

RESEARCH ARTICLE

NON TYPHOIDAL SALMONELLOSIS IN A PATIENT WITH ULCERATIVE COLITIS –MULTI DRUG RESISTANT SALMONELLA TYPHIMURIUM AND MOLECULAR CHARACTERISATION OF RESISTANT GENES; A CASE REPORT

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Manuscript Info

Abstract

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Key words:-

Non Typhoidal Salmonellosis, Gastroenteritis, Multidrug Resistance, Antimicrobial Susceptibility Test, Inflammatory Bowel Disease **Background:** Non typhoidal Salmonellosis are widely prevalent in developed as well as developing countries caused mostly by S.typhimurium and S enteritidis. Transmission of NTS to humans can occur by many routes including consumption of food of animal products mainly egg, poultry, undercooked ground meat and dairy products. Gastroenteritis is the most frequent manifestation, while less frequently may lead to complication like Bacteremia and Septicemia.

Case summary: This is a case report of a 69 years old male admitted in Medical Gastro Enterology department with complaints of loose stools about 15-20 episodes per day with blood in some episodes and associated with diffuse abdominal pain. Culture of the stool sample detected Salmonella typhimurium which was sensitive to Cotrimoxazole & Azithromycin and resistant to Ciprofloxacin, Ampicillin & Ceftriaxone by disc diffusion method. Genotyping was done by PCR and this showed the presence of CTX-M and TEM genes. **Conclusion:** Non Typhoidal Salmonellae though causes self-limiting Gastroenteritis but in immunosuppressed individual it leads to focal infections & life-threatening bacteremia. The isolate from stool showed high level resistance and this could be due to increased usage of antibiotics in poultry and transfer of plasmids carrying resistance genes among enteric bacteria.

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Introduction:-

Non TyphoidalSalmonellosis are widely prevalent in developed as well as developing countries.Non typhoidal salmonellae (NTS) include the pathogenic salmonella other thanS.typhi,S.paratyphi A, B,C.Majority of infection due to NTS are caused by S.typhimurium and S.enteritis. Human infections with Salmonellae are most commonly caused by ingestion of food, water or milk contaminated by human or animal excreta. Salmonellae are the primary pathogens of lower animals .Transmission of NTS to humans can occur by many routes including consumption of food of animal products mainly egg,poultry, undercooked ground meat and dairy products

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Multidrug resistance among human NTS isolates is increasing worldwide [1]. Of particular concern has been the worldwide emergence of a distinct strain MDR S.typhimuriumcharacterized as definite phage104 (DT104) that is resistant to atleast five antimicrobials (R.TypeACSSUT).Gastroenteritis is the most frequent manifestation ranging from mild to fulminant diarrhea accompanied by low grade fever, nausea& vomiting. Other manifestations of Non-

Typhoidal Salmonellosis include Bacteremia/Septicemia, endovascular infections with pre-existing valvular heart disease & metastatic localized infection in liver, spleen, brain& kidney.

Case Report:

A 69 year old male was admitted in Medical Gastro Enterology department with complaints of loose stools about 15-20 episodes per day with blood in some episodes and associated with diffuse abdominal pain.

Patient is a known case of Inflammatory Bowel Disease-Ulcerative Colitis on medication with oral Tab.Mesalamine and Tab.Azathioprine. He has mixed dietary eating habits

On Examination:

Palpation per Abdomen-Soft, mild diffuse tenderness and on auscultation -bowel sounds normal.

Investigations:

Blood Hb-8.8gms/dl, Total count-5.7 X 10³/µl, Covid-19RTPCR-Negative

Biopsy: showed Acute on chronic inflammatory etiology. Colonoscopy: Multiple superficial ulcers.

Microbiological investigation& results:

On macroscopic examination of Stool, it was found to be yellow, watery, slightly mixed with blood. Microscopy revealed plenty of pus cells, No parasitic ova/cysts.Modified Acid fast Staining was negative for any coccidian parasites.

Faeces Culture:

On standard microbiological media non lactose fermenting colonies and preliminary identification showed as short gram negative motile bacilli further characterized biochemically. It was found to be Catalase-Positive, Oxidase-Negative, Indole-Not produced

Citrate-Utilized, Urease-Not hydrolyzed, TSI- Alkaline slant/Acid butt with abundant H₂S

Except Lactose all the sugars are fermented with acid and gas, Lysine decarboxylated and slide agglutination with polyvalent O antisera of Salmonella group, prompt agglutination was noted. With the above biochemical identification tests, the pathogen was identified as Salmonella typhimurium.



Figure1:- Gram Stain, Gram Negative Bacilli observed in culture.



Figure 2:- Slide agglutination with Salmonella polyvalent O Antisera.

Antimicrobial sensitivity testing:

The isolate was sensitive to Cotrimoxazole and Azithromycin. Resistant to Ciprofloxacin, Ampicillin & Ceftriaxone by disc diffusion method



Figure 3:- Antimicrobial susceptibility test for the Salmonella typhimurium showing sensitivity to Cotrimoxazole and Azithromycin and resistant to Ciprofloxacin, Ampicillin & Ceftriaxone.

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GENOTYPING was done by PCR- showed the presence of CTX-M and TEM genes

Figure 4.:- Genotyping by PCR. The S1(Sample)was positive for the presence of TEM and CTX-M gene. PC-Positive control; NTC-No template control.

The patient was treated with IV fluids, IV metronidazole and oral Cotrimoxazole along with his other regular medications for IBD. His condition improved after 4 days and the patient was discharged.

