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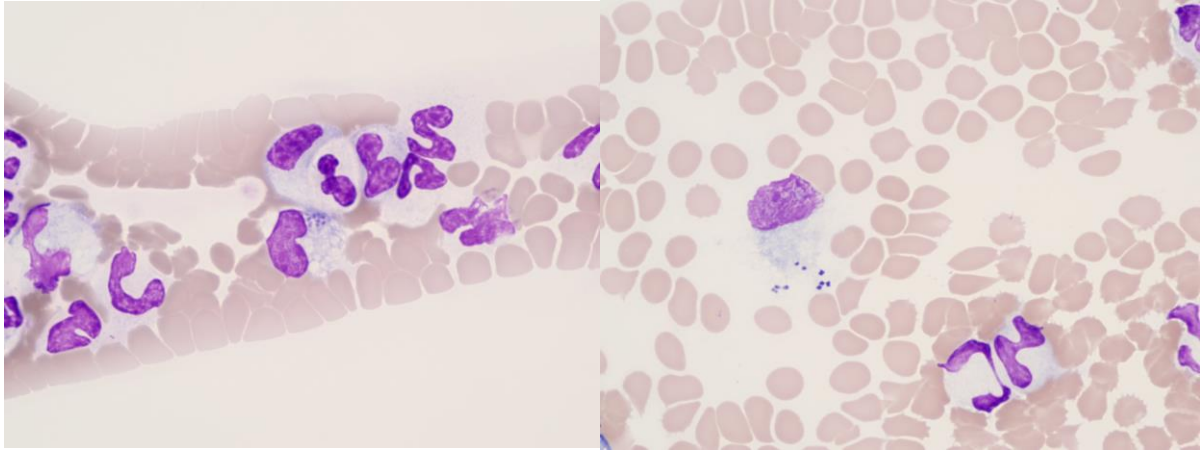
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Case report

Septicaemia and thrombocytopenia associated with blood culture of *Salmonella gallinarum* in a dog fed raw meat

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Abstract

In recent years, it has become increasingly popular for pet owners to feed their dogs and cats raw meat, as an alternative to processed, manufactured diets. Owners appear unaware of the potential risks this may pose for their animals and for themselves, despite the published literature. A five-month-old female French Bulldog was referred for investigation of acute vomiting, diarrhoea and pyrexia. She was diagnosed with septicaemia, believed to be associated with *Salmonella gallinarum* (identified on blood culture), as well as a positive faecal culture for *Campylobacter coli* and severe thrombocytopaenia (presumably secondary to infection). She received supportive treatment and marbofloxacin, going on to make a full recovery. Considering the *Salmonella* serovar identified (which is host-specific to poultry) and the patient's lifestyle, it is possible the septicaemia originated from her raw meat diet. *Salmonella spp.* is potentially zoonotic and can cause acute enteritis in humans. This is the first report of septicaemia with positive blood culture for *Salmonella gallinarum*, with secondary severe thrombocytopenia (presumably immune-mediated), in a dog that was fed a raw meat diet.
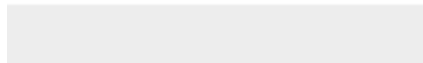
Conflict of Interest

The authors declare no conflict of interest.

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Abstract

In recent years, it has become increasingly popular for pet owners to feed their dogs and cats raw meat, as an alternative to processed, manufactured diets. Owners appear unaware of the potential risks this may pose for their animals and for themselves, despite the published literature. A five-month-old female French Bulldog was referred for investigation of acute vomiting, diarrhoea and pyrexia. She was diagnosed with septicaemia, believed to be associated with *Salmonella gallinarum* (identified on blood culture), as well as a positive faecal culture for *Campylobacter coli* and severe thrombocytopaenia (presumably secondary to infection). She received supportive treatment and marbofloxacin, going on to make a full recovery. Considering the *Salmonella* serovar identified (which is host-specific to poultry) and the patient's lifestyle, it is possible the septicaemia originated from her raw meat diet. *Salmonella spp.* is potentially zoonotic and can cause acute enteritis in humans. This is the first report of septicaemia with positive blood culture for *Salmonella gallinarum*, with secondary severe thrombocytopenia (presumably immune-mediated), in a dog that was fed a raw meat diet.

