

Case Report

Recurrent Non Typhoidal *Salmonella* infection of the thyroglossal duct cyst in a diabetic patient - A Case Report

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Abstract

The occurrence of extra-intestinal *Salmonella* neck infections is uncommon, especially with non-typhoidal *Salmonella* (NTS). We report a case of non-typhoidal *Salmonella* infection of a thyroglossal cyst in a 78-year-old diabetic woman admitted with gastroenteritis along with a neck swelling. The ultrasound revealed a thyroglossal cyst and fine needle aspiration cytology (FNAC) was done. Culture of the aspirate grew *Salmonella* species *enterica* subspecies *enterica* serogroup C. The patient was treated with amoxicillin/clavulanic acid for 10 days on discharge. She was readmitted two months later with an increasing neck mass and FNAC was repeated. Culture of the aspirate grew *Salmonella* species *enterica* subspecies *enterica* serogroup C. She was treated with amoxicillin/clavulanic acid for 5 days on discharge. Extra-intestinal infections, though uncommon, should be considered among immune-compromised patients presenting with gastrointestinal symptoms caused by *Salmonella* species.

Keywords: *Salmonella* neck infection, thyroglossal duct cyst, extra-intestinal infection, non-typhoidal *Salmonella*

Introduction

Salmonella is a non-sporulating, Gram-negative, facultative anaerobic bacteria which belongs to the family Enterobacterales.¹ Within the two species of *Salmonella*, namely *Salmonella bongori* and *Salmonella enterica*, there are over 2500 different serotypes. In 2017, it was estimated that *Salmonella* enterocolitis resulted in 95.1 million cases, 50,771 deaths, and 3.10 million disability-adjusted life-years (DALYs) according to the global burden of diseases, injuries, and risk factors study (GBD).²

Non-typhoidal *Salmonella* (NTS) are most frequently encountered in self-limiting diarrhoea and, to a lesser extent, in urine. NTS can also cause serious life-threatening infections such as invasive

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blood stream infections, meningitis, and may infect other normally sterile sites.^{3,4,5} The case fatality rate for non-typhoidal salmonellosis has decreased from 10-30% to 1-4% with appropriate antibiotic treatment. However, nearly 80% of deaths occur in Asia, Africa, and Latin America.⁶ Though the incidence of non-typhoid salmonellosis is estimated to be over 2 million cases annually, extra-intestinal manifestations account for less than 1% of cases, with infection of the neck region an uncommon site of focal extra-intestinal infection.⁷

Embryonically, the first, second and third embryonic pharyngeal pouches give rise to the tonsils, thymus, parathyroid glands, and parafollicular thyroid cells, as well as the middle ear canal and eustachian tube. The thyroglossal duct serves as the path of descent of the thyroid primordium from the foramen cecum which is located at the junction of the anterior two-thirds and posterior third of the tongue, down to the thyroid cartilage where it develops into the thyroid. The inferior portion of the thyroglossal duct may develop into the pyramidal lobe and the remainder involutes by the 10th week of gestation. The duct is usually obliterated by the 10th week of gestation. However, if any part of the duct remains after the 10th week, it forms a thyroglossal duct cyst. Common among the congenital cervical abnormalities is the thyroglossal cyst, with a population prevalence of 7%. It can occur anywhere from the base of the tongue to the inferior neck during development. Cysts seen in the midline are suprahyoid thyroglossal duct cysts, while infrahyoid thyroglossal duct cysts may be para-midline.^{8,9,10}

Case Report

A 78-year-old woman presented to the accident and emergency department with diarrhoea and vomiting of 5 days duration. She had loose stools of more than 10 episodes per day with occasional vomiting which was associated with upper abdomen pain. The patient denied any history of fever or blood in her stools. There was no relevant travel history or close contact, but she admitted to occasionally eating at restaurants. She was a known non-insulin dependent diabetic and hypertensive patient, both under control with medication.

