

SPONDYLODISCITIS INVESTIGATION AND THERAPEUTIC PROTOCOL: NEUROSURGERY SERVICE RESULTS

PROTOCOLO INVESTIGATIVO E TERAPÊUTICO DE ESPONDILODISCITE: RESULTADOS DE UM SERVIÇO DE NEUROCIRURGIA

INVESTIGACIÓN DE ESPONDILODISCITIS Y PROTOCOLO TERAPÉUTICO: RESULTADOS DEL SERVICIO DE NEUROCIRUGÍA

GUILHERME FINGER,¹ ANDRÉ MARTINS DE LIMA CECCHINI,¹ ERICSON SFREDDO,¹ FELIPE MARTINS DE LIMA CECCHINI,¹ LUCIANO WERLE LUNARDI,² TOBIAS LUDWIG DO NASCIMENTO,¹ ASDRUBAL FALAVIGNA³

1. Hospital Cristo Redentor, Department of Neurosurgery, Porto Alegre, RS, Brazil.

2. Hospital Cristo Redentor, Department of Infectology and Control of Infectious Hospital Diseases, Porto Alegre, RS, Brazil.

3. Universidade Caxias do Sul, Department of Neurosurgery, Caxias do Sul, RS, Brazil.

ABSTRACT

Objective: Spondylodiscitis is still a frequent pathology among neurosurgical services, and its correct treatment involves infectious, neurological and orthopedic goals. The authors describe the protocol and report the diagnostic and therapeutic results after its implementation. **Methods:** A prospective prognostic study (Level I) including patients with primary spondylodiscitis treated in the Neurosurgical Service of Cristo Redentor Hospital from January 2014 to March 2018. Demographic, spine, infectious and treatment-related variables were analyzed. The numerical variables are presented as mean and standard deviation or median and interquartile range (according to their parametricity), and are compared by the student's t-Test or Mann-Whitney U Test, respectively. **Results:** Thirty seven patients were included. The sexes were evenly distributed, with predominantly Caucasians, and a mean age of 56.89 ± 15.33 . Hypertension and type 2 diabetes were the most frequent comorbidities. Vertebral lumbar level was the most involved segment. Pathogens were identified in 34 cases (91%), with *Staphylococcus aureus* being the most prevalent, followed by Koch Bacilli. Inflammatory markers are higher in pyogenic infections at hospital admission, but lower at hospital discharge when compared to tuberculous discitis ($p < 0.01$). Mean hospital stay was higher in the pyogenic group. **Conclusion:** The protocol described has a high diagnostic level of the pathogen, with cure of infection and satisfactory neurologic outcome in all cases. **Level of Evidence I, Diagnostic Studies - Investigating a Diagnostic Test.**

Keywords: Discitis; Spine; Infection; Neurosurgery.

RESUMO

Objetivo: Espondilodiscite é uma patologia frequente nas enfermarias neurocirúrgicas, cujo tratamento adequado envolve questões infecciosas, neurológicas e ortopédicas. Os autores descrevem um protocolo reportando resultados diagnósticos e terapêuticos após sua implementação. **Método:** Estudo prognóstico prospectivo (Nível I) incluindo pacientes com espondilodiscite primária tratados de janeiro 2014 a março de 2018. Variáveis relacionadas a dados demográficos, vertebrais, infecciosos e terapêuticos foram analisados. Variáveis numéricas serão apresentadas como média e desvio padrão ou mediana e intervalo interquartil (conforme sua parametricidade) e analisadas com Teste T-Student ou Teste Mann-Whitney, respectivamente. **Resultados:** 37 pacientes foram incluídos, cuja média de idade foi 56.89 ± 15.33 . Hipertensão arterial e Diabetes foram as comorbidades mais prevalentes. O segmento lombar foi o mais acometido. Houve identificação do patógeno em 34 casos (91%), sendo o *Staphylococcus aureus* o mais frequente, seguido pelo Bacilo de Koch. Os marcadores inflamatórios foram maiores no grupo de discite piogênica no momento da admissão hospitalar, mas com valores inferiores aos da discite tuberculosa na alta hospitalar ($p < 0.01$). A média de internação hospitalar foi maior no grupo piogênico. **Conclusão:** O protocolo descrito tem elevada taxa de identificação do patógeno com critérios de cura infecciosa e desfecho neurológico satisfatório em todos os casos descritos. **Nível de Evidência I, Estudos diagnósticos – Investigação de um exame para diagnóstico.**

Descritores: Discite; Coluna Vertebral; Infecção; Neurocirurgia.

