin	1 g/d (PO)	5 Days

The paucity of reliable point of care diagnostics for typhoid fever compels clinicians in the field to initiate presumptive antimicrobial therapy, often based on clinical judgment. In endemic settings, typhoid features high on the list of potential causes of undifferentiated febrile illness and

antimicrobial therapy is routinely started empirically with antimicrobials that are thought to be appropriate for local clads of S.Typhi [1]

All strains of antimicrobial resistant S.Typhi possess an R-factor which carries information for resistance to chloramphenicol, streptomycin, sulfonamides and tetracycline. When S.Typhi came into contact with R-factor bearing bacteria, through conjugation process this factor will be transferred.[2]

The decision of changing antibiotic on day 4 according to blood culture sensitivity report guided us proper treatment plan and thus avoided overuse of antibiotics.

The Indian Society of Critical Care Medicine guidelines for treatment of typhoid fever recommend ceftriaxone as a first line antibiotic to cover MDR variant and suggest azithromycin and ciprofloxacin as an alternative therapy[3]

But in this case as per sensitivity report in spite of giving antibiotics, after 1 month of discharge still he developed fever and residual symptoms, so we tried tetracycline as last resort and he showed full recovery after completion of dosage.

IV. CONCLUSION

In our case the patient on presentation having fever with chills, without typical presentation of typhoid fever treated empirically outside hospital with multiple antibiotics developed multidrug resistance. With the help of blood culture sensitivity report we treated him but not showed 100% recovery after discharge. Hence we thought to give tetracycline as last resort antibiotic and he responded well to it. S.Typhi rapidly acquires resistance to antimicrobials that are being used in the community but can also lose it once drugs are withdrawn. Therefore deployment of typhoid conjugate vaccines to control the disease may be the best defence against antimicrobial resistance in S.Typhi.

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