Gram-negative versus Gram-positive in primary pyogenic spondylitis and Analysis of risk factors for relapse

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Research Article

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Abstract

Objective: In the present study, we aimed to compare and analyze the clinical features, diagnosis, treatment and prognosis of primary pyogenic spondylitis caused by Gram-positive and Gram-negative bacteria.

Methods: A retrospective analysis consisting of 76 cases of primary pyogenic spondylitis with complete clinical information was carried out from January 2013 to January 2020 in our hospital. The patients were divided into two groups according to Gram staining: Gram-negative group (n=33) and Gram-positive group (n=43). The clinical characteristics, diagnosis, treatment and prognosis of the two groups were compared and analyzed.

Results: Staphylococcus aureus accounted for the highest proportion of the Gram-positive group, while Escherichia coli accounted for the highest proportion of the Gram-negative group. Before treatment, there were no significant differences in terms of age, gender, affected segment, spinal abscess, diabetes mellitus, course of disease, admission erythrocyte sedimentation rate (ESR), admission C-reactive protein (CRP), and admission white blood cell (WBC) count between the two groups (P>0.05). After treatment, there were no statistically significant differences in discharge ESR, discharge CRP, ESR decline rate, CRP decline rate, surgery, recurrence, follow-up time, hospital stay, and body temperature ≥38℃ between the two groups (P>0.05). The body temperature of the Gram-negative group was higher compared with the Gram-positive group, and the number of patients with urinary tract infection in the Gram-negative group was significantly greater compared with the Gram-positive group (P<0.05). Antibiotic treatment time <6 weeks was an independent risk factor for recurrent infection.

Conclusions: The body temperature of the Gram-negative group was higher compared with the Gram-positive group, and there were significantly more cases with urinary tract infection in the Gram-negative group compared with the Gram-positive group (P<0.05). Antibiotic treatment time <6 weeks was an independent risk factor for recurrent infection.

Introduction

Primary pyogenic spondylitis remains the most common type of spinal infection. Bacteria mainly spread through blood, which can affect the spine and intervertebral discs [1]. Pyogenic spondylitis can be clinically divided into discitis, vertebral osteomyelitis, epidural abscess and so on [2]. Known possible causes of spinal infection include history of infection in other sites, diabetes, advanced age, intravenous drug use, HIV infection, immunosuppression, and history of tumors as well as liver and kidney failure [1]. According to the results of Gram staining, pyogenic spondylitis can be divided into Gram-positive and Gram-negative pyogenic spondylitis, and Gram-positive bacteria dominate [3, 4]. Among Gram-positive bacteria, Staphylococcus aureus accounts for the highest proportion [5, 6], while Escherichia coli accounts for the highest proportion among Gram-negative bacteria [7]. At present, no report has compared the similarity and difference between pyogenic spondylitis caused by Gram-positive and Gram-

negative bacteria. In the present study, we aimed to compare and analyze the clinical features, diagnosis, treatment and prognosis of pyogenic spondylitis caused by Gram-positive and Gram-negative bacteria.

Materials And Methods

A retrospective analysis consisting of 76 cases of adult primary pyogenic spondylitis with complete clinical data was carried out in our hospital from January 2013 to January 2020. Inclusion criteria were set as follows: (1) the clinical symptoms and imaging examination of patients were consistent with spinal infection; (2) histopathological examination revealed pyogenic inflammation; and (3) blood culture and/or tissue bacterial culture were positive. Exclusion criteria were set as follows: (1) tuberculosis, brucella, fungus and other types of spinal infections; and (2) previous history of spinal trauma, spinal puncture and spinal surgery.

According to the results of bacterial culture and drug susceptibility test, treatment with sensitive antibiotics was conducted. The outcomes could be divided into two types: successful treatment and relapse. Criteria for successful treatment were as follows: (1) inflammatory indicators, such as admission erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), were controlled within the normal range, and body temperature was normal; (2) tissue bacterial culture was negative; and (3) there was no evidence of spinal infection. The criteria for recurrence were as follows: (1) after the initial improvement, the clinical symptoms and inflammatory indicators (ESR and CRP) re-emerged; and (2) after the treatment was completed, the clinical symptoms, imaging examinations and bacteriological examinations showed pyogenic spondylitis again.

Statistical analysis

The data were analyzed with SPSS 20.0 statistical software. The results were expressed as the mean ± standard deviation. Student's t-test was used to assess the normally distributed data, while Mann-Whitney U rank sum test was used to analyze the non-normally distributed data. Categorical variables were evaluated using Chi-square test, multi-categorical variables were analyzed using row-multiplied list Chi-square test, Fisher's exact test was used when the conditions of Chi-square test were not met, and Mann-Whitney U rank sum test was used for ordinal categorical variables. The binary logistic regression model was used to analyze the risk factors with significant differences in univariate analysis. $P < 0.05$ was considered statistically significant (two-sided test).