RESUMEN

Objetivo: La espondilodiscitis sigue siendo una patología frecuente en los servicios de neurocirugía y su tratamiento correcto incluye objetivos infecciosos, neurológicos y ortopédicos. Los autores describen un protocolo e informan los resultados diagnósticos y terapéuticos después de su implementación. **Métodos:** Estudio pronóstico prospectivo (Nivel I) que incluyó pacientes con espondilodiscitis primaria tratados en el Servicio de Neurocirugía del Hospital Cristo Redentor desde enero de 2014 hasta marzo de 2018. Se analizaron variables demográficas, vertebrales, infecciosas y relacionadas con el tratamiento. Las variables numéricas se presentan como promedio y la desviación estándar o mediana y rango intercuartil (según su parametricidad) y se comparan mediante la prueba t de Student o la prueba U de Mann-Whitney, respectivamente. **Resultados:** Se incluyeron 37 pacientes. Los sexos se distribuyeron uniformemente, con predominancia de caucásicos y una edad promedio de $56,89 \pm 15,33$. La hipertensión y la diabetes tipo 2 fueron las comorbilidades más frecuentes. El nivel

This study was conducted at the Cristo Redentor Hospital, Porto Alegre, Brazil.

Corresponding: Guilherme Finger. Rua Domingos Rubbo, 020, Cristo Redentor, Porto Alegre, RS, Brazil. 91040-000. guilhermefingermd@gmail.com



lumbar fue el segmento más afectado. Se identificaron patógenos en 34 casos (91%), siendo el *Staphylococcus aureus* el más frecuente, seguido por el bacilo de Koch. Los marcadores inflamatorios fueron más en las infecciones piógenas en el hospital, pero más bajos en el alta hospitalaria en comparación con la discitis tuberculosa ($p < 0,01$). La estancia hospitalaria promedio fue mayor en el grupo piógeno. Conclusiones: El protocolo descrito tiene un alto nivel de diagnósticos del patógeno, con curación de la infección y resultados neurológicos satisfactorios en todos los casos. **Nivel de Evidencia I, Estudios de diagnósticos - Investigación de un examen para diagnóstico.**

Descriptor: Discitis; Columna Vertebral; Infección; Neurocirugía.

INTRODUCTION

Spondylodiscitis is an infection of the intervertebral disc and adjacent vertebral end-plates.^{1,2} It can be classified as a primary or secondary infection, depending on whether the patient has had previous spinal surgery or not. Primary spondylodiscitis bears no relationship to previous spinal surgery and is commonly caused by bacteria. Primary spondylodiscitis is classified, according to its etiology, as pyogenic (or bacterial infection), and nonpyogenic disease, caused mainly by Tuberculous Bacilli.^{3,4} The incidence in the general population ranges between 0.2 and 2 cases per 100,000 per year.^{5,6} Risk factors observed in primary spondylodiscitis are age, with higher occurrence in the fifth decade of life, male sex, and medical comorbidities such as diabetes, alcoholism, HIV infection, malnutrition, use of illicit drugs, malignancy, long-term steroid use, and chronic renal failure.⁷⁻⁹

Clinical manifestations are back pain, fever, local tenderness, and neurological signs when there is deformity of the affected structures.^{10,11} The lack of specific symptoms usually results in delayed diagnosis, leading to potential spine deformities, neurological impairment and mortality.¹²

The diagnosis is made in a patient with back pain who presents image alterations suggestive of infection associated with elevated inflammatory markers. The pathogen can be identified in the blood culture or disc culture samples. If not properly treated, the infection can extend to the paravertebral area, epidural space, and adjacent vertebral bodies.⁵

The diagnosis and treatment strategy for spondylodiscitis need to be established based on specific variables of the country and institution where the patient is being treated. This paper describes the experience of a Neurosurgical Service in Southern Brazil in diagnosing and treating patients with primary spondylodiscitis, and describes the institutional protocol.

METHODS

Study design

A prospective study of patients with primary spondylodiscitis treated in the Neurosurgical Service of Cristo Redentor Hospital from January 2014 to March 2018. The protocol was established in January 2014, by the neurosurgical and infectious disease services combined, and implemented in the hospital as a new therapeutic model. Therefore there was no requirement for the protocol and study to be submitted to the Research Ethics Committee, or for the patients to sign an informed consent form, since the authors were only following the protocol and no personal information was gathered. All consecutive patients with spondylodiscitis, based on the clinical and radiological findings, were included in the study, except those who had undergone previous spine surgery.

Variables

The variables analyzed were sex, age, race, medical comorbidities, leukocytes, inflammatory markers such as C-Protein Reaction (CPR) and Erythrocyte Sedimentation Rate (ESR), the pathogen and the site of microorganism identification in the blood culture or disc culture, the profile of antibiotic sensitivity, the route of antibiotic administration, the length of antibiotic therapy, the level and number of vertebral bodies involved, hospitalization time, external immobilization, and the need for spine fixation.