Keywords

Salmonellosis, Campylobacter, bacteraemia, sepsis, raw diet.

Key Points

A 5-month-old, female French Bulldog was diagnosed with septicaemia which was believed to be associated with *Salmonella gallinarum* (identified on blood culture), as well as a positive faecal culture for *Campylobacter coli* and severe thrombocytopaenia. Considering the *Salmonella* serovar identified and the patient's lifestyle, it is possible the septicaemia originated from her raw meat diet. There is a growing tendency to feed companion animals raw meat, despite the increasing number of peer-reviewed publications showing that they

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carry substantially higher numbers of pathogens, compared with processed diets. This report discusses the risks that raw feeding may pose to pets and their owners, as well as the owners apparent lack of knowledge on this matter.

1) Introduction

There has been a recent trend to feed dogs and cats living in developed countries raw meat-based diets (RMBDs), with the UK being one of these countries [1]. Investigations of their nutritional value have suggested nutrient imbalances and vitamin deficiencies [2-4]. However, a topic often discussed is the risk to human and animal health from contamination or infection of these diets with parasites and zoonotic bacteria, including antimicrobial-resistant bacteria.

Surveillance of *Salmonella spp.* in pet diets by the Animal and Plant Health Agency in the UK has shown that raw meat diets are 20 times more likely to be positive for *Salmonella spp.* than processed diets [5]. In Brazil, dogs fed RMBDs were 30 times more likely to be positive for *Salmonella* than dogs on processed diets; some of the serovars that were isolated are commonly associated with human salmonellosis, and 88% of the isolates were resistant to at least one of the seven classes of antimicrobials tested [6].

2) Case Description

2.1) Clinical Presentation

A five-month-old female entire French Bulldog was referred to a specialist veterinary hospital for investigations of acute vomiting, diarrhoea and pyrexia. She was up-to-date with regular vaccines and prevention against internal and external parasites (Bravecto, MSD Animal Health; and Milprazon, KRKA UK Ltd). She was fed a commercially available poultry-based raw meat diet. She lived with another dog, who was fed a commercial dry diet and was clinically healthy. As the dog was deaf, she was always walked on the lead under strict supervision.

On presentation, the patient was dull, her mucous membranes were pink and dry, respiratory rate was 52 breaths per minute, heart rate was 115 beats per minute, and rectal temperature was 40.3°C. Pulses were of good quality and synchronous. Dehydration was estimated at 7%. Thoracic auscultation and palpation of peripheral lymph nodes were unremarkable. There was moderate abdominal pain diffusely. She weighed 5.2kg, with a body condition score of 4/9.

2.2) Investigations

Haematology showed a mild non-regenerative normocytic normochromic anaemia, monocytosis and eosinopaenia, compatible with systemic inflammation (Table 1). There was also a severe thrombocytopenia at 10,000/ul, which was confirmed by blood smear evaluation and persisted for 9 days. The neutrophils showed moderate toxic changes and bacilli were seen engulfed by poorly preserved leukocytes (Figure 1).

Table 1: Haematology results on presentation. The reference intervals given are for adult dogs, hence interpretation of the results needs to reflect this.

