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Salmonella Paratyphi A infection: implications for public health management of extra-intestinal presentations – case study of a neck abscess

Moniek Borsovszky, Sophie Norton, Shopna K Bag, Jen Kok

Abstract

This study explores the implications of unusual presentations of *Salmonella enterica* subspecies *enterica* serovar Paratyphi (*S. Paratyphi*) infection for public health management, through a literature review and case study. In 2016, a 36-year-old male presented with a five-day history of right sided painful neck swelling, coryza and a two-day history of fevers after arriving in Australia from India nine weeks earlier. *S. Paratyphi A* was isolated from a fine needle aspirate sample.

A descriptive epidemiological review was performed of confirmed cases of *S. Paratyphi* notified in New South Wales between 2008 and 2017. *S. Paratyphi* was isolated in blood and/or faecal samples in 247 cases (98.4%). Only four specimens (1.6%) were from a focal site. A literature review of extraintestinal infections of *S. Paratyphi A* or *B* was performed. Of the 41 such cases reported, 16 (39%) had a clear history of a prior gastroenteritis and/or febrile illness, or information suggested this was highly likely. No preceding gastroenteritis or febrile illness occurred in 15 (37%) of the cases.

Information was reviewed and presented with a public health lens, valuable for ‘evidence-informed’ public health risk assessment of contacts and exposures related to these types of *S. Paratyphi* infection. *S. Paratyphi* infection usually presents as an enteric fever illness. Our case illustrates the variable nature of infectious diseases and the importance of laboratory testing in obtaining a diagnosis. *S. Paratyphi* can have unusual presentations, which may require adjustment in the public health management of the case. Public health staff should keep an open mind when investigating possible sources and assessing risk. In Western Sydney, this disease is largely associated with residents travelling to high-incidence countries to visit family and friends, and receiving family visits from these countries. The increasing number of cases of *S. Paratyphi* (prior to COVID-19) in Western Sydney and the importance of awareness of the risk of enteric fever to travellers to endemic regions is highlighted.

Keywords: Focal infection, *Salmonella* Paratyphi A, public health

Introduction

Paratyphoid fever, caused by *Salmonella enterica* subspecies *enterica* serovars Paratyphi A, Paratyphi B, and Paratyphi C (*S. Paratyphi*), is a public health issue of global significance. Global age-standardised incidence rates of typhoid and paratyphoid fevers combined have been estimated at 197.8 cases per 100,000 person

years, with paratyphoid infections accounting for around 24% of these cases.¹ Developed countries such as Australia are not subject to the same levels of enteric infection risks, related to inadequate food handling and storage and poor sanitation, as developing countries are, and thus have lower age-standardised incidence rates than the global average.² International travel, however, increases infection risk, particularly

travel to visit friends and relatives in higher-risk countries, as duration of stay tends to be longer than travel for tourism, and likelihood of exposure to the disease is increased.³

In New South Wales (NSW), Australia, all cases of *S. Paratyphi* are notified to public health authorities under the *Public Health Act 2010* to prevent the spread of disease,⁴ particularly amongst those in high-risk settings such as food handlers or healthcare workers. In June 2016, the Western Sydney Public Health Unit (WSPHU) was notified of a *S. Paratyphi* infection in a patient with no travel within the incubation period and an atypical locus of infection, a right sided painful neck swelling.

The unusual nature of this case prompted further assessment of the case history, an epidemiological review of Western Sydney Local Health District (WSLHD) and NSW notification data, and a literature search for culture-positive cases of *S. Paratyphi* taken from sites other than faeces, blood, urine and gall bladder. This study describes the process and findings of these investigations which were undertaken by the WSPHU to review potential routes of infection at sites remote to the gut and the implications for public health actions, particularly in high-risk settings. The study remains relevant to public health officials and infectious disease clinicians, as it highlights a rare presentation of the disease. The possibility of a longer incubation period has implications for the public health management of such cases.

Methods

Case review

In June 2016, the WSPHU undertook public health follow-up of the case according to the NSW Health Communicable Diseases Salmonellosis Protocol.⁵ This entailed obtaining relevant clinical information including onset date and type of symptoms, travel history, details of contacts and an occupational risk assessment through review of the case's clinical notes and a case interview. Written consent to

publish was obtained from the case by the consultant physician; therefore, ethics approval was not required.

Epidemiological review

A descriptive epidemiological review was performed of all confirmed cases of *S. Paratyphi* infection notified in NSW over the ten-year period from 2008 to 2017. A confirmed case requires laboratory definitive evidence with isolation of *S. Paratyphi*.⁶

Notification data were extracted from the Notifiable Conditions Information Management System (NCIMS)⁷ via the Secure Analytics for Population Health and Research Intelligence system (SAPHaRI).⁸ Descriptive analysis of notification data was undertaken using demographic, clinical, risk factor and laboratory result data fields. Crude incidence rates were calculated using the mean number of notifications over the study period (2008–2017) and the mean of mid-year population estimates obtained from the Australian Bureau of Statistics (ABS) via SAPHaRI.

