Intramedullary reaming and irrigation in associated with antibiotic-loaded calcium sulfate implantation in the treatment of infection after intramedullary nailing: A retrospective study of 19 cases.

Hong-An Zhang
Guangdong Second Provincial General Hospital
Chun-Hao Zhou
Southern Medical University Nanfang Hospital
Xiang-Qing Meng
Guangdong Second Provincial General Hospital
Jia Fang
Guangdong Second Provincial General Hospital
Cheng-He Qin (orthoqin@163.com)
Guangdong Second Provincial General Hospital https://orcid.org/0000-0002-5472-7964

Research article

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Abstract

Background

The incidence of intramedullary infection is increasing with the frequent application of intramedullary fixations on long bone fractures in latest decades. However, appropriate treatment for those special infection remains a challenge. The aims of this study were to assess the efficiency of our treatment protocols: intramedullary nail removal, medullary canal reaming and irrigation, followed by antibiotic-loaded calcium sulfate implantation with or without distraction osteogenesis, for the treatment of infection after intramedullary nailing.

Methods

From 2014 to 2017, a total of 19 patients with intramedullary infection were treated in our center, with means of intramedullary nail removal, distal diaphysis fenestration, medullary canal reaming and irrigation, antibiotic-loaded calcium sulfate implantation, followed by distraction osteogenesis in 9 cases to repair bone defect. The infection remission rate, infection recurrence rate and post-operative complications rate were assessed during the follow-up.

Results

All of patients gained satisfactory outcomes with an average follow-up of 38.1 (24 to 55months). 94.7% (18/19) patients achieved infection remission after surgical treatment. 5.3% (1/19) patient developed reinfection, but healed at the end of follow up with re-debridement. 9 patients with surgery-related bone defects received bone transport and successfully restored the length of involved limbs, with a mean transport duration of 10.7 months (range, 6.7 to 19.5months). Majority of patients achieved pain free and full weight bearing during the follow-up. Postoperative complications mainly included prolonged aseptic draining (36.8%, 7/19) and refracture (5.3%, 1/19), which were successfully managed by regular dressing and refixation.

Conclusion

Intramedullary nail removal, canal reaming and irrigation in associated with antibiotic-loaded calcium sulfate implantation (with or without distraction osteogenesis) were effective in the treatment of infection after intramedullary nailing.

Introduction

The development of infection after fixation is an unusual complication of intramedullary nailing. There have been different reports for infection rate after intramedullary nailing, some researchers reported the rate as 0.9%-3.8%[1, 2]. In a retrospective analysis of more than 1000 cases of humeral shaft fractures with intramedullary nailing, the infection rate after closed fracture was up to 1.9%, and the postoperative infection rate of open fracture reached 7%[3, 4]. Although the incidence of infection is not high, if the infection is not treated timely and appropriately, it is easy to cause catastrophic consequences such as osteomyelitis, fracture non-union, physical disability and even systemic sepsis.

The management of this type of infection remains controversial. According to the study of *Makridis KG* et al, a total of three stages of infection after intramedullary nailing could be classified[5]. They are, stage Ⅰ: 2–6 weeks after operation, generally as cellulitis; stage Ⅱ: 2–9 months after operation, primarily manifested as delayed wound healing, exudation, osteonecrosis, and pathological fracture; stage Ⅲ: 9 months after operation, with definite osteomyelitis. Each stage has its own managements. In the treatment of infections at stage I, a more conservative approach is widely accepted. With regard to stage II and III infection with unhealed fracture, however, the opinions on treatment become different from person to person[5–7]. At present, there has been no uniform and standard treatment protocol for those types of intramedullary infection[8].

To our experience, intramedullary nail as a foreign fixator lacks of adequate blood supply, which means systemic antibiotics cannot reach to the interface of fixator and kill the biofilm bacteria effectively. Furthermore, pathogens spread quickly to the whole medullary canal along with the nail, leading local infection developing to diffused one, if without appropriate treatment. Therefore, nails removal and surgical debridement are keystone for the treatment of infection after intramedullary nailing, since it removes the involved tissues and destroy the biofilm produced by bacteria, which enhances the efficiency of antibiotics in turn and improve the infection remission rate. In order to remove organisms efficiently, surgical debridement mainly includes local debridement and medullary canal managements. Reaming and irrigation is one of the most important components of surgical debridement, since it eliminates the endosteal sequestra of the canal, lower the intraosseous pressure, vascularize the bone and of course, remove the biofilm bacteria[9]. The efficiency of intramedullary reaming and irrigation on intramedullary infection or osteomyelitis has been reported in some former studies[10–12].

