Salmonella enterica subspecies *enterica* serotype Typhimurium induced pyelonephritis and suspected multifocal myositis in a cat

Remon Wilson[1] iD **and Vanessa R Barrs**[2,3] iD

Abstract

Case summary A 2-year-old male neutered domestic shorthair cat presented with an acute onset of muscular pain, ataxia and fever. Serological tests for *Toxoplasma gondii* IgM and IgG, cryptococcal antigen, feline immune deficiency virus antibody and feline leukaemia virus antigen were all negative. Brain and spinal MRI showed evidence of myositis and bilateral renal parenchymal abnormalities and pyelectasis. *Salmonella enterica* subspecies *enterica* serotype Typhimurium 1,4, [5],12:i:1,2 was isolated from urine and was susceptible to amoxycillin, amoxycillin–clavulanic acid, enrofloxacin and trimethoprim–sulfonamide. All clinical signs resolved after a 2-week treatment course with oral amoxycillin–clavulanate. A repeat urine culture 7 days after completing the antimicrobial course was negative.

Relevance and novel information Infection with *Salmonella* species is uncommon in cats and has not previously been reported in association with pyelonephritis or generalised myositis. The importance of performing urine culture in the initial diagnostic investigation of cats with pyrexia is highlighted in this case report.

Keywords: *Salmonella*; salmonellosis; atypical; pyelonephritis; myositis

Introduction

Salmonella is a genus of Gram-negative bacteria comprising two species, *Salmonella bongori* and *Salmonella enterica.* The latter infects humans and animals and is further classified into six subspecies (I *enterica*, II *salamae*, IIIa *arizonae*, IIIb *diarizonae*, IV *hountenae*, VI *indica*) with over 2600 serotypes. *S enterica* subspecies *enterica* serotype Typhimurium (*Salmonella* Typhimurium) has a broad host-range and causes acute gastroenteritis within 24h of ingestion There are also host-restricted serovars of *S enterica*, including *S* Typhi and *S* Paratyphi (humans), *S* Choleraesuis (pigs), *S* Dublin (cattle) and *S* Gallinarum (poultry).[1] Rarely, *S enterica* causes infection in extra-intestinal sites.[2] Several case reports describe extra-intestinal salmonellosis in cats in association with conjunctivitis, cholangiohepatitis, pneumonia, pyothorax and endocarditis.[3–7] To the

best of our knowledge, this is the first report to describe extra-intestinal salmonellosis in a cat with evidence of both pyelonephritis and multifocal myositis.

[1]Queensland Veterinary Specialists, North Lakes, QLD, Australia
[2]Department of Veterinary Clinical Sciences, Jockey Club College of Veterinary Medicine and Life Sciences, and Centre for Animal Health and Welfare, City University of Hong Kong, Kowloon Tong, Hong Kong, SAR China
[3]Centre for Animal Health and Welfare, City University of Hong Kong, Kowloon Tong, Hong Kong, SAR China

Corresponding author:
Remon Wilson BVSc, MANZCVS (Small Animal Internal Medicine), Queensland Veterinary Specialists, 53 Flinders Parade, North Lakes, QLD 4509, Australia
Email: wilson.remon@yahoo.com

Case description

A 2-year-old male neutered domestic shorthair cat was referred to the Internal Medicine Department at Queensland Veterinary Specialists, Brisbane for further investigation of acute onset of high fever. The owner reported a 24 h history of severe lethargy, anorexia and suspected fever (the owner noted the cat was unusually warm to touch). There was no vomiting or diarrhoea, but for 48 h before presentation, the time taken to urinate was noticed to be longer than normal. The cat had a history of chronic bilateral ocular discharge, was housed indoors and had access to an enclosed outdoor area. The cat's diet included a mix of commercial dry and wet food but no cooked or raw meat. There was one other cat in the household with no signs of illness.

