World Journal of Clinical Cases

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DOI: 10.12998/wjcc.v2.i7.304

World J Clin Cases 2014 July 16; 2(7): 304-308
ISSN 2307-8960 (online)

CASE REPORT

One-stage revision in two cases of *Salmonella* prosthetic hip infection

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Received: December 28, 2013 Revised: April 17, 2014
Accepted: May 28, 2014
Published online: July 16, 2014

Abstract

We describe two cases of prosthetic joint infection (PJI) of the hip due to *Salmonella*. The first patient presented with an early infection 5 d after being discharged following a total hip replacement and the second patient presented at the emergency ward with a late infection, thirteen years following a total hip replacement. Both cases occurred within one month of each other at our institution and both were successfully treated with a one-stage revision. PJI caused by *Salmonella* species is very rare: so far only 20 *Salmonella* PJIs of the hip have been described. Therefore, full consensus on the best treatment approach has not yet been reached. An aggressive two-stage approach is advised because of the virulence of *Salmonella*, although a limited number of successful one-stage approaches have been described as well. According to the latest guidelines, one-stage revision has comparable success rates and less morbidity compared to two-stage treatment, when selecting the right patients. In our opinion, PJI caused by *Salmonella* should be treated just as PJI caused by other bacteria, with consideration of the selection criteria as mentioned in several treatment guidelines. As illustrated by these two cases, one-stage revision can be successful in both early and late *Salmonella* PJI of the hip.

Key words: *Salmonella*; Prosthetic joint infection; One-stage revision; Two-stage revision; Treatment

Core tip: Prosthetic joint infection (PJI) of the hip by *Salmonella* species is rare. There is an ongoing debate whether treatment of prosthetic joint infection should consist of a one- or two-stage approach and also whether or not PJI caused by *Salmonella* should be treated similarly to PJI caused by other bacteria. We report two cases of *Salmonella* PJI, one early and one late infection, successfully treated by one-stage revision.

Jeroense KTV, Kuiper JWP, Colen S, Schade RP, Saouti R. One-stage revision in two cases of *Salmonella* prosthetic hip infection. *World J Clin Cases* 2014; 2(7): 304-308 Available from: URL: http://www.wjgnet.com/2307-8960/full/v2/i7/304.htm DOI: http://dx.doi.org/10.12998/wjcc.v2.i7.304

INTRODUCTION

Salmonella infections are usually associated with food consumption, specifically raw egg and related products, which account for at least one third of all outbreaks in the United States[1]. In the Netherlands, a Salmonellosis incidence of around 300/100000 is seen, mostly manifesting as gastroenteritis[2]. Although a general decline in human Salmonellosis has occurred in the last two

decades[1,2], because of demographic changes, the excess mortality due to *Salmonella* infections was predicted to double in the next 50 years[3].

The same demographic changes, i.e. the relatively and absolutely growing elderly population, will account for an increase in the number of total hip arthroplasties (THAs), and subsequently prosthetic joint infections (PJIs) of these hips[4]. PJI occurs in around 1%-2% of all THAs[5], and is one of the most severe and costly complications, usually requiring additional surgery, a prolonged hospital stay and administration of antibiotic agents, and (temporary) decreased function and quality of life[6,7].

PJI caused by *Salmonella* is nevertheless rare: only 28 patients (30 joints) have been described in the literature, of which 20 were prosthetic hip infections[8]. In the case of *Salmonella typhi*, the most common serotype, the prevalence of involvement of the bones or joints is only 1% or even less[9]. A higher frequency of *Salmonella* infections is seen in patients with sickle cell disease, systemic lupus erythematosus (SLE) and other immunocompromised states[5,10], and in children aged under five[3,11,12]. Most cases of *Salmonella* joint infections are caused by hematogenous spread[5,13].

An aggressive approach with two-stage revision is advised in cases of *Salmonella* PJI, because of the bacterial virulence[8].

We describe two cases of *Salmonella* prosthetic hip infection, both occurring within one month of each other, treated with one-stage revision.

CASE REPORT

Case 1

A 68-year-old female patient visited our outpatient clinic for severe osteoarthritis of the right hip. Her medical history further included clubfoot correction in her early youth, pneumonectomy for carcinoid tumor, hypophysectomy after pituitary adenoma, hypertension, renal failure grade 3, heart failure grade 3, atrial flutter and a stroke. She was using anticoagulants (acenocoumarol) and steroids (hydrocortisone) among other medication. She also mentioned an allergy for cephalosporins. In accord with the patient THA was planned.