On presentation to the Accident and Emergency department, the patient was found to be alert, oriented, mildly lethargic but otherwise comfortable. Systemic examination was within normal parameters. Blood biochemistry revealed a slightly elevated hemoglobin A1C of 7.1% (normal <6.0%). C-reactive protein was elevated at 8.52 mg/dL (normal ≤0.3 mg/dL) with normal white blood cell count of 7,700/uL (normal 4.2-12.0 × 10³/uL) and 59.1% neutrophils. She had mild hypokalemia of 3.4 mmol/L (normal 3.5-5.1 mmol/L) with elevated serum creatinine 17.78 mg/dl (normal 0.6-1.1 mg/dl) indicating severe acute kidney injury (AKI) following dehydration leading to hypovolemia. A raised troponin of 60.9 ng/L (normal 0-40 ng/L) too was most likely due to secondary hypovolemia and AKI. A diagnosis of acute gastroenteritis with invasive infection was proposed and the patient started on intravenous (IV) meropenem 1g eight hourly after obtaining blood and stool for culture and sensitivity.

On the second day of admission, the patient complained of increasing pain while swallowing and a neck mass along the upper neck region. The patient was referred to otolaryngology. On examination, the mass was found to be soft and non-tender with normal overlying skin at the level of the hyoid and noted to move with the protrusion of the tongue. The diagnosis of thyroglossal cyst was confirmed by ultrasound imaging. This mass was an irregular cystic lesion in the midline

of the neck superior to the thyroid measuring 2.9 x 2.5 x 2.1 cm. This acute enlargement was thought to be due to infection. Hence an ultrasound guided FNAC was performed and around 8 ml of cystic fluid was aspirated aseptically for culture and sensitivity.

The blood culture taken on the day of admission was negative after 5 days of incubation. Interestingly, both stool and cyst fluid cultures (from the neck lesion) grew non-hemolytic moist non-lactose fermenting colonies. *Salmonella* species *enterica* subspecies *enterica* serogroup C was identified and confirmed with VITEK MS (Biomerieux SA, France), Vitek 2 XL (Biomerieux SA, France) and serogrouping (Serotest, S&A Reagents Lab, Thailand) from both stool and cystic fluid cultures. Antibiotic susceptibility patterns for stool and cystic fluid were similar with both susceptible to ampicillin, ceftriaxone, trimethoprim–sulfamethoxazole, ciprofloxacin, chloramphenicol, and azithromycin. The patient was then switched to intravenous (IV) ceftriaxone 2g twenty four hourly for five days.

The patient's condition gradually improved with reduced inflammatory markers during hospitalisation and the patient was deemed fit for discharge on oral amoxicillin/clavulanic acid 625mg eight hourly for ten days. The patient's neck swelling was still persistent and upon discharge the patient was advised to have an otolaryngology follow-up regarding further management of her thyroglossal cyst.

Two months later the patient came to the accident and emergency department again with complaints of an increased neck mass and pain while swallowing for the past two days. However, the patient had no gastrointestinal symptoms. While systemic examination of the patient was found to be within normal limits, local examination of the neck revealed a soft, non-tender swelling with normal overlying skin. Given the previous history of an infected thyroglossal cyst an emergency ultrasound was conducted. The ultrasound revealed an irregular cystic lesion with septations measuring 4.2 x 3.9 x 4.1 cm

The patient's inflammatory markers were raised, with a C-reactive protein of 17.38 mg/dL (normal ≤ 0.3 mg/dL) and white blood cell count of 16,600/uL (normal $4.2-12.6 \times 10^3$ /uL) with 79.1% neutrophils. Based on this, a diagnosis of an infected thyroglossal cyst was made. The patient was started on intravenous (IV) amoxicillin/clavulanic acid 1.2g eight hourly for five days on the day of admission. An USG guided FNAC under local anaesthesia was done the following day and 15mL cystic fluid aspirated and sent for culture and sensitivity. *Salmonella* species *enterica* subspecies *enterica* serogroup C was isolated from the cystic fluid and confirmed by VITEK MS (Biomerieux SA, France), Vitek 2 XL (Biomerieux SA, France) and serogrouping (Serotest, S&A Reagents Lab, Thailand). Antibiotic susceptibility with Vitek 2 XL (Biomerieux SA, France) and Kirby Bauer Disk Diffusion (Oxoid Thermofisher, UK) was done. The isolate was susceptible to ampicillin, ciprofloxacin, trimethoprim-sulfamethoxazole, ceftriaxone, chloramphenicol, and azithromycin, a similar antibiotic susceptibility pattern to the previous isolate. The swelling reduced on the fourth day of admission and the patient's general condition improved with reduced inflammatory markers: white blood cell count of 8,500/uL (normal $4.2-12.6 \times 10^3$ /uL) and 67.4% neutrophils. The patient was discharged on oral amoxicillin/clavulanic acid 625 mg twelve hourly for five days. Review and further management of the thyroglossal cyst on a later date with otolaryngology was advised.