After debridement, bone substitute is vital to regenerate bone defect, and even serves as a local antibiotic carrier. Absorbable local antibiotic delivery system, the antibiotic-impregnated calcium sulfate, is an increasingly popular bone substitute applied in clinical practice, which has exhibited excellent osteogenesis and drug loading property. Related studies have reported the good outcomes could be received when applying antibiotic-loaded calcium sulfate as a local antibiotic carrier on bone infection.

The aims of this study were to demonstrate our experience on the management of infection after intramedullary nailing, and assess the efficiency of those surgical debridement technique combined with antibiotic-loaded calcium sulfate spacer and distraction osteogenesis in the treatment of infection after intramedullary nailing.

Methods And Materials

Those patients diagnosed with infection after intramedullary nailing fixation and treated in our department from 2014–2017 were included in the study. The inclusion criteria of study were: 1). Cases with infection after the initial intramedullary nailing fixation and retained the intramedullary nail when admitted to hospital. 2). Cases persisted to follow-up and has been followed up for more than 24 months. 3). Cases received debridement and antibiotic-loaded calcium sulfate as the only treatment method. The exclusion criteria were: 1) those with severe dysfunction of liver or kidney, severe cardiovascular disease and diabetes with uncontrolled blood glucose. 2) cases did not receive our treatment methods or received other surgical treatments during the follow-up. 3) the follow-up was less than 24 months.

In total, nineteen cases with infection after intramedullary nailing met the criteria were retrospectively analyzed. There were 15 men and 4 women with a mean age of 39 years (range, 23 to 56). Side involved was the right in 9 cases and the left in 9 cases. Site involved the femur in 7 cases and tibia in 12 cases. All of patients received physical examinations, imaging examinations and laboratory tests to evaluate the situations and guide the surgical treatment. Preoperative laboratory results showed, mean erythrocyte sedimentation rate (ESR) 49.8 mm/h, mean C-reactive protein (CRP) level 32.9 mg/L, and mean white blood cell (WBC) 12.7×10^9/L. The further details of those patients were listed in Table 1. All of patients were presented with chronic sinus at their first physical examination in our department. According to the preoperative X-ray results, 10 patients were with healed fracture at the time of diagnosis, while 9 cases remain unhealed. Antibiotic administration was not begun until samples had been obtained for culture during surgery. Before surgical interventions, patients were informed with the details of treatment protocols, and the contents were signed by patients themselves.

Surgical Technique

Surgical interventions were performed as follows: The intramedullary nail was removed at first, and the subsequent debridement procedures were dependent on whether the fracture had healed:

1. For 10 cases with fracture healing, the entry point of the intramedullary nail was enlarged, and subsequently, fenestration was performed on the distal diaphysis to drain the irrigation fluid and necrosis tissues. The medullary canal was reamed repeatedly with a larger-diameter reamer head (depending on preoperative measurement and the information of initial surgery) to debride out all the contents.
2. For 9 cases suffered with non-union, after intramedullary nail removal, the non-union site was segmentally resected, for preventing the infection recurrence as possible[13]. The boney defects of those cases were managed by osteotomy and distraction osteogenesis in a secondary surgery, if inflammatory markers had returned to normal.

The involved surrounding soft tissues were debrided also. Samples collected during the reaming were sent for cultures and pathological examination. After radical debridement, medullary canal was irrigated with at least 3L of saline using an impulsive irrigation gun. Then, the antibiotic-loaded calcium sulfate

(Stimulan, Biocomposites Ltd.) was prepared with appropriate ratio (VA 0.5 g + CN 2 ml + CS 5 ml), stirred with proper saline and injected into the medullary canal and bone defect site. Considering the economic situations of patients as well as the potential cytotoxic effect of calcium sulfate, the total volume of antibiotic-loaded calcium sulfate used per patient was no more than 50 ml. Since the species of pathogens were still unclear, vancomycin and gentamicin were both employed to cover Gram-positive and negative bacteria. After implantation, an external fixator was used in 13 cases for supporting the limbs or secondary distraction osteogenesis in cases with bone defects.