	Result	Reference interval	SI units
Red blood cells	4.2	5.6 - 8.4	x 10^12/l
Haematocrit	26.0	37.3 - 61.7	%
Haemoglobin	9.1	13.1 - 20.5	g/dl
Mean corpuscular volume	61.9	61.6 - 73.5	fL
Mean corpuscular haemoglobin concentration	35.0	21.2 - 25.9	g/dl
Reticulocytes	19.7	10 - 110	K/ul
White blood cells	12.4	2.9 - 11.6	x 10^9/l
Neutrophils	8.8	2.9 - 11.6	x 10^9/l
Monocytes	1.2	0.2 - 1.1	x 10^9/l
Eosinophils	0.03	0.06 - 1.2	x 10^9/l
Basophils	0.01	0.0 - 0.1	x 10^9/l

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Platelets	10	148 - 484	x 10^9/l

Figure 1: Blood smear – neutrophils showing toxic changes and bacilli (arrows) engulfed by poorly preserved leukocytes.
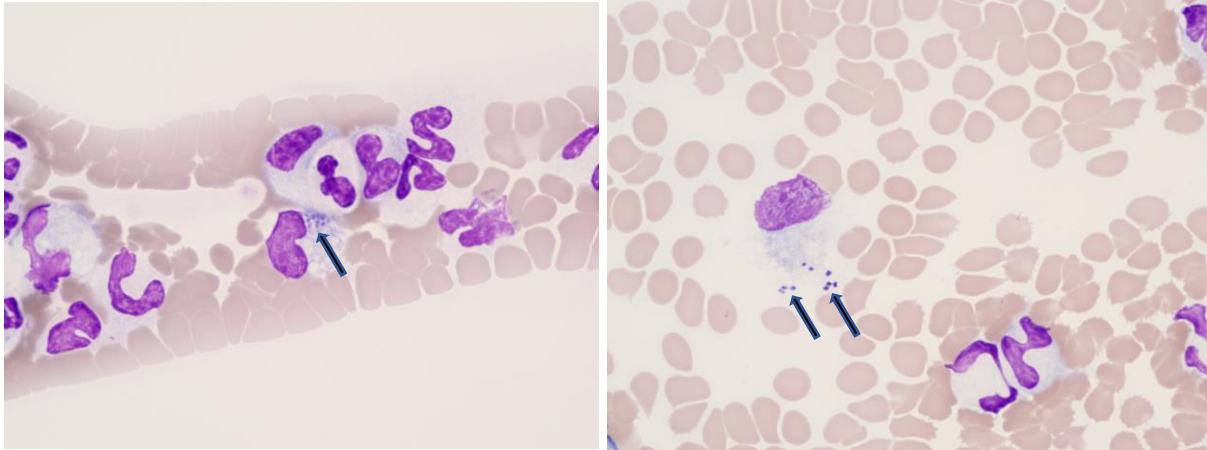
Biochemistry (Table 2) identified hypoalbuminemia (15.5 g/l, reference interval 26-35 g/l), likely a combination of intestinal loss and negative acute phase response; and mild total hypocalcaemia, presumably due to a reduction in protein-bound calcium. Alkaline phosphatase (ALP) was markedly elevated (1289 U/l, reference interval 20-60 U/l), potentially due to raised endogenous glucocorticoids, growth in a young animal and as a result of cholestasis, the latter supported by the mild elevation in bile acids and cholesterol. Mild hypokalaemia was suspected to be the result of reduced dietary intake and loss through vomiting and diarrhoea. Prothrombin Time and Activated Partial Thromboplastin Time were within reference interval.

Table 2: Biochemistry results on presentation. The reference intervals given are for adult dogs.

	Result	Reference interval	SI units
Total protein	54.9	58 - 73	g/l
Albumin	15.5	26 - 35	g/l
Globulin	39.4	18 - 37	g/l