Table 1: Databases and search terms used in the *S. Paratyphi* literature search

| Review database | Review search |
|-----------------|---|
| Medline | <p>MeSH terms Paratyphoid fever, <i>Salmonella Paratyphi A</i></p> <p>Keywords <i>Salmonella Paratyphi B</i></p> <p>AND</p> <p>MeSH terms Empyema, abscess, supp*</p> <p>Keywords Pyogenic, purulent, pus, unusual, extra intestinal, extraintestinal, lump, paratyphoid, paratyphi, enteric fever, focal, aberrant, meningitis</p> |
| PubMed | <p>MeSH terms Paratyphoid or paratyphi</p> <p>AND</p> <p>MeSH terms Abscess, suppuration, suppurative, pus, purulent, unusual, ulcer, pyogenic, extra intestinal, extraintestinal, empyema, focal, lump, meningitis.</p> |
| Google Scholar | Keyword searches using abovementioned search terms and previously retrieved article titles to search for other related articles |

Literature review

The literature review aimed to find publications describing a focal infection where *S. Paratyphi* A or B was isolated. In Stage 1, literature items (including case reports, case series, letters and descriptive studies) were identified from searches of computerised databases (Table 1). In Stage 2, full papers were obtained for items that met the review criteria in Stage 1 and were then reassessed against the review criteria. In Stage 3, reference lists of the included publications were scanned for other articles that might meet the review criteria.

Studies included in the review met the following criteria:

- they were published in the English language from 1 January 1990 to 9 September 2019;
- they clearly described instances of a focal infection with *S. Paratyphi* A or B that were confirmed from culture; and
- the full text article could be obtained at no cost.

Studies that were excluded after Stages 1 and 2 were those that:

- described instances of non-typhoidal *Salmonella* infection, or where the identification of the isolated organism was unclear;
- did not include confirmation of culture from the extra-intestinal site; or
- were articles likely to be about the same case as an included article.

Results

Case review

A 36-year-old male presented to hospital in June 2016 with a five-day history of right sided painful neck swelling, coryza and a two-day history of fevers. *S. Paratyphi* A was isolated from a fine needle aspirate of the neck swelling. Incision and drainage of the abscess was subsequently performed. Stool and blood cultures

were negative; however, antibiotic therapy had commenced prior to stool collection. No gall-bladder ultrasound was performed. Diarrhoea was reported post-operatively.

The case had arrived in Australia from India, nine weeks earlier, with his wife and eight-year-old child. His past medical history was unremarkable. He had no recent history of trauma to the area or of dental problems. He reported no recent hospitalisations, no sick contacts, or overseas visitors. The patient, his wife and his child had no history of fever or gastro-intestinal illness in India or since arrival in Australia. The only procedure he recalled was the removal of wisdom teeth in December 2014.

Epidemiological review

During the ten-year review period, there were 251 *S. Paratyphi* cases notified in NSW. Of these, 71/251 cases (28.3%) were WSLHD residents. The average annual incidence rate was 0.3 cases per 100,000 population in NSW and 0.8 cases per 100,000 population in WSLHD.

Table 2 summarises some demographic and clinical characteristics of *S. Paratyphi* cases notified in NSW. Most notified cases during the review period were in young adults with 95 (37.8%) aged 25 to 34 years. India was the most commonly identified country of disease acquisition, making up 39.8% of notified cases in NSW (100/251) and 63.4% of notified cases in WSLHD (45/71). There were 9/251 cases in NSW (3.6%) where it was thought that infection was acquired in Australia, although one of these mentioned recent travel to India that fell slightly outside the incubation period. The majority of cases (231/251, 92.0%) were caused by *S. Paratyphi* serotype A. Most cases (247/251; 98.4%) were confirmed in the laboratory by testing blood (204/251; 81.3%) and/or faeces (84/251; 33.5%) samples. The remaining four cases' specimens included bile and fluid that had been aspirated from a breast abscess, gall bladder, and lymph node from the case presented herein.

Table 2: Demographic and clinical characteristics of *S. Paratyphi* cases notified in New South Wales, 2008 to 2017 (N = 251)

| Characteristic | n | % |
|---|-----|-------|
| Sex | | |
| Female | 108 | 43.0 |
| Male | 142 | 56.6 |
| Not stated | 1 | 0.4 |
| Age group | | |
| < 5 years | 20 | 8.0 |
| 5–14 years | 24 | 9.6 |
| 15–24 years | 49 | 19.5 |
| 25–34 years | 95 | 37.8 |
| 35–44 years | 23 | 9.2 |
| 45–54 years | 26 | 10.4 |
| 55–64 years | 8 | 3.2 |
| ≥ 65 years | 6 | 2.4 |
| Country of disease acquisition^a | | |
| India | 100 | 39.8 |
| Bangladesh | 34 | 13.5 |
| Indonesia | 20 | 8.0 |
| Pakistan | 15 | 6.0 |
| Cambodia | 14 | 5.6 |
| Nepal | 13 | 5.2 |
| Australia | 9 | 3.6 |
| Other and unknown | 46 | 18.3 |
| Serotype | | |
| Paratyphi A | 231 | 92 |
| Paratyphi B | 19 | 7.6 |
| Paratyphi untyped | 1 | 0.4 |
| Positive specimen site | | |
| Blood only | 163 | 64.9 |
| Faeces only | 42 | 16.7 |
| Blood & faeces | 42 | 16.7 |
| Bile/gall-bladder/breast abscess/neck lump | < 5 | < 2.0 |

a Countries listed individually are Australia and those where n > 10.

