MEDDOCS Open Access Publisher

ISSN: 2637-9627

Annals of Pediatrics

Open Access | Case Report

Epidemiology and Management of Pyogenic Spondylodiscitis in a Tertiary Paediatric Center, over 10 Years

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Received: Aug 13, 2021

Accepted: Sep 06, 2021

Published Online: Sep 09, 2021

Journal: Annals of Pediatrics

Publisher: MedDocs Publishers LLC

Online edition: http://meddocsonline.org/

Abstract

Background: Pyogenic Spondylodiscitis (PSD) is the concurrent bacterial infection of the intervertebral disc and the adjacent vertebral bodies. There is a substantial lack of structured reviews about this topic. Many aspects of the treatment are under debate, mainly because there are no guidelines for paediatric PSD.

Methods: Data from children, aged > 1 month, admitted for PSD to a third level paediatric hospital, between 1st January 2010 and 31 December 2019 were retrospectively reviewed, and analysed. Logistic regression analysis was performed to investigate possible risk factors for sequelae.

Results: Overall, 21 children with PSD were identified. Male to female ratio was 1.3:1. The median age was 9.3 years (IQR: 1.7-11.5). Thirteen (61.9%) cases of lumbar-lumbosacral PSD were identified. The most common symptom was persistent back/lower limp pain (42.8%). ESR was found to be more sensitive than CRP (sensitivity 94.4% vs. 19.04%). One or more bacterial pathogens were identified in 6 (28.6%) children; *S. aureus* was the most commonly isolated. Magnetic resonance imaging confirmed the diagnosis of PSD showing typical vertebral bone and intervertebral disc involvements in all the children. All children were treated with an extended course of antibiotics and one child underwent surgical treatment. The most commonly prescribed intravenous regime was oxacillin + 3rd generation cephalosporin (10/18; 55.5%). Switch to oral therapy was performed in 19/21 (90.5%) children and amoxicillin-clavulanate was the most commonly used drug (6/19; 31.6%). Immobilization was carried out in 12/21 (57.1%) children. Five (25%) children presented occasional episodes of very mild back pain/discomfort, or minimal deformity of the spine. Radiological sequelae were reported in 10/21 (47.6%) children. At logistic regression analysis age class ≤ 5 years was the only factor significantly associated with sequela (p=0.05).

Cite this article: Ferri I, Musso P, Ristori G, Galli L, Chiappini E. Epidemiology and Management of Pyogenic Spondylodiscitis in a Tertiary Paediatric Center, over 10 Years. Ann Pediatr. 2021; 4(1): 1079.

Conclusions: Ours is a recent and large case series study, that reports 25% of sequelae (clinical and/or radiological), although no severe sequela was observed. PSD diagnosis should be considered in children with back pain, but also unspecific symptoms such as irritability. Increased ESR can be a useful marker for the diagnosis.

Introduction

Spondylodiscitis (SD) is a term commonly used to describe the concurrent infection of the intervertebral disc and the adjacent vertebral bodies. It has also been used for encompassing a continuum of spinal infections, from discitis to vertebral osteomyelitis through SD [1]. Childhood SD is a relatively rare disease, accounting for only 1-2% of all osteomyelitis [2] and with an estimated incidence of 0.3 per 100,000 children/year [3]. However, if not treated promptly, SD can lead to substantial clinical problems, such as severe spinal deformities, segmental instabilities, or neurological damages if the infection spreads into the spinal channel [1,4].

Historically, discitis and vertebral osteomyelitis were considered two different entities [2,5]; however, in more recent studies authors agree that they are two aspects of the same spectrum, which appear in two different stages of the pathological process [6].

The nonspecific clinical manifestations of SD, especially back pain in the older children and irritability in toddlers, and the inability of younger children to verbalize the nature of their pain, are the main factors that contribute to the delay in diagnosis [3,7,8] which may lead to a worse outcome and lifelong disability [9]. In the pre-antibiotic era, mortality due to PSD was 25%-56% [10,11]. Currently, due to better diagnostic tools and improvements in medical and surgical treatment, mortality is significantly reduced, and it is lower than 5% [1,12]. Children between 2 and 8 years of age are more frequently affected, although SD can also occur in infants and children of any age [13]. The lumbar and the lumbar-sacral spine are the most frequently involved sites, but every segment of the spine can be affected [14]. Pathogens can infect the spine via three routes: by hematogenous spread (the most frequent), by direct external inoculation, and by spread from infections of adjacent tissues. The pathophysiology of SD is assumed to be different in adults and children because of the persisting vascular channels in the ID space in children (3,15). SD aetiology can vary, and it is changing, according to bacterial susceptibility pattern modification over time and implementation of PCR techniques. SD is usually divided into pyogenic forms; unspecific granulomatous; specific (such as tuberculosis); and parasitic forms. In high-income countries, Pyogenic Spondylodiscitis (PSD) is the most common form, and other presentations are exceptional and *S. aureus* is the most commonly isolated pathogen [1]. Since the 1980s [14], *K. kingae* has emerged from being a previously poorly recognized cause of PSD in children to the second most commonly responsible for most cases of hematogenous PSD in children aged between 6 months and 4 years [16]. Gram-negative organisms are rarely implicated in children as in adults, and they may account for up to 30% of cases [17,18]. However, in many cases, the identification of the causative microorganism is not possible, and it often requires invasive procedures (*i.e*. CT-guided biopsy), unless the blood culture is positive [19]. The results of laboratory tests (WBC, CRP, ESR, and PCT) often provide nonspecific information since they are usually normal or slightly raised [14]. Another significant problem concerns the radiological imaging, that is poorly contributive in the first period of the disease's development. The use of x-rays is limited for diagnosis and helpful only in advanced cases [13]. MRI is the mainstay mode of investigation with high specificity and high sensitivity [2]. Finally, the best therapeutic approach is not precisely defined: Contrary to adult SD, for which treatment guidelines have been issued [20]; no guidelines exist for paediatric patients. Optimal antimicrobial treatment is still under debate in terms of molecule and duration, and the empirical therapeutic choice is based on local epidemiological data. Several data suggest that a long-term therapeutic course is usually required to control symptoms and normalize laboratory tests [19]. Treatment also involves spine immobilization and surgery in advanced cases. Surgical indications include doubtful diagnosis, progressive neurological deficits, progressive spinal deformity, failure to respond to treatment, and unresolved pain [21-23].

The case series regarding the childhood SD, which are reported in the literature, are limited, and they are very heterogeneous. They derive from different countries, and they report data that were collected in different years; therefore, the aetiology, the investigation methods, and also the antimicrobial therapies are widely different [2,3,5,6,13,14]. Moreover, the clinical studies describing outcomes, complications, and sequelae of PSD are limited.

To review the clinical presentation, management, causative organisms, and therapeutic strategies adopted in children with PSD, a cohort referred to a single centre over ten years was evaluated.

Methods

Definitions

PSD was defined as any suspected or ascertained bacterial infection of the intervertebral disc and the adjacent vertebral bodies [1]. PSD was diagnosed in the presence of clinical features (back pain, limping, movement limitations, refusal to walk/to sit/to bear weight, motor regression, and irritability/general malaise), laboratory findings (elevated inflammatory indices: ESR, CRP and/or WBC), and compatible radiologic imaging, with or without bacteriological isolation [13,14]. In order to exclude children with possible TSD all the study children underwent Tuberculin Skin Test (TST)/QuantiFERON-TB Gold (QFT) at admission, and positive children were excluded from the analysis.

PSD sequelae

The sequelae were differentiated in

1) Radiological sequelae, with no clinical symptoms associated (*i.e*. narrowing of disk spaces, permanent reduction of the intervertebral disc height, vertebral fusion) [7];

2) Sequelae associated with mild clinical symptoms (*i.e.* persistent mild back pain/discomfort but with no limitations of the activities) [3,13];

3) Severe clinical sequelae (permanent deformities of the spine or neurological damages) [24].

Study design and population

Data from all children aged between 1 month and 18 years, consecutively admitted to Meyer Children's Hospital with a discharge code consistent with the diagnosis of SD (ICD codes M46.2-46.5; M46.8-M46.9), according to the World Health Organization International Classification of Diseases (WHO ICD-10),

between 1 January 2010 and 31 December 2019. Two authors independently reviewed data from these children. Exclusion criteria were age ≤ 30 days, or isolated discitis. Data were collected from medical records, electronic records for laboratory, and radiology results. Demographic and clinical details, microbiological and radiologic results, and clinical management including type, route and duration of antibiotic treatment, need for surgery, and readmission to hospital within 6 months after initial diagnosis were entered into an electronic database. Reasons for changes in the antibiotic regimen were also recorded (*i.e*. clinical and/or radiological failure; switch from intravenous therapy to oral therapy; switch from empirical therapy to a targeted antimicrobial therapy after bacterial isolation). Surgery was performed in selected cases (*i.e.* children needing draining an abscess). The antibiotic treatment duration and the targeted choice of the molecule was guided by clinical picture, microbiological information, interval inflammatory markers and MRI imaging [2].

Laboratory and microbiological investigations

All the laboratory tests, including serology tests, were performed in the same laboratory at the author's institution using standardized techniques and according to the manufacturer's instructions. Haematological parameters (WBC, CRP, ESR, PCT) were collected at admission before administration of any antimicrobial therapy. Blood cultures and cultures from vertebral bone, intervertebral disc or other specimens were processed using standard methods. All samples were processed for detection of common human bacteria (or cultured for detection of MRSA isolates) using rich and selective culture media. Universal real-time PCR (RT-PCR) assay targeting the gene coding for 16S ribosome RNA coupled with the sequencing of amplified products was performed on blood and/or tissue samples, as previously described [25,26]. RT-PCR for several bacteria (Staphylococcus aureus, *Streptococcus pyogenes*, Klebsiella pneumoniae, Streptococcus pneumoniae, Pseudomonas aeruginosa, Kingella kingae, Bartonella spp, Escherichia coli) were performed using specific primers and probes [26-28].