Postoperative Management

Postoperatively, intravenous antibiotics were empirically administrated until culture results were available, and then adjusted based on the results. Due to the topical application of antibiotic-loaded calcium sulfate, a total course of antibiotics usage we recommended was less than 2 weeks. Regular infection markers test (WBC, CRP, ESR) and standard AP and lateral radiographs were suggested in outpatient to assess the efficiency of infection elimination and bone formation. 9 cases with bony defects received osteotomy in a secondary surgery. Bone transport was carried out 1 weeks after surgery, with an initial rhythm of 1 mm/day and then regulated according to the quality of regenerate formation and feedbacks of patients. External fixations were removed once the bones were assessed strong enough for weight bearing.

Outcome Evaluation

We defined infection remission as the absence of any signs of infection and a completely healed wound. Bone union proved by the formation of new bone tissues on the X-ray presentations. infection recurrence was defined by the positive clinical symptoms, radiographic findings and elevated inflammatory markers. We defined continuous drainage without topical infection symptoms for more than 1 month as prolonged aseptic drainage.

Results

Totally, 19 cases who received intramedullary reaming and antibiotic-impregnated calcium sulfate implantation in our center were included for study. 13 cases needed external fixation, and 9 of which suffered with segmental bone resection and needed bone transport to repair the bone defect. The average bone defect of those cases was 4.7 cm (range, 3.3 to 7.6 cm). After surgery, clindamycin, cephalosporin or quinolones was the commonly applied intravenous antibiotics, with a mean duration of 8.3 days (range, 3–14). Another 4 weeks of oral antibiotics usage was omitted in our study, since we deemed extremely high concentrations and long curative duration produced by local antibiotics delivery system was far enough to eradicated the residual organisms. The mean time for normalization of infection markers after surgery was 3.5 weeks (range, 2 to 8). 9 cases with segmental bone resection received osteotomy after the infection markers became normal, and started bone transport one week after surgery (Fig. 2).

With regard to the culture results, a total of 20 strains of bacteria in 17 cases were isolated, with a positive rate of 89.5% (17/19). *Coagulase-negative staphylococcus* (30.0%, 6/20) was the most commonly isolated pathogen by culture, followed by *MRSA* (25.0%, 5/20), *MSSA* (25.0%, 5/20), *Escherichia coli* (15%, 3/20) (Fig. 3). 3 cases (15.8%, 3/19) were polymicrobial infections and the bacteria species of which were *Coagulase-negative staphylococcus, Escherichia coli* and *MRSA*, respectively.

With a mean follow-up of 38 months (range, 24 to 55), 18 (94.7%, 18/19) cases achieved infection remission after first surgical treatment, 1 case (5.3%, 1/19) developed infection recurrence three months after surgery and underwent segmental resection and bone transport. Majority of patients achieved pain free and full weight bearing during the follow-up. 1 case (5.3%, 1/19) re-fractured four months after surgery and underwent external fixation. Both patients mentioned above healed at the end of follow-up. Prolonged aseptic drainage was the most frequently detected complications followed by application of calcium sulfate, which reached 36.8% (7/19) in this study. With regular dressing change, all of cases achieved healing eventually. Bone defects in 9 cases were successfully restored by bone transport technique, with a mean fixation duration of 10.7 months (range, 6.7 to 19.5months). The details of surgery and follow-up outcomes were listed in Table 2.

Discussion

After surgical debridement and antibiotic-loaded calcium sulfate implantation, most of patients received satisfying results. 94.7% (18/19) cases achieved infection remission after first surgical treatment, while only 1 case received secondary treatment for infection recurrence. Undoubtedly, the high remission rate should be attributed to the radical debridement and the use of local antibiotics delivery system, which removed the infected tissues in a more thorough way and eliminated the residual organisms by a longer therapeutic duration. This remarkable result was similar to the previous report. In their study, *N. Kanakaris et al* used intramedullary removal, intramedullary debridement with reamer-irrigator-aspirator (RIA) device and antibiotic-loaded cement rods in the treatment of 24 such patients. The cement rods were removed once the infections were well controlled. With a mean follow-up of 21 months, 23 (96%) patients had no evidence of recurrent infection[14]. The difference of their study lies in the application of RIA device and antibiotic cement. The RIA system is a device that was initially developed to prevent fat embolism and lessen the systemic inflammatory process after reaming the femur in nailing procedures[15, 16]. Due to its versatility, it has been expanded to the treatment of long bone osteomyelitis[17, 18]. However, RIA system is not introduced into our country by now, yet the methods we used were similar to RIA system, and with a pretty good outcome as we demonstrated. Antibiotic cement was non-absorbable, requiring a secondary removal intervention, or its long existence might lead to infection recurrence. It is one of the conspicuous shortcomings compared to calcium sulfate in our study.