Literature review

There were 38 manuscripts included in the literature review, describing 41 different cases with an infection in one or more aberrant sites due to *S. Paratyphi* A or B (Table 3; Appendix A, Table A.1). A wide range of anatomical sites were identified. The most common locations were: brain/cerebrospinal fluid (n = 10);^{9–18} breast (n = 7);^{19–24} reproductive organs (n = 4);^{25–28} bone/joint (n = 4)^{10,29–31} and liver (n = 4).^{32–35} Other sites described included: soft tissue/perianal (n = 3);^{35–37} neck (n = 2);^{38,39} spleen (n = 2);^{35,40} kidney (n = 2);^{41,42} and single cases involving the pericardium,⁴³ parietal wall,⁴⁴ psoas muscle,³¹ thyroid,⁴⁵ and pleura.⁴⁶

The majority of cases detailed (33/41, 80%) were in articles authored in South Asia, or were cases in travellers to South Asia.^{10–12,16–25,27,28,31–38,40–46} The eight remaining cases were from articles authored in the following regions: the Middle East;^{9,13,14,29,39} and South East Asia.^{15,26} One case was from the United Kingdom and the ‘source of the infection could not be established’.³⁰ Cases were assumed to be residents of the country the paper was authored in, unless otherwise specified.

A prior, or highly likely, history of an enteric fever illness preceding the focal symptoms was described in 16/41 cases (39%).^{11,12,17,19,21,24,26,27,31–34,37,40,43,46} Such a history was unlikely in 15/41 cases (37%),^{18,22,23,25,28–30,35,38,39,41,42,45} and was not discussed or clearly described for the remaining ten cases.^{9,10,13–16,19,20,36,44}

There was pre-existing trauma,^{10,42} surgery,⁴³ medical comorbidities,^{18–20,24,26,27,29,30,32,34,35,37} pregnancy,³⁹ age of less than 12 months,^{11,12,14–18} or age 12 months to less than 5 years^{13,46} in 25/41 cases (61%), which may have increased the risk of *S. Paratyphi* gaining a foothold in the focal area discussed, or may have caused complications that led to infection. In 11/41 cases (27%), no pre-existing medical condition was reported,^{9,21–23,25,31,33,35,38,41,45} and pre-existing conditions were not discussed in the remaining 5/41 cases (12%). The relationship between

pre-existing conditions and location of infection is examined in Table 3. Where trauma to a site is noted, the infection occurs in the same location. The location of the infection was the brain for all infants. There is no link between pregnancy and breast abscess.

Similarly to the case in this study, for the two neck abscesses in the literature review,^{38,39} there was no mention of a preceding gastro-intestinal illness or enteric fever. One case did, however, describe having a sore throat two weeks prior to the onset of abscess symptoms and was pregnant.³⁹

Discussion

The disease burden of *S. Paratyphi* in NSW is low compared to other regions in the world, such as South Asia where age-standardised incidence rates were estimated at 549.2 cases per 100,000 in 2017. This is the region with the highest age-standardised incidence rate of typhoid and paratyphoid globally.¹ Enteric diseases will, however, continue to pose a challenge to public health authorities in NSW through travel.³ Travel back to India was associated with almost two-thirds of infections notified in WSLHD residents and with almost half of those notified in NSW during the period reviewed. Western Sydney has also seen an increasing number and proportion of residents born in India, from 42,968 (5.3% of the population) in 2011, to 69,807 (7.5% of the population) in 2016.⁴⁷ Due to the changing demographics of the population, rates of infection have increased. This underpins the importance of increasing awareness and education of travellers to areas where enteric fever is endemic, and of clinicians who provide care for these persons and may be unfamiliar with this pathogen.

There were two documented cases of abscess due to *S. Paratyphi* found in the Australian and New Zealand literature, one from a breast abscess²¹ and one from a renal abscess.²⁶ The current Typhoid and Paratyphoid Fevers New South Wales Control Guidelines for Public Health Units⁶ focuses on transmission via the

faecal-oral route and an ensuing relatively short incubation period of one to 10 days for *S. Paratyphi*. All subsequent risk assessments related to acquisition and potential transmission are based on this focus. However the case presented here, and the two neck abscesses in the literature review,^{38,39} demonstrate a less certain disease pathway, blurring the lines on which public health decisions are made, such as time of exposure, at what point a patient becomes an infectious risk to others, for how long they pose this risk, and to what degree. In these three cases of *S. Paratyphi* infection involving the neck, there was an absence of systemic symptoms, suggesting an alternate mode of acquisition of some extra-intestinal salmonella infections.