Statistical methods

Data were reported as median and Interquartile Range (IQR) or absolute numbers and percentages. Nineteen five percent of confidence interval of percentages were calculated using Agresti-Coull method. Nonparametric Mann-Whitney, Fisher's exact or Chi Square tests were used to compare continuous or categorical variables, as appropriate. All significant tests were two-sided. Uni- and multi-variate logistic regression analyses were performed to investigate the association between several parameters and risk of PSD with sequelae (both clinical and radiological), calculating Odds Ratios (ORs) and 95% Confidence Intervals (CIs). Variables included in univariate analyses were gender, age, interval time between symptoms onset and diagnosis, comorbidities, previous trauma, recent febrile episode, involved spinal segment (lumbar-lumbosacral or others) , isolated pathogen, WBC (≥ or <10,000 cell/μL) CRP (≥ or <10 mg/L), ESR (≥ or <20 mm/h), PCT (positive or negative), at least one elevated inflammatory index, median length of total antibiotic therapy, median length of IVT, and immobilization. Factors significantly associated with sequelae in PSD at univariate analysis were included in the multivariate analyses if p0.05. All statistical analyses were carried out using the SPSS (Statistical Package for the Social Sciences, SSPS Inc., Chicago, IL, USA) for Windows software program version 19.0. A **p**-value ≤ 0.05 was considered significant. The study was approved by the Ethics Committee at the authors' institution (121/2016).

Results

Overall, 21 children with PSD were included in the study. Male to female ratio was 1.3:1 (12 males to 9 females). The median age at the admission was 9.3 years (IQR:1.7-11.5). Nineteen out of twenty-one (90.4%) children were Caucasian, 1/21 (4.7%) child was Hispanic, and 1/21 (4.7%) child was Arab. Overall, 20/21 (95,2%) cases had unifocal involvement of the spine. Twelve out of twenty (60.0%) cases of lumbar or lumbosacral PSD were identified, with 2/20 (10%) cases of cervical involvement, 4/20 (20%) cases of thoracic involvement, and 2/20 (10%) cases of sacral involvement. One out of twenty-one (4.7%) child presented a multifocal affection of the spine (with contemporary thoracic, lumbar and sacral involvement) (Tables 1, 2).

Clinical features, physical examination, and comorbidities

The median interval time (days) between onset symptoms and PSD diagnosis was ten days. Nine (42.8%) children presented persistent back/lower limp pain (children with thoracic and lumbar SD); 1/21 (4.7%) case had torticollis (child with cervical SD); 13/21 (14.2%) children showed irritability; 2/21 (9.5%) cases had previous/persistent fever, associated with antalgic gait or persistent back pain.

At physical examination localized pain was observed in 15/21 (71.4%) cases; movement limitations and regression in mobility were observed in 14/21 (66.6%) cases; isolated antalgic gait/position/limping was observed in 4/21 (19%) cases; refusal to walk/to sit/to stand was observed in 4/21 (19%) cases; fever was found in 7/21 (33.3%) patients. One child (Table 2; #6) with a complicated neurological condition of spinal dysraphism presented spinal tumefaction, near a pre-existing pressure ulcer. Another child (Table 2; #11) presented with a reddened secreting intergluteal fistula.

Two children presented with particularly unusual clinical conditions at the admission. One four-month male infant (4.7%) (Table 2; #2) was admitted for fever, irritability, excessive crying, and feeding difficulties. Sepsis was diagnosed, and the child was first admitted to the neurosurgery unit and subsequently to the intensive care unit. During the imaging investigations an inflammatory and infectious process of the thoracic segment (D4-D5-D6) compatible with the diagnosis of PSD, and a subperiosteal abscess, were documented. The microbiological investigations allowed the isolation *S. aureus* and *Candida parapsilosis* (isolated from the central venous catheter). Because of the expansive nature of the infection, it was presumed that the PSD was derived from a congenital spinal neuro-enteric cyst.

One 21-month-old female (4.7%) (Table 2; #18) was admitted for spinal stiffness, and antalgic hyperextension of the spine (especially of the cervical segment). At physical examination refusal to walk/to stand, and a slightly positive straight raise leg test were observed. Due to these clinical symptoms/signs, a diagnosis of meningitis was initially presumed, and the child underwent a lumbar puncture. After laboratory and imaging investigations, PSD was diagnosed.

Five (23.8%) children had severe comorbidities. One child had pre-existent humpback of the cervical-thoracic spine (Table 2; #2); one child had a complicated clinical condition, including Arnold-Chiari malformation type 2, myelomeningocele, hydro syringomyelia and dysraphism (Table 2; #6); one had Arnold-Chiari malformation (Table 2; #16); one child had quadriplegia as an outcome of a polytrauma (Table 2; #20); one child presented a neurological complicated condition of flaccid lower

limb paraplegia, associated with tetra ventricular hydrocephalus, neuromotor dysfunction, and scoliosis (Table 2; #11).

The presence of a documented prodromal illness before attending hospital was noticed in 10/21 (47.6%) children, 9/10 (90%) children reported a previous febrile episode, and 1/10 (10%) an episode of diarrhoea in apyrexia.

Finally, 4/21 (19%) patients had history of a recent trauma (1/4 was a polytrauma victim) (Table 2).

Laboratory investigations

At admission, WBC and CRP were performed in all the study children. WBC was increased (>10.000/μL) in 7/21 (33.3%, 95%CI:17.0-54.8) cases; CRP was elevated (>10 mg/L) in 4/21 (19.04%, 95%CI: 7.0-40.6). ESR was performed in 18/21 (85.7%) children and it was elevated (>20 mm/h) in 17/18 (94.4%,95%CI:72.3-100.9) cases. PCT was performed in 6/21 (28.6%) cases, and it always was negative.

ESR was found to be more sensitive than CRP (sensitivity 94.4% vs. 19.04%) in our cohort (Table 2).

Microbiological tests

Blood cultures were performed in 7/21 (33.3%) children, and 2/7 (28.6%) were positive for *S. aureus.* Other specimens' cultures were performed in 4/21 (19.0%) cases, and 3/4 (75%) yielded positive results. PCR technique was used on blood, throat swab, pus, pleural fluid, or liquor in 14/21 (66.7%) cases; 3/14 (21.4%) PCR were positive. Biopsy was performed in 3 cases, none of them showed positive bacterial growth on cultures. Regarding the microbiology findings, overall one or more bacterial pathogens were identified in 6/21 (28.6%) cases. A total of 9 microorganisms were isolated. *S. aureus* was the most commonly isolated (in 4 cases). No *K. kingae* infection was documented. Other identified pathogens were *Candida parapsilosis* (from cvc culture) (n=1)*, S. agalactiae* (n=1)*, S. pneumoniae* (n=1)*, S. pyogenes* (n=1)*,* and *E. coli* (n=1) (Table 2).

Regarding the microbiological investigations stool samples or rectal swabs were collected and tested for rotavirus and adenovirus antigens using the immuno-chromatography test (ICT) in 7/21 (33.3%) children. Moreover, serology testing results for detecting *Salmonella tiphy/Salmonella paratiphy/Bartonella* spp*./Borrelia* spp*./Listeria* spp. antibodies, were available in 12/21 (57.1%) children, and they all yielded negative.

Imaging studies

At admission X-rays was performed in 14/21 (66.6%) cases, 11/14 (78.6%) were negative. Three out fourteen (21.4%) x-rays revealed not specific abnormalities including reduction of the physiologic lumbar lordosis, retrolisthesis, and mild scoliosis.

MRI at the time of diagnosis was performed in all cases and it always confirmed the diagnosis of PSD. The MRI showed typical vertebral bone involvements: oedema appeared as a dark signal on T1-weighted images and as a bright signal on T2-weighted images (Table 3). Other performed imaging methods were: CT scan (n=5), BS (n=1) and PET (n=1). Of all 21 cases, 3/21 (14.3%) showed subperiosteal/muscular abscesses (#2, #17, #20 of table 3). At follow-up, the following imaging controls were performed: x-rays in 14/21 (66.6%) cases and MRI in 19/21 (90.4%) cases. CT was performed in 1 case. They showed radiological resolution of the inflammatory process and signs of bony healing (sclerosis with partial fusion of the vertebrae) without any osteolytic lesions, or muscular-skeletal modifications. However, in 10/21 (47.6%) children presented residual degenerative changes (irregularities of the endplates, persistent narrowing of the disc space, or decreased height and thickness of the ID space) were still visible. One out of ten (10%) case showed spinal deformity (evident dorsal kyphosis) (Table 3).

Treatment

All patients were treated with an extended course of antibiotics, and one child underwent surgical treatment.