Demographics And Clinical Characteristics

A total of 76 patients with pyogenic spondylitis were included in the present study, including 43 cases in the Gram-positive group and 33 cases in the Gram-negative group (Table 3). There were five cases of cervical spine infection, six cases of thoracic spine infection, and 32 cases of lumbosacral spine infection in the Gram-positive group. There were 0 cases of cervical spine infection, 10 cases of thoracic spine infection, and 27 cases of lumbosacral spine infection in the Gram-negative group (Table 1).

Table 1
Clinical characteristics of 76 cases of pyogenic spondylitis

	Gram-negative (n = 33)	Gram-positive (n = 43)	P
General			1.000
Sex			
male	20	25	
female	13	18	
Age, _x±s	63.94±12.54	62.77±16.69	0.737
Diabetes	3	4	1.000
Clinical feature			
Spinal pain	33	43	
Temperature	38.24±1.12	37.76±0.92	0.042
≥ .04	18	16	0.165
admission WBC (·10^9/L), ±s	8.28±2.75	8.65±3.53	0.621
admission CRP (mg/dL), ±s	68.26±37.94	67.14±35.30	0.895
admission ESR (mm/h), ±s	78.42±25.33	77.44±25.45	0.868
Spine level	37	43	
Cervical vertebra	0	5	0.065
Thoracic vertebra	10	6	0.097
Lumbar vertebra	27	32	0.581
Spinal abscess	18	18	0.355
Paravertebral abscess	7	11	0.788
Epidural abscess	5	4	0.490
Psoas abscess	7	4	0.193
Course (day), ±s	65.91±117.21	41.23±32.69	0.192
History of urinary tract infection	7	2	0.035

Treatment Procedure

Among the 76 patients in this analysis, nine patients with epidural abscess were treated with emergency surgery. Specimens were collected during the operation for tissue culture, and all cultures were positive. The remaining 67 patients had complete blood cultures, and 20 were positive. The remaining 47 patients underwent CT-guided puncture of infected lesions under strict aseptic conditions, and all were positive. All patients were routinely given vancomycin + imipenem or vancomycin + fluoroquinolones or fluoroquinolones + third-generation cephalosporin antibiotics intravenously, strict bed rest, nutritional support and other conservative treatments. Sensitive antibiotic treatment was adjusted according to the results of drug susceptibility experiments, antibiotics were adjusted according to changes of the conditions, and the changes in body temperature, ESR, CRP and white blood cell (WBC) count were regularly monitored. Indications for surgical treatment were as follows: conservative treatment was ineffective, combined with spinal instability, impaired spinal nerve compression, and progressive symptoms. Indications for conservative treatment were as follows: conservative treatment was effective, and there was no spinal instability, spinal cord nerve compression damage, and progressive symptoms.

Results

Pathogenic microorganisms

There were 76 cases with positive bacterial culture, of which 43 cases were Gram-positive bacteria, and Staphylococcus aureus (n = 23) accounted for the largest proportion. There were 33 cases in the Gram-negative group, and Escherichia coli (n = 16) accounted for the largest proportion (Table 3).

Treatment Outcome And Recurrence

There were no significant differences in terms of hospital stay, antibiotic treatment duration, and follow-up time between the two groups ($P > 0.05$). In the Gram-negative group, 29 cases underwent surgery in combination with antibacterial treatment, four cases underwent antibacterial treatment alone, and four cases relapsed. In the Gram-positive group, 32 cases underwent surgery in combination with antibacterial treatment, 11 cases underwent antibacterial treatment alone, and six cases relapsed. The course of intravenous antibiotics was 2–6 weeks, and then the regimen was changed to oral antibiotics for 4–8 weeks (Table 2).

Table 2
Comparative analysis of treatment and prognosis of the two groups

	Gram-negative (n = 33)	Gram-positive (n = 43)	P
Laboratory			
Discharge ESR, (mm/h), $\bar{x} \pm s$	35.48±19.13	34.81±17.83	0.875
Decreased ESR, (mm/h), $\bar{x} \pm s$	42.94±20.22	42.60±17.02	0.938
Discharge CRP, (mg/dL), $\bar{x} \pm s$	15.56±13.44	12.88±14.47	0.413
Decreased CRP, (mg/dL), $\bar{x} \pm s$	52.70±36.16	54.21±31.05	0.845
Hospital stays (day), $\bar{x} \pm s$	25.33±11.52	22.72±12.66	0.357
History of antibiotic use before culture	22	25	0.484
Duration of antibiotic (week)	7.18±1.63	7.60±1.56	0.254
Follow-up (month)	13.82±2.71	14.60±2.90	0.232
Surgery	29	32	0.244
Relapse	4	6	1.000