Medical notes from the referring veterinary hospital documented a rectal temperature of 41.1°C before referral. A complete blood count (CBC) showed severe leucocytosis (24.93×10^9/l) (reference interval [RI] 5.5–19.5) mainly due to severe neutrophilia (23.68×10^9/l [RI 3.12–12.58]). A serum biochemistry panel and blood gases were within the RIs. A rapid cage-side blood test for feline immune deficiency virus (FIV) antibody and feline leukaemia virus (FeLV) antigen was negative for both (FIV/FeLV Witness; Zoetis). Urinalysis had not been performed due to the stressed and defensive behaviour of the cat and the need for sedation for cystocentesis. The cat was hospitalised and administered intravenous crystalloid fluid therapy overnight.

On clinical examination at referral the next day, the cat was lethargic and vocal. Vital signs were normal, except for rectal temperature, which was 41.0°C. The cat was well hydrated with moist mucous membranes and no prolonged skin-tent. The cat was reluctant to walk and did so with an arched back posture and severe generalised ataxia, causing it to fall repeatedly to both the left and right. On neurological examination, the cat had dull mentation but cranial nerve testing, postural reaction testing and spinal reflexes were normal. Spinal palpation elicited signs of severe, diffuse pain that could not be localised to a specific region.

On initial assessment, given the cat's young age, infectious or inflammatory disease was considered the most likely cause of the fever and neutrophilic leucocytosis, although immune-mediated or paraneoplastic causes could not be excluded. Diffuse or multifocal central nervous system disease was suspected to be causing the dull mentation, ataxia and spinal pain and an infectious cause was considered most likely. Serum was submitted to test for *Toxoplasma gondii* IgG and IgM by ELISA and for *Cryptococcus* antigen by a latex cryptococcal agglutination titre test (LCAT).

Supportive treatment with intravenous fluid therapy (Hartmann's crystalloid solution, 3 ml/kg/h) and analgesia were administered (methadone 0.2 mg/kg IV q4h and a ketamine continuous rate infusion 5 µg/kg/min IV). Pending *Toxoplasma* species serology results, treatment was also commenced with clindamycin (Apex Clindamycin; Apex) at 15 mg/kg PO q12h. The LCAT was zero, excluding cryptococcosis as a differential diagnosis.

On day 4 after referral, although there was some improvement, given the persistence of fever (39.5°C), spinal pain and ataxic gait, additional diagnostic investigations were undertaken. MRI of the brain and spinal cord, and lumbar cerebrospinal fluid (CSF) collection were performed under general anaesthesia using propofol 3 mg/kg IV to effect for induction and isoflurane in oxygen inhalation to maintain general anaesthesia. Sagittal and transverse MRI sequences performed using a Siemens Magnetom Prisma 3-T MRI machine included T2, pre- and post-contrast T1, T1 VIBE, and T1 VIBE and FS, as well as short inversion time inversion recovery (STIR) dorsal images. The MRI scans showed no evidence of abnormalities in the brain or spinal cord and were submitted for reporting to a board-certified radiologist. The results of the CSF analysis performed by an external reference laboratory (QML Vetnostics Laboratory, Queensland) were within the normal RIs. The cat was discharged from the hospital after these procedures at the owner's request, with ongoing clindamycin administration and the addition of oral gabapentin from a veterinary compounding pharmacy (BOVA Aus) at 12.5 mg/kg (50 mg) q12h.

The MRI report received from the board-certified radiologist the next day (day 5 after referral) confirmed that the brain and spinal cord were of normal size and signal intensity, and no lesions were identified. However, on the STIR sequence, the right kidney was normal in size but irregular in contour, with lack of the normal corticomedullary definition, mild pyelectasis and there was a small volume of fluid in the peri-nephric space (Figure 1). In addition, multifocal lesions were identified in the paraspinal muscles, including the deep axial muscles at L5 and L6, at C7, at T2, and the caudal thoracic paraspinal muscles and in the skeletal muscle of the left brachium. These lesions were ill-defined and showed peripheral enhancement post-contrast on the T1-weighted VIBE sequence (Figure 2) and were hyperintense on STIR sequences post-contrast (Figure 3).

