Salmonella meningitis and septicaemia in a non-immunocompromised adult, associated with a cluster of *Salmonella* Enteritidis PT 14b, Ireland, November 2009

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Citation style for this article:

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This article has been published on 18 February 2010

We report a fatal case of meningitis caused by *Salmonella* Enteritidis phage type 14b in a middle-aged man who had no history or findings to suggest he was immunocompromised. To our knowledge, this is the first reported case of *Salmonella* meningitis in an adult in Ireland, and the first case of meningitis in an adult caused by phage type 14b. This case was associated with a nationwide cluster of salmonellosis which is still under investigation at the time of writing.

Introduction

Salmonella infection is recognised as a common cause of gastroenteritis which can result in large outbreaks [1]. Acute bacterial meningitis is a rare manifestation of *Salmonella* infection, and when it does occur, it is most commonly a disease of infants [2,3]. In adults, *Salmonella* meningitis, although rare, is most commonly seen in patients with impaired immunity, particularly in infection with human immunodeficiency virus (HIV) [4,5].

In this report, we describe a case of a non-immunocompromised adult with *Salmonella* Enteritidis meningitis and severe sepsis, with a rapid onset and a fatal outcome, that occurred in Dublin in November 2009.

This case is one of a cluster of at least 15 cases of *Salmonella* Enteritidis phage type 14b infection in Ireland that started in October 2009 [6; Health Protection Surveillance Centre, personal communication]. This variant has also been implicated in over 443 cases, including 14 outbreaks, in the United Kingdom since August 2009 [7,8].

Case description

The patient was a man in his late 40s who had a stable chronic mental illness and lived in a community psychiatric hostel in an urban area, supervised by 24-hour nursing staff. His regular medications included clozapine, amisulpride and valproate. Regular blood tests

for potential side effects such as agranulocytosis did not show any abnormalities. He was a regular smoker. There was no abuse of alcohol or intravenous drugs and no known risk factors for HIV infection.

The patient woke in the early morning hours with a headache, which was relieved by treatment with 1 g paracetamol. After a quiet night he was found agitated and feverish six hours later. He was seen by a doctor and, due to rapid deterioration, was transferred by ambulance to the nearby acute hospital as an emergency with a seven-hour history of headache and a two-hour history of fever (38.5 °C), rigors, inability to stand and progressive reduction in level of consciousness. He was admitted to the intensive care unit on the same day.

On admission, a lumbar puncture revealed turbid cerebrospinal fluid, with a milky-brown colour. Three samples of cerebrospinal fluid (CSF) were taken at the time of admission. All of them showed a white blood cell count of >5,000 and a red blood cell count of zero. Microscopy of the CSF, performed urgently, showed abundant Gram-negative bacilli. A blood sample taken on admission showed a leukocyte count of $8.97 \times 10^9/L$, with a neutrophil count of $8.13 \times 10^9/L$. Plasma urea, electrolytes, liver enzymes, total protein and albumin concentration were all within the normal range at that time.

A progressive neutrophilia was documented, with a count of $17.73 \times 10^9/L$ on day 2, rising to $31.61 \times 10^9/L$ on day 4 of hospitalisation. The patient developed acute renal failure on day 2 of hospitalisation.

The patient received one dose of 2 g cefotaxime and 2.4 g benzylpenicillin in the emergency department. After Gram-negative organisms were identified in the CSF samples taken on admission, this treatment was discontinued and the patient received 2 g meropenem

three times a day and 1 g vancomycin twice a day for the following three days. On day 4 of hospitalisation, cultures from the CSF samples and a series of three blood samples taken on the day of admission grew *Salmonella* sensitive to cefotaxime, and the patient's treatment was changed to 1 g cefotaxime every four hours.

In view of known association between *Salmonella* meningitis in adults and immunodeficiency, and despite the absence of risk factors, the patient was tested on day 5 for HIV, hepatitis B virus and hepatitis C virus infections, all of which were negative. Nor were there any incidental clinical signs, radiographic or laboratory findings to suggest underlying malignancy or opportunistic infection.

Despite treatment with appropriate antibiotics and interventions to support failing organ systems, he deteriorated and died five days after admission. The final *post mortem* report was not available at the time of writing this report.

