Uncommon presentations of *Listeria monocytogenes* infection

**Authors**

1) Chavada R- Department of Microbiology and Infectious diseases, Liverpool Hospital, Liverpool, NSW, 2170, Australia

   ruchirchavda@gmail.com

2) Keighley C- Department of Medical Oncology, Bankstown hospital, Bankstown, NSW, 2200, Australia

   Caitlin.is@gmail.com

3) Quadri S- Department of Medical Oncology, Bankstown hospital, Bankstown, NSW, 2200, Australia

   zuzuj@hotmail.com

4) Asghari R- Department of Medical Oncology, Bankstown Hospital, Bankstown, NSW, 2200, Australia

   ray.asghari@sswahs.nsw.gov.au

5) Hofmeyr A- Department of Microbiology and Infectious diseases, Liverpool Hospital, Liverpool, NSW, 2170, Australia

   ann.hofmeyr@sswahs.nsw.gov.au

6) Foo H- Department of Microbiology and Infectious diseases, Liverpool Hospital, Liverpool, NSW, 2170, Australia

   hong.foo@sswahs.nsw.gov.au

**Corresponding author**

Chavada R- Department of Microbiology and Infectious diseases, Sydney South Western Area Pathology Services (SSWPS), Corner Goulburn street, Liverpool Hospital, Liverpool, NSW, 2170, Australia

Phone:+61 02 87385121 Fax:+61 02 87385129
Introduction

Listeriosis is a serious food borne disease caused by the bacterium *Listeria monocytogenes*, affecting mostly pregnant women, neonates and immune-compromised hosts with relatively high mortality rates in these groups. Listeria may cause life threatening meningitis and bacteraemia in these groups. However it may only manifest as self-limiting gastrointestinal illness in immunocompetent hosts. A multitude of focal infections with *Listeria monocytogenes* have been reported in the literature affecting various organs. There have been multi-jurisdictional and statewide outbreaks of listeriosis in Australia associated with contaminated food items in the past. However sporadic cases occur more often than cluster outbreaks. [1, 2] The source of infection in sporadic cases remains largely unknown. We present three epidemiologically unrelated cases of sporadic origin presenting as focal infections.

Case presentation

Case 1

A 73 year old Caucasian woman presented with acute onset of right knee pain for 1 week. She had a background of metastatic colorectal carcinoma for which she was receiving 5-Fluorouracil and oxiplatin chemotherapy, bilateral total knee replacements and type 2 diabetes. There was a preceding history of gastrointestinal illness 3 weeks prior to current presentation. A technetium 99m-bone scan (figure 1) demonstrated increased tracer uptake in the right knee suggestive of a septic arthritis. On arthroscopic washout of the knee, microscopy of the aspirated fluid revealed $>10^9 200 \times 10^6 /L$ polymorphs and gram-positive bacilli. Cultures of the aspirate confirmed *Listeria monocytogenes* on horse blood agar at 3 days. The minimum inhibitory concentration (MIC) of this organism to penicillin tested by Etest® (AB Biodisk; Solna, Sweden) was 0.5 mg/L. Blood cultures were negative. The patient completed a 2 week course of
intravenous ampicillin followed by benzyl penicillin (14.4 gram/daily) as intravenous infusor and then completed a 6 month course of amoxicillin (1 gram/TDS). She remained asymptomatic at the end of therapy.

The local public health unit was notified. On telephonic interview with the patient they found that she had a penchant for raw meat; an environmental investigation was not undertaken as this was deemed to be a sporadic case.

Case 2

An 86 year old Caucasian man with history of peripheral vascular disease and a prosthetic (polytetra-fluroeythelene) left femoro-popliteal bypass graft in 2011, atrial fibrillation and mild mitral regurgitation presented with a discharging skin sinus in the left groin. He also had abdominal pain, fever and a raised neutrophil count (14600×10⁶/L) on admission. An abdominal computerized tomographic (CT)) revealed left femoro-popliteal graft leak with haematoma formation which was in close proximity to the graft.(Figure 2) The patient subsequently underwent an operative excision of the femoro-popliteal graft with ovine graft replacement and femoral endarterectomy. *Proteus mirabilis* and *Listeria monocytogenes* were isolated from the operative samples of prosthetic fluid and graft tissue. He was commenced on intravenous ampicillin (2 grams every 4 hours) to which both of the above organisms tested sensitive [MIC of *Proteus mirabilis* to ampicillin <2 mg/L by Vitek2,(bioMérieux, France) and of *Listeria monocytogenes* to penicillin was 0.5 mg/L by Etest]. His post operative course was complicated by a surgical site infection with an extended spectrum β lactamase (ESBL) producing *Enterobacter cloacae*. He required a subsequent washout and addition of meropenem (1 gram/TDS) to the antibiotic regimen. He had a good clinical response after 6 weeks of parenteral antibiotic therapy. In follow-up, he was clinically stable and
a plan was made for continuing oral amoxicillin (500 mg/TDS) with an aim of lifelong antibiotic suppression.