The original route of infection is likely to have been via the faecal-oral route with the case experiencing no symptoms, or only mild fever and/or gastrointestinal symptoms which he failed to recall. This could have led to chronic carriage with possible gall-bladder involvement and eventual subclinical seeding to the lymph node.⁴⁸ Alternate modes of acquisition, however, have previously been discussed in the literature. Leiberman et al. propose that invasion occurs through direct seeding from tonsillar tissue causing cervical lymphadenitis.³⁹ Our case denied having a sore throat or cough; however, he did report rhinorrhoea. Other literature suggests seeding can also occur through the teeth with dental decay, or poor oral hygiene.⁴⁹ Our case denied any dental pathology, only a history of dental surgery 18 months prior to the appearance of the abscess symptoms. The organism may have entered either via the surgical site of the wisdom teeth extractions or from unknown dental decay, which caused a transient bacteraemia, with a mild fever that the case did not notice or remember, leading to focal infection. The considerable length of time between the dental extractions and the onset of case symptoms could be explained by the 'reactivation of a past dormant focus'⁵⁰ where the pathogen 'reached an intracellular location' where it was able 'to avoid immune system components' during an episode of 'silent bacteraemia'.^{24,36}

Table 3: The relationship between pre-existing conditions and location of *S. Paratyphi* infection

| Pre-existing condition/trauma | Further details of risk condition ^a | Location of infection ^a | Further details of infection | Reference |
|-------------------------------|--|------------------------------------|--|-----------|
| Immunosuppression | Diabetes | Breast | Breast abscess | 19 |
| Immunosuppression | ITP on steroids | Breast | Breast abscess | 20 |
| Immunosuppression | Type II DM - poorly controlled | Breast | Breast abscess | 24 |
| Immunosuppression | Renal failure | Skin/soft tissue | Necrotising fasciitis right lower limb | 35 |
| Immunosuppression | Long term methotrexate 5 mg prednisone daily Infliximab | Skin/soft tissue | Soft tissue left arm | 37 |
| Immunosuppression | Sickle cell disease | Bone/joint | Osteomyelitis - spondylitis | 29 |
| Immunosuppression (possible) | Pre-renal azotemia | Abdominal organ | Liver abscess | 35 |
| Immunosuppression > 65 years | 66 years old Diabetes | Bone/joint | Septic arthritis | 30 |
| Less than 12 months of age | 10 days old | CNS | Pyogenic meningitis | 11 |
| Less than 12 months of age | 10 days old Delivered at 36 weeks Foetal distress | CNS | Intracerebral abscess | 12 |
| Less than 12 months of age | 15 days old | CNS | Meningitis | 14 |
| Less than 12 months of age | 4 months old | CNS | Meningitis | 15 |
| Less than 12 months of age | 90 days old | CNS | Meningitis | 16 |
| Less than 12 months of age | 11 months old | CNS | Meningitis | 17 |
| Less than 12 months of age | 6 months old Meningitis 2 months prior | CNS | Subdural empyema | 18 |
| Less than 5 years of age | 13 months old | CNS | Bilateral subdural empyema | 13 |
| Less than 5 years of age | 2.5 years of age | Pleura | Pleural effusion | 46 |
| Liver condition | Probable amoebic liver abscess | Abdominal organ | Liver abscess | 32 |
| Liver condition > 65 years | 74 years old Liver cyst | Abdominal organ | Liver abscess | 34 |
| Pregnancy | 16 weeks pregnant | Neck | Neck abscess | 39 |
| Reproductive organ condition | Ovarian cyst or endometrioma | Reproductive | Ovarian abscess | 26 |
| Reproductive organ condition | Polycystic ovaries | Reproductive | Tuboovarian abscess | 27 |
| Trauma - flank | L flank injury due to MVA 4/12 ago with transient haematuria | Renal | Perinephric abscess | 42 |
| Trauma - head | MVA 2 years prior with burr hole for SDH 15/12 later had evacuation of chronic SDH | CNS & bone | Subdural empyema & osteomyelitis | 10 |
| Trauma - surgery | CABG 7/52 prior | Thoracic | Pericardial abscess | 43 |

^a Abbreviations used: ITP: idiopathic thrombocytopenic purpura; DM: diabetes mellitus; CNS: central nervous system; MVA: motor vehicle accident; SDH: subdural haematoma; CABG: coronary artery bypass graft.

Consideration should be given to the possibility of chronic carriage of *S. Paratyphi* in a household/travel contact which led to more recent transmission to the case. Unfortunately, the patient's wife and child were not tested. Whilst these alternate routes align with aspects of our case's history, due to the sparse details of their history, we are unable to draw definitive conclusions as to the origin of the infection.

The incubation periods for most cases presented in the articles reviewed were unable to be determined as they mostly lived in endemic areas, or it was not discussed. In many cases it was difficult to distinguish which symptoms related to the enteric illness and which related to the development of the abscess. However, one article described a case having symptom onset four weeks after returning from a trip to India.³⁴ In our case, the length of time from arrival in Australia to the onset of symptoms was nine weeks, well beyond the typical incubation period considered by many non-endemic countries.⁵¹ An article which discusses local cases from South-Eastern Sydney⁵² describes a case of *Salmonella* Typhi (*S. Typhi*) for which the onset was nine months after arrival from Saudi Arabia. They conclude that the infection is presumed to be overseas acquired; however, the authors do question whether the case may have been infected from an unidentified source in Australia.