Discitis Protocol

Every patient who presented back pain associated with radiological or tomographic findings suggestive of discitis was promptly investigated by complete blood count, VHS and CPR dosage, and submitted to magnetic resonance of the suspected spine level. Discitis was diagnosed based on the presence of elevated inflammatory markers associated with MRI findings suggestive of infection. First, the patient's neurologic status and spine stability were examined, then every patient who presented neurological deficit or spine instability was promptly submitted to surgical intervention. If the patient was neurologically intact and the spine was stable, the physicians looked for signs of a severe infectious condition (sepsis criteria, neutropenia or hemodynamic instability). If the patient presented any of these signs, a blood culture was quickly collected and antibiotic treatment started (Oxacillin 1g 4/4h and Cefepime 2g 8/8h based on the bacterial pattern found at our institution). If there was no evidence of uncontrolled infectious condition, no antibiotic was started empirically, and two blood cultures and one urine culture were collected on the same day. Blood cultures were collected from two different sites of the body and sent for aerobic and anaerobic cultures. The period of culture growth is 72 hours. If a pathogen was identified based on the blood cultures, then antibiotic therapy was selected and started, based on a table of resistance/sensitivity. If no bacteria was identified in the both blood cultures after 72 hours, the patient was submitted to percutaneous disc biopsy guided by fluoroscopy, and the material was sent for aerobic, anaerobic, tuberculous and fungi culture. The physicians also performed a GeneXpert TB test and microscopic analysis looking for Koch bacilli or fungi. The physician waited for the results of the GeneXpert, pathology, and culture tests, and if no bacteria were identified after 72 hours, a second percutaneous fluoroscopic guided biopsy was performed. If a pathogen was then identified, antibiotic treatment was begun, based on the sensitive bacterial pattern. However, if no bacteria was identified, the physicians performed an open disc biopsy, and the material collected was sent for aerobic, anaerobic, tuberculous and fungi culture, GeneXpert TB test exam, and microscopic analysis looking for Koch bacilli or fungi. The pathogen identified was treated as proposed in the literature. If no bacteria were identified and TB infection was ruled out, the patient received empirical antibiotic therapy with Oxacillin and Cefepime (based on hospital results). Patients with spine instability were submitted to spine arthrodesis, and those with stable spine alignment were fitted with an external body cast while receiving treatment for discitis (Figure 1).

Statistical Analysis

Data were collected using the software Microsoft Excel 2007. Statistical analysis was performed using the software Statistical Package for the Social Sciences (SPSS) 22.0. The numerical variables were presented as mean and standard deviation or median and interquartile range, according to their parametricity, and compared by the Student's t-test or the Mann-Whitney U Test, respectively.

RESULTS

Epidemiology

A total of 37 patients were diagnosed with discitis and analyzed. The sexes were evenly distributed, with 19 males (51.4%), predominantly Caucasian, and a mean age of 56.89 ± 15.33 .