The average duration of Intravenous Therapy (IVT) was 28 days, of OT was 32 days, of total Antibiotic Therapy (ABT) was 60 days. Oxacillin was the most commonly used first intravenous antibiotic (16/21; 76.1%), with ceftriaxone as the second most commonly prescribed antibiotic (10/21; 47.6%), followed by ceftazidime (8/21; 38%), either as single agents or in combination with other antibiotics. Eighteen out of twenty-one (85.7%) children received a combination of two broad-spectrum antibiotics as first antibiotic IVT; the most common antibiotic combinations were: ceftriaxone + oxacillin (5/18; 27,8%) and oxacillin + ceftazidime (5/18; 27.8%). Other combinations were: ceftriaxone + teicoplanin (1/18; 5.5%), meropenem + teicoplanin (1/18; 5.5%), ceftazidime + rifampin (1/18; 5.5%), clindamycin + oxacillin (1/18; 5.5%), oxacillin + ceftazidime + ciprofloxacin (1/18; 5.5%), ceftriaxone + ceftazidime + cefazolin (1/18; 5.5%), and oxacillin + ceftriaxone + clindamycin (2/18; 11.1%). Three out of 21 (14.3%) children received a single therapy based on oxacillin (2/3; 66.7%) or ceftriaxone (1/3; 33.3%). The antibiotic intravenous regimen was modified in 11/21 (52.3%) cases, due to the identification of the microorganism and its antibiotics susceptibility profile (n=3), the need of a therapy simplification (n=3), worsening of the clinical conditions and/or persistence of high inflammatory laboratory indices (n=2). In 3/11 (27.3%) cases the switch's motivation was missing.

Oral Therapy (OT) were administered to 19/21 (90.5%) children. Amoxicillin-clavulanate was the most commonly used oral antibiotic (6/19; 31.6%) followed by amoxicillin- clavulanate + rifampin (4/19; 21.0%) and sulfamethoxazole/trimethoprim + rifampin (4/21; 21.0%). Clindamycin was administered to 2/19 (10.5%) children. Linezolid and sulfamethoxazole/trimethoprim were respectively used 1/19 (5.3%) child. In one case a triple antibiotic OT consisting of sulfamethoxazole/trimethoprim + linezolid + rifampin was given. Two out of twenty-one (9.5%) children did not receive any OT.

The conservative treatment also comprehended the immobilization of the spine. Immobilization with spinal bracing was carried out in 12/21 (57.1%) children, combined with the administration of antibiotics. Only one child (Table 4; #2) required spinal surgery, more precisely he underwent abscess drainage (Table 4).

Follow up results

A favourable and relatively benign long-term outcome was observed in the majority of cases. The clinical sequelae of one child (Table 2; #20) could not be evaluated and summarized, due to his previous complex clinical condition. At the latest follow-up assessment (13.5; 8-22-5), 16/20 (80%) children were completely pain-free, with no restriction in the activity. They made a full clinical recovery and they were reported as being free from symptoms despite abnormal radiological signs in ten. Five (Table 2; #5 #12 #13 #15 #16) (25%) children presented occasional episodes of very mild back pain /discomfort (local back pain due

to long-sitting or long-standing) with no impact on their daily activities, or minimal spinal deformity. Ten out of twenty-one (47.6%) children presented with radiological residual sequelae including the decreased height of the Intervertebral Disc (ID) and the residual irregularities of endplates (Table 3). One out of these ten children reported an evident dorsal kyphosis and a reduction of the width of the vertebral canal, associated with compression of the ependymal canal. Interestingly, these children were clinically healed, and they usually have no functional impairment or pain.

Tables 1,2, 3, and 4 merged and summarised all the characteristics of the 21 study children.

Logistic regression analyses for risk of sequelae (clinical and/or radiological) in children with PSD

At univariate logistic regression analysis, a significant association was observed between the development of sequelae and age < 5 years (p=0.05), immobilization (p=0.024) (Table 5).

Since only one possible risk factor (age) was significantly associated with sequelae, multivariate analysis was not performed.

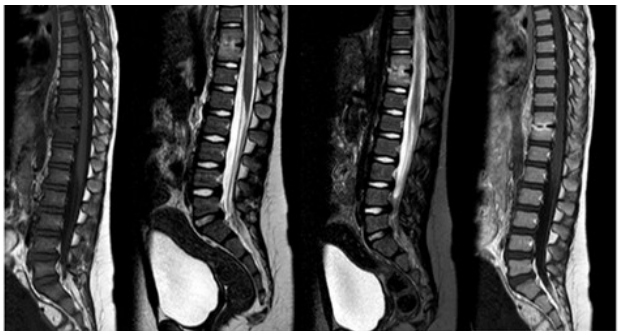

Figure 1: Child #5 of Table 3. Imaging findings at admission.
MRI images acquired in T1 sequence before and after injection of paramagnetic contrast agent and T2 sequence, in sagittal section. There is a marked reduction in thickness of intervertebral disc between D10-D1 with alteration of the signal affecting the endplates, evident post contrast enhancement, and prevertebral swelling.

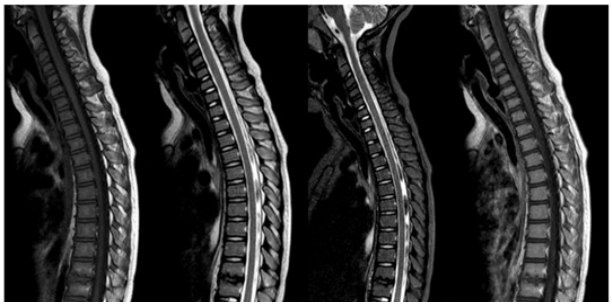

Figure 2: Child #5 of Table 3. Follow up imaging findings.
MRI images acquired in T1sequence before and after injection of paramagnetic contrast agent and T2 sequence, in sagittal section. At the follow-up check irregularities of the endplates can be appreciated. In T1sequence adipose degeneration of the endplates (bone marrow fat, BMF) is noticed, while in T2 the intervertebral disc appears dehydrated and reduced both in thickness and in height. In post contrast T1 images, the enhancement disappears and thickening of the prevertebral soft tissue is noted.

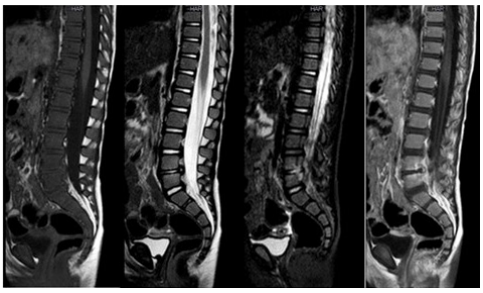

Figure 3: Child #12 of Table 3. Imaging findings at the admission.
Images acquired in T1 sequence before and after the injection of the paramagnetic contrast agent, T2 sequence and FAT SAT, in sagittal section. In T1 there is a reduction in thickness of the intervertebral disc of L4-L5 and a thickening in the epidural space below the posterior longitudinal ligament. In T2 a reduction of the intervertebral disc thickness is documented; in T2 FAT SAT there is an alteration of the vertebral bodies, involving the endplates. An evident post contrast enhancement was also observed.

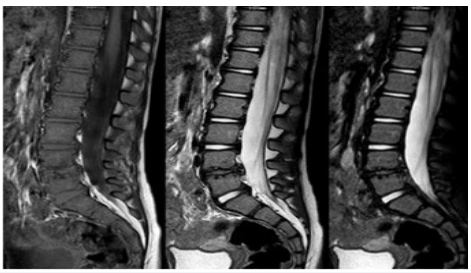

Figure 4: Child #12 of Table 3. Follow-up imaging findings.
MRI images acquired in T1 sequence before and after the administration of the paramagnetic contrast agent and T2 in sagittal section. Irregular fine erosions of the endplates, due to the sclerotic outcome were described. Reduction of the intervertebral height and thickness and a protrusion of the intervertebral disc were also documented.

Table 1: Characteristics of the 21 study children.

Sex (n, %)	Female	9/21 (42.85%)
	Male	12/21 (57.14%)
Median age (years; IQR)		9.3 years (IQR:1.7-11.5)
Onset symptoms/hospitalization (median interval time) (days)		10 days
Comorbidities (n, %)		5/21 (23.8%)
Previous trauma (n, %)		4/21 (19.0%)
Recent febrile episode (n, %)		9/21 (42.8%)
Lumbar/lumbosacral involvement (n, %)		13/21 (61.9%)
Microbiological identification (all methods)		6/21 (28.6%)
Positive blood culture (n, %)		2/10 (20.0%)
Positive pus/another specimen culture (n, %)		4/5 (80.0%)
Positive blood/another specimen PCR (n; %)		3/14 (21.42%)
Biopsy executed (n; %)		3/21 (14.28%)
Staphylococcus aureus infection (n, %)		4/21 (19.0%)
IV therapy; days (median, IQR)		28 (20-33)
Oral therapy; days (median, IQR)		32 (14-54)
Total ABT therapy; days (median, IQR)		60 (39-83)
IV drugs	Single therapy	3/21 (14.28%)
	Combination therapy	18/21 (85.71%)
Oral therapy	Single therapy	10/19 (56.63%)
	Combination therapy	9/19 (47.36%)
	No oral switch	2/21 (9.52%)

Notes: IQR: Interquartile Range; PCR: Polymerase Chain Reaction; IV: Intravenous; ABT: Antibiotic Therapy.

Table 2: Characteristics of the 21 study children.