This discussion highlights the challenge to public health of determining an incubation period which covers all case scenarios. Information from the case and literature review supports the notion that a longer incubation period should be considered, beyond the one to ten days stated by various national public health guidelines.^{53,54} The Public Health England Guidelines (2019), for example, have a longer 'working definition for travel related infection for public health investigation and management' of 28 days, developed from observed surveillance data.⁵³ Our case presented during a transition period before the current guidelines were approved in December 2016, and as such was managed according to the previous salmonellosis

guidelines, where screening of household contacts was not required.⁵ In the current guidelines, stool testing would have been undertaken to ensure that an unidentified chronic carrier was not the source of infection to the case, as the onset of symptoms was well beyond the accepted range for an episode of enteric fever to be considered 'travel related'.⁵¹

Differences in the case study presented, and in cases in the literature, from gut-based infections support a broader approach to public health management of extra-intestinal *S. Paratyphi*. The public health implications for cases with *S. Paratyphi* infection at aberrant sites were not discussed in the articles from the literature search. Additional measures such as management of household, travel and close contacts should be considered and instituted. The case and their household contacts, who may be involved in caring for the case and the wound, should be given advice on the precautions that should be taken, such as: covering the wound with a dressing; using gloves when touching the dressing or items that are at risk of contamination with wound exudate; and handwashing. When there is an active wound, consideration regarding exclusion of the case from high-risk occupations may be warranted. These conclusions can also be extended to the public health management of focal *S. Typhi* infections.

Limitations

We acknowledge that relevant articles may have been omitted from the literature review due to only including articles that were available free of charge and in the English language, and that omissions may have occurred where articles were indexed to refer to the enteric illness rather than the extra-intestinal infection or atypical presentations. Our interpretations were based on, in some cases, limited information provided by the author in the review literature. We were also reliant on the case providing a good clinical history, and assessment was made based on that history; however, recollection may have been impacted by the stress of recent migration to Australia.

Conclusion

S. Paratyphi presentation is generally as an enteric fever illness. Extra-intestinal occurrences are rare. While not questioning the risk-based approach of the CDNA guidelines, it would be beneficial for the guidelines to reflect consideration of longer incubation periods in these unusual circumstances. This would allow explanation of plausible time periods to encompass earlier overseas travel. Exploration of chronic carriers amongst close contacts should, however, still be carried out. Our case highlights that 'public health professionals must use their professional judgment when a case does not appear to be consistent with the rules'.¹³ This case illustrates the variable nature of infectious diseases and the importance of laboratory testing in obtaining a diagnosis, and the need to keep an open mind when investigating possible sources and assessing public health risk.

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Appendix A: Supplementary data

Table A.1: Summary of literature review canvassing extraintestinal infections of *S. Paratyphi A* or *B*

| Reference | Organism | Location of infection | Anatomical region/ structure | Country of acquisition | Pre-existing condition | Pre-existing condition details | Clinical details | Likely preceding enteric fever symptoms? | Length of time following illness to abscess symptoms |
|-----------|-----------------------|----------------------------------|---------------------------------|-------------------------|---------------------------|---|---|---|--|
| 9 | <i>S. Paratyphi A</i> | Meningitis | CNS | Assumed Qatar resident | — | Nil | 20 y/o M 5 day history of fever, severe headache, vomiting, neck pain, chills, decreased LOC BC and stool culture negative CSF – <i>S. Paratyphi A</i> | Unclear – fever and vomiting associated with neurological symptoms | N/A |
| 10 | <i>S. Paratyphi A</i> | Subdural empyema & osteomyelitis | CNS Bone/joint | Assumed Indian resident | Trauma – head trauma | MVA 2 years prior with burr hole for SDH 15/12 later had evacuation of chronic SDH | 42 y/o M Headache & purulent discharge from burr hole wound for 2/7 No enteric fever symptoms discussed Aspirated pus and bone fragments – <i>S. Paratyphi A</i> | Not discussed | N/A |
| 11 | <i>S. Paratyphi A</i> | Pyogenic meningitis | CNS | Pakistani resident | Less than 12 months | 10 day old neonate | 10 day M Diarrhoea & fever 2 days later developed seizures & vomiting BC & initial faeces negative CSF & faeces – <i>S. Paratyphi A</i> | Likely | 2 days |
| 12 | <i>S. Paratyphi B</i> | Intracerebral abscess | CNS | Pakistani resident | Less than 12 months | 10 day old neonate | 10 day F Cyanotic spells and respiratory distress following birth At 4 days of age developed diarrhoea, dehydration At 10 days of age developed hypertonia, peripherally shut down & seizures BC & CSF <i>S. paratyphi B</i> 4/52 after treatment for meningitis-parieto- occipital intracerebral abscess organism multi drug resistant Spinal and ventricular CSF – <i>S. Paratyphi B</i> | Likely | 6 days |