The owner was contacted on day 5 and recommended to return the cat for further investigation but did not re-present the cat until day 12 due to perceived improvement at home. A limited physical examination was performed because of the cat's stressed and defensive behaviour. The cat's gait was normal and no spinal pain was detected on palpation. An abdominal ultrasound was performed under sedation using medetomidine 0.005 mg/kg IM and methadone 0.2 mg/kg IM (Troy Laboratories). A focal hyperechoic area was identified in the right renal cortex, the renal pelvis was assessed to be
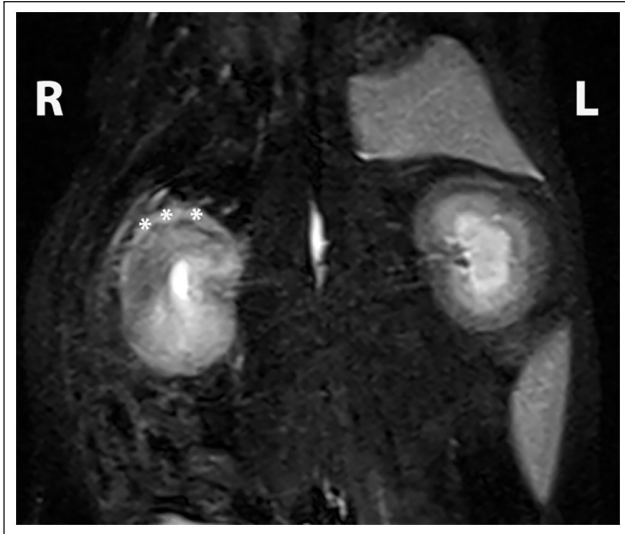
Figure 1 MRI short inversion time inversion recovery dorsal plane image of the kidneys. The right kidney has distorted architecture and accumulation of fluid in the pelvis and peri-nephric space (asterisks)
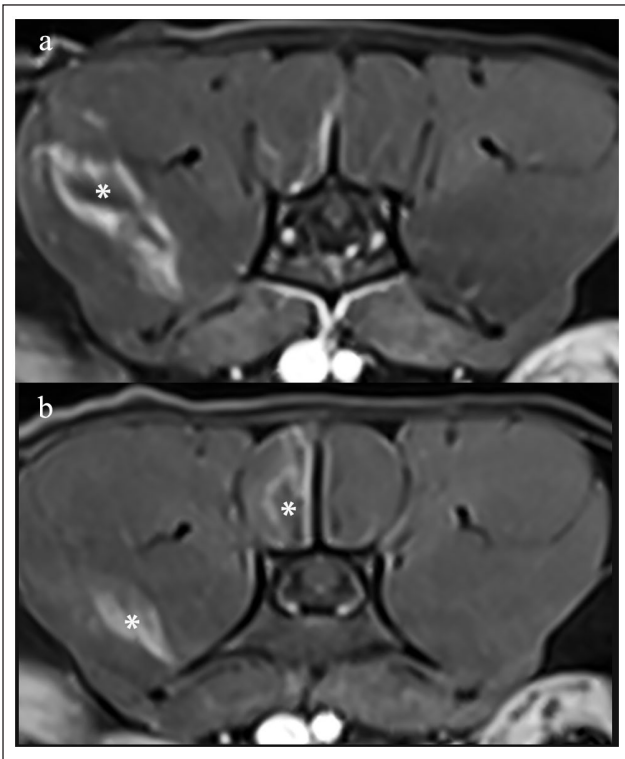