This study also included nine cases with fracture non-union. They were treated by intramedullary nails removal, segmental bone resection, medullary canal reaming and irrigation, delivery of local antibiotic and secondary bone transport. All of patients received infection remission and length restorage of involved limbs. Although the results were satisfying, the best protocol on the management of infected non-union is still controversial. Those who prefer to retain the nails believe that fracture healing is more important, management of intramedullary infection could be postponed until bone healing, yet those who are more radical recommend that removal of intramedullary nails will take infection control in prior consideration. Based on different concepts, the treatment methods are various, which include: 1). Local debridement and antibiotics usage but retaining the nail, 2). Current nail removal, re-reaming and replacement of a larger diameter intramedullary nail or a resorbable antibiotic coating one, 3). Nail removal, segmental bone resection, re-reaming, local antibiotics delivery and bone reconstruction. To our opinion, management with infection is more important than bone healing, since incomplete debridement and internal fixation are unsuitable for infection disease. Persistent infection or infection recurrence, however, might prevent the healing process and even lead to diffused osteomyelitis, disability and even amputation. We are inclined to the third protocol mentioned above, and has been well proved by results.

Local antibiotic-carriers were proposed in 1970s[19, 20], and has been recommended as a bone substitute in the management of bone defect, or as a local antibiotic carrier in bone infection. Calcium sulfate as one of the local applied carriers was approved by the US FDA in 1996 with osteoconductivity for non-diabetic patients, and now has been practically long applied in orthopedic surgery, including as an antibiotic carrier, filling bone defects, expanding solvent for bone graft[21–23]. As an absorbable carrier, it has stable curve of releasing antibiotics and maintain about 6–8 weeks higher than MIC. The local concentration is about 100–1000 times higher than the serum levels resulting from intravenous treatment[24]. It is sufficiently high to penetrate biofilm and eliminate the stubborn bacteria. Furthermore, calcium sulfate exhibits similar microstructure to cancellous bone. After being absorbed in situ, the network structure is left, and the presence of trabecular bone can be observed under the light microscope, which contributes to the crawling and growing of blood vessels and bone cells[25, 26]. Calcium sulfates applied in clinical practice are mostly injectable, and they are very suitable for filling the marrow canal.

Prolonged aseptic drainage was the most frequent recorded complication in our study, with a relatively high rate of 36.8% (7/19). The drainage rate was similar to the previous studies, in which the drainage rate ranged from 4.2–33%[27–29]. To our experience, poor soft tissue coverage, scar formation and excessive calcium sulfate implantation may be the reasons for the high incidence of postoperative exudation. Although this kind of aseptic exudation is not a sign of infection, management of this postoperative drainage is of great necessity, or a soggy gauze is prone to cause wound infection. Generally, routine treatment of prolonged drainage includes regular dressing and wound care. Other effective methods to prevent prolonged aseptic drainage may include good soft tissue coverage and reduction of calcium sulfate implantation.

The weakness of our study is still obvious. Firstly, our outcomes were not compared with those of other surgical methods. In addition, our study included multiple situations, such as different location of infection and different surgical treatment on unhealed and healed bone, which inevitably leaded to the outcomes more complex. However, we have to point out that the emphasis of our study was to introduce an effective method to eliminate the infection after intramedullary nailing (not focusing on the management of nonunion only), and all cases received the same management methods of infection, so we think the study is still meaningful.

Conclusion

Intramedullary nailing removal, medullary reaming and irrigation combined with antibiotic-loaded calcium sulfate implantation is effective in the treatment of infection after intramedullary nailing.

Abbreviations

Abbreviations

CoNS, coagulase-negative staphylococcus

E. coli, Escherichia coli

Ent. Cloacae, Enterobacter cloacae

MRSA, methicillin-resistant Staphylococcus aureus

MSSA, methicillinsensitive Staphylococcus aureus

CN, Gentamicin

VA, Vancomycin

CS, calcium sulfate

EF, external fixator

IM, intramedullary

CRP, C-reactive protein

ESR, erythrocyte sedimentation rate

WBC, white blood cells

FWB, full weight bearing

Declarations

Ethics approval and consent to participate

Medical Ethical Committee of Guangdong second provincial general hospital has approved the research ethics approval. All included patients consented to participate in this study and a signed consent form was obtained from each subject before testing. All procedures were conducted according to the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and material

The data used and analyzed during the current study is available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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This study was not externally founded.