Table 3
Classification of bacteria (n = 76)

Species	Values
Gram-positive	43
staphylococcus aureus	23
coagulase negative staphylococcus	8
Streptococcus	8
enterococcus faecium	3
Staphylococcus Koch	1
Gram-negative	33
E.coli	16
klebsiella pneumoniae	7
pseudomonas aeruginosa	3
salmonella	2
bacteroides fragilis	2
acinetobacter baumannii	1
enterobacter cloacae	1
Brevendimonas diminuta	1

Risk Factors Associated With Recurrent Infection

Tables 4 and 5 show the variables related to the recurrence of pyogenic spondylitis. In the univariate analysis, patients with body temperature ≥ 38℃ and antibiotic treatment time < 6 weeks showed recurrent infection. In the multivariate logistic analysis, antibiotic treatment time < 6 weeks was an independent risk factor for recurrent infection (Tables 4 and 5).

Table 4
Analysis of risk factors for relapse

Variables	Cure (n = 66)	Relapse (n = 10)	P
Age (_x±s)	63.09±14.05	64.50±20.82	0.783
Sex (male/female)	40/26	5/5	0.732
Admissions-WBC (_x±s)	8.64±3.28	7.50±2.55	0.297
Admissions-ESR (_x±s)	78.30±25.43	75.00±25.01	0.702
Discharge-ESR (_x±s)	34.77±17.03	37.30±26.18	0.687
Admissions-CRP (_x±s)	64.57±36.28	87.80±30.11	0.058
Discharge-CRP (_x±s)	14.60±14.00	10.40±14.22	0.381
course (day) (_x±s)	52.09±85.45	51.00±48.64	0.969
Temperature (_x±s)	37.91±1.08	38.35±0.59	0.209
≥ .20	26	8	0.036
hospital stays (day)(_x± s)	23.20±11.81	28.20±14.26	0.228
Spinal abscess	31	5	1.000
staphylococcus aureus	19	4	0.479
E.coli	14	2	1.000
Bacteremia	17	3	0.717
Surgery	53	8	1.000
Diabetes	7	0	0.584
Other surgical or trauma history	16	1	0.441
Other site of infection history	17	3	0.717
neurological sign	27	4	1.000
History of antibiotic use before culture	39	8	0.301
antibiotic therapy6 weeks	1	9	0.001

Table 5
Multivariate logistic regression analysis

Variables	B	S.E	Wals (χ^2)	P	Exp(B)/ (OR)	95%CI
Temperature ≥ 38℃	0.977	1.528	0.409	0.522	2.658	0.133–53.135
antibiotic therapy□6 weeks	6.156	1.468	17.581	0.000	471.365	25.529-8375.286

Discussion

Our data showed that the average body temperature of the Gram-negative group was higher compared with the Gram-positive group, and the number of patients with urinary tract infection in the Gram-negative group was significantly greater compared with the Gram-positive group ($P < 0.05$). In the univariate analysis, patients with body temperature ≥ 38℃ and antibiotic treatment time < 6 weeks showed recurrent infection. In the multivariate logistic analysis, antibiotic treatment time < 6 weeks was an independent risk factor for recurrent infection.

Pyogenic spondylitis is mainly caused by the spread of bacteria through the blood source. The arterial route is more common than the venous route. The spinal blood supply is abundant, and it is more susceptible to bacterial transmission and infection [8]. In the Gram-negative group, E. coli accounted for the highest proportion, followed by Klebsiella pneumoniae. Among the 62 cases of Gram-negative bacterial infection reported by Seung-Ji Kang et al. [9], Escherichia coli accounts for the highest proportion, followed by Pseudomonas aeruginosa. In our Gram-positive group, Staphylococcus aureus accounted for the highest proportion, followed by coagulase-negative Staphylococcus. It is widely reported that Staphylococcus aureus is the most common strain [1, 5, 10]. Pyogenic spondylitis usually affects the elderly [11, 12], and the most common site is the lumbar spine, followed by the thoracic spine and cervical spine [10]. Usually, pyogenic spondylitis is more frequently detected in males compared with females [2]. The most common symptom is focal spinal pain, and other symptoms include fever and neurological symptoms [13]. The above-mentioned characteristics were also well reflected in this research.

