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A case series

## BRUCELLA INFECTION FOLLOWING TOTAL JOINT ARTHROPLASTY

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### Abstract

*Brucellosis is a common zoonotic infection that carries a high economic burden in China especially in Xinjiang.*

**Purpose of the message:** To discuss the treatment of brucella infection following total joint arthroplasty and find out its curative effect.

**Methods.** We analyzed 8 patients with who infected joint brucella after received arthroplasty in our department from March 2009 to March 2019, whose ages were from 55 to 79 years old (average age was  $65.6 \pm 1$  years). The following parameters were measured in the pre- and post-operation periods: HSS and Harris score, range of knee motion (ROM), VAS, erythrocyte sedimentation rate (ESR) and C-reactive Protein (CRP). From x-ray to find out post-operate curative effect of revision operation.

**Results.** All cases had pain and elevated ESR. Deep vein thrombosis (DVT) and nerve damage were not found in these cases. There were no sinuses on the skin have be found. All patients received total joint arthroplasty and infected with brucella post operation receive revision operation at last. All cases were followed-up for 6-30 months; the average follow-up period was  $14 \pm 0.5$  months. Post-operation we took an HSS and Harris score and X-rays to find out its curative effect after revision operation. There were also no patients with aseptic loosening or fracture of prosthesis during or post- revision operation, no recurrence had been found. The average ROM of knee was improved to  $90 \pm 3^\circ$ .

**Conclusions.** Recent clinical results indicate that systemic antibrucellosis chemotherapy and surgery technical is effective to treat the patients following. Revision operation can significantly improve the function of the joint and relieve pain.

**Key words:** brucella, arthroplasty, infection.

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### Introduction

Brucellosis is a zoonotic disease caused by the gram-negative bacilli of brucella. From the history we know that Hippocrates may have described brucella in his treatise "on epidemics" and there is some evidence to prove that the disease was common in the ancient world [1]. Nowadays, is still endemic in west part of China.

As is arthroplasty widely used, more and more papers are reporting on arthroplasty used in kinds of infection joints, like tuberculosis joint [2,3]. Our hospital has 3200 beds for patients, including 150 beds for the

orthopedics department, 15 beds for special infections disease for example, joint tuberculosis. Based on these clinical experiences we carried out revision operation on brucella infection after total arthroplasty.

**The aim of this paper** is to discuss our experience concerning about the patients with brucella prosthetic joint infection and find out its curative effect.

### A series of clinical cases

This study was approved by the People's Hospital of Xinjiang Uygur Autonomous Region Orthopedics center. According to China's brucellosis diagnosis and treatment guidelines [4] the diagnosis of brucellosis should be combined with epidemiological history, clinical manifestations and laboratory examination. Between March 2009 to March 2019, we analyzed 8 patients with who have one stage of revision infected joint brucella after received arthroplasty. Patients hip dysplasia, fractures secondary to tumors, Paget's disease, or metabolic bone disease were excluded from the study.

In our study, all of the cases were unilateral, five cases were male, and three cases were female. Patients' age range was from 55 to 79, with an average age of  $65.6 \pm 1$  years old. 6 patients were herdsmen, 2 was lived in city. Based on the clinical examination we found pain, swelling of joint, joint dysfunction, clinical weight loss and 4 patients have febrile. 1 patient has testicle swollen and treated in urology department before. On X-ray examination, we found prosthesis loosening (Fig.1,2,3,4).



