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Case Report

Salmonella Enterica Serovar Paratyphi A Carrying the CTX-m Gene Sepsis in a 9 Year Old Asian Girl-First Reported Case in UK

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Abstract

We report a case of a 9-year old girl who presented with fever, recurrent gastrointestinal disturbances, and consequent dehydration, after a visit to Pakistan 3 months previously.

From her blood culture, Salmonella Enterica *serovar paratyphi* A was isolated, carrying the CTX-m gene and demonstrating resistance to amoxicillin, co-amoxiclav, pipericillin+tazobactam,ceftazidime, cefepime, cefotaxime, tobramycin, ciprofloxacin and tigecyclin.

This is the first case of its kind in the UK, underlining a worrying trend both toward higher proportions of enteric fever caused by *S. paratyphi* (an organism for which no vaccine is available), and toward increasing loss of antimicrobial effectiveness against the organism in South Asia and elsewhere. This is the first organism of its kind in the UK to be found to be resistant to all cephalosporins and narrower-spectrum beta lactamases such as amoxicillin. Further typing revealed that production of cephalosporinases by this organism contributed to this.

As geographical context typically provides the predicted bacterial sensitivities, which in turn permit our empiric antibiotic treatment (while we await lab-confirmed cultures), our empiric antibiotic selection in these cases must appropriately reflect these resistance patterns. Moreover, they starkly illustrate our vital need for appropriate antibiotic stewardship now and in the future, to preserve our ability to treat the potentially-fatal condition.

As an additional point of interest, we have identified in this case the co-existence of entamoeba histolytica species with this *S. paratyphi*, which we believe may be the first such finding documented in the literature. Further study is required to elucidate their pathophysiological relationship and its effects on the clinical picture.

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Our Case

A 9 year old girl was transferred to our paediatric inpatient unit for correction of dehydration arising in the context of presumed viral gastroenteritis. Of note, this was her 4th episode of diarrhoeal illness since becoming unwell during a visit to Pakistan 3 months previously.

She had developed diarrhoea and nausea during the first week of month-long visit to Pakistan in July 2016. She had been recovering from chickenpox in the week prior to this trip, but had no other ill contacts before travelling to Pakistan. On returning to the UK, she experienced 3 further episodes of gastroenteritis, with each episode lasting approximately 3 to 5 days before self-resolving. No blood or mucus was present in her stools, and her vomitus was not bile-stained. No other family member suffered similar symptoms. Her past medical history included a modified Norwood procedure for hypoplastic left heart syndrome and she was taking warfarin, sildenafil and enalapril as per her usual prescription.

She experienced continuous spikes of temperature >40 degrees celsius (controlled with simple antipyretics) associated with diarrhoea and vomiting. In addition, she began experiencing nose bleeds. She had vomited approximately 8 times, passed 8 diarrhoeal stools and was intolerant of oral fluids. In context of worsening pattern of recurrent diarrhoea and vomiting, she presented to hospital and was found to be clinically dehydrated, lethargic/miserable and with generalised abdominal tenderness.

At the point of presentation, she had a metabolic alkalosis (pH 7.55, pCO2 3.5, HCO3 26.1) accompanied by hyponatraemia (126mmol/L), hypokalaemia (3.3mmol/L) and hypocalcaemia (2.21mmol/L) was demonstrated. Leukopaenia of 3.2 x 10^9/L was noted. CRP initially was 167mg/L.

Initial diagnosis considered was sepsis for which she was screened and commenced on broad-spectrum antibiotics. Other differentials considered included Urinary Tract Infection and Infective Gastroneteritis. A thick and thin film were sent but demonstrated no evidence of malaria. Films looking for evidence of Dengue fever were sent but proved negative. Stool sample demonstrated neither ova, nor cysts, nor parasites. Although C.Difficile was detected, associated toxins were not present. In view of the presentation and travel abroad, extensive serological testing was undertaken which ruled out Dengue virus, Leptospirosis, Phleobovirus, Chikungunya virus, West Nile virus, Japanese Encephalitis and *Ricketssia* infections.

Her blood Cultures grew gram negative bacilli within 24 hours of incubation. Initially, she was prescribed ceftriaxone and metronidazole, but despite these antibiotics she continued to be intermittently pyrexial. These blood cultures subsequently cultured Salmonella *Paratyphi* A, which was sensitive to ertapenem, meropenem and co-trimoxazole. It was resistant to amoxicillin/co-amoxiclav/

pipericillin+tazobactam, and to ceftazidime/cefepime/cefotaxime, and to tobramycin and ciprofloxacin, and to tigecycline. Public Health England were notified.