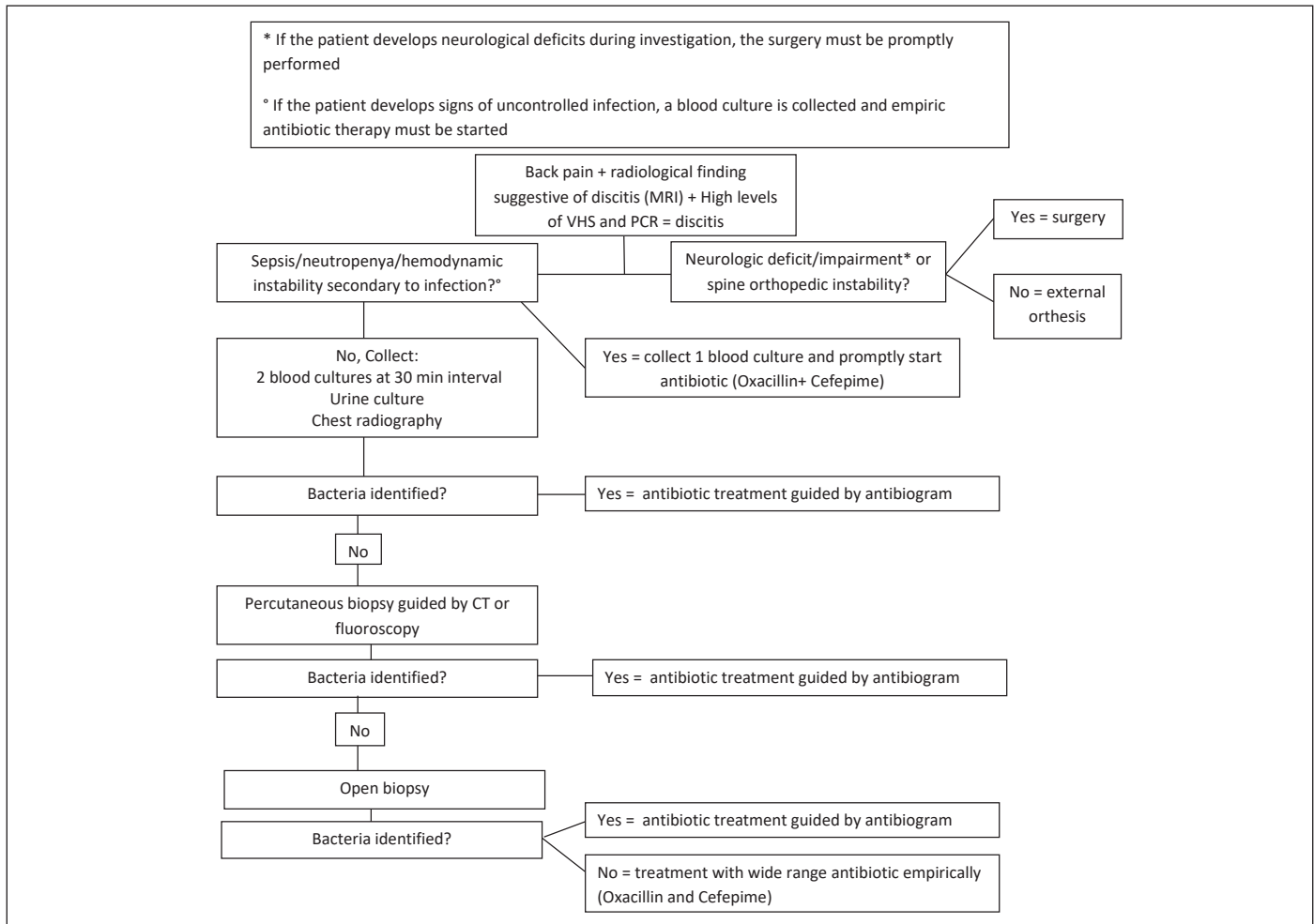


Figure 1. Discitis protocol.

Comorbidities

Hypertension was the most common previous pathology presented in our population (29.7%), followed by type 2 diabetes (24.3%) and obesity (13.5%). Three patients were HIV positive, and another three patients were immunocompromised due to immunosuppressive therapy for autoimmune diseases or lymphoma. Two patients presented chronic renal failure. (Table 1)

Radiology

Thirty patients had infection restricted to one level (81.8%) and 7 patients had infection in 2 vertebral segments. Among the patients with two infected levels, five had contiguous lesion and 2 had involvement of distant segments. Therefore, although the study included 37 patients, a total of 44 vertebral intervertebral discs were diagnosed with discitis. The vertebral lumbar segment was the most involved, with 19 cases (43.1%), followed by the thoracic and cervical regions. (Table 1)

Microorganisms

The pathogen was identified in all 34 out of the 37 cases (91.8%), 13 cases by open disc biopsy during spinal surgery, eleven cases by hemoculture and ten cases by percutaneous disc biopsy (Table 3). The most prevalent bacterium isolated was *Staphylococcus aureus* (35.1%), closely followed by Koch Bacilli (32.4%) (Table 1). Two patients had two or more bacteria identified.

Inflammatory serum markers

Analyzing the whole sample, the median CPR at hospital admission and discharge were 72 (38.5 - 160) and 17.1 (6.16 - 41),

respectively. The mean and standard deviation of leukocytes and VHS at admission were 9550 ± 4276 and 64.78 ± 27.14 , respectively. (Table 2) Stratifying the sample in pyogenic and nonpyogenic groups, the inflammatory markers are higher in pyogenic infections at hospital admission, but lower at hospital discharge when compared to tuberculous discitis ($p < 0.01$).

Leucocytes and age were not different between groups (Table 3), even though the difference of admission CPR was almost significant.

Surgical and Antibiotic therapy

A total of fifteen patients required surgical stabilization of the spine during antibiotic therapy. External immobilization with a cast was performed in six patients.

Antibiotic treatment varied according to the microorganism identified. Tuberculosis infections were treated with Rifampicin, Isoniazid, Pyrimethamine and Ethambutol for two months, followed by seven months of Rifampicin and Isoniazid. Pyogenic discitis were treated according to the protocol previously described. After the antibiogram results, during hospitalization, gram positive microorganisms were mostly treated with Oxacillin and only three patients required treatment with Vancomycin. All gram negative bacteria were treated with Cefepime. After discharge, most of the patients received Ciprofloxacin until cure criteria.

The mean hospital stay was 34.6 ± 25.9 among patients with TB, and 46.9 ± 19.3 ($p = 0.02$) among patients with pyogenic discitis.

DISCUSSION

Primary pyogenic spondylodiscitis commonly arises from haematogenous spread from a lung, bladder or skin infection.⁶ In adults,

Table 1. Demographic characteristics and infection data.

Variable	Total Value (%)
Sex	
Male	19 (51.3)
Race	
Caucasian	34 (91.8)
Black	2 (5.4)
Hispanic	1 (2.7)
Comorbidities	
SAH	11 (29.7)
Type 2 Diabetes	9 (24.3)
Obesity	5 (13.5)
Immunocompromised	3 (8.1)
HIV infection	3 (8.1)
CRD	2 (5.4)
Number of spine levels involved	
One segment	30 (81.8)
Two segments	7 (18.9)
Spinal Segment Involved	
Cervical	8 (18.1)
Thoracic	16 (36.3)
Lumbar	19 (43.1)
Bacteria	
Staphylococcus aureus	13(35.1)
Koch Bacilli	12 (32.4)
Escherichia coli	3 (8.1)
Enterobacter complex	2 (5.4)
Staphylococcus epidermidis	1 (2.7)
Staphylococcus capitis	1 (2.7)
Streptococcus viridans	1 (2.7)
Moraxella specie	1 (2.7)
Pseudomonas aeruginosa	1 (2.7)
Acinetobacter spp	1 (2.7)
Proteus mirabilis	1 (2.7)
Diagnostic Method	
Open disc biopsy culture	13 (47.6)
Blood culture	11 (28.5)
Percutaneous biopsy culture	10 (23.0)

1. Systemic Arterial Hypertension; 2. Chronic Renal Disease. Immunosuppression: patients using immunosuppressive drugs due to auto-immune disease or lymphoma.