Four days prior to surgery, her anticoagulants were replaced by therapeutic low molecular weight heparins (LMWH, nadroparin 5700 IE two times daily). Perioperatively, prophylactic clindamycin was administered. A non-cemented Trident cup with polyethylene insert (Trident system, Stryker Orthopaedics, Mahwah, New Jersey, United States) and a cemented Exeter stem (Exeter Total Hip system, Stryker Orthopaedics, Mahwah, New Jersey, United States) using Simplex P bone cement with Tobramycin (1 g tobramycin, Stryker Orthopaedics, Mahwah, New Jersey, United States) were implanted.

After an uncomplicated rehabilitation course of 5 d the patient was discharged. However, she was readmitted at her local hospital just 2 d later, with anemia (hemoglobin of 4.1 mmol/L, reference value 7.5-10.0 mmol/L). She was given 2 units of packed red blood cells (PRBC) and was transferred to our center.

Due to a sudden onset of right flank pain and elevated liver enzymes, an abdominal computed tomography was performed, which revealed a retroperitoneal hematoma, possibly with ongoing bleeding. Administration of nadroparin was discontinued, the patient received another 4 units of PRBC and after fluid resuscitation her hemodynamic status remained stable.

Gram staining of joint aspirate and superficial wound cultures revealed gram negative rods, while blood parameters showed a C-reactive protein (CRP of 334 mg/L (reference value < 8 mg/L). DAIR (debridement, antibiotics, irrigation and retention) was performed soon after. Intra-operatively 5 cultures were gathered, the insert and prosthetic head were exchanged, and 3 resorbable gentamicin sponges (130 mg gentamicin per sponge; Garacol, EUSA Pharma, Oxford, United Kingdom) were left in the surgical area. Afterwards, intravenous ciprofloxacin was started at 400 mg 3 times daily combined with intravenous vancomycin 1000 mg once daily.

After one week the cultures taken intra-operatively yielded Group E *Salmonella* species. At that moment the vancomycine was stopped while intravenous ciprofloxacine was continued for another week. This was followed by 4 wk of 750 mg ciprofloxacine orally twice a day. Then, due to her existing renal failure, the dosage of ciprofloxacine was lowered to 500 mg twice a day for one week and 500mg once a day for yet another week.

Due to sanguinous wound drainage, the dosage of nadroparin was changed to the prophylactic dosage (0.3 mL = 2850 IE, once a day). Because of the continuing wound drainage and increasing CRP from 119 to 147 mg/L, it was decided to proceed with a one-stage revision, nearly two months after the initial arthroplasty.

Intra-operatively, all components and cement were removed and the wound was thoroughly debrided and irrigated. Subsequently the medullary canal was reamed and an uncemented Restoration Modular stem (Restoration Modular System, Stryker Orthopaedics, Mahwah, New Jersey, United States) and Trident cup were inserted. Antibiotic treatment was continued with ciprofloxacin, according to the antibiogram from the cultures taken previously.

A subsequent debridement, antibiotics and implant retention (DAIR) procedure was performed because of persistent leakage, which appeared to be due to a fracture of the proximal femur around the stable stem. After wiring of this fracture and after exchanging the insert and prosthetic head of THA again, the patient recovered quickly and wound leakage cessated.

The 5 cultures taken during the one-stage revision, as well as the 2 cultures from the second DAIR procedure, all taken during antibiotic treatment, turned out negative. After the second DAIR procedure oral ciprofloxacin dose was administered at 750 mg 2 times daily again. After 5 wk this was lowered back to 500 mg once a day (because of the renal failure).

At the first follow up, two months since the one-stage revision, the patient was walking with a walker. The wound still showed a little redness, but CRP had declined

to 26 mg/L and erythrocyte sedimentation rate (ESR) was 43 mm/h (reference value < 20 mm/h).

At 5 mo follow-up, antibiotic treatment was stopped, the wound showed no signs of infection and ESR had normalized.

Case 2

A 59-year-old man presented at the emergency department with pain in the right groin since four days, along with a progressive fever and nausea. At the age 16 he underwent screw osteosynthesis, because of epiphysiolysis capitis femoris, which was followed by THA in 1999 at the age of 46. No other comorbidities were present.

On physical examination of the hip the patient showed a painless function of 100 degrees flexion, 0 degrees extension, 20 degrees endorotation, and 30 degrees exorotation. Pressure in the groin was painful, however. The psoas sign was negative.