Authors' contributions

HAZ, CHZ and XQM contributed equally to this work. Scientific idea: CHQ, HAZ and CHZ; Project planning: CHQ, CHZ, XQM, JF; Manuscript writing: HAZ, CHZ and XQM. Manuscript revision: HAZ, CHZ and XQM; All authors read and approved the final manuscript.

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Tables

Table 1. Preoperative characteristics of nineteen cases.

Case No.	Age	Initial trauma	Site/Side	Open or closed fracture	history (months)	Sinus	Fracture healed or not	Infection markers before surgery
1	44	Falling height	Femur/R	Closed	36	Yes	Yes	WBC: 6.4×10^9 CRP: 56.7 ESR: 14
2	52	Traffic trauma	Tibia/L	Open	13	Yes	Yes	WBC: 5.7×10^9 CRP: 9 ESR: 26
3	33	Falling height	Tibia/R	Closed	3	Yes	No	WBC: 11.3×10^9 CRP: 77 ESR: 101
4	37	Traffic trauma	Femur/R	Open	48	Yes	Yes	WBC: 5.7×10^9 CRP: 7.4 ESR: 45
5	24	Falling height	Tibia/R	Open	6	Yes	Yes	WBC: 6.3×10^9 CRP: 5.3 ESR: 29
6	26	Falling height	Tibia/L	Closed	14	Yes	No	WBC: 5.7×10^9 CRP: 7.4 ESR: 45
7	44	Heavy pound injury	Tibia/L	Open	4	Yes	No	WBC: 10.5×10^9 CRP: 23.2 ESR: 15
8	44	Traffic trauma	Femur/L	Closed	20	Yes	Yes	WBC: 18.3×10^9 CRP: 37.3 ESR: 114
9	47	Traffic trauma	Femur/R	Open	36	Yes	Yes	WBC: 12.6×10^9 CRP: 35.3 ESR: 89

Case No.	Age	Initial trauma	Site/Side	Open or closed fracture	history (months)	Sinus	Fracture healed or not	Infection markers before surgery
10	45	Falling height	Tibia/L	Open	40	Yes	Yes	WBC: 10.3 $\times 10^9$ CRP: 42.6 ESR: 67
11	52	Heavy pound injury	Tibia/L	Closed	5	Yes	Yes	WBC: 7.5 $\times 10^9$ CRP: 18.3 ESR: 5
12	37	Traffic trauma	Tibia/L	Open	19	Yes	No	WBC: 22.1 $\times 10^9$ CRP: 51.0 ESR: 78
13	46	Traffic trauma	Femur/L	Open	13	Yes	No	WBC: 9.3 $\times 10^9$ CRP: 11.3 ESR: 25.7
14	27	Traffic trauma	Femur/R	Closed	15	Yes	Yes	WBC: 17.7 $\times 10^9$ CRP: 77.5 ESR: 32
15	34	Traffic trauma	Tibia/R	Open	30	Yes	Yes	WBC: 28.3 $\times 10^9$ CRP: 44.9 ESR: 29
16	56	Falling height	Tibia/L	Closed	7	Yes	No	WBC: 8.1 $\times 10^9$ CRP: 65.3 ESR: 29
17	23	Traffic trauma	Tibia/R	Open	11	Yes	Yes	WBC: 17.5 $\times 10^9$ CRP: 10.6 ESR: 76
18	28	Traffic trauma	Femur/R	Closed	11	Yes	Yes	WBC: 21.8 $\times 10^9$ CRP: 28.9 ESR: 23

Case No.	Age	Initial trauma	Site/Side	Open or closed fracture	history (months)	Sinus	Fracture healed or not	Infection markers before surgery
19	42	Falling height	Tibia/L	Closed	17	Yes	No	WBC: 16.1 × 10^9 CRP: 17.3 ESR: 103

Table 2. The details of surgery and follow-up outcomes of nineteen cases.

Case No.	Microbiology	Description of surgery	Time for normalization of infection markers	Follow-up (months)	Recurrence	Outcome
1	MRSA	IM nail removal + Debridement + CS + EF	2 weeks	36	No	Pain free, FWB mobilisation
2	E. coli	IM nail removal + Debridement + CS	4 weeks	24	No	Pain free, FWB mobilisation
3	CoNS + E. coli	IM nail removal + Debridement + CS + EF+ Bone transport	8 weeks	38	No	Mild pain with movement, FWB mobilisation
4	-	IM nail removal + Debridement + CS	4 weeks	37	No	Pain free, FWB mobilisation
5	MSSA	IM nail removal + Debridement + CS + EF+ Bone transport	3 weeks	27	No	Mild pain and movement limitation on right ankle
6	MRSA	IM nail removal + Debridement + CS + EF+ Bone transport	2 weeks	26	No	Pain free, FWB mobilisation
7	CoNS	IM nail removal + Debridement + CS + EF	5 weeks	41	Yes, 3 months after the first surgery	Segmental resection and bone transport
8	Ent. Cloacae	IM nail removal + Debridement + CS	2 weeks	46	No	Pain free, FWB mobilisation