Table 2. Variables analyzed and their distribution in our sample.

Variable	Mean \pm SD*	Median (IQ ^a)
Age	56.89 \pm 15.33	
Leucocytes	9550 \pm 4276	
VHS	64.78 \pm 27.14	
CPR Hospital admission		72 (38.5 - 160)
CPR Hospital discharge		17.1 (6.16 - 41)
Days of Hospital care	43.09 \pm 22.01	

*SD: standard deviation; ^aIQ: Interquartile interval.

Table 3. Comparison of variables analyzed between pyogenic and nonpyogenic groups.

Variable	TB group	Pyogenic group	P value
Age	55.02 \pm 14.9	57.79 \pm 15.7	0.61 ¹
Leucocytes	7853 \pm 2770	10365 \pm 4667	0.09 ¹
VHS	47.1 \pm 23.9	73.5 \pm 24.5	< 0.01 ¹
CPR Hospital admission	53.6 (22 - 104.6)	100 (44.9 - 186)	0.06 ²
CPR Hospital discharge	31.1 (23.3 - 49.5)	9.14 (4.9 - 23.5)	< 0.01 ²
Days of Hospital care	34.6 \pm 25.9	46.9 \pm 19.3	0.02 ¹

Mean \pm Standard deviation; Median (interquartile interval); 1. Student's t-test; 2. Mann-Whitney U test.

the disc is avascular, therefore, bacteria reach the vertebral body capillaries and invade the end-arterial arcades into the subchondral region, adjacent to the intervertebral disc. The infection then spreads through the end-plates to the intervertebral disc.⁶

Tuberculosis used to be the most common cause of spinal infections,⁶ however according to most articles published in recent medical literature, *S. aureus* is the most common organism isolated.^{2,5,13-15} In our study, *S. aureus* was the most common pathogen identified, especially oxacillin-susceptible *S. aureus*, closely followed by Koch Bacilli.

Moreover, patients with spontaneous discitis demonstrate a wide variety of gram-positive and gram-negative organisms,¹⁶ whose incidence differs according to each center.^{6,17,18} Gram-negative bacilli such as *Escherichia coli*, *Proteus* and *Pseudomonas* are often seen in association with diabetes, immunocompromised patients or intravenous drug abuse. In our sample, 3 patients out of 9 (33%) with one of the risk factors described above were affected by a gram negative pathogen.

Spine Involvement

According to Legrand and Cheung^{6,15} the lumbar segment is the segment most commonly involved among discitis cases, closely followed by the thoracic segment; which is in agreement with our results.

Even though any level of the spine may be involved singly, two or more vertebral levels may be concomitantly affected. In our population, 18.9% presented the involvement of two discs, and 85.72% had a single level infection, with distribution similar to that described by Legrand.¹⁵

Investigation and diagnose

Once the diagnose of spondylodiscitis is suspected, the physician should dose acute-phase reactants (CPR and ESR) and perform an image exam of the spine at the level where the pain is occurring.¹⁶ Magnetic resonance imaging (MRI) is the gold standard for the diagnosis of spinal infection.^{6,19} A rise in the ESR and CRP occurs in over 90% of patients^{14,20} and the average ESR in patients with pyogenic spondylodiscitis ranges from 43–87 mm per hour.²¹ Among our patients, 100% presented high levels of CRP and ESR. Leukocytosis is present in less than 50% of cases,²² which was also found in our study.

Our study compared inflammatory markers between tuberculous and pyogenic spondylodiscitis, and found a significant difference among groups, with higher levels of ESR and CPR in the pyogenic group. The difference in CRP is also seen after antibiotic therapy, with a drastic reduction in pyogenic infections, which is not seen in the TB group.

Pathogen identification

Spondylodiscitis investigation begins with two blood culture samples in an attempt to identify the pathogen. If these are negative, a percutaneous disc biopsy guided by computed tomography (CT) or fluoroscopy is indicated.²³ In our service, we perform fluoroscopic percutaneous biopsy when both blood cultures are negative. The authors performed a second fluoroscopic percutaneous biopsy if the first failed to identify the bacteria, which is also recommended by other centers.^{24,25} However, even though this procedure is recommended by literature, there is no report about the sensitivity of a second percutaneous biopsy, and an open biopsy could perhaps be performed if the first percutaneous biopsy fails to identify a pathogen.

Biopsy specimens should be sent for Gram smear, aerobic and anaerobic cultures, tuberculosis culture and polymerase chain reaction, fungal culture and histopathology. The accuracy of percutaneous vertebral biopsy in patients with infective spondylodiscitis has been reported to be about 70%. If the initial biopsy is negative, and withholding antibiotics is clinically safe, a further biopsy can be attempted. If two fluoroscopic or CT guided percutaneous biopsies fail to identify the organism, an open biopsy should be performed.^{6,16}

Even though it is important to identify the pathogen in order to guide antibiotic therapy, this is not always possible. According to

Sapico, in one-third of cases, the pathogen is never identified.²⁶ Kapsalaki describes a better rate of pathogen identification (87.5%), even though only 8 patients were included in that study.¹⁰ In our series of 37 patients, the pathogen was identified in 91.8%; 11 from blood cultures and 23 from disc cultures (the disc samples were collected by open surgery in 13 cases, and by percutaneous biopsy).