Figure 2 (a,b) T1-weighted VIBE transverse images; asterisks indicate a contrast-enhanced lesion, consistent with an inflammatory aetiology in the paraspinal muscles

moderately dilated (measurement not available) and there was hyperechoic fat in the peri-renal area. Urine was collected using ultrasound-guided cystocentesis

and had a urine specific gravity (USG) of 1.028. An in-house urine sediment examination revealed a moderate number of bacterial rods and neutrophils. The urine sample was submitted for bacterial culture (QML Pathology) and a *Salmonella* species with >100,000 colony-forming units/ml was isolated. Pending susceptibility results, since *Salmonella* species are rarely isolated from urine, a second urine sample collected several days later by cystocentesis immediately after presentation without the need for sedation was submitted to rule out contamination or an error in laboratory identification, and a *Salmonella* species was again isolated. Bacterial strain identification and serotyping performed by an enteric pathogen reference laboratory (QLD Health Microbiology Laboratories) confirmed *S* Typhimurium serotype 1,4, [5],12:i:1,2.

On antimicrobial susceptibility testing (AST) by agar gel diffusion, the isolate showed susceptibility to amoxycillin, amoxycillin–clavulanic acid, enrofloxacin and trimethoprim–sulfonamide but was resistant to cephazolin and cefovecin. The AST panel did not include clindamycin. The cat was treated for 2 weeks with amoxicillin–clavulanate (Amoxyclav; Apex) (20 mg/kg q12h PO). At recheck examination 1 week after completing therapy, the cat was clinically normal and afebrile (rectal temperature of 38.2°C) A third follow-up urine sample collected via cystocentesis for bacterial culture was negative.

Discussion

Clinical salmonellosis is uncommon in cats.[8] In our case, the route of infection was not identified, while in other reported cases of *S* Typhimurium infections in cats, infection was suspected to result from ingestion of raw meat or predation.[9–11] However, the cat in this report was only fed commercial food and had limited outdoor access to an enclosed space. Salmonellosis in cats has also been reported in association with immunosuppression from chemotherapy or treatment with cyclosporine.[12,13] There was no evidence of immunosuppression in the current case.

In humans, *Salmonella* species urinary tract infections are rare and occur as a result of haematogenous dissemination, faecal contamination of the urethra, urolithiasis or secondary intraluminal ascending infection.[14–16]

Only one report in a cat has described *Salmonella* species isolated from the urine and faeces of a 9-year-old male neutered cat that was being investigated for weight loss and a chronic history of feline lower urinary tract disease; that cat had been fed a *S* Typhimurium-contaminated commercial diet.[11]

Although clinical improvement occurred in our case before discharge from hospital, this was unlikely to be a result of clindamycin administration, as *S* Typhimurium isolates are uniformly resistant to clindamycin.[17]
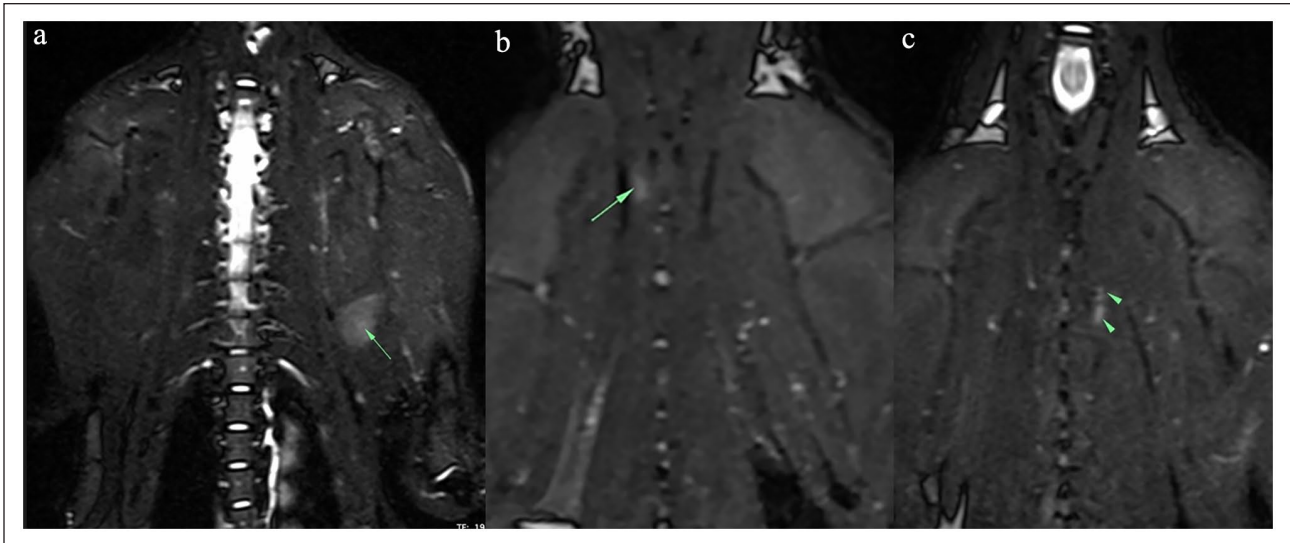
Figure 3 Short inversion time inversion recovery sequence dorsal plane images; inflammatory lesions in (a) the left brachium (arrow) and (b, c) paraspinal muscles (arrow in panel b, arrowheads in panel c)