Additional blood tests showed a C-reactive protein of 193 mg/L and ESR 23 mm/h. On X-ray the prosthetic head appeared not to be centered (sign of polyethylene wear), though there were no signs of loosening of the prosthesis. Ultrasound of the groin revealed a 5.5 cm × 7.5 cm abscess. Aspiration produced some drops of pus, along with serosanguinous synovial fluid. After culturing the aspirated fluid revealed *Salmonella enteritidis*.

Antibiotic treatment was postponed until after intra-operative cultures could be taken, as the patient was not septic.

Six days after admission the patient underwent a one-stage revision. The decision to proceed with a one-stage revision rather than performing a DAIR procedure, was made intra-operatively, when osteolytic lesions were found around the femoral stem. A Trident cup and Omnifit stem (Omnifit system, Stryker Orthopaedics, Mahwah, New Jersey, United States) were inserted. Ciprofloxacin was started at 400 mg intravenously three times daily.

After the operation, CRP declined to 49 mg/L (from 245 mg/L at the day of operation) and the incision showed no redness or wound drainage. All 5 cultures obtained intra-operatively showed *Salmonella enteridis*. The patient was discharged with a regimen of oral ciprofloxacin (750 mg twice a day) after having received ciprofloxacin intravenously for 8 d.

At follow up, two weeks after discontinuing the antibiotic treatment (3 mo regime in total) and a total of 3 mo after discharge, the patient had no infectious signs or symptoms. Blood results showed a CRP of 5 mg/L, and an ESR of 9 mm/h. At 6 mo follow up the clinical and radiological findings were normal.

DISCUSSION

PJIs are a severe complication seen in 1%-2% of cases after arthroplasty, causing additional costs and morbidity, including serious impairment in quality of life for the patient[7]. PJI due to *Salmonella* is especially uncommon.

Although most patients having a *Salmonella* infection are suffering from gastro-intestinal complaints, in the presented cases no overt gastro-intestinal symptoms were present (one patient presented only with mild nausea), indicating that PJI by *Salmonella* can occur without general gastro-intestinal complaints as has been previously stated[12].

Even though our cases presented within the same month, the course of infection was different. In the first case, symptoms occurred only 2 wk after initial THA, classifying this as an early infection[14,15] suggesting intra-operative contamination, although *Salmonella* usually spreads *via* the hematogenous route[16]. Another possibility is a carrier state of *Salmonella* species, however, we did not take fecal cultures to rule this out. Hematogenous spread in the early postoperative phase, although unlikely, is of course also possible.

The second PJI would be classified as a late infection[14,15] occurring 13 years after initial surgery.

When comparing this with other case-reports, there seems to be no outspoken trend in time since THA before infection: out of the 20 cases of *Salmonella* PJI in THA, 9 were late (> 24 mo) [11,14,17-22], 5 were delayed (3-24 mo)[23-26] and 5 were early infections (< 3 mo)[10,15,17,27]. In one case time until infection was not specified[28].

In bone infections the most encountered serotypes of *Salmonella* are *S. typhimurium* (group D) and S. *enteritidis* (group B)[15]. In the first case PJI was caused by group E *Salmonella*, which has not been reported before. The other patient's culture turned out to be the more common *Salmonella enteritidis*, reported previously in 5 PJIs of the hip[8,11,20,23,28] and in 6 PJIs of the knee[8,10,23,29-31].

For both our patients, the original treatment plan was to perform a DAIR procedure. In the first patient however, DAIR treatment failed, and a one-stage revision was performed.

During surgery in the second patient we proceeded with a one-stage revision rather than a DAIR procedure because of the encountered osteolysis. Because of good previous experiences by the surgeon, we opted for a one-stage revision rather than a two-stage revision. Only one case treated with a one-stage revision has been described before. In that case it was performed instead of the preferred two-stage procedure, because of the patient's co-morbidity[11].

In 2004, Zimmerli *et al*[15] already set ground rules for choosing between retention or resection of the prosthesis. This choice is based on duration of symptoms, (absence of) prosthetic loosening, tissue status and bacterial susceptibility.

In a recent systematic review by Leonard *et al*[32], functional outcome and reinfection rates were compared between one- and two-stage revision for PJI of the hip. There seems to be a trend toward better functional outcome in single-stage surgery, whereas reinfection rates turn out to be comparable between the two approaches. Besides this, a two-stage revision is associated with a significantly higher morbidity and mortality, and tissue changes associated with a period without a hip implant can lead to important functional deficits after reimplantation[32].

Furthermore, if the selection criteria, mentioned by Zimmerli *et al*[15] and by multiple other articles as summarized in the infectious diseases society of America (IDSA) guidelines[14], are strictly followed, retention and debridement and one-stage revision have high success rates, with less morbidity, in selected patients.