The prevalence of polymicrobial infection is not uncommon. In a series of 35 cases described by Danner, 68% of the cases revealed a single organism, 21% revealed two organisms and 11% more than two organisms (27). In our series, a single bacterium was isolated in 32 cases (86.4%), two bacteria (Koch Bacilli and *Enterobacter complex*) in one case, and three bacteria in another case (2.94%).

Antibiotic Therapy

Antimicrobial treatment should not be started until the organism is identified, except when clinical circumstances dictate otherwise (patients with neutropenia or sepsis).²⁵ If the patient requires urgent treatment, empirical therapy with a broad spectrum antibiotic regimen should be initiated right after collection of the blood cultures.²⁹ According to Cottle, an antibiotic regimen using a combination of ciprofloxacin and clindamycin may be used, since its association provides both staphylococcal and Gram-negative coverage, and has good bone and disc penetration.⁵ On the other hand, Cheung⁶ describes an empirical antibiotic use of penicillin or first generation cephalosporin only. This author prescribes broader spectrum antibiotics (third generation cephalosporin) only for immune-compromised patients and intravenous drug abusers, since they require better gram negative bacteria coverage.

In stable patients, once the pathogen has been identified and a table of resistance/sensitivity formulated, agent-sensitive intravenous antibiotics should be started.¹ Based on the antibiogram chart, physicians should choose an antibiotic characterized by good intraosseous penetration and oral bioavailability (fluoroquinolones, clindamycin, fusidic acid, metronidazole and rifampin).^{5,10,15,28} Agents that are known to have poor penetration into disc tissue, such as Penicillin and Vancomycin, should not be the first choice of treatment.⁵ However, some authors report that Vancomycin has good bone penetration and should be considered when treating spinal infections, especially for patients in whom beta-lactam antibiotic sensitive bacteria were identified.⁶ Nevertheless, according to Honan, cephalosporins are relatively contraindicated in discitis, due to their poor disc penetration.¹⁶ Among the cases of pyogenic discitis in our sample, the most frequent bacterium identified was *S. aureus*, and according to the resistance chart performed in our hospital, only one case was caused by MRSA and all other 8 cases were caused by Oxacillin-susceptible bacteria. Among the gram negative pathogens, no case of Carbapenem-resistant infection was detected, and all pathogens were susceptible to Cefepime (table 1). Therefore, our protocol states that empiric antibiotic therapy should be started with Oxacillin and Cefepime.

Therapy duration

The optimal duration of antibiotic therapy (intravenous plus oral) is unclear.²⁸ As a general rule, it is advisable to administer antibiotics intravenously for two to four weeks.¹ Studies recommend that antibiotics should be given intravenously for 4 to 6 weeks until sufficient clinical improvement has been achieved and CPR and ESR levels are reduced.^{10,21} The reduction of inflammatory markers is evident in pyogenic discitis, but the same pattern is not found in tuberculous cases, and this difference is significant between groups. Therefore, we conclude that CPR and ESR should be used as parameters to follow the infection in pyogenic cases.

If ESR and CPR show a 50% reduction, and the patient is pain free, without instability or neurological deficits, the physician may switch to oral therapy⁵ for an additional 6 weeks of treatment.^{5,21}

If the infection parameters remain persistently elevated, with intravenous antibiotics, an image study should be repeated searching for any abscess collection (epidural or paravertebral abscess).

Antibiotic therapy for less than four weeks may result in a high

rate of recurrence.³⁰ A good response is indicated by resolution of the fever and back pain, and a 50% drop in the CPR level every week until normal values are reached after about 4 weeks.³¹ The erythrocyte sedimentation rate decreases more slowly. However, if the ESR level goes down 50% after 4 weeks of treatment, the infection is usually cured.³²

Antibiotic discontinuation criteria

According to a multicenter study, antibiotic therapy can be safely discontinued when patients meet all the following criteria: free of spine pain with disappearance of inflammatory pattern, normal body temperature, normal CPR and/or ESR values and stabilization or improvement in the disk and vertebral abnormalities on plain radiographs.¹⁵

In our service, we recommend a total of 6 weeks of antibiotic treatment: 4 weeks by the intravenous route followed by 2 weeks by the oral route. However, if CPR and ESR values do not drop by 50% by the end of the 4th week, or if the pathogen is not sensitive to oral antibiotic, intravenous treatment is extended to 6 weeks.

