Typhoid fever in a traveller returned from Samoa

Dr Maria Brand
Middlemore Hospital, Counties Manukau District Health Board

Maria is a surgical house officer who has been working in the Auckland region since graduating from the University of Auckland in 2015. This case report was written during her time in General Medicine, as a sixth year medical student. Maria intends to pursue a career in surgery (specialty TBC) and particularly enjoys working in the busy and diverse environment at Middlemore Hospital.

Case

A 39 year old male patient presented to Middlemore Hospital directly from Auckland Airport on his return from Samoa, with a 13 day history of febrile illness. His symptoms began with high fevers, chills and polyarthralgia, and diarrhoea developed around day five of his illness. Other associated symptoms included sweating, nausea, intermittent headaches, myalgia and weight loss (10 kg over 2 weeks).

Five days after becoming unwell, the patient was admitted to Apia Hospital overnight. He was diagnosed with presumed Chikungunya fever based on his clinical presentation. Definitive blood tests for viral illnesses such as this are not routinely performed in Samoa. He received intravenous fluids and analgesia and was discharged the following day. When his condition failed to improve the following week, he decided to return to New Zealand.

The patient had been volunteering as a builder in Samoa, including work with septic tanks. He was mostly working outside and had suffered many insect bites. He had also eaten at two local restaurants in the days before becoming unwell. He is normally fit and well, with no significant past medical history and no regular medications. He normally works as a builder, is a non-smoker and drinks minimal alcohol (2-4 standard drinks per week).

On physical examination the patient appeared unwell, with rigors and sweating. His vital observations were normal, other than a low-grade fever (37.6°C). He was clinically dehydrated with dry mucous membranes and his JVP was not visible. There was no rash, joint swelling or tenderness. His liver edge was palpable 1cm below the costal margin, but non-tender. Examination of his abdomen was otherwise normal. Cardiovascular and respiratory examinations were unremarkable.

Investigations

Bloods

- LFTs deranged
- GGT 875 [<60 IU/L]
- ALP 268 [40-110 U/L]
- AST 216 [<45 U/L]
- ALT 455 [<45 U/L])
- CRP 110 mg/L (n = <5mg/L)
- Normal full blood count, electrolytes, creatinine, albumin, bilirubin, mosquito-borne viral panel, hepatitis/ EBV/CMV serology
- Microbiology: normal faecal pathogen screen and midstream urine test, peripheral blood cultures: growth of gram negative bacilli, Salmonella typhi isolated

Imaging

- normal chest x-ray and upper abdominal ultrasound scan

Problem list

- Typhoid fever
- Dehydration, secondary to diarrhoea and reduced oral intake

A 39 year old male patient presented after returning from Samoa with a 13 day history high fevers and diarrhoea, resulting in significant dehydration and weight loss. He appeared visibly unwell with rigors, a low grade fever, and was clinically dehydrated. Laboratory investigations showed deranged liver enzymes, and peripheral blood cultures grew Salmonella typhi.

Although a positive blood culture offers a reasonably confident diagnosis in this case, prior to this result the differential diagnosis was broader. Chikungunya virus, which had been the diagnosis given by the doctors at Apia Hospital the week before, was still a possibility, especially given the current outbreak in Samoa. Chikungunya virus commonly presents with fever and polyarthralgia as the main symptoms and can cause diarrhoea and deranged LFTs (mainly affecting transaminases)[1] which fits relatively well with the clinical picture that this patient first presented with. However, Chikungunya virus is usually self-limiting and symptoms typically resolve within 7-10 days.[1] Other differentials included typhoid fever, acute hepatitis (including hepatitis A, EBV and CMV), or Dengue fever.

Discussion

There are a number of vital pieces of information required when presented with a case of fever in a returned traveller. These include where the patient was travelling, their purpose of travel and the specific activities they undertook, timing of the illness, including symptom onset, duration of travel, how long since they have returned and what measures had been taken against contracting diseases, eg. vaccinations, prophylactic medications.[2] Knowing this information is important when developing a differential diagnosis, combined with knowledge of endemic diseases in the travel destination, current outbreaks and incubation periods.