This patient, although elderly was not immunosuppressed with other medical conditions and no clear risk factors were identified for *Listeria* infection apart from consuming meats from a local delicatessen.

**Case 3**

A 60 year old Asian man was admitted with a perianal abscess present for 3 weeks prior to presentation. He had a history of atrial fibrillation and was on oral flecainide. There were no concurrent neurological symptoms or any history of underlying immunosuppression. He underwent a surgical incision and drainage of the perianal abscess which revealed positive microbiological culture of *Listeria monocytogenes* and mixed bowel organisms. The MIC of the organism to penicillin tested by Etest was 0.38 mg/L. A brain CT did not demonstrate the presence of any cerebral abscesses. The patient received a 10 day course of oral ampicillin (1 gram/TDS) and ciprofloxacin (500 mg/BD).

The public health unit was notified, however apart from an interview with the patient, no further investigation was carried out as the case did not meet the local case definition of invasive listeriosis.

**Discussion**

We performed Pubmed search with terms-“*Listeria monocytogenes*”, “prosthetic joint septic arthritis”, “prosthetic vascular graft infection” and “perianal abscess” and reviewed articles in literature. To the best of our knowledge, these are the first reported cases of prosthetic joint septic arthritis, prosthetic vascular graft infection and perianal abscess due to *Listeria monocytogenes* in Australia. None of these 3 cases appear to be
epidemiologically linked to each other. All three of them were unrelated strains (non-outbreak). [2, 3]

Listeria monocytogenes is a gram-positive bacillus that is ubiquitous in the environment; it is present on unwashed vegetables and also found from foods that have been contaminated after processing. It has a mortality rate of 10-44% in food borne outbreaks. In Australia the incidence of listeriosis is 2.5-3.6 cases per million of population per annum.[4] According to the New South Wales (NSW) Health Department statistics of the 21 cases of listeriosis in 2011, 61% of patients were over 65 years and had underlying immunosuppression compared to 24% patients who were under 65.[5] A similar incidence of invasive listeriosis has been found in the United States with 24% of patients under 65 on some form of immunosuppressive therapy (glucocorticoids or chemo-radio therapy).[6]. Solid organ or haematological malignancy is also an established risk factor for invasive listeriosis, with certain conditions like chronic lymphocytic leukaemia being associated with >1000 fold increased risk compared to the general population. [7, 8] In NSW during 2011-2012, it was found that in patients who developed invasive listeriosis 24% had history of malignancy and 28% were on immunosuppressant medications. [Musto J, Health Protection NSW, personal communication]

Septic arthritis is an unusual manifestation of infection with L. monocytogenes with less than 80 reported cases in the literature. In the largest series of 43 patients from France[9], the most frequently involved joint involved was the hip (60%) followed by the knee (21%). 84% patients had associated orthopaedic devices, and 26% had underlying malignancy, as in our first case. Subacute infection with a median duration of 4 weeks occurred in the majority. There were no fatal cases. Other case reports with
Septic arthritis have demonstrated a link with tumour necrosis factor (TNF) inhibitors, which was not present in case 1. [10]

Prosthetic graft infections caused by *Listeria species* are rare, with only 8 cases reported in world literature, [11] of which 6 patients were elderly or had underlying immunosuppression. In all these cases haematogenous dissemination was the mode of infection, as was thought to be the case in our second patient, and the organism was less frequently isolated in blood culture than fluid or tissue from the graft site. Most patients were treated with definitive surgery as was case 2.

*Listeria* can cause abscess formation, the most common sites being brain and liver. Only two cases of perianal abscesses have been described so far in literature from a Danish series. [12] Both these patients died as a result of septicaemia. Our case 3 was quite well after surgical drainage of the abscess with a short course of oral antibiotics.

Laboratory confirmation of listeriosis requires isolation or detection of *L. monocytogenes* from a site that is normally sterile. A presumptive identification of *Listeria* can be made on basis of typical short Gram positive bacilli with characteristic “tumbling motility” by light microscopy (at room temperature and at 37 °C) and aesculin hydrolysis. The availability of Matrix-assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS) has made confirmation of *Listeria monocytogenes* relatively quick in laboratories using it. In our laboratory MALDI-TOF MS has been validated for this purpose. Phenotypic strip tests (API ®, bioMérieux, France) can also be used for identification of *Listeria monocytogenes*. Various methods of antibiotic susceptibility testing like Etest strips and disk diffusion have been used. We routinely employ an Etest for penicillin and trimethoprim-sulfamethaxazole for susceptibility testing on the *Listeria* isolates.
It is mandatory to report cases of listeriosis in all jurisdictions in Australia. Public health officers assess each of these notified cases to determine the epidemiological links and the necessity for carrying out further investigations such as food sampling, tracing the food borne source etc. Molecular analysis with binary typing and Multiple-Locus Variable number tandem repeat Analysis (MLVA) is performed in the state public health laboratory on all clinically significant *Listeria* isolates. Binary typing (BT) is a polymerase chain reaction (PCR) detection method of 8 gene loci on the *Listeria* genome. In binary typing, each strain is assigned a signature based on the presence (1) or absence (0) of a set of defined DNA sequences. The results of BT are combined with MLVA typing (involves testing of another 9 gene loci) to provide laboratory evidence for an outbreak. The isolates also undergo pulsed field gel electrophoresis (PFGE) and molecular serotyping at another reference laboratory in Australia. In our cases molecular analysis (Figure 3) revealed the following BT types: BT 158 (case 1), BT 254 (case 2) and BT 50 (case 3). All three cases were molecularly unrelated to the listeriosis outbreak in NSW in 2011-2012. A national network of foodborne diseases epidemiologists called OzFoodNet exists in Australia, which coordinates the analysis of the epidemiological data and molecular typing for determination of clusters and outbreaks. (See Table 1)