Figure 1- Patient have knee joint dysfunction pre-operation

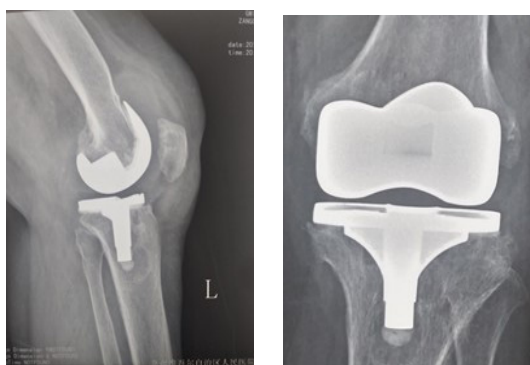


Figure 2 - Pre-operation X-ray showed prosthesis loosening

From computed tomography (CT) scans we found a low-density area that means joint purulent tissue formation around the joints. Blood tests showed erythrocyte sedimentation rate (ESR) 39-87 mm/H

(normal 0-20 mm/H). All patients C-reactive Protein (CRP) was 12-112mg/L (normal 1-8mg/L) higher than normal. Figure 2 - Synovial partial necrosis, purulent and necrotic tissue around prosthesis



Figure 3 - Synovial partial necrosis, purulent and necrotic tissue around prosthesis

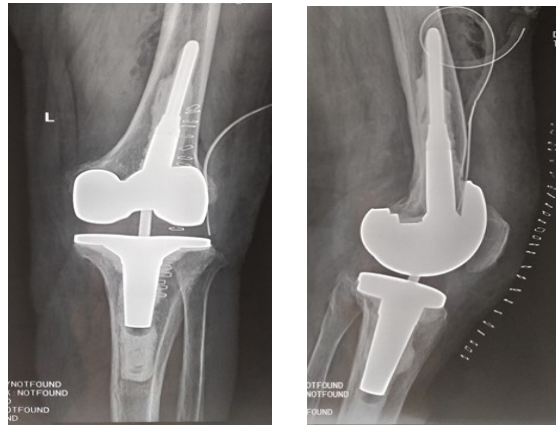


Figure 4 - Post-operation x-ray shows no prosthesis loosening happened, Implants placed good position

Anti-brucellosis treatment was started 2 weeks before surgery, and the medication regimen was doxycycline (100 mg, 2 times/d) combined with rifampicin (600 mg/d). All these we call pre-operation nutritional support therapy considering it as an important part of treatment. VAS score was taken before and post-operation to get know the relief of pain. Two kinds scores were taken

to evaluate the function, for knee revision patients we use HSS score, preoperative HSS scores were 25 to 45 points (average  $29.0 \pm 2$  points), average ROM was  $60 \pm 5^\circ$ , and for hip Harris scores were 30-50 points (average  $36.5 \pm 8.5$  points). All cases were followed-up for 6-30 months; the average follow-up period was  $14 \pm 0.5$  months.



Figure 5 - Patient has painless and good function knee joint post-operation

All patients had general anesthesia, and surgical procedures were performed by one group using a standard medial patellar arthrotomy technique with a tourniquet for knee arthroplasty, and lateral-posterior approach for hip replacement. During the operation we could see purulent or necrotic tissue around prosthesis. The liquor puris was a turbid, pale yellow, and synovial hyperplasia edema, synovial partial necrosis. We did the debridement first; pulse pressure washing could help to clean out the brucella bacillus. After this step we change the gloves and use new operation instrument for revision. After debridement and installing the prosthesis, we use pressure washing after bone cement was dry and used doxycycline powder(100mg) directly around the prosthesis. No drainage was placed. The most conclusive means of establishing the diagnosis of brucellosis is by positive cultures from normally sterile body fluids or

tissues. During the operation pus was cultured, and the tissues were removed and sent for routine pathological examination.

SPSS 19.0 statistical software was used for data analysis. The measurement data conforming to the normal distribution are expressed as  $X \pm S$ , and the paired-sample t test was performed on before and after the operation. The difference is statistically significant with  $p < 0,05$  (SPSS19.0, SPSS Inc., Chicago, IL, USA).

In this Study length of operation performed was 70min (arrange from 50-90 minutes), the amount of intraoperative blood loss 350ml (arrange from 250-450 ml). During the operation no nerve injury and prosthesis fracture happened.