Case No.	Microbiology	Description of surgery	Time for normalization of infection markers	Follow-up (months)	Recurrence	Outcome
9	-	IM nail removal + Debridement + CS	4 weeks	25	No	Refracture four months after first surgery, followed by EF fixation
10	CoNS	IM nail removal + Debridement + CS + EF+ Bone transport	2 weeks	33	No	Pain free, FWB mobilisation
11	MSSA	IM nail removal + Debridement + CS + EF	3 weeks	52	No	Pain free, FWB mobilisation
12	CoNS	IM nail removal + Debridement + CS + EF+ Bone transport	3 weeks	41	No	Mild pain with movement, FWB mobilisation
13	MSSA	IM nail removal + Debridement + CS	2 weeks	38	No	Pain free, FWB mobilisation
14	MSSA	IM nail removal + Debridement + CS + EF	2 weeks	40	No	Pain free, FWB mobilisation
15	MSSA	IM nail removal + Debridement + CS + EF+ Bone transport	3 weeks	30	No	Mild pain with movement, FWB mobilisation
16	MRSA	IM nail removal + Debridement + CS + EF	2 weeks	55	No	Pain free, FWB mobilisation
17	E.coli + MRSA	IM nail removal + Debridement + CS	2 weeks	44	No	Pain free, FWB mobilisation

Case No.	Microbiology	Description of surgery	Time for normalization of infection markers	Follow-up (months)	Recurrence	Outcome
18	CoNS	IM nail removal + Debridement + CS + EF+ Bone transport	6 weeks	37	No	Mild pain with movement, FWB mobilisation
19	CoNS + MRSA	IM nail removal + Debridement + CS + EF+ Bone transport	6 weeks	54	No	Pain free, FWB mobilisation

CoNS, coagulase-negative staphylococcus; E. coli, Escherichia coli; Ent. Cloacae, Enterobacter cloacae; MRSA, methicillin-resistant Staphylococcus aureus; MSSA, methicillinsensitive Staphylococcus aureus

† CS, calcium sulfate; EF, external fixator; IM, intramedullary

‡ CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; WBC, white blood cells FWB, full weight bearing