Cases	Age	Ethnicity	Sex	Onset symptoms/ hospitalization (days)	Comorbidities	Sport Activity	Trauma/ Recent febrile episode	Initial presentation	Level	WBC/ mm3	CRP mg/dL	ESR Mm/h	PCT	Blood/ Pus Culture	PCR	Biopsy	Isolated Pathogen	Sequelae	Notes
#1	10 m	Caucasian	F	8	No	No	No; no	Torticollis; PE: dolor and movement limitation.	C1-C2	7210	0.71	61	n.a.	n.a.	n.a.	n.a.	n.a.	No	Associated arthritis
#2	4 m	Caucasian	M	73	Pre-existent humpback of the cervical-thoracic spine.	No	No; no	Suspected expansive spinal injury; Feeding's difficulties; Irritability. PE: fever, dolor.	D4-D5-D6	17620	14.13	n.a.	Neg	Blood culture: neg Pleural fluid culture: *S. aureus*	n.a.	Neg	*S. aureus* *Candida parapsilosis* (cvc)	No	Subperiosteal abscess; Sepsis; ICU Suspected congenital neuroenteric cyst.
#3	5.8 y	Caucasian	M	66	No	Fencing	No; Yes (treated with amoxicillin-clavulanate).	Suspected spinal infection. PE: dolor and movement limitation.	S1-S2	5950	2,32	42	n.a.	n.a.	n.a.	n.a.	n.a.	No	Suspected Arnold-Chiari syndrome
#4	3.2 y	Caucasian	M	10	No	No	No; No.	15 d of pelvis pain. PE: dolor and refusal to sit.	L1-L2	7650	0,34	72	n.a.	n.a.	Neg	n.a.	n.a.	No	
#5	4.3 y	Caucasian	F	10	No	No	Yes (thoracic injury); No.	Back pain. PE: dolor and movement limitation.	D10-D11	8300	<0.29	20	n.a.	n.a.	n.a.	n.a.	n.a.	2 y later: 2 m of back pain	
#6	9.3 y	Hispanic	F	n.a.	Arnold-Chiari type II malformation, myelomeningocele, hydro syringomyelia and dysraphism.	No	No; No.	Suspected spinal abscess. PE: tumor.	D1-D6	8220	0.69	n.a.	n.a.	Pus culture: *S. Aureus*	PCR (pus): *Streptococcus agalactiae*	n.a.	*S. aureus* *Streptococcus agalactiae*	No	
#7	14.5 y	Caucasian	M	46	No	No	No; No.	Back pain. PE: dolor, movement limitation and antalgic gait.	D12-L4 S1-S2 (multifocal)	6470	2.3	33	n.a.	n.a.	Neg	Neg	n.a.	No	

#8	10.5 y	Caucasian	M	6	No	No	No; Yes (treated with efixime 400 mg)	Suspected coxo-femoral arthritis PE: dolor and movement limitation.	S1-S2	6410	9.95	53	n.a.	n.a.	n.a.	n.a.	n.a.	No	
#9	2.9 y	Caucasian	M	8	No	No	No; No.	Back pain. PE: dolor, movement limitation, limping, antalgic hiperlordotic position and antalgic gait.	L3-L4	18280	<0.29	27	n.a.	Neg	PCR (throat swab): *S. pneumoniae*	n.a.	*S. pneumoniae*	No	
#10	1.7 y	Caucasian	M	4	No	No	No; No.	Suspected SD. PE: dolor and movement limitation.	L4-L5	11140	1.57	20	n.a.	n.a.	Neg	n.a.	n.a.	No	
#11	12.5 y	Caucasian	F	3	Flaccid lower limb paraplegia, tetra ventricular hydrocephalus, neuromotor retardation, sacrum coccygeal fistula and scoliosis with fulcrum in D12.	No	No; No.	PE: fever, rubor and dolor.	C1	18440	7.14	76	n.a.	Blood culture: neg; Pus culture: *S. Pyogenes, E. coli.*	PCR (blood): neg; PCR (pus): *S. pyogenes*	n.a.	*S. Pyogenes, E. coli.*	No	
#12	1.5 y	Caucasian	F	16	No	No	No; Yes	Pre-existent fever associated to antalgic gait. PE: movement limitation, irritability and antalgic hiperlordotic position.	L4-L5	8650	1.94	66	n.a.	n.a.	Neg	n.a.	n.a.	Occasional episodes of sacral pain when sitting in the car.	
#13	11.5 y	Caucasian	F	15	No	Skating	No; Yes.	Worsening back pain. PE: fever, dolor and movement limitation.	L4-L5	7370	1.32	29	Neg	Blood culture: *S. aureus* Pus culture:neg.	Neg	Neg	*S. aureus*	Occasional episodes of backpain while standing for long time	
#14	12.8 y	Arab	M	8	No	No	No; yes	Back pain and persistent fever.	L4-L5 S1-S2	1068	31.14	n.a.	Neg	Neg	n.a.	n.a.	n.a.	No	
#15	11.2 y	Caucasian	M	121	No	Volleyball and cycling	Yes, No.	Persistent back pain since the trauma. PE: dolor, Movement limitation, asthenia.	D11-D12	6920	1.84	61	Neg	Neg	Neg	n.a.	n.a.	Minimal asymmetry of the trunk with a very slight hump on the right	

#16	10 y	Caucasian	M	29	Arnold-Chiari malformation	No	No; Yes.	Refusal to walk and to sit. PE: fever and movement limitation.	L5-S1	1109	2.24	120	n.a.	n.a.	Neg	n.a.	n.a.	Predilection of the right lower limb to climb the stairs.	
#17	13.8 y	Caucasian	F	6	No	Kickboxing	No; Yes.	Persistent back pain especially located in the right sacral-lumbar area. It disturbed sleeping and walking. PE: fever, dolor and movement limitation.	L2-S3	3390	17.4	90	n.a.	n.a.	Neg.	n.a.	n.a.	No	Muscular abscess
#18	1.7 y	Caucasian	F	2	No	No	No; No. (Episode of diarrhoea in a pyrexia)	Stiffness of the spine with hyperextension, rejection of walking and sitting PE: irritability, hyperextension of the spine (cervical spine). Lasegue test slightly +	L4-L5	17920	<0.29	47	Neg	Neg	(liquor) neg	n.a.	n.a.	No	
#19	10.5 y	Caucasian	F	12	No	Yes	Yes, suspected. Yes.	Pain in the left gluteus, in the posterior part of the left leg and back pain. Limitation in walking. PE: fever, dolor, limitation in walking. Left lumbo-sacral back pain evoked with the flexion movement of the thigh with the lower limb extended and with the abduction with the limb flexed.	L5-S1	8870	4	62	Neg	Blood culture: *S. aureus*	Neg	n.a.	*S. aureus*	No	
#20	16.2 y	Caucasian	M	11	Quadriplegia	No	Yes (polytrauma); Yes (treated with levofloxacin).	PE: fever, dolor, movement limitation (difficult to evaluate).	L3-L4	8600	>20	38	n.a.	Neg	Neg	No	n.a.	Fever (7 d), pain and movement limitation after ABT. Unstable clinical condition, but related to the previous situation	Paravertebral psoas abscess
#21	1.5 y	Caucasian	M	9	No	No	No; No.	PE: movement limitation and refusal to sit.	L3-L4	9670	0.93	18	n.a.	n.a.	n.a.	n.a.	n.a.	No	

Notes: WBC: White Blood Cells; CRP: C Reactive Protein; ESR: Erythrocyte Sedimentation Rate; PCT: Procalcitonin; PCR: Polymerase Chain Reaction; D: Days; M: Months; Y: Years; F: Female; M: Male; PE: Physical Examination; Neg: Negative; S. Aureus: Staphylococcus Aureus; S. Pneumoniae: Streptococcus Pneumoniae; E.Coli: Escherichia Coli; ABT: Antibiotic Therapy; SD: Spondylodiscitis; Cvc: Central Venous Catheter; ICU: Intensive Care Unit.

Table 3: Summary of radiologic characteristics of study children.

Cases	Imaging findings at admission	Follow-up (months)	Follow-up imaging	Radiologic sequelae
#1	X-rays: Negative; MRI: MRI images acquired in T1 sequence before and after injection of paramagnetic contrast agent and T2 sequence, in sagittal section. There is a marked reduction in thickness of ID between C1-C2, with alteration of the signal affecting the endplates, evident post contrast enhancement, and prevertebral swelling.	n.a.	X-rays: No osteolytic lesions. No morpho-structural alterations. MRI: resolution of the inflammatory process.	
#2	MRI: pathological tissue with a large central colliquative component. Erosion of D5 and compression of the spinal cord. CT: suspected expansive lesion.	122	MRI: Marked acute angle kyphosis of the dorsal spine. X-rays: Unchanged kyphotic curvature, accentuated at the level of the stabilization between D3-D6 and slight accentuation of lumbar lordosis. CT: Evident dorsal kyphosis secondary to previous stabilization of D2-D4 segment. D3 was hypoplastic and it showed fusion of the 4th rib to the bilaterally transverse processes. Disc spaces was obliterated. Reduction of the width of the vertebral canal with compression of the anterior surface of the ependymal canal was observed.	Evident dorsal kyphosis. Reduction of the width of the vertebral canal, with compression of the anterior surface of the ependymal canal.
#3	X-rays: negative. MRI: MRI images acquired in T1 sequence before and after injection of paramagnetic contrast agent and T2 sequence, in sagittal section. There is a marked reduction in thickness of ID between S1-S2, with alteration of the signal affecting the endplates, evident post contrast enhancement, and prevertebral swelling. CT: Uncertain. No densitometric alterations of the vertebral bones. Dysmorphic appearance of S2 with paramedian butterfly cleft.	n.a.	MRI: n.a.	n.a.
#4	MRI: SD process associated with pathological tissue in the surrounding soft tissues. BS: positive.	1	MRI: Persistent inflammatory process.	n.a.
#5	X-rays: Negative. MRI: MRI images acquired in T1 sequence before and after injection of paramagnetic contrast agent and T2 sequence, in sagittal section. There is a marked reduction in thickness of ID between D10-D1 with alteration of the signal affecting the endplates, evident post contrast enhancement, and prevertebral swelling.	25	X-rays MRI: MRI images acquired in T1sequence before and after injection of paramagnetic contrast agent and T2 sequence, in sagittal section. At the follow-up check irregularities of the endplates can be appreciated. In T1sequence adipose degeneration of the endplates (bone marrow fat, BMF) is noticed, while in T2 the ID appear dehydrated and reduced both in thickness and in height. In post contrast T1 images, the enhancement disappears and thickening of the prevertebral soft tissue is noted. The presence of small schmorl nodules persisted.	Irregularities of D10-D11 endplates and height reduction of ID.
#6	MRI: Arnold-Chiari 2 malformation. Hypotrophy and large hidrosyringomelia in D1-D6. Spinal dysraphism with segmental dysplasia. Kyphoscoliosis of upper lumbar tract. Marked lumbar scoliosis. inflammatory signal alterations compatible with the diagnosis of SD.	21	X-rays MRI: Unchanged radiological condition.	
#7	X-rays: Negative. MRI: MRI images acquired in T1 sequence before and after injection of paramagnetic contrast agent and T2 sequence, in sagittal section. There is a marked reduction in thickness of ID between D12-L4 / S1-S2 with alteration of the signal affecting the endplates, evident post contrast enhancement, and prevertebral swelling. Presence of inhomogeneity and T2 hyperintensity of the left adductor insertion and of the right spinal muscles. PET 18F-FDG: Compatible with the presence of tissue with high glucose metabolism.	17	X-rays MRI: The signal alterations of D12 and L4 were no longer recognizable. S1-S2 signal alterations persisted.	
#8	X-rays: negative. MRI: MRI images acquired in T1 sequence before and after injection of paramagnetic contrast agent and T2 sequence, in sagittal section. There is a marked reduction in thickness of ID between S1-S2 with alteration of the signal affecting the endplates, evident post contrast enhancement, and prevertebral swelling. + signal alterations of the superolateral margin of the right sacral wing of S1, which suggested osteomyelitis.	23	X-rays: No structural skeletal alterations, no focal bone lesions affecting the pelvic bones. Normally sacroiliac and coxo-femoral joints. MRI: No more appreciable signal alterations of the superolateral margin of the right sacral wing of S1.	