In our case, the omission of urinalysis and urine culture earlier in the investigation was unfortunate, as the presence of bacteriuria would likely have curtailed the further more invasive and expensive neurological and serological diagnostic testing undertaken. In retrospect, the prolonged urination time reported by the owner was a flag for underlying urinary tract disease. This report also highlights the importance of urinalysis, including urine sediment examination, as part of routine diagnostic investigations of sick cats, especially where there is fever, as in this case. Another shortcoming of this case was that renal function was not assessed at the completion of therapy and the cat was lost to follow-up. The USG of 1.028 in a cat could indicate loss of urine-concentrating ability.

In this case, the ataxic gait and severe spinal pain displayed by the cat were initially interpreted as neurological disease. However, the perceived spinal pain on clinical examination could have been referred abdominal pain arising from the kidneys, as has been reported in human *Salmonella*-induced pyelonephritis.[14–16] Alternatively, or in addition, the pain in this case could be associated with the multifocal muscle lesions identified on MRI in the paraspinal and brachial muscles, which were very similar to the MRI images described in human *Salmonella*-induced myositis.[18,19] Unfortunately, creatine kinase was not part of the serum biochemistry test profile in this case.

Salmonella-induced myositis has not been reported in cats, but has been described in humans, including cases with MRI evidence of focal myositis.[18,19] Generalised *Salmonella*-associated myositis has also been reported in people and can be associated with creatine kinase elevation (CK).[19] The underlying mechanisms

of *Salmonella*-induced myositis are not clearly understood but could include bacterial invasion of the muscle, sepsis-related, tissue hypoxia and altered muscle metabolic capacity.[20]

In the Australian state of Queensland, the notification rate of non-typhoidal *Salmonella* species invasive disease in humans is among the highest in Australia, with *S* Virchow followed by *S* Typhimurium being the most common serotypes to cause invasive disease.[21,22]

Conclusions

This is the first case report to describe clinical *S* Typhimurium-induced pyelonephritis with suspected multifocal myositis in a cat with isolation and identification of the organism from the urine.

Ethical approval The work described in this manuscript involved the use of non-experimental (owned or unowned) animals. Established internationally recognised high standards ('best practice') of veterinary clinical care for the individual

patient were always followed and/or this work involved the use of cadavers. Ethical approval from a committee was therefore not specifically required for publication in *JFMS Open Reports*. Although not required, where ethical approval was still obtained, it is stated in the manuscript.

ORCID iD Remon Wilson [iD] https://orcid.org/0009-0002-6705-3089
Vanessa R Barrs [iD] https://orcid.org/0000-0001-6761-8022

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