Discussion:-

Infection with NTS most often results in acute Gastroenteritis with the frequent manifestation ranging from mild to fulminant diarrhea accompanied by low grade fever, nausea& vomiting. In this case, patient presented with diffuse abdominal tenderness and bloody diarrhea as observed by Hung-Ming Chen et al in his studies

Here the patient was a known case of IBD,the treatment strategy of immunosuppression in patients with Inflammatory Bowel Disease (IBD) leads to remission or reduction of symptoms in most patients. But this strategy also induces an increased risk of intestinal as well as extra intestinal infections. The incidence of gastrointestinal infections among IBD varies between 9% & 13%.

Intestinal infections are common in patients with IBD and may mimic IBD flares. This patient was admitted as a suspected case of IBD flares but routine stool culture identified the pathogenic salmonellae highlighting the importance of stool culture in patient with IBD flares. In case of Non typhoidal Salmonellosis, S.Typhimurium has been the most frequently reported serotype accounting for >20% isolates reported to CDC annually [2].

In India, Typhimurium and Enteritidis are the commonest non- typhoidal serotypes but occurrence of rare serotypes like S.worthington, S.wien, S.virchow& S.dublin have been reported in literature[3].

The major risk factors for non-typhoidal Salmonellosis are certain immuno-compromised conditions including extremes of age, alterations of the endogenous bowel flora, malignancy, HIV, autoimmune disorders & therapeutic immunodeficiency [4]. In this case, patient is a known case of Ulcerative colitis, hence lead to alteration of endogenous bowel flora. In addition, as the patient is on Immunosuppressants, it promotes colonization with intestinal pathogen.

The fluoroquinolones and the third-generation cephalosporins are appropriate antibiotic choices for the management of invasive NTS infections [5]. NTS are more drug resistant than typhoidal Salmonellae [6,7, 8]. In this case also, antimicrobial susceptibility testing of the NTS isolate showed high level resistance to Flouroquinolones, Ceftriaxone and Ampicillin. In 2014, 2.1% of NTS human isolates in United States were Ceftriaxone resistant: with Minimum inhibitory concentration (MIC)>4 and this isolate also showed MIC >4 confirming the increasing resistance among NTS.But Ceftriaxone resistance is more common among NTS isolated from blood than stool[9]. In contrary, our isolate though it was from stool showed increased resistance to Ceftriaxone.

Over the last decade, the strains of NTS showing resistance to Ciprofloxacin with MIC>1 have emerged and are showing more treatment failure [10]. The isolate from this patient has also showed high level resistance to quinolones.

Salmonella gastroenteritis is usually a self-limiting disease. Antimicrobial therapy should be considered for neonates, persons older than 50 years and those with immunosuppression.

Conclusion:-

Non Typhoidal Salmonellae causes self-limited illness to severe gastroenteritis, focal infections & life threatening bacteremia. In patients with IBD, due to continuous immunosuppresion and repeated antibiotic usage for any mild infections leads to colonization with resistant pathogens. So early recognition of complicating infections with targeted therapeutic approach is needed for better prognosis. The isolate from stool showed high level resistance and this could be due to increased usage of antibiotics in poultry and transfer of plasmids carrying resistance genes among enteric bacteria.

References:-

- 1. Patrick F McDermott¹, Shaohua Zhao¹, Heather Tate- Antimicrobial Resistance in Nontyphoidal Salmonella, 2018 Jul;6(4). doi: 10.1128/microbiology spectrum [Pubmed]
- 2. Hohmann EL.2012. Microbiology epidemiology of and salmonellosis. http://www.uptodate.com/contents/microbiology-and-epidemiology-ofsalmonellosis?source=search_result&search=nontyphoidal+salmonella&selectedTitle=3~15 Varsha PreetiBehl -NonTyphoidal Salmonellosis(NTS) :AGlobal Gupta, concern https://www.jgi-gisi.com > JOGI > pdf > jogi-2-1-1
- 4. Matheson N, Kingsley RA, Sturgess K, et al. Ten years experience of salmonella infections in Cambridge, UK. J Infect 2010;60:21–5
- 5. Hohmann EL.2012. Nontyphoidal salmonella bacteremia. http://www.uptodate.com/contents/nontyphoidal-salmonella-bacteremia?source=search_result&search=nontyphoidal+salmonella&selectedTitle=1~15
- 6. Stevenson JE, Gay K, Barrett TJ, et al. Increase in nalidixic acid resistance among non-typhi salmonella enterica isolates in the United States from 1996 to 2003. Antimicrob Agents Chemother 2007;51:195–7
- 7. Lee HY, Su LH, Tsai MH, et al. High rate of reduced susceptibility to ciprofloxacin and ceftriaxone among nontyphoid salmonella clinical isolates in Asia. Antimicrob Agents Chemother 2009;53:2696–9
- 8. Lee HY, Su LH, Tsai MH, et al. High rate of reduced susceptibility to ciprofloxacin and ceftriaxone among nontyphoid salmonella clinical isolates in Asia. Antimicrob Agents Chemother 2009;53:2696–9
- AgilaKumariPragasam, ShaliniAnandan, James John, AyyanrajNeeravi, VigneshNarasimman, DhiviyaPrabaaMuthuirulandiSethuvel, DivyaaElangovan, Bala jiVeeraraghavan-An emerging threat of ceftriaxone-resistant non-typhoidal salmonella in South India: Incidence and molecular profile.Indian J Medical Microbiology. Apr-Jun 2019;37(2):198-202. doi: 10.4103/ijmm.IJMM_19_300.
- 10. RinaKarunakaran, Sun Tee Tay, FairuzFadzilah Rahim, Bee Bee Lim, Savithri D Puthucheary-Molecular analysis of ciprofloxacin resistance among non-typhoidal Salmonella with reduced susceptibility to ciprofloxacin isolated from patients at a tertiary care hospital in Kuala Lumpur, Malaysia. Jpn Journal of Infectious Diseases. 2014;67(3):157-62. doi: 10.7883/yoken.67.157.