The national case definition requires laboratory evidence in the form of isolation or detection of *Listeria monocytogenes* from a site that is normally sterile, including foetal gastrointestinal contents. Clinical and epidemiological evidence is not required. Table 1 provides information about the public health unit investigations that were carried out on our three cases.

The recommended management of invasive listeriosis is with a combination of penicillin or ampicillin with the synergism of an aminoglycoside in severe cases. The
duration of therapy for focal infections is based on evidence from small case series. Optimal duration of therapy is unknown and should be based on person’s immune status and response to antimicrobials. Both patients with septic arthritis and graft infection received 6 weeks of intravenous therapy. Debridement or replacement of prosthetic material is generally considered necessary for cure, which was not performed in our case given her underlying morbidities. Thus far case 1 patient has had a good outcome. Case 2 had treatment with almost complete removal (small piece adjacent to anastomotic site left behind) of the infected graft and drainage of the collection which has been shown to have good outcomes. [14] Case 3 also was managed with antibiotics alone. Although only Case 1 had a history of gastroenteritis, these cases highlight the fact that gastrointestinal symptoms may not be present in all patients. Asymptomatic and subclinical infections are known to occur in immunocompetent patients. [13] We speculate that case 2 and 3 may have had sporadic subclinical infections in the past with carriage of the organism in the gastrointestinal tract. About 5% of healthy adults can have asymptomatic carriage of Listeria. [15] Diagnosis of these focal infections can be extremely challenging based on their clinical presentation. However modern techniques in the laboratory like MALDI-TOF have vastly improved the detection of such infections especially when they are polymicrobial, as was demonstrated in cases 2 and 3. It also raises the importance of providing dietary advice to patients who are undergoing chemotherapy or other immunosuppressive therapy, such as mycophenylate mofetil or TNF inhibitors. Whilst consumption of raw meat is uncommon in Australian society, large scale outbreaks of listeriosis have also occurred even with consumption of pasteurised milk in other countries. [16] We recommend extending the advice that is provided to pregnant women regarding the dangers of raw and unpasteurised foods
and soft cheese to all patients undergoing immunosuppression. There is a need for heightened awareness amongst clinicians of unusual organisms causing these focal infections where requirement for obtaining a microbiological specimen is crucial for diagnosis. Treatment is often prolonged and inappropriate therapy may lead to progression of the infection.

**Conclusion**

Although localised and focal infections with *Listeria* are rare, they present with challenges associated with diagnosis and may not have clear risk factors for their development. A thorough clinical history is vital and improved microbiological techniques have improved their detection. We suggest appropriate dietary advice to immunosuppressed patients.

**Figure legends** – Fig 1, Fig 2, and Fig 3 as indicated in the body of text

**Table** – Table 1 as indicated in the text

**Consent**

Written informed consent was obtained from all patients for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

**Competing interests**

The author(s) declare that they have no competing interests.

**Authors’ contributions**

RC- Conceived the case report, wrote the initial manuscript, performed literature review, managed Case 3 in this report, and liaised with local public health unit and reference laboratories in Sydney and Melbourne

CK- Managed Case 1 and Case 2, performed literature review and liaised with Health Protection NSW, Sydney
SQ- Managed and followed up on Case 1
RA-Consultant in charge of Case 1
AH-Consultant in charge of Case 1, provided input into the manuscript
HF- Consultant in charge of Case 2, provided input into the manuscript
All authors read and approved the final manuscript.

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References


Figure 1-Technetium-99m bone scan depicting increased uptake in the region of tibial tuberosity of the prosthetic knee joint (images 1 and 2-red pointer denotes increased uptake in the region indicative of synovitis). Image 3 is suggestive of hyperaemia in the right knee which is also indicative of the same.
Figure 2- Abdominal CT scan showing the left femoro-popliteal graft and surrounding collection (see arrow)
Case 1                      Case 2                       Case 3                   Outbreak strain (2012)
BT 158                    BT 254                      BT 50                    BT 255

Figure 3-Results of binary typing (BT) of the isolates
Additional files provided with this submission:

Additional file 1: Table 1.doc, 31K
http://www.biomedcentral.com/imedia/1977208008124695/supp1.doc