| Reference | Organism | Location of infection | Anatomical region/structure | Country of acquisition | Pre-existing condition | Pre-existing condition details | Clinical details | Likely preceding enteric fever symptoms? | Length of time following illness to abscess symptoms |
|-----------|-----------------------|----------------------------|-----------------------------|--------------------------|-------------------------|--------------------------------|---|--|--|
| 13 | <i>S. Paratyphi A</i> | Bilateral subdural empyema | CNS | Assumed Turkish resident | Less than 5 years old | 13 months old | 13 month F 4 days of irregular fever, poor feeding, irritability and vomiting BC and stool negative Aspirate fluid from brain – <i>S. Paratyphi A</i> | Unclear – fever and vomiting associated with neurological symptoms | N/A |
| 14 | <i>S. Paratyphi A</i> | Meningitis | CNS | Assumed Turkish resident | Less than 12 months old | 15 day neonate | 15 day old M Fever 39C Urine and stool negative BCS. <i>Paratyphi A</i> CSF <i>S. Paratyphi A</i> Relapse of illness approx 4 weeks later CSF <i>S. Paratyphi A</i> | Unclear – fever associated with neurological symptoms | N/A |
| 15 | <i>S. Paratyphi B</i> | Meningitis | CNS | Assumed Malay resident | Less than 12 months old | 4 months old | 4 month old M Fever Subdural effusions CSF – <i>S. Paratyphi B</i> | Insufficient details provided | N/A |
| 16 | <i>S. Paratyphi B</i> | Meningitis | CNS | Assumed Indian resident | Less than 12 months old | 90 days old | 90 day old M 2 days of fever, 1 episode of vomiting, 1 episode of vacant stare for 5 minutes, bulging anterior fontanelle, lethargy BC and CSF – <i>S. Paratyphi B</i> | Unclear if fever and vomiting commenced before neurological symptoms | Unclear (1 day?) |
| 17 | <i>S. Paratyphi B</i> | Meningitis | CNS | Indian resident | Less than 12 months | 11 months old | 11 month old M Intermittent fevers from previous week, gradually becoming lethargic, irritable, decreased intake. Sudden onset of vomiting with generalised convulsion Bulging fontanelle, marked neck stiffness, decreased reflexes CSF – <i>S. Paratyphi B</i> | Likely | 1 week |

| Reference | Organism | Location of infection | Anatomical region/ structure | Country of acquisition | Pre-existing condition | Pre-existing condition details | Clinical details | Likely preceding enteric fever symptoms? | Length of time following illness to abscess symptoms |
|-----------|-----------------------|-----------------------------|---------------------------------|-------------------------|--|--|---|--|--|
| 18 | <i>S. Paratyphi B</i> | L Subdural empyema | CNS | Assumed Indian resident | Less than 12 months old Recent CNS infection | 6 month infant Meningitis 2 months prior | 6 month old M 2 weeks prolonged fever and enlarging head, bulging fontanelle, extensor posturing, unequal pupils, pus drained from burr hole Pus – <i>S. Paratyphi B</i> | No | N/A |
| 19 | <i>S. Paratyphi A</i> | Breast abscess | Breast | Assumed Indian resident | — | Not discussed | 27 y/o F 2 month painful lump in L breast Stool, urine & BC negative Pus drained – <i>S. Paratyphi A</i> | Yes | 3 months |
| 19 | <i>S. Paratyphi A</i> | Breast abscess | Breast | Assumed Indian resident | Immuno-suppression | Not discussed | 29 y/o F 20 day history of lump in L breast BC negative Pus drained – <i>S. Paratyphi A</i> | Unable to be determined | N/A |
| 20 | <i>S. Paratyphi A</i> | Breast abscess | Breast | Assumed Indian resident | Immunosuppression | ITP on steroids | 35 y/o F 3 week duration of lump L breast No history of pain, fever, trauma BC negative Pus culture – <i>S. Paratyphi A</i> | Unable to be determined | N/A |
| 21 | <i>S. Paratyphi A</i> | Breast (multiple abscesses) | Breast | Travel to Bangladesh | — | Well | 33 y/o F 2/12 prior fevers & rigors No subsequent systemic Sx Dec 2009 painful lump Core needle biopsy of two lesions revealed granulomatous mastitis and fibroadenoma Over next 4/12, experienced two further episodes of painful breast Was prescribed antibiotic with no improvement — repeat surgical review — pus aspirated Pus aspirated from breast collections on a further 6 occasions Abdo u/s & stool culture NAD Pus from breast — <i>S. Paratyphi A</i> | Likely | 2 months |

| Reference | Organism | Location of infection | Anatomical region/ structure | Country of acquisition | Pre-existing condition | Pre-existing condition details | Clinical details | Likely preceding enteric fever symptoms? | Length of time following illness to abscess symptoms |
|-----------|----------------|-----------------------|---------------------------------|---------------------------------|---------------------------------|--|--|--|--|
| 22 | S. Paratyphi A | Breast abscess | Breast | Assumed Indian resident | — | well | 31 y/o F R breast lump past 2 years Pain for 15/7 Discharge for 2–3/7 BC negative No history of recent fever Pus x 2 – S. Paratyphi A | No | N/A |
| 23 | S. Paratyphi A | Breast abscess | Breast | Assumed Indian resident | — | None | 33 y/o F 2yr lump in R breast 15/7 pain in lump 2–3/7 discharge No past history suggestive of enteric fever BC NAD Pus – S. Paratyphi A | No | N/A |
| 24 | S. Paratyphi A | Breast abscess | Breast | Assumed Indian resident | Immunosuppression | Type II DM – poor control | 37 y/o F 15/7 Intermittent fevers & pain in R breast 4/7 noticed lump in R breast Abdo u/s hepatomegaly BC negative Pus samples x 2 – S. Paratyphi A | “...history of intermittent fever suggestive...” | 11 days |
| 25 | S. Paratyphi A | R testicular abscess | Reproductive | Indian resident | — | Well | 63 y/o M 1/52 progressive R testicle swelling pain, dysuria, low grade fever No GI symptoms mentioned Urine culture negative No stool culture or GB u/s done Abscess pus – S. Paratyphi A | No | N/A |
| 26 | S. Paratyphi A | Ovarian abscess | Reproductive | Travel to Vietnam & Cambodia | Reproductive organ condition | Previously well ovarian cyst or endometrioma | 29 y/o F 3/52 intermittent fevers, abdo discomfort & assoc. diarrhoea RIF tenderness BC & stool INAD Abscess fluid – S. Paratyphi A | Yes | 3 weeks |