The patient did not have any further clinical incidents following this second episode. She was reviewed after 18 months with an ultrasound scan which revealed an irregular cystic lesion in the midline of her neck with an internal echo measuring 3.0 x 1.4 x 2.1cm confirming the thyroglossal cyst. FNAC was performed by aspirating a minimal quantity of thick fluid, which did not grow any organisms. Considering her age and absence of any further infection, surgery was excluded. The timeline of her illness is shown in Figure 1.

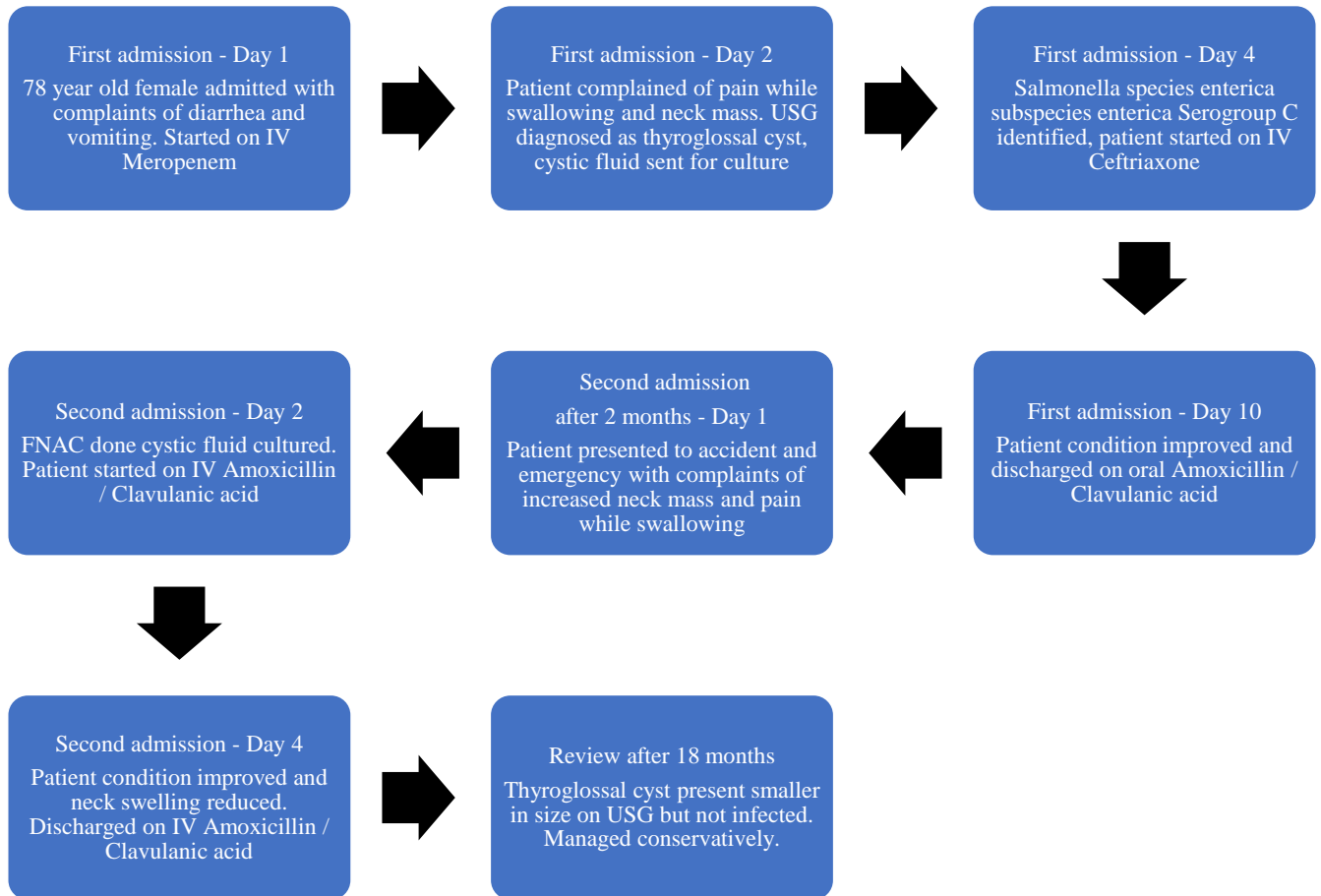


Figure 1. Timeline of illness

Discussion

Salmonella enterica contains six subspecies, with almost all strains belonging to *S. enterica* subspecies *enterica*. Further classification into serogroups can be done with surface O antigens, with additional flagellar H antigen and biochemical tests. *Salmonella* serogroup C is subdivided into groups C1 (presence of O: 6,7 antigen) and C2 (presence of O: 6,8 antigen). *Salmonella* group C1 serovar Paratyphi C can be detected with the Vi capsule¹¹. Clinical presentations vary with *salmonella* infections. Our patient had diarrhoea and vomiting. According to a study by Bedada teshome et al. (2019), salmonellosis manifests with symptoms such as diarrhoea, fever, vomiting,

and abdominal cramps after 12–72 h of infection. The infection can be more serious in those with debilitated illnesses, infants, and elders.¹²

In this patient, the organism was identified as *Salmonella* species *enterica* subspecies *enterica* serogroup C by both VITEK MS (Biomérieux SA, France), Vitek 2 XL (Biomérieux SA, France) and serogrouping (Serotest, S&A Reagents Lab, Thailand). Studies have shown that identification using both systems are comparable.^{13,14} The route of infection is usually through the gastrointestinal tract. Subsequent blood stream invasion with distal infection sites can present even after an acute gastrointestinal illness and remote abscesses may occur because of haematogenous or lymphatic dissemination of primary gastrointestinal tract infections. However, given that this patient's blood culture was negative, with stool culture growing *Salmonella* species *enterica* subspecies *enterica* serogroup C, the exact mode of spread was uncertain, showing that a negative blood culture should not rule out potential spread of infection to other sites.^{11,15} The 78-year-old patient was diabetic, which could be a possible contributing factor for extra-intestinal focal spread to the thyroglossal cyst. A study by Chen et al. (2007), showed that extra-intestinal focal infections occurred more frequently in patients with diabetes and hypertension.¹⁶