For TB, 9 months of treatment are recommended, with an antimicrobial regimen that includes Rifampicin, Isoniazid, Ethambutol and Pyrazinamide for the first two months of treatment; with isoniazid and rifampicin continued alone after 2 months. This is the treatment performed in our service.³

External immobilization

Bed rest is recommended in the early phase of the treatment, until the acute pain improves. Subsequently, walking with an appropriate cast or brace should be advised. External immobilization helps to stabilize the spine, decrease pain and prevent deformity. The duration of bracing ranges from three to four months, depending on the amount of bony destruction or deformity.^{5,6}

Surgical Treatment

Half to three-quarters of all patients respond successfully to non-operative treatment.^{2,6} However, in some cases, surgery must be performed to achieve proper cure of the disease and prevent neurologic or orthopedic disability. Surgery may be indicated for the following reasons: resolution of significant spinal cord or radicular compression, prevention or correction of biomechanical instability and deformity, management of severe persistent pain and/or drainage of abscesses.¹ Fifteen of our patients met those criteria, and were submitted to surgical stabilization. The goals of surgery are debridement and removal of the septic focus, decompression of the spinal canal, with stabilization and restoration of the infected spine segment, and subsequent bone fusion.³¹

Although some authors believe that emergency decompression is indicated only if complete paraplegia develops, and that paresis can be resolved by antimicrobial treatment alone,⁵ the Neurosurgery Department at the Cristo Redentor indicates surgery in all patients with discitis (whether harboring epidural abscess or not) who present neurological deficit secondary to the infection. This conduct is in agreement with other neurosurgeons, such as Cottle, based on the view that the presence of neurological dysfunction is a sign of spinal cord disturbance that can progress rapidly to irreversible neurologic impairment.^{5,32} However, it is important to highlight that TB may cause a vascular reaction (vasculitis) that leads to ischemia in the spinal cord, and that even with decompression, neurological recovery may not be as significant as expected.

A grafting structure with autograft, allograft, and titanium cages has been placed safely and successfully in the presence of infection after most of the purulent material has been removed.³

Strengths and Limitations of the Study

One limitation of our study is the short time span of four years, since only 37 patients with primary discitis were treated in our service. However, the protocol showed a high level of pathogen identification and excellent results, with no recorded deaths.

The authors expect that in coming years, more patients will be included, with the objective of maintaining the high level of diagnosis,

which may optimize the therapy (identifying the pathogen earlier) and reduce hospitalization times, thereby decreasing costs and the risks of secondary hospital complications.

CONCLUSION

Spondylodiscitis is a disease that is still clinically difficult to diagnosis, as there are no specific signs or symptoms. Therefore, neurosurgeons must have a high level of suspicion when examining a patient with back pain. Institutional protocols have a

significant impact on the treatment of these patients, since they guide the physician on the proper investigation and treatment, improving pathogen diagnosis and antibiotic treatment and guiding surgical indications, which can result in a shorter hospitalization times and better outcomes.

All authors declare no potential conflict of interest related to this article.

CONTRIBUTION OF THE AUTHORS: Each author made significant individual contributions to the manuscript. GF (0000-0001-8365-8032), AMLC (0000-0002-6186-5361), ES (0000-0001-8539-4202), FMLC (0000-0002-7724-6709) conceived the project; GF, AMLC, ES, LWL(0000-0002-6269-2212) elaborated the protocol; GF, LWL applied the protocol; GF, AMLC, ES, FMLC, TLN (0000-0001-6161-1348) performed the surgeries; GF, ES, TLN, collected the data; GF, LWL, TLN filled out the database; GF, LWL, TLN, AF (0000-0002-0016-3198) performed a review of the literature; GF, AMLC, AF interpreted the results; GF, AMLC, LWL, AF, wrote the article; GF, AMLC, ES, EMLC, LWL, AF, reviewed and approved the final manuscript; LWL applied the protocol and provided the discussion of the results; TLN gave final approval of the manuscript, and AF performed the statistical analysis. *ORCID (Open Researcher and Contributor ID).