| Reference | Organism | Location of infection | Anatomical region/ structure | Country of acquisition | Pre-existing condition | Pre-existing condition details | Clinical details | Likely preceding enteric fever symptoms? | Length of time following illness to abscess symptoms |
|-----------|-----------------------|-------------------------------|---------------------------------|---|--|--|---|--|--|
| 27 | <i>S. Paratyphi A</i> | Tuboovarian abscess | Reproductive | Assumed Indian resident | Reproductive organ condition | Polycystic ovaries | 36 y/o F Intermittent fevers for 7/12 BC & stool cultures negative Pus – <i>S. Paratyphi A</i> | Likely | 7 months |
| 28 | <i>S. Paratyphi A</i> | Testicular abscess | Reproductive | Assumed Pakistani resident | — | Not discussed | 5 y/o M 2/52 R testicular swelling No urinary Sx No fevers, chills, vomiting or loss of appetite Normal bowel habits Urine culture NAD Pus from abscess – <i>S. Paratyphi A</i> | No | N/A |
| 29 | <i>S. Paratyphi B</i> | Osteomyelitis – spondylitis | Bone/joint | Assumed Turkish resident | Immunosuppression | Sickle cell disease | 5 y/o M 1/12 of back pain, difficulty in walking, kyphosis BC and stool negative Operative bone fragments – <i>S. Paratyphi B</i> | No | N/A |
| 30 | <i>S. Paratyphi B</i> | Septic arthritis | Bone/joint | Assumed UK resident Travel not discussed | Immunosuppression Over 65 years old | 66 years old Diabetic on oral hypoglycaemics | 66 y/o F 2 month history of R sided groin and buttock pain following a perforated duodenal ulcer BC, urine and stool cultures all negative Washout of R hip – <i>S. Paratyphi B</i> | Duodenal ulcer only No evidence of gastrointestinal disturbance Author unable to determine source of infection | N/A |
| 31 | <i>S. Paratyphi A</i> | Psoas abscess & osteomyelitis | Muscle Bone/joint | Assumed Indian resident | — | None | 21 y/o F 2/52 high intermittent fevers & chills 7/7 recurrence of fever 2/7 painful restriction of movement L hip radiating L leg Normal examination for other systems BC & abscess fluid – <i>S. Paratyphi A</i> | Likely | 3 weeks |

| Reference | Organism | Location of infection | Anatomical region/ structure | Country of acquisition | Pre-existing condition | Pre-existing condition details | Clinical details | Likely preceding enteric fever symptoms? | Length of time following illness to abscess symptoms |
|-----------|-----------------------|---------------------------------------|----------------------------------|--|--------------------------------------|-----------------------------------|---|--|--|
| 32 | <i>S. Paratyphi A</i> | Liver abscess | Abdomen | Arrived in UK from India 3 weeks prior | Liver condition | Probable amoebic liver abscess | 23 y/o M 8/7 abdominal pain & fevers Watery diarrhoea & vomiting day before admission & subsequent constipation No Hx of GI disturbance prior Abscess fluid – <i>S. Paratyphi A</i> | Likely | 1 day |
| 33 | <i>S. Paratyphi A</i> | Liver | Abdomen | Likely acquired from Pakistan | — | Previously well | 25 y/o M 5/7 fever, sweating, R upper abdo pain, vomiting & diarrhoea BC <i>S. Paratyphi A</i> Stool negative FNA – <i>S. Paratyphi A</i> | Yes | 5 days |
| 34 | <i>S. Paratyphi A</i> | Liver abscess | Abdomen | 3/12 stay in India | Liver condition Over 65 years old | Liver cyst 74 years old | 74 y/o M 4/52 following return from travel Daily episodes of fever and night sweats BC <i>S. Paratyphi A</i> Liver abscess fluid – <i>S. Paratyphi A</i> | Likely | Unknown |
| 35 | <i>S. Paratyphi A</i> | Necrotising fasciitis R lower limb | Soft tissue (other than neck) | Assumed Indian resident | Immunosuppression | Renal failure | Male Not discussed Purulent aspirate from skin and soft tissue – <i>S. Paratyphi A</i> | No | N/A |
| 35 | <i>S. Paratyphi A</i> | Splenic abscess | Abdomen | Assumed Indian resident | — | None | Not discussed Purulent aspirate from spleen – <i>S. Paratyphi A</i> | No | N/A |
| 35 | <i>S. Paratyphi A</i> | Liver abscess | Abdomen | Assumed Indian resident | Immunosuppression | Pre-renal azotemia | Not discussed Purulent aspirate from liver – <i>S. Paratyphi A</i> | No | N/A |
| 36 | <i>S. Paratyphi A</i> | Perianal abscess | Anus | Assumed Indian resident | — | Not discussed | 55 y/o M 5–7 day history of pus and swelling from perianal region, fever BC negative Stool <i>S. Paratyphi A</i> Pus from abscess – <i>S. Paratyphi A</i> | Unclear | N/A |