Co-incidentally her blood test for Entamoeba Histolytica serology (sample tested at London School of Tropical Medicine) was suggestive of invasive amoebiasis.

IV Meropenem led to a rapid clinical resolution from an infection standpoint, and once she was stabilised from both a hydration and an anticoagulation perspective, she was discharged to complete 3 weeks of intravenous meropenem with the aid of the community nursing team. Further typing revealed that the causative organism was capable of producing cephalosporinases, which contributed toward its resistance to cephalosporins and narrower-spectrum beta-lactamases.

Introduction

Enteric fever is a systemic infection caused by the gram negative Salmonella enterica serovars typhi ("typhoid fever") and paratyphi ("paratyphoid fever"). Its faecal-oral transmission cycle means that poor hygiene and sewage contamination of water supply are the most important sources of person-to-person transmission for these human-host restricted pathogens [1]. In this context, Salmonella enterica is a leading cause of community-acquired bloodstream infections in many low- and middle-income countries [2], whereas, in high-income countries, it has become a disease predominantly associated with travel to areas of endemicity or with food-preparers who are chronic carriers of the pathogen [3]. The Global Burden of Disease (GBD16) project's Institute for Health Metrics and Evaluation estimated an annual prevalence in 2016 of 11.8 million, resulting in 8.8 million disability-adjusted life years, and 128,200 deaths [4]. One systematic review estimating that between 11.9 and 15.9% of Pakistani enteric fever cases affecting children <16 years were caused by serovar paratyphi A [5].

This is the first recorded incident in the UK of paratyphoid fever caused by an organism resistant to extended spectrum cephalosporins (such as ceftriaxone). The implications for future management are discussed below:

No effective vaccine for prevention of S. *Paratyphi* A is currently licensed [6]. The proportion of documented cases of enteric fever caused by S. *Paratyphi* A is growing, particularly in south Asia. Given these trends toward extended-spectrum resistance, priority should be given to developing a vaccine to prevent these infections

Similarly, those issues which currently limit the usefulness in a paediatric setting of the two vaccines available for S. *Typhi* must be addressed. The oral capsule administration route limits the use of Ty21a in preschool children, and ViPS provokes an inferior immune response in children <2 years of age [6].

Further efforts towards effective vaccines would likely benefit not only those health systems serving endemic areas but also lessen the risks of infection in travelers returning to non-endemic regions. This case contributes further evidence that bacterial resistance to multiple broad-spectrum antibiotics is emerging [7]; in such circumstance, prevention will be better than cure.

It is important to consider the diagnosis of enteric fever in a febrile returning traveller, particularly where gastrointestinal disturbance is evident. This case illustrates the clinical features which may raise the suspicion of enteric fever. Typically, after an asymptomatic initial period (lasting usually 7 to 14 days) the predominant symptom is fever. The temperature rises gradually during the first week of the illness and reaches a high plateau of 39 to 40˚C the following week. There is little diurnal variation, although the pattern may be modified by anti-pyretic medications [1].

Beyond this, the clinical presentation of enteric fever varies from a mild illness with malaise, and slight dry cough to a severe clinical illness with multiple complications including intestinal perforation. Toxic apathy, blanching 'rose spots' on the trunk, and diarrhoea are also associated with enteric fever. Constipation is a frequent early symptom. A slightly distended abdomen with a "doughy" consistency and diffuse tenderness is common, and abdominal organomegaly may develop. Occasionally, the pain and tenderness is intense in the right iliac fossa, mimicking appendicitis, and a relative bradycardia is described as being common in enteric fever [1].

Important differences in children, compared to adults, are a greater frequency of diarrhoea and vomiting, jaundice, febrile convulsions, nephritis, or typhoid meningitis. South Asian data has suggested that the presentation of typhoid may be more dramatic in children younger than 5 years, with higher rates of complications and hospitalization [8].

Where clinical suspicions, the recommended means of laboratory confirmation is by blood or bone culture. Although commercial point-of-care Rapid Diagnostic Tests (RDTs) are available, a 2017 Cochrane Database systematic review could not support their use as a replacement for blood culture for diagnosing enteric fever, owing to their moderate sensitivity and specificity of the RDTs evaluated [9].

It is also worth noting that, whilst *Salmonella enterica* may be isolated from faeces in up to 30% of patients with typhoid fever, this finding could either indicate acute enteric fever infection, or alternatively represent chronic carriage (with the acute infection syndrome caused by a different organism) [1].