REFERENCES

- Zarghooni K, Rölinghoff M, Sobottke R. Treatment of spondylodiscitis. *Int Orthop*. 2012;36(2):405–11.
- Hadjipavlou AG, Mader JT, Necessary JT, Muffoletto AJ. Hematogenous pyogenic spinal infections and their surgical management. *Spine (Phila Pa 1976)*. 2000;25(13):1668–79.
- Gouliouris T, Aliyu SH, Brown NM. Spondylodiscitis: Update on diagnosis and management. *J Antimicrob Chemother*. 2010;65(Suppl 3):11–24.
- Menon KV, Sorour TMM. Epidemiologic and Demographic Attributes of Primary Spondylodiscitis in a Middle Eastern Population Sample. *World Neurosurg*. 2016;95:31–9.
- Cottle L, Riordan T. Infectious spondylodiscitis. *J Infect*. 2008;56(6):401–12.
- Cheung WY, Luk KDK. Pyogenic spondylitis. In *Orthop*. 2012;36(2):397–404.
- Reihsaus E, Waldbaur H, Seeling W. Spinal epidural abscess: a meta-analysis of 915 patients. *Neurosurg Rev*. 2000;23(4):175–204; discussion 205.
- Soehle M, Wallenfang T. Spinal epidural abscesses: clinical manifestations, prognostic factors, and outcomes. *Neurosurgery*. 2002;51(1):77–9.
- Forestier E, Sordet C, Cohen-Solal J, Remy V, Javier RM, Kuntz JL, et al. Bone and joint infection due to *Streptococcus pneumoniae* in two immunocompetent adults. *Jt Bone Spine*. 2006;73(3):325–8.
- Kapsalaki E, Gatselis N, Stefanos A, Makaritsis K, Vassiou A, Fezoulidis I, et al. Spontaneous spondylodiscitis: presentation, risk factors, diagnosis, management, and outcome. *Int J Infect Dis*. 2009;13(5):564–9.
- Lehovskey J. Pyogenic vertebral osteomyelitis/disc infection. *Baillieres Best Pract Res Clin Rheumatol*. 1999;13(1):59–75.
- Colmenero JD, Jiménez-Mejías ME, Sánchez-Lora FJ, Reguera JM, Palomino-Nicás J, Martos F, et al. Pyogenic, tuberculous, and brucellar vertebral osteomyelitis: a descriptive and comparative study of 219 cases. *Ann Rheum Dis*. 1997;56(12):709–15.
- Hopkinson N, Stevenson J, Benjamin S. A case ascertainment study of septic discitis: clinical, microbiological and radiological features. *QJM*. 2001;94(9):465–70.
- Lam KS, Webb JK. Discitis. *Hosp Med*. 2004;65(5):280–6.
- Legrand E, Flipo R, Guggenbuhl P, Masson C, Maillefert J, Soubrier M, et al. Management of nontuberculous infectious discitis. Treatments used in 110 patients admitted to 12 teaching hospitals in France. *Jt Bone Spine*. 2001;68(6):504–9.
- Honan M, White GW, Eisenberg GM, Ridge P. Spontaneous Infectious Discitis in Adults. *Am J Med*. 1996;100(1):85–9.
- Clamp JA, Grevitt MP. Spinal infections. *Surgery*. 2009;27(7):306–10.
- Yee DKH, Samartzis D, Wong Y-W, Luk KDK, Cheung KMC. Infective Spondylitis in Southern Chinese: A Descriptive and Comparative Study of Ninety-One Cases. *Spine (Phila Pa 1976)*. 2010;35(6):635–41.
- Govender S. Spinal infections. *J Bone Jt Surg Br*. 2005;87(11):1454–8.
- An H, Seldomridge J. Spinal infections: diagnostic tests and imaging studies. *Clin Orthop Relat Res*. 2006;444:27–33.
- Carragee EJ, Kim D, van der Vlugt T, Vitum D. The clinical use of erythrocyte sedimentation rate in pyogenic vertebral osteomyelitis. *Spine (Phila Pa 1976)*. 1997;22(18):2089–93.
- Fang A, Hu SS, Endres N, Bradford DS. Risk factors for infection after spinal surgery. *Spine (Phila Pa 1976)*. 2005;30(12):1460.
- University of Michigan Health System. Vertebral Osteomyelitis, Discitis, and Spinal Epidural Abscess in Adults. 2013;1–12.
- Chidiac C, Bru J, Choutet P, Decazes J, Dubreuil L, Lepout C, et al. Recommandations pour la pratique clinique spondylodiscites infectieuses primitives, et secondaires a un geste intradiscale, sans mise en place de materiel. *Med Mal Infect*. 2007;37(9):554–72.
- Grados F, Lescure FX, Senneville E, Flipo RM, Schmit JL, Fardellone P. Suggestions for managing pyogenic (non-tuberculous) discitis in adults. *Jt Bone Spine*. 2007;74(2):133–9.
- Sapico FL. Microbiology and antimicrobial therapy of spinal infections. *Orthop Clin North Am*. 1996;27(1):9–13.
- Danner RL, Hartman BJ. Update on spinal epidural abscess: 35 cases and review of the literature. *Rev Infect Dis*. 1987;9(2):265–74.
- Sobottke R, Seifert H, Fatkenheuer G, Schmidt M, Gossmann A, Eysel P. Current diagnosis and treatment of spondylodiscitis. *Dtsch Arztebl Int*. 2008;105(10):181–7.
- Jaramillo-de la Torre JJ, Bohinski RJ, Kuntz C. Vertebral osteomyelitis. *Neurosurg Clin N Am*. 2006;17(3):339–351.
- Legrand E, Massin P, Levasseur R, Hoppe E, Chappard D, Audran M. Strategie diagnostique et principes therapeutiques au cours des spondylodiscites infectieuses bacteriennes. *Rev Rhum*. 2006;73(4):373–9.
- Berbari E, Kanj S, Kowalski T, Darouiche R, Widmer A, Schmitt S, et al. 2015 Infectious Diseases Society of America (IDSA) Clinical Practice Guidelines for the Diagnosis and Treatment of Native Vertebral Osteomyelitis in Adults. *Clin Infect Dis*. 2015;61(6):e26–46.
- Osenbach RK, Hitchon PW, Menezes AH. Diagnosis and management of pyogenic vertebral osteomyelitis in adults. *Surg Neurol*. 1990;33(4):266–75.