| Reference | Organism | Location of infection | Anatomical region/ structure | Country of acquisition | Pre-existing condition | Pre-existing condition details | Clinical details | Likely preceding enteric fever symptoms? | Length of time following illness to abscess symptoms |
|-----------|-----------------------|-----------------------------|-------------------------------------|----------------------------|---------------------------|-----------------------------------|--|--|--|
| 37 | <i>S. Paratyphi A</i> | Soft tissue infection L arm | Soft tissue (other than neck) | History of travel to India | Immuno-suppression | Long-term immuno- suppressants | 54 y/o M Acute gastro during travel with complete resolution after 3/7 of rifamixin 3/52 later developed sweating, cough & intermittent fevers Abdo u/s cholelithiasis Stool culture MAD BC x 4 <i>S. Paratyphi A</i> Skin biopsy <i>S. Paratyphi A</i> | Yes | 3 weeks |
| 38 | <i>S. Paratyphi A</i> | Neck abscess | Neck | Assumed Indian resident | — | Well HIV negative | 22 y/o M 7/7 painful swelling R neck Febrile Gross cellulitis Stool BC & urine MAD 'No classic presentation of enteric fever' Aspirate – <i>S. Paratyphi A</i> | No | N/A |
| 39 | <i>S. Paratyphi A</i> | Neck | Neck | Assumed Israeli resident | Pregnancy | Pregnant | 25 y/o F 2/52 earlier sore throat febrile L neck swelling & pain L IJ vein thrombosis u/s GB NAD BC NAD No GI Sx mentioned Thought to be through tonsillar tissue Samples from neck abscess – <i>S. Paratyphi A</i> | No | N/A |
| 40 | <i>S. Paratyphi A</i> | Splenic abscess | Abdomen | Assumed Indian resident | — | Not discussed | 8 y/o M 15/7 fever 5/7 upper L abdo pain Typhoid 3 years ago BC no growth No gastro symptoms mentioned Aspirate – <i>S. Paratyphi A</i> | Likely | 10 days |

| Reference | Organism | Location of infection | Anatomical region/ structure | Country of acquisition | Pre-existing condition | Pre-existing condition details | Clinical details | Likely preceding enteric fever symptoms? | Length of time following illness to abscess symptoms |
|-----------|-----------------------|-----------------------|---------------------------------|-------------------------------|---------------------------|--|---|---|--|
| 41 | <i>S. Paratyphi A</i> | Renal abscess | Abdomen | Assumed Indian resident | — | Previously well HIV negative | 17 y/o M 15/7 L flank pain & fever No V or D or dysuria Urine & BC NAD Aspirate – <i>S. Paratyphi A</i> | Unlikely – fever associated with L flank pain | N/A |
| 42 | <i>S. Paratyphi A</i> | Perinephric abscess | Abdomen | Assumed Indian resident | Trauma – flank | L flank injury due to MVA 4/12 previously with transient haematuria | 35 y/o M 10/7 worsening L loin pain & high fevers no fever, chills or bowel symptoms after accident No UTI or haematuria ever in the past CT showed # 10th rib with large perinephric haematoma /abscess causing displacement and compression of L kidney Drainage of collection – <i>S. Paratyphi A</i> | No | N/A |
| 43 | <i>S. Paratyphi B</i> | Pericardial abscess | Cardiothoracic | Assumed Pakistani resident | Surgery | CABG 7/52 prior | 45 y/o F 2/52 intermittent fevers Severe R chest pain No GI symptoms documented BC negative Abscess wall – <i>S. Paratyphi B</i> | Speculated as likely | ? |
| 44 | <i>S. Paratyphi A</i> | Parietal wall abscess | Abdomen | Assumed Indian resident | — | Not discussed | No other information provided <i>S. Paratyphi A</i> isolated from a parietal wall abscess | Not discussed | N/A |
| 45 | <i>S. Paratyphi A</i> | Thyroid abscess | Neck | Assumed Indian resident | — | None | Not “...suspected of having salmonella etiology until culture of the surgically obtained specimen was performed” No other information provided Abscess – <i>S. paratyphi A</i> | Unlikely | N/A |
| 46 | <i>S. Paratyphi A</i> | Pleural effusion | Cardiothoracic | Indian resident | Less than 5 years old | 2.5 years old Previously well | 2.5 y/o M 1 month of abdominal pain, loose stools, fever, chills & rigors for 1 week, peripheral oedema, oliguria, & mild jaundice Urine and Stool NAD BC and pleural fluid – <i>S. Paratyphi A</i> | Yes | 1 month |

a Not stated but speculated to have been in the immediate post operative period.