The average age of the Gram-negative group was higher compared with the Gram-positive group, while the difference was not statistically significant ($P > 0.05$), which was similar to the data reported by Ching-Yu Lee et al. [14]. The admission body temperature of the Gram-negative group was significantly higher compared with the Gram-positive group ($P < 0.05$). Because the two pathogenic mechanisms are different, and Gram-negative bacteria rely on endotoxin to cause disease. The toxic component is mainly lipid A, which is not easy to be dissolved in blood vessels and surrounding tissues. However, it can cause fever, microcirculation disorders, endotoxin shock and disseminated intravascular coagulation in blood vessels. Therefore, the body temperature of the Gram-negative group was higher compared with the

Gram-positive group. Gram-positive bacteria can produce special pathogenic factors, such as protein A and coagulase, which can invade tissues or blood vessels, causing necrosis and dissolution of surrounding tissues. Subsequently, a large number of neutrophils infiltrate, forming a cavity filled with pus. In the present study, there was no statistically significant difference in spinal abscess between the two groups.

Our research showed that there were significantly more patients with urinary tract infection in the Gram-negative group compared with the Gram-positive group ($P < 0.05$). KH Park and other studies have shown that the main source of infection of Gram-negative pyogenic spondylitis is urinary tract infection [15]. Ching-Yu Lee et al. have also shown that Gram-negative pyogenic spondylitis is more complicated with a history of urinary tract infection [14]. Diabetes is the most common underlying disease, although there are reports that pyogenic spondylitis caused by Gram-negative bacteria is related to diabetes [15]. However, our study and Dong Youn Kim et al. [16] did not find any connection between these two factors.

There is no clinical guideline for conservative treatment and surgical treatment [11]. When conservative treatment is effective, and there is no spinal instability, spinal nerve compression damage, or symptoms that are progressively worsening, conservative treatment, such as antibiotics, can be used [11]. In the selection of antibiotics, sensitive antibiotics should be selected for treatment based on the results of Gram staining and drug sensitivity experiments. There is no uniform conclusion on the duration of antibiotic treatment. The American Academy of Infectious Diseases believes that antibiotic treatment should last at least 6 weeks [17]. A published randomized controlled trial shows that 6 weeks of antibiotic treatment for pyogenic spondylitis is as effective as 12 weeks [18], while this study has only included patients with positive microbial cultures. Research by Park KH and others has concluded that antibiotic therapy should be continued for at least 8 weeks for patients with a high risk of recurrence [19]. Generally speaking, the duration of antibiotic treatment should be no less than 6 weeks [20]. Most of the patients (66/76) in this study were treated with antibiotics for more than 6 weeks. Some studies have shown that treatment of less than 6 weeks is associated with an increased recurrence rate [19]. Similarly, our research revealed that the duration of antibiotic treatment < 6 weeks was an independent risk factor for recurrence.

When conservative treatment is ineffective, and there are spinal instability, impaired spinal nerve compression and progressive symptoms, surgery in combination with antibiotic therapy can be used [11, 21, 22]. E Pola et al. have reported a minimally invasive surgery in combination with antibiotic treatment regimen, and good clinical results have been achieved [23].

Conclusions

In the present study, certain conclusions could be drawn by comparing and analyzing the clinical features, diagnosis, treatment and prognosis of Gram-positive and Gram-negative pyogenic spondylitis. Before treatment, there were no statistically significant differences ($P > 0.05$) in terms of age, gender, affected segment, spinal abscess, diabetes mellitus, course of disease, admission ESR, admission CRP, admission WBC between the two groups. After treatment, there were no statistically significant

differences in terms of discharge ESR, discharge CRP, ESR decline rate, CRP decline rate, surgery, recurrence, follow-up time, hospital stay, and body temperature ≥ 38℃ between the two groups ($P > 0.05$). The body temperature of the Gram-negative group was higher compared with the Gram-positive group, and the number of patients with urinary tract infection in the Gram-negative group was significantly greater compared with the Gram-positive group ($P < 0.05$). Antibiotic treatment time < 6 weeks was an independent risk factor for recurrent infection.

Limitations

This was a retrospective, single-center study with small sample size. More reliable conclusions need to be verified by multi-center, randomized controlled studies with large sample size.

List Of Abbreviations

erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cell (WBC)

Declarations

Ethics approval

This study was approved by the ethics committees of Affiliated Hospital of Qingdao University.

Conflict of interest

The authors declare that they have no conflict of interest.

Informed consent

All patients involved gave written informed consent to review their medical records. All personal details were erased before analysis to cover patient data confidentiality and comply with the Declaration of Helsinki.

Consent for publication

Written informed consent was obtained from all of the patients for publication of this research and any accompanying images.

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Availability of data and material

All the data and material can be available from Dai guohua and Wang ting for reasonable request.

Authors' contributions

GuoHua Dai, Ting Wang, Shuzhong Li designed the study; ZhongYing Wang, LiangRui Luan ZhiChao Wang and JianWen Hou enrolled subjects and collected data; GuoHua Dai, ChuQiang Yin, YuanLian Sun analyzed the data; GuoHua Dai, Ting Wang, Shuzhong Li discussed the results and wrote the manuscript. All authors reviewed and approved the manuscript.

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