Febrile diseases that are currently prevalent in Samoa include mosquito-borne viruses, such as Dengue fever, Chikungunya virus and Zika virus and diseases which are spread via faecal-oral transmission, often through contaminated food or water, such as hepatitis A and typhoid fever.[3]

Little information is available regarding ill travellers returning to New Zealand. A study from sites in Auckland and Hamilton published in 2003 found that 14% of travellers who were unwell upon returning to New

Zealand had a febrile illness, of which the majority were of unknown origin. Tropical diseases such as Dengue fever and typhoid fever, although important and potentially fatal, were uncommon.[4]

Salmonella are gram negative bacilli of which there are seven subspecies and >2500 serotypes.[5] Infection with Salmonella enterica serotypes typhi and paratyphi (often shortened to S. typhi and S. paratyphi) causes typhoid fever, also known as enteric fever.[5,6] S. typhi is more common in typhoid fever from the Pacific region,[6] and generally causes a more severe infection than that of S. paratyphi.[5,7] Infection is initiated by ingestion of organisms, usually through contaminated food or water. The organisms leave the gut by being phagocytosed by M-cells in the Peyer's patches of the small intestine, thus crossing the epithelial layer. They are then phagocytosed again by macrophages, which proceed to carry the organisms throughout the body within the lymphatic system, leading to colonisation within tissues including liver, spleen, lymphatics and bone marrow.[5]

The average incubation period of S. typhi is 10-14 days, with typhoid fever often presenting non-specifically with symptoms of prolonged fever and abdominal pain. Other symptoms may include headache, chills, cough, sweating, anorexia, nausea, vomiting, myalgia, arthralgia and diarrhoea or constipation. A 'rose spot' maculopapular rash may be present on the trunk or chest of about 30% patients during the first week of illness. If untreated for 3-4 weeks, there is a risk of developing life-threatening complications of gastrointestinal bleeding and perforation.[5]

Initial investigations should include a full blood count, urea and electrolytes, and peripheral blood cultures.[2,5] Typhoid fever can only definitively be diagnosed by isolates in blood, stool or bone marrow. Peripheral blood cultures may only be 40-80% sensitive; thus if typhoid fever is suspected and no other cause is found, or if the patient has already been given antibiotics, a bone marrow culture (55-95% sensitive) may be helpful.[2,5]

Once S. typhi has been isolated, targeted treatment should replace any empiric therapy which has already been started. Susceptibility to antibiotics differs in different regions and likely susceptibility profiles based on local strains are available to guide initial empiric antibiotic therapy.[5-7] Fluoroquinolones are most effective in fully susceptible strains and ciprofloxacin is used most commonly.[2,5-7] Nalidixic acid resistance is a growing concern in some areas, particularly South-East Asia.[5,7] However, most of the S. typhi in the Pacific region does not appear to have developed this feature.[6]

If untreated, up to 5% of infected patients may become chronic carriers and unknowingly spread the infection, especially if they are involved in activities such as food preparation. Thus, typhoid fever is a notifiable disease in New Zealand and Ministry of Health can investigate and manage cases and contacts in order to prevent further spread.[8]

Typhoid fever is considered to be partially vaccine preventable with limited efficacy against S. typhi and none against S. paratyphi.[5,7] There are currently two commercially available vaccines, which include Ty21a (oral) and Vi-polysaccharide (parenteral).[5,7,9] This patient had received no vaccination. A recent Cochrane review evaluating these, along with another emerging modified Vi vaccine, found Ty21a to be between 33-50% effective in the first two years, with no benefit after the third year.[9] Vi-polysaccharide vaccine showed efficacy of around 69% in the first year dropping to around 55% in the third year following vaccination. The new vaccines showed promise with similar efficacy but potentially offering longer-term immunity.[9]

A recent New Zealand study found 25% of cases of typhoid fever in Auckland were from patients returning from the Pacific; mostly from Samoa.[6] Although there is a medium incidence (10-100/100000) of typhoid fever in the Pacific region, incidence in Samoa is significantly greater (134-406/100,000) and has been increasing since 2002.[7] Furthermore, 25% of cases of typhoid fever in Auckland between 2005-2010 were found to have been locally acquired; 55% of these within the Samoan population.[6] This demonstrates this disease is an important consideration in the South Auckland population, even in the absence of a history of recent travel.

Conclusion

Fever in a returned traveller presents a diagnostic challenge and it is important to take an accurate history, gathering key information about travel details and the time-course of illness. Knowledge of endemic diseases in particular areas and incubation periods of common tropical diseases is helpful to develop a relevant differential diagnosis. It is particularly important to always consider potentially life-threatening causes of fever in returned travellers, such as typhoid fever and Dengue fever, despite these being relatively uncommon in New Zealand.

Conflict of Interest: None

Correspondence: Dr Maria Brand, wilson.mkr@gmail.com

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