Environmental investigation

In view of the fatal outcome, and despite the fact that no staff member or resident at the hostel had a history of gastroenteritis, stool samples from staff and fellow residents were obtained as part of the public health investigation. In addition to testing samples of food, eggshells and water from the hostel, other food premises where the patient was known or thought to have eaten were inspected, foods sampled and distribution chains traced. Particular attention was paid to foods containing chicken, eggs or egg products of any kind. None of the dozens of stool or food samples grew *Salmonella*.

The *Salmonella* species involved was nalidixic acid-resistant *Salmonella* Enteritidis phage type 14b. The same phage type has been identified in a cluster of cases notified to Irish departments of public health since November 2009, all of whom had gastro-enteritis alone and made a full recovery [6]. As with the above case, meticulous tracing of relevant foods through the distribution chains was and is being conducted for all cases, but to date the source of infection has not been identified.

Discussion

Human *Salmonella* infection is categorised into four manifestations: enteric infections, sepsis, non-enteric focal infections (including meningitis) and a chronic carrier state [3]. Bacterial meningitis is characterised by acute onset of fever, headache and one of the following signs: neck stiffness, altered consciousness or other meningeal signs [9].

The first case of *Salmonella* meningitis in the literature was reported in 1907 by Ghon [10]. In a study of 7,779 infections identified at the New York *Salmonella* Centre, meningitis accounted for only 0.8% [3]. In

adults, *Salmonella* meningitis is most commonly seen in patients with intercurrent illness [11,12], including particularly immunosuppression associated with HIV [4,5].

Irish legislation requires doctors to send notifications of infectious diseases, including *Salmonella* infections, to medical officers of health in regional public health departments. Notification of bacterial meningitis from any cause must also be given. These data are collated at the national level by the Health Protection Surveillance Centre (HPSC). In a review of national data for the ten-year period from 2000 to 2009, the number of notifications of bacterial meningitis in Ireland was 1,229 and the number of notifications of *Salmonella* infection was 4,395, including 88 cases of typhoid and/or paratyphoid. The data from this period include only one case of *Salmonella* meningitis, a three-week-old baby with S. Dublin (medical officer of health, personal communication). Before this period, Foley *et al.* published in 1980 one series of three cases of childhood *Salmonella* meningitis in Ireland; all were infants [13].

Of all *Salmonella* infections listed in 2008 in the database of enteric infections collected by Enter-net, the European surveillance network for human gastrointestinal infections, *Salmonella* Enteritidis was by far the most common serotype, while S. Typhi, Oranienburg, Paratyphi and Berta were not listed among the top ten [14]. However, the European literature includes only two previous case reports of adults with meningitis due to *Salmonella* Enteritidis, one of whom was immunocompromised [15,16]. Other cases of *Salmonella* meningitis in adults previously reported in the literature have involved a diversity of serotypes, including at least 19 cases of S. Typhi [17-22], two cases of S. Typhimurium [18,11], and one case each of S. Oranienburg [23], S. Virchow [24], S. Paratyphi [21] and S. Berta [25].

The case described here is the only notified case of *Salmonella* meningitis in an adult in Ireland in the last ten years, and the first published adult case in Ireland. Kauffman *et al.* reported that *Salmonella* meningitis, arising in association with a variety of serotypes, may present without preceding symptoms of gastroenteritis [11], as was also true in our case.

There were no clinical signs, laboratory or radiographic findings to suggest a compromised immune system in this case. While agranulocytosis is a recognised adverse effect of clozapine, the fact that the patient's white blood cell count was monitored regularly and that he developed a marked neutrophilia indicates that this was not a factor.

Conclusion

We describe the first reported case of *Salmonella* meningitis in an adult in Ireland, who was not immunocompromised. The association of this fatal case with a phage type that has also been implicated in a large

number of sporadic cases and several recent outbreaks in the United Kingdom indicates the need for continuing vigilance in terms of surveillance and investigation to reduce the risk of further such infections with *Salmonella* Enteritidis PT 14b.

Acknowledgements

We would like to thank the Departments of Public Health, the Department of Microbiology, Department of Intensive Care Medicine and other staff at Mater Misericordiae University Hospital, the National *Salmonella* Reference Laboratory, Environmental Health Officers of the Communicable Diseases Unit and regional offices, the Food Safety Authority of Ireland and the Health Protection Surveillance Centre for their assistance.

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