ALT	27	21 - 102	U/l
ALP	1289	20 - 60	U/l
Bile acids	29	0 - 10.5	umol/l
Bilirubin	3.3	0 - 6.8	umol/l
Cholesterol	7.6	3.8 - 7	mmol/l
Triglycerides	1.14	0.57 - 1.14	mmol/l
Urea	3.5	1.7 - 7.4	mmol/l
Creatinine	41	22 - 115	umol/l
Total calcium	2.16	2.3 - 3	mmol/l
Phosphate	1.6	0.9 - 2	mmol/l
Sodium	148	144 - 160	mmol/l
Potassium	3.2	3.5 - 5.8	mmol/l
Chloride	114	109 - 122	mmol/l
Glucose	5	3 - 5	mmol/l
Prothrombin Time	12	11 - 14	seconds
Activated Partial Thromboplastin Time	81	60 - 93	seconds

Urine analysis was unremarkable and with no proteinuria identified. A faecal Parvovirus antigen test (SNAP Parvo Test, IDEXX) and serology for tick-borne diseases that could cause thrombocytopenia (*Borrelia burgdorferi*, *Anaplasma spp.* and *Ehrlichia spp.*) (SNAP 4Dx Plus, IDEXX) were negative.

Faecal parasitology and an antigen-based Giardia test (SNAP Giardia Test, IDEXX) were negative. Faecal culture was positive for *Campylobacter coli*, and negative for *Salmonella spp.* and *Yersinia spp.* The faecal sample was collected two days after antimicrobial therapy had started, as this was the first time the patient defecated since admission.

Abdominal ultrasound identified a fluid-filled, hypomotile small intestine throughout its length consistent with a functional ileus. Additionally, there were mildly enlarged jejunal and mesenteric lymph nodes, which were considered normal for a puppy. Thoracic radiographs and echocardiography were performed to exclude a focus of infection outside the gastrointestinal tract and both were unremarkable.

The left jugular vein was shaved and prepared for aseptic blood collection. Five millilitres of blood were obtained and injected aseptically into a blood culture bottle (Oxoid Signal Blood Culture System, Thermo Fisher Scientific). The needle on the syringe was replaced, and the stopper of the blood culture bottle was cleaned with alcohol before the blood was inoculated. The culture bottle was incubated at 37.C for 48 hours. Blood culture was positive for *Salmonella gallinarum*, as identified by VITEK®2 (Biomerieux Diagnostics) at a veterinary referral laboratory. The sample was sent to the Scottish Microbiology Reference Laboratories, which confirmed the species and serovar using whole genome sequencing.

2.3) Treatment

The patient was treated with fluid therapy to correct dehydration initially, then to address maintenance requirements as well as ongoing losses. Additionally, the dog received maropitant (Prevomax, Dechra; 1mg/kg intravenously every 24 hours) for an anti-emetic effect, methadone (Comfortan, Dechra; 0.2mg/kg intravenously every 4 - 6 hours) for analgesia, fenbendazole (Panacur, MSD Animal Health; 50mg/kg orally every 24 hours for five days) to treat potentially unidentified parasites on faecal parasitology, and amoxicillin-clavulanate (Augmentin, GlaxoSmithKline UK; 20mg/kg intravenously every 8 hours) for septicaemia.

The pyrexia persisted for a further 24 hours. Due to the lack of clinical response, marbofloxacin was commenced (Marbocyl, Vetoquinol; 5mg/kg intravenously every 24 hours). Within 12 hours, the pyrexia resolved and the dog's mentation and abdominal comfort improved.

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Treatment was continued with marbofloxacin (Marbocyl P, Vetoquinol; 3.7mg/kg orally every 24 hours for 16 days) and paracetamol (Paracetamol Oral Suspension, Crescent; 13mg/kg orally every 12 hours for 4 days).

2.4) Outcome

The patient had no further vomiting or diarrhoea following admission. Marked thrombocytopenia (<5,000/ul) persisted for nine days, although the patient did not show any clinical signs of petaechiation or haemorrhage.

On day nine of hospitalisation, the platelet count normalised (198 x 10^9/l; reference interval 148-484 x 10^9/l) and the patient was discharged on oral marbofloxacin. At this point, serum C-reactive protein was measured to allow for a more objective decision on when to stop the antimicrobial, as the volumes necessary for reliable blood cultures and patient size were deemed to be limiting factors. The value was elevated at 21.5 mg/l (reference interval < 5 mg/l).