The VAS score of the patients', ESR and CRP level have significant statically difference  $p < 0,05$ .

## Discussion

Brucellosis is a zoonotic disease, more and more report showed it was becoming risen in some undeveloped country. Over 500 thousand cases of brucellosis are reported yearly to the World Health Organization, it is estimated that annual losses from

bovine brucellosis in Latin America is approximately US\$ 600 million [5,6]. As we know, if incidence of brucellosis was well controlled in the animal reservoirs, there will be a corresponding and significant decline in the incidence in humans. China implemented large-scale animal

brucellosis prevention and control work in the 1960s and 1970s, which significantly reduced the prevalence of brucellosis, but since the 1990s, the number of cases has risen significantly, especially in west part of China. There was a paper from our region (The Sixth People's Hospital of the Xinjiang Uygur Autonomous Region, hereafter called especial infection Hospital), they reported A total of 2041 patients with laboratory confirmed brucellosis were admitted to the hospital between January 1st and December 31st of 2014 and were included in, the patients numbers were so large [7].

From 1990's, more and more Arthroplasty have been performed in China, so we have to face more cases about periprosthetic joint infection (PJI). Although bacterial infections of prosthetic joints have been abundantly documented, but brucella infection following arthroplasty was rare reported, the first described in 1991, in a Saudi woman with bilateral involvement caused by direct spread from knee abscesses [8,9].

One stage or two stage revision it is still in the dispute phase in China. At present, bacterial biofilm is considered to be a key factor in implant infection, and in vitro experiments have confirmed that the adhesion of brucellae to metals is lower than that of other bacteria. Studies showed that we got good result in treated brucellae of spine infection, and it proof that internal fixation was safety based on good debridement. all these studies provide a reliable theoretical basis for prosthesis implantation that we choose one stage revision [10,11]. We believe that one stage revision combined with sufficient antimicrobial therapy throughout the course can relief pain, get good joint function, and also reduce the patient's hospitalization cycle and treatment costs. Thorough debridement uses high concentration of rifampicin to wash, before new implant inserts. Up to 10% of patients relapse after antimicrobial therapy was reported [12]. This is big challenge for us. The key point is debridement with pulse pressure washing and make sure purulence and necrosis synovial tissue was cleaned out clearly. In our study, we followed-up all patient for 6-30 months, from the x-ray no prosthesis loosening happened, we allowed patients to walk as tolerated using a walker on the 1st day post-operation, no DVT happened. VAS score is lower than pre-operation this means their pain relieved. Post-operation HSS average scores were up to  $80.7 \pm 5.5$ , the average ROM was improved to  $90 \pm 3^\circ$ , post-operation Harris average scores were  $75.5 \pm 0.5$  thus, pre-operative scores were 30-50 points (average  $36.5 \pm 8.5$  points).

ESR and CRP level are also important in PJI infection diagnosis and treatment.

Elevated CRP and increased ESR were the most common laboratory findings seen in our series, T. Buzgan et al. [13] reported similar results. ESR average were 39-87 mm/H (normal 0-20 mm/H), and CRP were 12-112 mg/L (normal 1-8 mg/L) pre-operative. It was very important to know whether anti-brucellas treatment was effective or not. If 2 weeks of using doxycycline (100 mg, 2 times/d) combined with rifampicin (600 mg/d), but ESR and CRP did not show a downward trend, it means there was a brucellae drug resistance, or patient

## Conclusions

Revision for the treatment of brucella infection following total joint arthroplasty is rare in China and abroad, and there is a need for further in-depth research and long-term follow-up reports. Systemic antibrucellosis

has other kinds of infection, also means high risk of recurrence. So, our suggestion is using doxycycline and rifampicin for 2 weeks until there is a downward trend in ESR and CRP levels, then we can carry out the operation. In our study we use doxycycline (100 mg) powder directly around the prosthesis. Patients were encouraged to perform quadriceps strengthening exercise after they had recovered from anesthesia. All patients were allowed to walk on the 1st day post-operation. We found that from 7th, 30th, 90th day post operation ESR and CRP goes down and nearly become normal at 3months, VAS score is lower than pre-operation, these differences have statistically significant ( $p < 0.05$ ). This means operation can help patient receive relief from pains and have good function, which is our aim. The reports said that they have good results in using arthroplasty in treating joint brucellae infection.