#9	X-rays: Negative. MRI: L3-L4 ID space was reduced with a fluid collection contained in the anulus fibres. Longitudinal ligament showed post contrast enhancement. Hyperintense signal in T2 and STIR sequences. Hypointense signal in T1 sequences. Inflammatory reaction with hyperintense signal post contrast enhancement of the right iliopsoas, near L3-L4 segment.	13	X-rays: No structural bone modifications. No osteolytic lesions. MRI: the posterior fluid collection was no longer detectable. Differences of the signal and contrast impregnation of the root of the pedicle and of the right pedicle of L4 remained. Thinning of the ID of L3-L4 showing a reduction in T2 intensity due to initial dehydration. The muscular inflammatory reaction of the iliopsoas on the right near the rachis disappeared.	Thinning of L3-L4 intervertebral disc.
#10	X-rays: Negative. MRI: MRI images acquired in T1 sequence before and after injection of paramagnetic contrast agent and T2 sequence, in sagittal section. There is a marked reduction in thickness of ID between L4-L5 with alteration of the signal affecting the endplates, evident post contrast enhancement, and prevertebral swelling. + Fluid sub-ligament collection at L4-L5 level.	59	X-rays: L4-L5 endplates irregularities, with reduction of disc thickness. MRI: Outcomes of SD were observed with ID space thinning and central hypo intensity with degenerative-dehydrating significance of the disc itself.	Irregularities of L4-L5 endplates and height reduction of the ID.
#11	MRI: MRI images acquired in T1 sequence before and after injection of paramagnetic contrast agent and T2 sequence, in sagittal section. Alteration of the signal affecting the endplates, evident post contrast enhancement, and prevertebral swelling. CT: Bone erosions and inhomogeneity of endplates + reduction of ID height	n.a.	MRI	n.a.
#12	X-rays: Negative. It showed the presence of left-convex scoliotic deviation with fulcrum on L2-L3. MRI: Images acquired in T1 sequence before and after the injection of the paramagnetic contrast agent, T2 sequence and FAT SAT, in sagittal section. In T1 there is a reduction in thickness of the ID of L4-L5 and a thickening in the epidural space below the posterior longitudinal ligament. In T2 a reduction of the ID thickness is documented; in T2 FAT SAT there is an alteration of the vertebral bodies, involving the endplates. An evident post contrast enhancement was also observed.	38	X-rays MRI: MRI images acquired in T1 sequence before and after the administration of the paramagnetic contrast agent and T2 in sagittal section. Irregular fine erosions of the endplates, due to the sclerotic outcome were described. Reduction of the ID height and thickness and a protrusion of the ID were also documented.	Height reduction of L4-L5 ID
#13	X-rays: Negative. MRI: Alteration of the signal of hyperaemic and oedematous significance of L5 peduncles, with non-specific contrast enhancement. Alteration of the signal of similar significance in L3 endplates with prevalent involvement of the upper half of the soma. Intraspongious hernia of schmolr. CT: positive	12	X-rays: No morpho structural alteration of the lumbar spine metamers except residual, minimum focal depression of the upper endplate of L3. MRI: Reduction of the alteration of the signal of L3 endplate, barely noticeable.	
#14	X-rays: Uncertain. Reduction of the physiological lumbar lordosis with wide-ranging scoliotic attitude. No bone lesions MRI: Swollen appearance of L4-L5, with signal alteration also extended to the surrounding tissues. Spinal cord moved forward due to collection. In a subsequent MRI made during hospitalization: minimal alterations of the signal of spondylitis significance are observed in the process of regression at the level of S1-S2.	4	MRI: An almost complete resolution of the inflammatory process, with modest alteration of the signal appreciable in the T2 FAT SAT sequences	
#15	MRI: oedematous signal alteration of D11-D12. Tumefaction of paravertebral soft tissue. Suspected paramedian hernia in D11-D12. CT: There were no morpho structural alterations in the examined metamers. Modest sclerotic aspect of the anterior superior endplate of D12, but with preservation of the cortex and the anterior wall. reduction of the D11-D12 ID.	5	X-rays: A reduction of ID is documented in D11-D12 with prevalence on the left side. Fine irregularities of the endplates in the absence of reduction of the vertebral height. MRI: Always appreciable the extensive alteration of the oedematous signal of the bone marrow of the vertebral bodies D11 D12, with extension to the peduncles, especially the left. The ID was thinned. Partial involvement of the surrounding paravertebral tissues persisted.	Reduction of ID height in D11-D12
#16	X-rays: uncertain. Retrolisthesis in L5. MRI: Alteration of the signal of L5-S1, the disc was markedly reduced thickness. The disc was protruding with a tissue sleeve that imprints the Dural sac and the roots of the cauda	20	X-rays: The alterations of the profile of the L5-S1 endplates appeared excavated and it was more evident in S1. The reduction in height of the corresponding interbody space remained. MRI: healing process and resolution of the inflammatory process were evident.	Reduction of the height of the intervertebral disc L5-S1.
#17	MRI: Swelling of the retro vertebral muscles on the right from L2 to S1 in which context there was a collection, anteriorly in continuity with the first right sacral foramen and the vertebral canal. Alteration of the signal with reactive oedema also in the posterior arch of L5, which corresponded to post contrast enhancement.	12	MRI: Complete resolution of the inflammatory process, as the signs of residual extradural endorachid involvement between L5-S1 were no longer appreciable. The alteration of the signal of edematous significance described at the level of the right paravertebral muscles was no longer evident.	

#18	MRI: Inflammatory signal alterations were appreciated, which coincided with the diagnosis of SD	14	X-rays: Evolution of the healing process of L4-L5, where the interbody space remained reduced, while the sclerosis of the endplates, whose surfaces showed irregularities, appeared more evident and delimited. MRI: thickness reduction of L4-L5 intervertebral disc. Anterior protrusion of the disc. hypointense Alteration of the signal of the upper hemi some of L5, as a resolution of phlogistic process and evolution in the sclerotic process. The alteration of the signal remained as a minimum of oedema. Resolved the inflammatory thickening at the anterior paravertebral site, where the presence of an osteophyseal bridge, between the upper limiting of L5 and L4 was documented.	Reduction of the height of the intervertebral disc L4-L5 + endplates irregularities
#19	X-rays: Uncertain. Mild scoliotic dorsal attitude. MRI: MRI images acquired in T1 sequence before and after injection of paramagnetic contrast agent and T2 sequence, in sagittal section. There is a marked reduction in thickness of ID between *L5-S1,* with alteration of the signal affecting the endplates, evident post contrast enhancement, and prevertebral swelling.	3	X-rays: No signs of disease. Reduction of rarefaction of L5 endplate.	
#20	X-rays: Negative. MRI: Thinning of L3-L4. Altered signal of the disc fibrocartilage. An abscess collection involving the iliopsoas muscle was highlighted.	8	X-rays: Slight reduction of the L3-L4 interbody space without significant irregularities of endplates MRI: Reduction of the signal in the muscle tissues, while the alteration of the signal and the post contrast enhancement in both vertebrae appeared more evident and extensive.	Reduction of the height of the intervertebral disc L3-L4.
#21	X-rays: No evident radiographically appreciable bone alterations of the metamers under examination, the height of the vertebral body was apparently preserved. Reduction of the L3-L4 ID space. MRI: MRI images acquired in T1 sequence before and after injection of paramagnetic contrast agent and T2 sequence, in sagittal section. There is a marked reduction in thickness of ID between L3-L4, with alteration of the signal affecting the endplates, evident post contrast enhancement, and prevertebral swelling.	8	X-rays: A slight reduction in the amplitude of the posterior ID space L3-L4 remained.	Reduction of the height of the intervertebral disc L3-L4.