One week later, the patient represented to the primary veterinary surgeon for clinical examination with haematology, albumin and C-reactive protein measurements obtained. All clinical parameters and blood results were within normal limits, with the C-reactive protein levels below the limit of detection. Due to the complete clinical response, marbofloxacin was stopped and the patient has remained asymptomatic since.

3) Discussion

Raw meat is claimed by some to be a more natural diet for dogs and cats, with proposed health benefits for the teeth, skin, behavioural disorders and an extensive range of infectious, inflammatory, neoplastic and endocrine diseases [3,7,8]. Aside from improved faecal quality in some studies [5,9,10], the other health benefits of feeding RMBDs are anecdotal, and there are no controlled studies supporting these statements [11,12]. Feeding RMBDs may answer

a psychological desire among owners to improve their pet's health and care for them, through a route that is simple and easy to understand, compared with more complex and confusing interventions advised by health professionals [3].

Investigations of RMBDs' nutritional value have proposed nutrient imbalances and vitamin deficiencies [2-4]. While commercial RMBDs may meet European pet food industry standards, they are commonly formulated without evaluation in feeding trials [1,13]. It is not known whether the RMBD fed to the dog here reported was nutritionally balanced for a puppy. One of the paramount concerns regarding RMBDs is the growing number of peer-reviewed publications showing that they carry substantially higher numbers of pathogens, some of which have the potential to cause life-threatening illness in animals and humans.

Parasites that have been shown to be possibly harboured by RMBDs include *Toxoplasma gondii* [3,14-16], *Sarcocystis* [16], *Neospora caninum*, *Isospora spp*, *Cryposporidium parvum*, *Giardia*, *Echinococcus spp*, and *Taenia spp* [12,17-19]. The risk to human health or livestock from pets shedding some of these organisms has been well characterised but objective data on the role of RMBDs with respect to infection by these organisms is limited.

In contrast with the sparse data on the association between RMBDs and parasitic infection, zoonotic bacteria have often been cultured from RMBDs directly, or from the faeces shed by the pets that are fed these diets. These include *Salmonella spp* [20,13,21,22], *E. coli* spp [3,16,23,24], *Campylobacter spp*, *Clostridium perfringens*, *Clostridium difficile* [6,20], *Listeria monocytogenes* [16,25,26], *Yersinia enterocolitica* [27], and *Brucella spp* [28]. A recent study has also identified a large number of cats with gastrointestinal lesions caused by *Mycobacterium bovis*, which were fed raw meat from a single reputable RMBD manufacturer [29].

Another emerging concern is the isolation of ==antimicrobial==-resistant bacteria from commercial raw diets, including extended-spectrum beta-lactamase *E. coli* [16,30], AmpC-positive *Enterobacteriaceae* [31-33] and multi-resistant strains of *Salmonella* [6,34,35].

Salmonellosis is a food borne disease of massive public health significance. It is estimated to cause illness in over 20 million people worldwide, and death in 150,000 people per year. There is a great concern regarding the increasing number of ==antimicrobial==-resistant *Salmonella* strains [26,36]. Analysis of commercial raw diets for pets have shown *Salmonella* contamination in proportions ranging from 7% [20,23] to 21% [16,22] in the USA and Europe. ==Processed pet diets can also be contaminated with *Salmonella*, but this is 20 times less likely compared with raw diets [5].==

The dog reported here was infected with *Salmonella gallinarum*. Considering the patient's lifestyle, which was predominantly indoors and always walked on a lead under close supervision, the in contact dog not displaying clinical signs, and the fact *Salmonella gallinarum* is host-specific to poultry, it is suspected this infection originated from the raw poultry meat the patient was fed. Dogs may be infected with *Salmonella* from contaminated food and water, but *Salmonella gallinarum* is found almost exclusively in poultry. Unfortunately, we were not able to definitively confirm the source of *Salmonella gallinarum* as a sample of the diet was not available to submit for culture, which we recognise as a major limitation. ==The relevance of the positive culture of *Campylobacter coli* is uncertain, as we have no evidence that it originated from the patient's diet or that it caused disease.== Several studies have shown that healthy dogs can carry *Campylobacter spp.*, questioning the pathogenic role of these organisms in dogs [37,38].