Figures

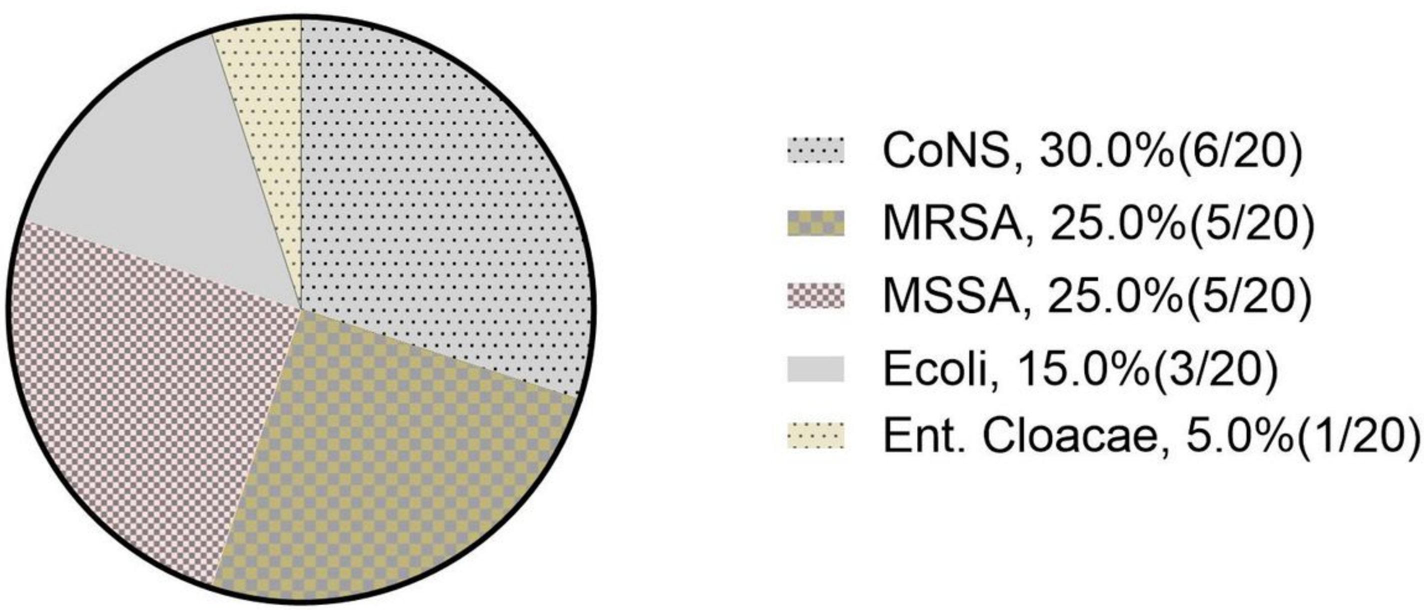

Figure 1

Distribution of bacterial culture results after operation.

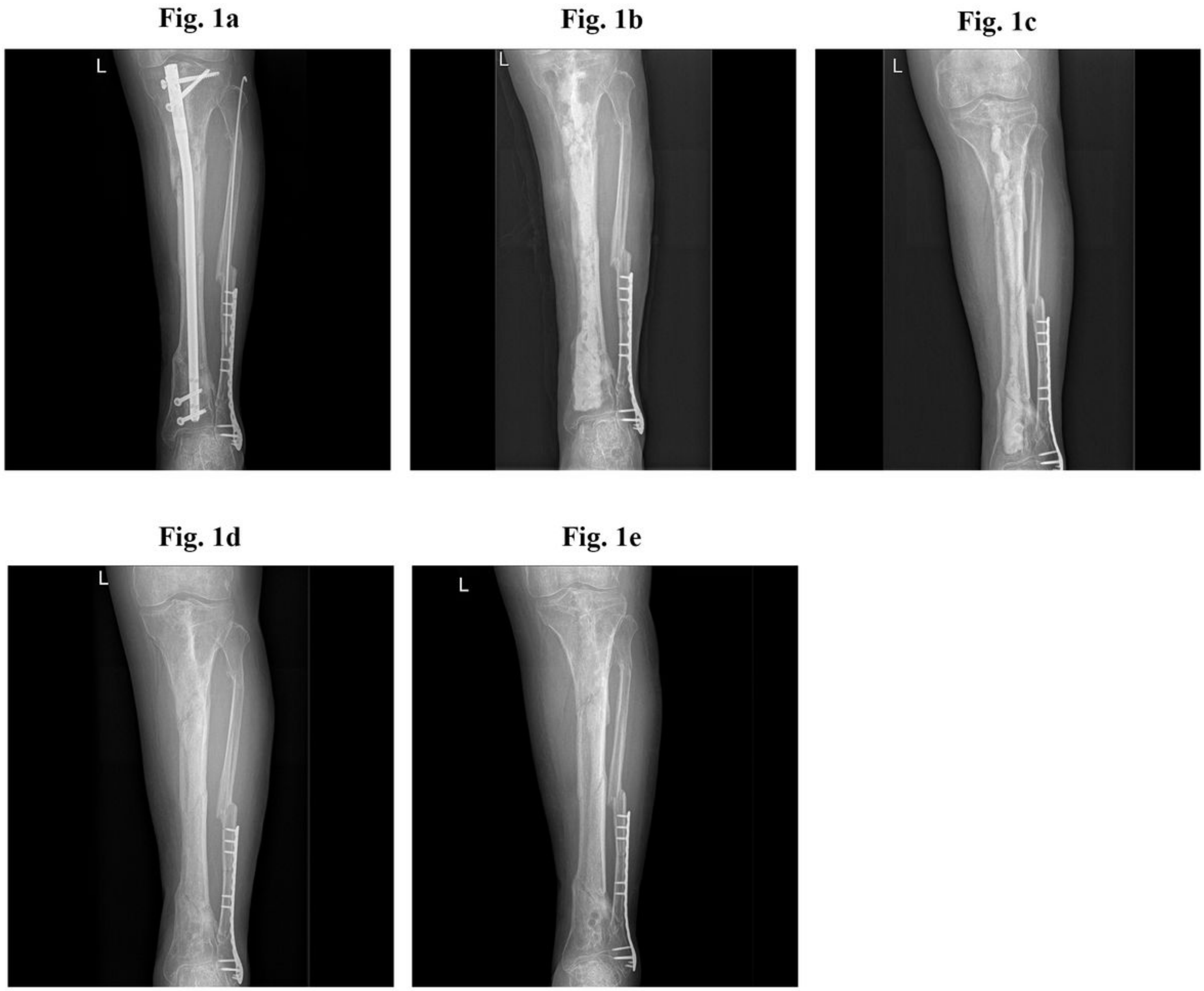

Figure 2

The typical case of IM nail removal+Debridement+CS.