Notes: X-rays: radiography; MRI: magnetic resonance imaging; CT: computed tomography; BS: bone scan; PET 18F-FDG: positron emission tomography fluorodeoxyglucose 18F;SD: spondylodiscitis; ID: intervertebral disc.

Table 4: Summary of treatment of study children.

Cases	Intravenous Antibiotic Therapy	Switch to another IVT. Why?	Oral antibiotic therapy	Total Duration of ABT	Other Pharmacological Treatment	Surgery	Immobilization
#1	Ceftriaxone Duration: 19 d Oxacillin Duration: 12 d	Yes (simplification of therapy) Teicoplanin Duration: 7 d	Amoxicillin-Clavulanate Duration: 13 d	39 d	Unspecified pain relief therapy	No	No
#2	Ceftazidime Duration: 4 d Oxacillin Duration: 4 d	Yes (targeted ABT) Meropenem Duration: 23 d Vancomycin Duration: 32 d Teicoplanin Duration: 16 d Gentamycin Duration: 7 d	Amoxicillin-Clavulanate Duration: 17 d Rifampin Duration: 17 d	69 d	Tramadol, ibuprofen, paracetamol, clonidine, fluconazole, ranitidine, heparin, ketorolac, tromethamine, beclomethasone.	Abscess drainage	Antigravity valve corset
#3	Ceftriaxone Duration: 18 d Teicoplanin Duration: 18 d	No	Amoxicillin-Clavulanate Duration: 14 d	32 d	No	No	No
#4	Ceftriaxone Duration: 30 d Oxacillin Duration: 30 d	No	Amoxicillin-Clavulanate Duration:13 d	43 d	No	No	Antigravity valve corset
#5	Ceftriaxone Duration: 22 d Oxacillin Duration: 15 d	Yes (simplification of therapy) Teicoplanin Duration: 7 d	Amoxicillin-Clavulanate Duration: 14 d	36 d	No	No	Orthopaedic brace
#6	Oxacillin Duration: 14 d Ceftazidime Duration: 14 d Ciprofloxacin Duration: 19 d	Yes (targeted ABT) Rifampin Duration: 11 d Metronidazole Duration: 11 d	No	26 d	No	No	No

#7	Oxacillin Duration: 18 d Ceftazidime Duration: 18 d	No	No	18 d	Unspecified pain relief therapy	No	No
#8	Ceftriaxone Duration: 9 d Oxacillin Duration: 9 d	No	Clindamycin Duration: 61 d	70 d	No	No	No
#9	Ceftriaxone Duration: 29 d Oxacillin Duration: 2 d	Yes, Clindamycin Duration: 27 d	Amoxicillin-Clavulanate Duration: 19 d	48 d	No	No	Orthopaedic brace
#10	Ceftriaxone Duration: 28 d Oxacillin Duration: 4 d Clindamycin Duration: 24 d	No	Amoxicillin-Clavulanate Duration: 12 d Rifampin Duration: 12 d	40 d	No	No	Bivalve orthopaedic brace
#11	Meropenem Duration: 16 d Teicoplanin Duration: 23 d	Yes (simplification of therapy) Amikacin Duration: 7 d	Sulfamethoxazole/Trimethoprim Duration: 6 d	30 d	Pain relief therapy (paracetamol)	No	No
#12	Oxacillin Duration: 43 d Ceftazidime Duration: 43 d	No	Amoxicillin-Clavulanate Duration: 87 d	130 d	Pain relief therapy (paracetamol)	No	No
#13	Oxacillin Duration: 28 d	No	Sulfamethoxazole/Trimethoprim Duration: 32 d Rifampin Duration: 32 d	60 d	Pain relief therapy (paracetamol)	No	Orthopaedic brace
#14	Ceftriaxone Duration: 2 d Oxacillin Duration: 31 d Clindamycin Duration: 31 d	Yes. Teicoplanin Duration: 28 d	Sulfamethoxazole/Trimethoprim Duration: 52 d Rifampin Duration: 52 d	83 d	No	No	Orthopaedic brace
#15	Oxacillin Duration: 9 d	No	Sulfamethoxazole/Trimethoprim Duration: 86 d Rifampin Duration: 86 d	95 d	No	No	Orthopaedic brace (c35)
#16	Oxacillin Duration: 33 d Ceftazidime Duration: 32 d	No	Amoxicillin-Clavulanate Duration: 56 d Rifampin Duration: 56 d	89 d	No	No	Bivalve orthopaedic brace
#17	Clindamycin Duration: 3 d Oxacillin Duration: 3 d	Yes Clindamycin Duration: 16 d Ceftazidime Duration: 10 d	Clindamycin (300 mg 4/d) Duration: 40 d	59 d	No	No	No
#18	Ceftriaxone Duration: 7 d Ceftazidime Duration: 21 d Cefazoline Duration: 21 d	Yes (reappearance of symptoms) Teicoplanin Duration: 24 d CVC: Ceftriaxone Duration: 37 d Teicoplanin Duration: 43 d	Sulfamethoxazole/Trimethoprim Duration: 39 d Rifampin Duration: 39 d	112 d	Corticosteroids	No	Orthopaedic brace
#19	OxacillinDuration: 5 d Ceftazidime Duration: 11 d	Yes (teicoplanin sensibility) Teicoplanin Duration: 19 d Linezolid Duration: 5 d	Linezolid Duration: 40 d	65 d	Pain relief therapy (paracetamol)	No	Orthopaedic brace
#20	Ceftazidime Duration: 22 d Rifampin Duration: 6 d	Yes (due to the slow decline of the phlogosis indices) Linezolid Duration: 4 d	Linezolid Duration: 23 d Sulfamethoxazole/Trimethoprim Duration: 21 d Rifampin Duration: 21 d	66 d	No	No	No
#21	Ceftriaxone Duration: 15 d	No	Rifampin Duration: 15 d Rifampin Duration: 78 d Amoxicillin-Clavulanate Duration: 78 d	93 d	No	No	Bivalve orthopaedic lumbar brace

Notes: IVT: Intravenous Therapy; ABT: Antibiotic Therapy; D: Days; Mg: Milligrams; Ml: Millilter.

Table 5: Characteristics of the 21 children of the study and univariate analysis results.

Characteristics		Total	Sequelae in PSD (Clinical and/or radiological) 11/21 (52.4%)	No sequelae in PSD 10/21 (47.6%)	*p*-Value
Sex (**n**; %)	Female	12	4 (36.4%)	8 (80%)	0.530
	Male	9	7 (63.6%)	2 (20%)	
Median age (months; IQR)			35 (19-128)	128 (80.5-153)	
Age class ≤5 years >5	≤5 years	9	7 (77.8%)	2 (22.2%)	0.050
	>5 years	12	4 (33.3%)	8 (66.7%)	
Interval time between onset symptoms and diagnosis (days; IQR)			11 (8.5-22.5)	8 (6-12)	
Comorbidities (*n*; %)	Yes		3 (27.3%)	2 (20%)	0.697
Recent Trauma (*n*; %)	Yes		3 (27.3%)	1 (10%)	0.332
Recent febrile episode (**n**; %)	Yes		4 (36.4%)	5 (50%)	0.530
Involved spinal segment (**n**; %)	Lumbar/lumbosacral		8 (72.7%)	5 (50%)	0.290
	Others		3 (27.3%)	5 (50%)	
Isolated pathogen (*n;* %)	Yes		3 (27.3%)	3 (30%)	0.896
WBC	>10.000/mm3		5 (45.5%)	2 (20%)	0.227
CRP	>10 mg/dL		2 (18.2%)	2 (20%)	0.916
PCT	Positive		0 (0.0%)	0 (0.0%)	0.413
ESR	>20 m/h		9 (90.0 %)	8 (100%)	0.827
At least one elevated inflammatory index			10 (90.9%)	9 (90%)	0.944
Median length of total antibiotic therapy (IV plus oral) (days; IQR)			69 (54-94)	41 (30.5-63.5)	
Total duration of ABT (class) ≤40 days >40 days	≤40 days	7	2 (28.6%)	5 (71.4%)	0.060
	>40 days	14	9 (64.3%)	5 (35.7%)	
Median length of IVT (days; IQR)			29 (27-39.5)	24 (18.5-29)	
Total duration of IVT (class) ≤10 days > 10 days	≤10 days	2	1 (50%)	1 (50%)	0.944
	>10 days	19	10 (52.6%)	9 (47.4%)	
Immobilization (*n*; %)	Yes		9 (81.8%)	3 (30%)	0.024

Notes: PSD: Pyogenic Spondylodiscitis; IQR: Interquartile Range; WBC: White Blood Cells; CRP: C-Reactive Protein; PCT: Procalcitonin; ESR: Erythrocyte Sedimentation Rate; IV: Intravenous; ABT: Antibiotic Therapy; IVT: Intravenous Therapy.

Discussion

In the present study characteristics and outcomes of 21 children admitted for PDS to a paediatric hospital were retrospectively analysed.

Our study on 21 children referred to a single tertiary paediatric Italian centre, over 10 years (2010-2019), is one of the largest studies on paediatric PSD performed in Italy.

Previous case series studies in Germany [5,6], Spain (29,30), Switzerland [14]. UK [7,13], and other extra-European countries [2,3,31] are heterogenous and they analyse small population data; including less than 25 children [3,5,7,13]. Few larger studies have been published by Dayer and Fernandez including 103 and 50 children, respectively [2,14].