The blood culture technique followed manufacturer recommendations. In the largest study of dogs with suspected bacteraemia performed to date (n=939 dogs), positive blood cultures were obtained from only 15% of dogs – none was positive for *Salmonella spp*. Only 4% of

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dogs had blood culture performed from two or three different sites, and a third had a positive bacterial culture from only one of the samples [39].

The decision to treat the patient with a fluoroquinolone was based on the previous lack of response to a lower-tier antimicrobial and the recommendation in human medicine to use fluoroquinolones in severe salmonellosis whilst pending sensitivity results [40]. Fluoroquinolones are also advised in septicaemia caused by *Salmonella* in dogs [41]. As the dog was septic, a dose at the higher end of the recommended range was chosen [42]. The risk of arthropathy in a growing animal and the off-license use of a dose above manufacturer's recommendations were discussed with the owner, who consented to these given the potential benefits were felt to outweigh the risks.

A definitive cause for this dog's thrombocytopenia was not confirmed, however, immune-mediated destruction was considered to be most likely, presumably associated with infection. Immune-mediated destruction of platelets has been reported in dogs with a variety of infections [43-46]. Platelet-bound antibody testing can confirm that the thrombocytopenia is immune-mediated in origin. However, the test is not readily available and cannot distinguish between primary and secondary immune-mediated destruction [47]. Hence, diagnosis of immune-mediated thrombocytopenia is based on a persistent low count (less than 35,000/ul) and exclusion of other causes of thrombocytopenia [48]. As there was no evidence of gross haemorrhage with this patient, and coagulation times were within reference interval, microthrombi formation secondary to disseminated intravascular coagulation was unlikely, but it cannot be fully excluded as a source of thrombocytopenia. Specific treatment for thrombocytopenia was not required in this dog, with platelet count normalisation coinciding with improved clinical signs following the institution of marbofloxacin.

The owner of this dog appeared unaware of the potential risks associated with the feeding of RMBDs. A recent study has confirmed that 99% of owners that feed their pets RMBDs believe

this does not pose a health risk to themselves; and 88% of owners believe it does not pose a health risk to their pets either [6]. There are several ways through which pet owners can become infected with ==diets== that are contaminated with bacteria. This can happen through contact with an infected pet, direct contact with the food when preparing a meal, through ingestion of cross-contaminated human food, or via contact with contaminated surfaces in the house [49,50]. *Salmonella*, for example, can persist in food bowls of pets fed a RMBD for at least several days at room temperature, even after cleaning with soap or bleach, or after washing the bowls in the dishwasher [21]. Dogs can shed *Salmonella* for several days after a single meal of contaminated raw meat; and the shedding may continue for up to eight months if the dog is fed contaminated raw meat over a prolonged period of time [51].

4) Conclusions

This is the first report of septicaemia believed to be associated with *Salmonella gallinarum*, with secondary severe thrombocytopenia, in a dog fed a commercially available raw meat diet. It was not possible to confirm whether the *Salmonella* originated from the raw meat, as a sample of the diet was not available to submit for culture. This report discusses the risks that raw feeding may pose to pets and their owners, as well as their lack of knowledge on this matter. It is important to better communicate with pet owners about these potential risks; at the very least, veterinarians should advise careful handling of the raw meat and of the faeces of pets that are raw fed. From a clinical perspective, it also highlights the importance of obtaining a dietary history in those patients where systemic infections are suspected, to aid in the clinical decision-making process.

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