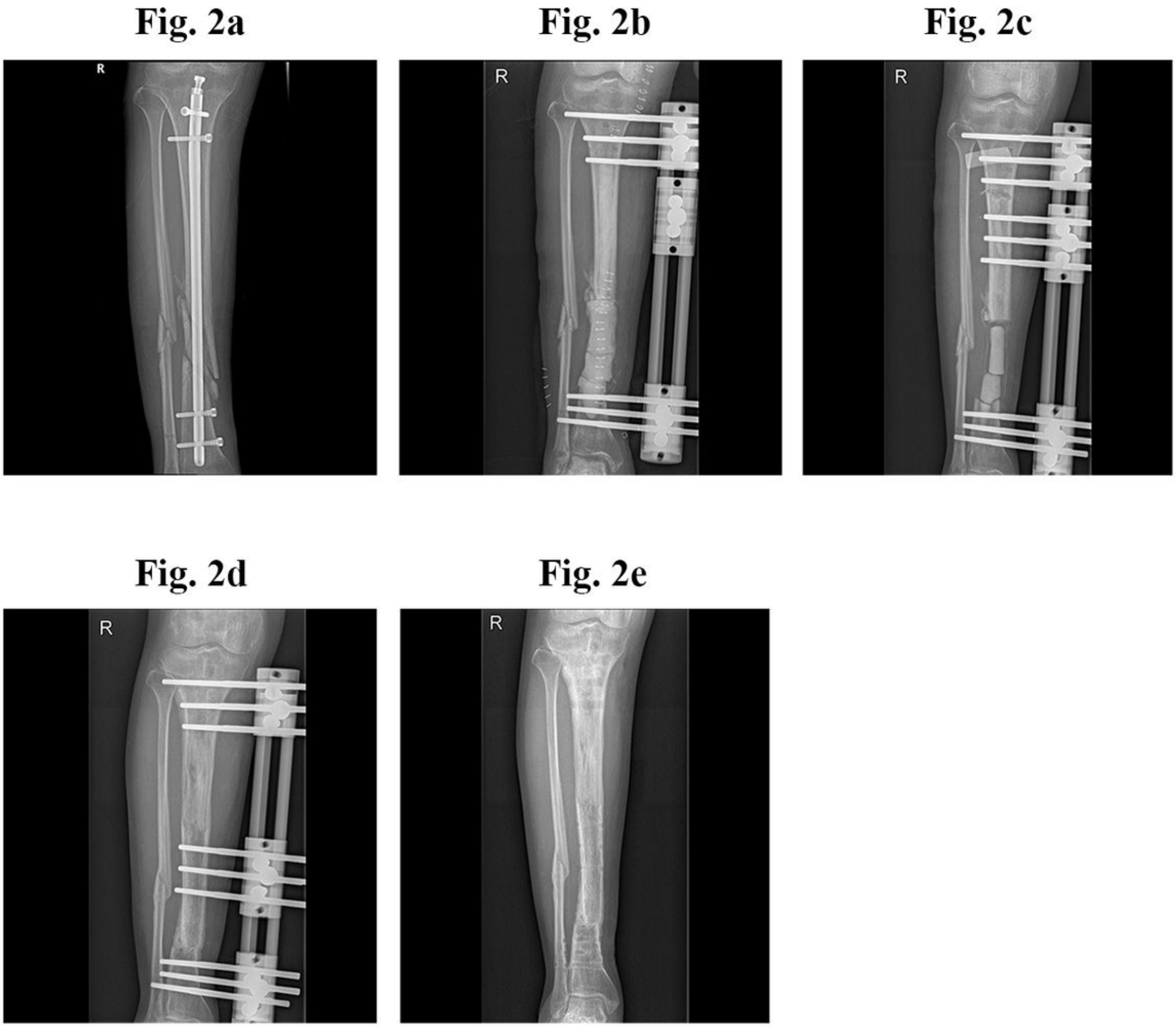

Figure 3

The typical case of IM nail removal +Debridement+CS+EF+Bone transport.