The median age at presentation in our cohort was 9.3 years (IQR:1.7-11.5). This finding is in line with previous published data. SD affects most frequently children between 2 and 8 years of age, although it can also occur in infants and children of any age [13].Interestingly, SD usually peaks in three age groups with three main different clinical forms: 1) children aged under 6 months, 2) those aged between 6 months and 4 years, and 3) those aged between 4 and 16 years. A recent multicentre study suggested a biphasic age distribution of SD, primarily affecting the young toddler, with a second peak in adolescence [14]. Chandrasesan et *al.* attempted to exemplify the age distribution, the related clinical features, and outcomes, and subdivided the children into those aged less than 24 months, and those aged 24 or over [7].

In our study the male to female ratio was 1.3:1 (12 males to 9 females). In previous paediatric studies, sex prevalence was unclear. The multi-centre retrospective study by Dayer et *al*. highlighted the male prevalence, with 1.9 times more boys being affected than girls (14). Kayser *et al.* reported a higher incidence among girls than boys, in their cohort [6].

The lumbar/lumbosacral spine was the most common area of involvement (61.9%) in our cohort, as previously reported. The underlying reason for susceptibility of the lumbar region to PSD is not fully understood but is likely to be partly related to venous drainage, through Batson plexus [13,14].

In our study, the median time (days) between onset symptoms and PSD diagnosis was 10 days, reaching 121 days in one child. The nonspecific clinical manifestations, the inability of younger and non-communicating children to verbalize the nature of their pain, the nonspecific laboratory findings, and the late plane radiology detection are the main factors that contribute to the delay in diagnosis [13], which may lead to a worse outcome (severe spinal deformities, segmental instabilities, or neurological damages [1] and lifelong disability [9]. Sapico and Montgomerie reported that 50% of patients had symptoms lasting for greater than 3 months before the diagnosis was established [12]. In Waizy *et al*. study the mean interval from onset symptoms and final diagnosis was 36 days [5]. In Afsahri *et al.* the average duration of symptoms prior to presentation to neurosurgical unit was 6 weeks [13]

Clinical characteristics of our children were similar to those previously reported [3,7,13,19,29,32-34]; back pain was the most common symptom in patient that were old enough to verbalize the nature of the pain, present in more than 40% of cases. However, in younger patients, irritability was the leading symptom. At physical examination fever was present only in seven children in this study, which is unexpectedly low considering the pathogenesis of the disease. Accordingly, Kang *et al.* reported fever in half of their study children (n=25); for this reason, spine infections should be a part of the differential diagnosis in children with nonspecific symptoms (back pain, irritability, and movement limitations), even without fever at admission [3]

Confirming what is reported in previous case series, the patients of our study were almost all PHC, without any underlying pathological condition; however, about one fifth of the children presented with comorbidities, mostly related to neurological pathological conditions. Paediatric SD tends to occur without any known risk factors in the majority of cases, whereas in adults it is more common to identify a risk factor [13]. However, it has been also observed in children with comorbidities. Yazici et *al*. reported a case of SD following a lumbar puncture in a 13-year-old girl, affected by non-Hodgkin lymphoma [35].

Almost half of our children had a documented prodromal illness; an association between the PSD a previous infection (ear-nose-throat, gastrointestinal tract, or urogenital tract) has been frequently reported in literature [6,7].

When reviewing the laboratory data, we found that WBC was increased in 7/21 children, CRP in 4/21 children and ESR in 17/18 children. Raised ESR was found to be the most reliable test on presentation of PSD, with a sensitivity of 94.4% in our cohort. Accordingly, Chandrasenan *et al.* confirmed ESR to be the most accurate for plotting the clinical course of the condition [7]. Previous studies have reported that WBC and CRP are usually within normal limits and ESR in only moderately raised and of low sensitivity [36-39]. It is currently recognized that few laboratory findings show significant results [2,34,40,41].

In our study only the 28.6% of the performed blood cultures were positive. PCR technique was used on blood, throat swab, pus, pleural fluid, or liquor in more than half of the cases, and the 21.4% were positive. The most common aetiology of PSD is the result of hematogenous spread. Therefore, blood culture is considered a fondamental part of the diagnostic process; its positivity prevents the need for invasive diagnostic procedures and can help to select the appropiate antimicrobial therapy [3]. However, according to literature blood cultures are negative in the majority of children, ranging from 88% to 100% (14). In Kang et *al.*'s study, including 25 children, the reported sensitivity of blood culture was 18.8% [3].

Biopsy was performed in only 3 cases, none of them showed positive bacterial growth on cultures. In literature, the success rates of needle biopsy to identify the causative organism range from 40 to 96% [5].

Although in 71.4 % of cases, microbiological methods failed to identify causative organisms, *S. aureus* was confirmed to be the most commonly identified pathogen by culture (44.4% of identified bacteria). Despite the increasing recognition of *K. kingae* as responsible pathogen of childhood PSD [16], no *K. kingae* infection is documented in our patients. Our microbiological results are consistent with the published literature confirming that in most cases, the origin of PSD remains unidentified [6,42].

In our series, X-rays was performed in the majority of cases, but they are not helpful for the diagnosis process. MRI at the time of diagnosis was always performed and all 21 cases had confirmation of PSD based on MRI findings. On the latest radiological follow up (13.5; 8-22.5) X-rays and MRI showed evidences of residual degenerative changes (irregularities of the endplates, persistent narrowing of the disc space, or decreased height of the ID space) in ten children. Appropriate imaging is important in order to establish the diagnosis. Initial plain radiography is usually negative; degenerative changes, such as reduced ID height or erosion of the endplates, are evident only in advanced cases [1,2,32,34]. MRI is the most reliable mode of imaging for detecting PSD with high sensitivity and specificity. The excellent morphological resolution of the MRI leads to recognition of the early inflammatory response [2,7,30,34,43]. Some experts suggest that MRI should not be performed routinely in order to follow the healing process, because it can give false positive. Instead they propose to use only x-rays during the radiologic follow-up.

All patients in our cohort were treated with long courses of broad-spectrum antibiotics with a mean duration of 60 days, and with a switch to a targeted therapy when the responsible pathogen was isolated. Almost all the children received a combination of two broad-spectrum antibiotics as first Intravenous Therapy (IVT). Oxacillin + 3d generation cephalosporin was the most commonly used IVT. Amoxicillin-clavulanate was the most commonly used oral antibiotic. Despite the lack of micro-organism isolation on blood culture in most of cases in our cohort, broad spectrum antibiotics were effective in treating PSD. As a rule, decision for antibiotic therapy should be according to the culture results, when it is possible [35]. However, the reported antibiotic regimen is mainly empirical. Typical antibiotic therapy duration involved 6 weeks of intravenous antibiotics followed by a switch to oral antibiotics with interval imaging and monitoring of clinical picture and inflammatory markers. Many aspects of the treatment are still under debate, both as regard the choice of the antibiotic and the. In contrast to adult form, for which guidelines have been established [20], no such guidelines exist in paediatric PSD. Dayer *et al.* recommended the following empirical antimicrobial treatment: - for neonates and infants aged under 6 months, amoxicillin-clavulanate +

gentamycin; -for infants aged between 6 months and 4 years, amoxicillin- clavulanate or cefuroxime; - for children aged over 4 years, flucloxacillin or amoxicillin- clavulanate [14]. In Afshari *et al.* study, all children of their population were treated with a long course of broad-spectrum antibiotics with a mean duration of 9.3 weeks [13]. Bianchini *et al.* suggested, in accordance with what is currently recommended for osteomyelitis, that antibiotics should be administered for several weeks [19].

In accordance with Kayser *et al*. we consider spinal immobilization, combined with the administration of antibiotics, to be a decisive part of the treatment, spinal bracing was carried out in more than half of our children. Spinal immobilization allows the infection to heal and additionally maintains the spine in a normal position to prevent even worse deformities from occurring [6]. Chandrasenan *et al.* suggested the use of spinal bracing on its own, without antibiotics, when the child is asymptomatic and systemically well, with normal inflammatory indices and a negative blood culture [7].

Only one child of our cohort required spinal surgery, more precisely he underwent abscess drainage. Clinical conditions that require surgery are compression of neural elements and progressive neurologic impairment, mechanical derangement (instability, malalignment, severe bone destruction), and intractable pain [21-23]. Surgical treatment is also often required to evacuate an epidural or paravertebral abscess; however, if the abscess is limited and responsive to the antimicrobial treatment the drainage procedure can be avoided.

In accordance with the literature, a favourable and relatively benign long-term outcome was observed in the majority of our cases. On the latest follow-up clinical assessment, more than 80% of children were completely pain-free. Five children presented occasional episodes of very mild back pain /discomfort and minimal spinal deformity; ten children presented the radiological residual sequelae, previously described. In accordance with other Authors [6], we believe that a long-term follow- up is necessary for children with PSD, to follow the disease evolution over time. Long-term follow-up studies in paediatric PSD are very limited. After the resolution of the symptoms, patients should be followed for 12-18 months [32]. The follow up requires any recurrence of disease be evaluated, obtaining new radiographs and laboratory data. Generally, ESR and CRP should gradually return to normal values. The outcomes, when reported, were in most cases favourable, describing a large number of asymptomatic children at the follow up, free of pain and with normal spinal movements. Thus, many studies suggested a benign and self-limiting course of PSD in children [6,13,40,42]. However, some other studies have demonstrated the presence of clinical sequelae associated with mild clinical symptoms (i.e. persistent mild back pain/discomfort during sports activity) [3,13], and long-term clinical sequelae (permanent deformities of the spine, permanent spinal movement restriction or neurological damages) [6]. Interestingly, radiological sequelae with no clinical symptoms associated are frequently reported in studies *(i.e.* narrowing of the disk spaces for years, permanent reduction of the intervertebral disc height, vertebral fusion, sclerosis, and irregularities of the endplates) [7].