There is convincing evidence that symptoms in brucellosis were protean and nonspecific [3,7,14]. Brucella organisms may localize in almost any organ, bone, lung, testes or liver. In this study, 1 patient has testicle swollen and treated in urology department before. A study done in Iran [15] showed that pain, swelling of joint, joint dysfunction, clinical weight loss was common, nearly 87% of patient happened, it is similar as our study. Hepatosplenomegaly and lymphadenopathy may be found as well as signs and symptoms associated with other infected organs, but this was not found in our study.

Few cases reported in the published literature, and treatment of Brucella PJI is equally challenging. Previous meta-analyses have reached different conclusions regarding the preferred regimens for brucellosis. Generally, dual or triple regimens are advisable. In 1986, the World Health Organization recommended the use of doxycycline in combination with rifampin for 6 weeks as the preferred treatment of adult acute brucellosis. According to China's Practice Guideline for brucellosis diagnosis and treatment [4]: doxycycline (100mg every 12 h), rifampin (600 -900mg every 24 h) was suggested. The recovery rate of human brucellosis has been reported between 80.6% in A.A. Farazi et al. studies' [16], but no large number of patients' prognosis about brucella joint infection reported. The use of an aminoglycoside with doxycycline is believed to reduce relapse, but we didn't use. Another reason for choosing rifampin was many patients in west part of China also have same risk for tuberculosis [7,10], misdiagnosis of tuberculosis as brucellosis might lead to the inadvertent use of rifampin, this situation almost guaranteed to result in rifampin resistance. Patients on doxycycline for brucellosis may develop the Jarisch-Herxheimer reaction had been reported by John S [17], it's not happened in this study. Additionally, in our case series, the clinical results indicated that the treatment was satisfactory and safe and did not present obvious operation-related complications. Relapses most commonly occur within the first 6 months after completion of therapy. We followed-up for 6-30 months with no evidence of disease recurrence or relapse. Antimicrobial therapy was going for 12-24 weeks, when complete resolution of symptoms with normalization of inflammatory biomarkers.

chemotherapy and surgery technical are both important of treatment. Revision operation could make patient feel efficacy, safety and satisfactory.

Authors' contributions. MD. Habaxi Kaken designed the study. Wang Li attended and performed all the operations for specimen collection

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As no individual patient's identity is revealed by the photographs, verbal consent for publication was obtained from the patient or their relative, either telephonic or on a follow-up visit.

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## БУЫНДЫ ЭНДОПРОТЕЗДЕУДЕН КЕЙІН ДАМЫҒАН БРУЦЕЛЛЕЗ ИНФЕКЦИЯСЫ

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### Түйіндеме

Бруцеллез - бұл Қытайда, әсіресе Шыңжаңда үлкен экономикалық ауыртпалық болып табылатын кең таралған зооноздық инфекция.

Қолжазбаның мақсаты: буындарды толық ауыстырғаннан кейін бруцеллез инфекциясын емдеуді талқылау және оның емдік әсерін анықтау.

Әдістері. Біздің бөлімішеде 2009 жылдың наурыз айынан 2019 жылдың наурыз айына дейін 55 пен 79 жас аралығындағы (орташа жасы 65,6 ± 1 жас) буындардың бруцеллезімен ауырған 8 науқасқа талдау жасадық. Операция алдындағы және кейінгі кезеңде келесі параметрлер өлшенді: HSS және Харрис шкаласы, тізе буынындағы қозғалыс ауқымы (ROM), VAS, эритроциттердің шөгуге жылдамдығы және С-реактивті ақуыз. Ревизиялық хирургияның операциядан кейінгі емдік әсерін рентген сәулесі арқылы анықталды.