Salmonella species *enterica* subspecies *enterica* serogroup C isolated from the diarrhoeal source and both the isolates from the thyroglossal duct cyst were susceptible to ampicillin, ciprofloxacin, trimethoprim-sulfamethoxazole recommended for intestinal infections. Since the isolates from the thyroglossal duct cyst were from extraintestinal source the following antibiotics ceftriaxone, chloramphenicol, and azithromycin, recommended for extra-intestinal infections were also tested according to CLSI 2021 guidelines, and the isolates were found to be susceptible to all the antibiotics tested.¹⁷

Aspiration, surgical drainage, and removal of the cyst with appropriate antibiotics are needed for treatment of an abscess. Examination of the thyroglossal cyst aspirate allows for identification of the commonly involved organisms such as *Staphylococcus epidermis*, *Haemophilus influenzae*, and *Staphylococcus aureus*. A cytologic analysis should be conducted to rule out an underlying thyroglossal duct cyst carcinoma.^{18,19}

Given that the patient's blood culture was negative for *Salmonella* which was isolated from stool and cystic fluid highlights a possible spread of infection even without haematogenous involvement to extra-intestinal sites. The patient presenting for the second time with the same infection of the thyroglossal cyst without any obvious gastrointestinal symptoms may be due to the inadequate duration of treatment of the residual preliminary infection in a remote site.

To the best of our knowledge this is a rare case of extra-intestinal infection of the thyroglossal duct by a non-typhoidal salmonella species, namely *Salmonella* species *enterica* subspecies *enterica* serogroup C.

Take home message:

Extra-intestinal non typhoidal *Salmonella* infections in remote sites should be actively looked for with or without preceding gastrointestinal symptoms.

Declarations

Conflicts of Interest: None

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Ethics statement: Verbal consent obtained.

Authors' contributions: All the authors have contributed to collecting information on patient history, laboratory test results and preparation of manuscript.

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