Of further interest, this patient also tested positive for co-existent amoebaiasis. There is possibly the first ever documented co-infection of this kind; their pathophysiological relationship must be further teased out.

As happened in this case, a clinical suspicion of enteric fever can necessitate the initiation of empiric antibiotic treatment, whilst bacterial cultures are awaited.

Where enteric fever is suspected in a returning traveller, and whilst bacterial sensitivities are awaited, the initial antibiotic selection is guided by the travel history (which predicts likely bacterial sensitivities, based on known regional patterns of susceptibility and resistance). That this case featured a S. *paratyphi* serovar merely underscores the emergence of highly-resistant S. *paratyphi* serovars in South Asia; already, Extended-Spectrum β-Lactamase (ESBL) enzymes of the SHV-12 and CTX-M types and an AmpC β-lactamase of the ACC-1 type have been reported among *Salmonella* serovar *Typhi* isolates from Bangladesh, India and the Philippines [1]. This situation, unfolding in resource-limited settings where the few remaining effective antimicrobials are either unavailable or altogether too expensive to be afforded by either the general public or by public health services, is concerning.

Nor, as our case report plainly shows, will these resistance patterns remain restricted by the geographic context in which the infection was contracted [7]. This not only challenges our empirical antimicrobial prescribing to respond to these patterns, but provides further weight to the argument that today's appropriate antibiotic stewardship may be our best hope for managing and containing tomorrow's invasive infective diseases [1,7].

Learning Points

- Consider the diagnosis of enteric fever in the febrile returning traveler, and be vigilant for other clinical clues to this as a possible diagnosis
- Where enteric fever is suspected, blood or bone cultures should be sent to establish the diagnosis and provided bacterial sensitivities
- No vaccine is available to protect against enteric fever cases caused by Salmonella enterica serovar *paratyphi;* furthermore, both vaccines available for S. *typhi* are problematic in young children - this should be the focus of further study
- Travel history guides empiric antibiotic selection; rising proportions of enteric fever are being caused by S. *paratyphi* and resistance to broad spectrum antibiotics is emerging. Given this, we must both redouble our efforts in anatimicrobial stewardship, and also adjust our empiric antibiotic selection to reflect these changes in sensitivities
- This case might be the first ever documented co-infection of entamoeba histolytic and Salmonella Paratyphi; further investigation of their pathophysiological relationship must be undertaken to elucidate what impact they have on each other and on the clinical picture

References

1. Crump JA, Sjölund-Karlsson M, Gordon MA, Parry CM (2015) Epidemiology, Clinical Presentation, Laboratory Diagnosis, Antimicrobial Resistance, and Antimicrobial Management of Invasive Salmonella Infections. Clin Microbiol Rev 28: 901-937.
2. Deen J, von Seidlein L, Andersen F, Elle N, White NJ, et al. (2012) Community-acquired bacterial bloodstream infections in developing countries in south and southeast Asia: A systematic review. Lancet Infect Dis 12: 480-487.
3. Lynch MF, Blanton EM, Bulens S, Polyak C, Vojdani J, et al. (2009) Typhoid fever in the United States, 1999-2006. JAMA 302: 859-865.
4. Global Burden of Disease Study 2016 (GBD 2016) Covariates 1980-2016. Seattle, United States: Institute for Health Metrics and Evaluation (IHME), 2017, Global Burden of Disease Collaborative Network.
5. Howlader DR, Koley H, Maiti S, Bhaumik U, Mukherjee P (2017) A brief review on the immunological scenario and recent developmental status of vaccines against enteric fever. Vaccine 35: 6359-6366.
6. Akhtar S, Sarker MR, Jabeen K, Sattar A, Qamar A, et al. (2015) Antimicrobial resistance in Salmonella enterica serovar typhi and paratyphi in South Asia current status, issues and prospects. Crit Rev Microbiol 41: 536.
7. Bhutta ZA, Dewraj HL (2006) Current concepts in the diagnosis and treatment of typhoid fever. BMJ 333: 78-82.
8. Wijedoru L, Mallett S, Parry CM (2017) Rapid diagnostic tests for typhoid and paratyphoid (enteric) fever. Cochrane Database Syst Rev 5: CD008892.
9. Mawatari M, Kato Y, Hayakawa K, Morita M, Yamada K, et al. (2013) Salmonella enterica serotype Paratyphi A carrying CTX-M-15 type extended-spectrum beta-lactamase isolated from a Japanese traveller returning from India, Japan, July 2013. Euro Surveill 18.

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