*Нәтижелер.* Барлық жағдайларда ауырсыну және ЭТЖ жоғарылауы байқалды. Бұл жағдайларда терең тамыр тромбозы (DVT) және нервтердің зақымдануы анықталмады. Теріде синус табылған жоқ. Толық буын артропластикасынан өткен және отадан кейін бруцеллезді жұқтырған науқастардың барлығы ревизиялық операциядан соңғы болып өтеді. Барлық жағдайлар 6-30 ай бойы бақыланды; орташа бақылау кезеңі  $14 \pm 0,5$  айды құрады. Операциядан кейін біз ревизиялық операциядан кейінгі емдік әсерді білу үшін HSS және Харрис шкаласын, сондай-ақ рентген сәулелерін алдық. Сондай-ақ ревизиялық операция кезінде немесе одан кейін протездің асептикалық қолпсытуы немесе сынуы бар науқастар болған жоқ, рецидивтер анықталған жоқ. Тізе буынының орташа ROM  $90 \pm 3^\circ$  дейін жақсарды.

*Қорытынды.* Соңғы клиникалық нәтижелер бруцеллезге қарсы жүйелі химиотерапия және техникалық хирургия келесі науқастарды емдеуде тиімді екенін көрсетеді. Ревизиялық хирургия буын жұмысын айтарлықтай жақсартады және ауырсынуды жеңілдетеді.

Түйін сөздер: бруцеллалар, эндопротездеу, жұқпалы ауру.

## ИНФИЦИРОВАНИЕ БРУЦЕЛЛЕЗОМ ПОСЛЕ ТОТАЛЬНОГО ЭНДОПРОТЕЗИРОВАНИЯ СУСТАВОВ

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### Резюме

Бруцеллез является распространенной зоонозной инфекцией, которая несет большое экономическое бремя в Китае, особенно в Синьцзяне.

Цель сообщения: обсудить лечение бруцеллезной инфекции после тотального эндопротезирования суставов и выявить его лечебный эффект.

Методы. Проанализировано 8 пациентов, инфицированных бруцеллезом суставов после эндопротезирования в нашем отделении с марта 2009 г. по март 2019 г., в возрасте от 55 до 79 лет (средний возраст  $65,6 \pm 1$  год). В до- и послеоперационном периодах измеряли следующие параметры: шкалу HSS и Harris, амплитуду движений в коленном суставе (ROM), ВАШ, скорость оседания эритроцитов и С-реактивный белок. По рентгену выявить послеоперационный лечебный эффект ревизионной операции.

Результаты. Во всех случаях отмечалась боль и повышенная СОЭ. Тромбоз глубоких вен и повреждение нервов в этих случаях не были обнаружены. Синусов на коже не обнаружено. Всем больным, перенесшим тотальное эндо протезирование суставов и инфицированным бруцеллезом после операции, в последнюю очередь проводят ревизионную операцию. Все случаи прослежены в течение 6-30 месяцев; средний период наблюдения составил  $14 \pm 0,5$  мес. После операции мы взяли шкалу HSS и Harris, а также рентген, чтобы выявить лечебный эффект после ревизионной операции. Также не было пациентов с асептическим расшатыванием или переломом протеза вовремя или после ревизионной операции, рецидивов не выявлено. Средний ROM колена улучшился до  $90 \pm 3^\circ$ .

Выводы. Недавние клинические результаты показывают, что системная противобруцеллезная химиотерапия и техническая хирургия могут быть эффективны для лечения больных данной категории. Ревизионная операция позволяет значительно улучшить функцию сустава и облегчить боль.

Ключевые слова: бруцелла, эндопротезирование, инфекционное заболевание.