Nevertheless, despite commonly accepted directives and reported good results of one-stage revision in general PJI, both Tóth *et al*[11] and De la Torre *et al*[8] advocate a two-stage approach in patients with a *Salmonella* PJI.

De la Torre *et al*[8] propagate the aggressive treatment approach, because the virulence of *Salmonella* infections, difficulty in re-revision, and results of debridement procedures (based on a meta-analysis of studies published between 1977 and 1999)[8,33]. The virulence of *Salmonella* infections will generally cause a quick onset of symptoms. This means patients will present with symptoms quickly, and treatment can be started early (surgically and medically). If the bacterium has good susceptibility, a high cure rate can be expected, just like the guidelines propagate (Osmon 2013)[14].

In a recent study by Papavasileiou *et al*[34], the antimicrobial resistance of *Salmonella enteritidis* was compared between the planktonic form and the biofilm form in multiple antibiotics[34]. It appeared that the best results were obtained with ciprofloxacin and moxifloxacin[34]. None of the previously described case-reports in which ciprofloxacin was used reported recurrence of PJI[11,23,29,30,35]. This includes the one case treated with a one-stage revision[11].

So far neither of our patients, both treated with a one-stage approach and ciprofloxacin, show signs of reinfection. However, the first patient had undergone a DAIR procedure prior to, and after the one-stage approach, which might have influenced the outcome in a positive way: the IDSA guidelines describe that the thoroughness of debridement positively affects the success rate of a single stage surgery[14], and in our opinion, this might be true for multiple debridements as well.

In conclusion, good results can be achieved with one-stage revision, taking into consideration the guidelines for selecting the right patients[14,15], in combination with the use of appropriate antibiotics with a good activity against the causative micro-organism. One-stage revision is, in selected cases, a better alternative than the two-stage approach, causing less morbidity, less mortality and a much smaller burden of disease for the patient. In our opinion, *Salmonella* PJI could and should be treated as other bacterial PJIs, depending on the factors mentioned in the guidelines, and therefore one-stage revision could also be performed more often in these particular cases.

COMMENTS

Case characteristics

Case 1: A 68-year-old female with a history of severe osteoarthritis of the right hip was readmitted with anemia 5 d after right total hip arthroplasty; Case 2: A 59-year-old male with a history of total hip arthroplasty presented at the emergency department with pain in the right groin.

Clinical diagnosis

Case 1: Anemia and sudden onset of right flank pain shortly after right total hip arthroplasty; Case 2: Mildly declined function of the hip, painful pressure in the groin, along with fever and nausea.

Differential diagnosis

Case 1: Post-operative bleeding, periprosthetic joint infection, loosening of the prosthesis, periprosthetic fissure or fracture, total hip arthroplasty (THA) dislocation, intraabdominal pathology; Case 2: Periprosthetic joint infection, loosening of the prosthesis, THA dislocation, heterotopic ossification, hernia inguinalis

Laboratory diagnosis

Case 1: Hemoglobin 4.1 mmol/L; C-reactive protein (CRP) 334 mg/L; elevated liver enzymes; Case 2: CRP 193 mg/L; erythrocyte sedimentation rate 23 mm/h.

Imaging diagnosis

Case 1: Computed tomography revealed a retroperitoneal hematoma; Case 2: On X-ray the prosthetic head appeared not to be centered, without signs of loosening of the prosthesis, while an ultrasound of the groin revealed a 5.5 cm × 7.5 cm abscess.

Pathological diagnosis

Case 1: Intraoperatively taken cultures yielded group E *Salmonella* species; Case 2: Joint aspiration fluid revealed *Salmonella enteritidis*.

Treatment

Case 1: After one failed debridement, antibiotics and implant retention-procedure, one-stage revision was performed followed by ciprofloxacin; Case 2: Because of encountered osteolysis the patient was treated with a one-stage revision, followed by ciprofolxacin.

Related reports

There is an ongoing debate whether prosthetic joint infection of the hip is best treated by one- or two-stage revision surgery, but also whether Salmonella infections should be treated similarly to periprosthetic joint infections due to other bacteria.

Experiences and lessons

This case report illustrates that one-stage revision of periprosthetic joint infections of the hip can be a successful treatment even when infection is due to *Salmonella* species.

Peer review

This is a report of two case with a prosthetic joint infection cause by Salmonella treated with one-stage revision. The paper is very well presented with a clear message.

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P- Reviewer: Drosos GI **S- Editor**: Song XX **L- Editor**: A
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