Finally, logistic regression analysis was performed. The correlation between age (class ≤ 5 years) and the presence of sequelae (both clinical and radiological) was statistically significant (**p**-Value= 0.050). The age class ≤ 5 years represented a risk factor for the development of sequelae in PSD. However, the correlations between use of immobilization treatment and the presence of sequelae probably reflects the fact that children with a more severe disease were both more likely treated with immobilization and prone to develop sequelae.

Our study has several limitations. Due to its retrospective nature, there were difficulties in trying to remove possible biases. Data regarding previous use of antibiotics were lacking since this information was missed in many cases. Thus, previous antibiotic use might be a reason or a co-factor for the high rate of negative microbiological results. There was no predefined management protocol. There was a lack of useful data, especially regarding the follow up controls, both clinical and radiological; due to the fact that some children had the follow-up at other institutions or because for various reasons they did not carry out the radiological checks that were scheduled. Finally, the number of children is small, both because the extreme rarity of the disease and because of the non-negligible number of underdiagnosed or misdiagnosed paediatric PSD; although we believe it to be one of the largest case series so far.

PSD is a rare disease in children; however, if not treated promptly, it can lead to sequelae. Therefore, a high index of suspicion, an early diagnosis, and a targeted treatment are necessary to reduce these risks. Ours is a recent and large case series study, that reports 25% of sequelae (clinical and/or radiological), although no severe sequela was observed. PSD diagnosis should be considered in children with back pain, antalgic gait, refusal to walk, movement limitation, but also unspecific symptoms such as general malaise and irritability, especially in younger children. Increased ESR can also be a useful marker for the diagnosis since it was significantly higher than WBC and CRP in our study children. Imaging plays a very important role, not only as a diagnostic tool, but also during the follow-up, reviling often residual evidence of degenerative process.

References

1. Principi N, Esposito S. Infectious Discitis and Spondylodiscitis in Children. Int J Mol Sci. 2016; 17: 539.
2. Fernandez M, Carrol CL, Baker CJ. Discitis and vertebralosteomyelitis in children: An 18-year review. Pediatrics. 2000; 105: 1299-1304.
3. Kang HM, Choi EH, Lee HJ, Yun KW, Lee CK, et al. The etiology, clinical presentation and long-term outcome of spondylodiscitis in children. Pediatr Infect Dis J.2016; 35: e102-e106.
4. Cottle L, Riordan T. Infectious spondylodiscitis. J. Infect. 2008; 56: 401-412.
5. Waizy H, Heckel M, Seller K, Schroten H, Wild A. Remodeling of the spine in spondylodiscitis of children at the age of 3 years or younger. Arch Orthop Trauma Surg. 2007; 127: 403-407.
6. Kayser R, Mahlfeld K, Greulich M, Grasshoff H. Spondylodiscitis in childhood: Results of a long-term study. Spine (Phila Pa 1976). 2005; 30: 318-323.
7. Chandrasenan J, Klezl Z, Bommireddy R, Calthorpe D. Spondylodiscitis in children: A retrospective series. J Bone Jt Surg Br. 2011; 93: 1122-1125.
8. Garron E, Viehweger E, Launay F, Guillaume JM, Jouve JL. Non-tuberculous spondylodiscitis in children. J Pediatr Orthop. 2002; 22: 321-328.
9. Tsirikos AI, Tome-Bermejo F. Spondylodiscitis in infancy: A potentially fatal condition that can lead to major spinal complications. J Bone Jt Surg Br. 2012; 94: 1399-1402.

10. Kulowski J. Pyogenic osteomyelitis of the spine: An analysis and discussion of 102 cases. J Bone Joint Surg Am. 1936; 18: 343-364.

11. Bauman GI, Stifel RE. Osteomyelitis of the spine. Ann Surg. 1923; 78: 119-1121.

12. Sapico FL, Montgomerie JZ. Pyogenic vertebral osteomyelitis: Report of nine cases and review of the literature. Infect Dis Clin North Am. 1990; 4: 539-550.

13. Afshari FT, Rodrigues D, Bhat M, Solanki GA, Walsh AR, et al. Paediatric spondylodiscitis: A 10 year single institution experience in managment and cliinical outcomes. Child's Nerv Syst. 2020; 36: 1049-1054.

14. Dayer R, Alzahrani MM, Saran N, Ouellet JA, Journeau P, et al. Spinal infections in children: A multicentre retrospective study. Bone Joint J. 2018; 100-B: 542-548.

15. Prodi E, Grassi R, Iacobellis F, Cianfoni A. Imaging in spondylodiskitis. Magn Reson Imaging Clin N Am. 2016; 24: 581-600.

16. Yagupsky P, Porsch E, St Geme JW. 3rd Kingella kingae: An emerging pathogen in young children. Pediatrics.2011; 127: 557–565.

17. Gaschignard J, Geslain G, Mallet C, Lorrot M, Blot N, et al. Spondylodiscitis in a healthy 12-year-old girl with Extraintestinal pathogenic Escherichia coli (ExPEC) bacteraemia. BMC Infect Dis. 2017; 17: 380.

18. Barkai G, Leibovitz E, Smolnikov A, Tal A, Cohen E. Salmonella diskitis in a 2-year old immunocompetent child. Scand J Infect Dis 2005; 37: 232-235.

19. Bianchini S, Esposito A, Principi N, Esposito S. Spondylodiscitis in Paediatric Patients: The Importance of Early Diagnosis and Prolonged Therapy. Int J Environ Res Public Health. 2018; 15: 1195.

20. Berbari EF, Kanj SS, Kowalski TJ, Darouiche RO, Widmer AF, 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: e26-e46.

21. Gouliouris T, Aliyu SH, Brown NM. Spondylodiscitis: Update on Diagnosis and Management. J Antimicrob Chemother. 2010; 65: iii11-iii24.

22. Skaf GS, Domloj NT, Fehlings MG, Bouclaous CH, Sabbagh AS, et al. Pyogenic spondylodiscitis: an overview. J Infect Public Health. 2010; 3: 5-16.

23. Hadjipavlou AG, Mader JT, Necessary JT, Muffoletto AJ. Hematogenous pyogenic spinal infections and their surgical management. Spine (Phila Pa 1976). 2000; 25: 1668-1679.

24. Principi N, Esposito S. Kingella kingae infections in children. BMC Infect Dis. 2015; 5: 260.

25. Azzari C, Moriondo M, Indolfi G, Cortimiglia M, Canessa C, et al. Realtime PCR is more sensitive than multiplex PCR for diagnosis and serotyping in children with culture negative pneumococcal invasive disease. PLoS ONE. 2010; 5: e9282.

26. Lodi L, Ricci S, Nieddu F, Moriondo M, Lippi F, et al. Impact of the 13-Valent Pneumococcal Conjugate Vaccine on Severe Invasive Disease Caused by Serotype 3 Streptococcus Pneumoniae in Italian Children. Vaccines (Basel). 2019; 7: 128.

27. Tocchioni F, Tani C, Bartolini L, Moriondo M, Nieddu F, et al. The Role of DNA Amplification and Cultural Growth in Complicated Acute Appendicitis. Pediatr Rep. 2016; 8: 6487.

28. Gentile L, Benazzo F, De Rosa F, Boriani S, Dallagiacoma G, et al. A systematic review: characteristics, complications and treatment of spondylodiscitis. Eur Rev Med Pharmacol Sci.2019; 23: 117-128.

29. Moreno RT, Fernández ME, León MM, Gómez JG, Pascual PM.. Espondilodiscitis: diagnóstico y seguimiento a medio-largo plazo de 18 casos [Spondylodiscitis: Diagnosis and medium-long term follow up of 18 cases]. An Pediatr (Barc). 2009; 71: 391-399.

30. Ventura N, Gonzalez E, Terricabras L, Salvador A, Cabrera M. Intervertebral discitis in children. Int Orthop. 1996; 20: 32-34.

31. Nussinovitch M, Sokolover N, Volovitz B, Amir J. Neurologic abnormalities in children presenting with diskitis. Arch Pediatr Adolesc Med. 2002; 156: 1052-1054.

32. Early SD, Kay RM, Tolo VT. Childhood diskitis. J Am Acad Orthop Surg. 2003; 11: 413-420.

33. Crawford AH, Kucharzyk DW, Ruda RI, Smitherman Jr HC. Diskitis in children. Clin Orthop. 1991; 266: 70-79.

34. Brown R, Hussain M, McHugh K, Novelli V, Jones D. Discitis in young children. J bone Joint Surg Br. 2001; 83: 106-111.

35. Yazıcı N, Yalçın B, Cila A, Alnay A, Büyükpamukçu M. Discitis following lumbar puncture in non-hodgkin lymphoma. Pediatric Hematology and Oncology. 2005; 22: 689-694.

36. Scheuerman O, Landau D, Schwarz M, Hoffer V, Marcus N, et al. Cervical discitis in children. Pediatr Infect Dis J. 2015; 34: 794-795.

37. Mitha A, Boutry N, Nectoux E, Petyt C, Lagrée M, et al. Community-acquired bone and joint infections in children: A 1-year prospective epidemiological study. Arch Dis Child. 2015; 100: 126-129.

38. Mohanty CB, Fieggen G, Deopujari CE. Pediatric spinal infections-a review of non-tuberculous infections. Childs Nerv Syst. 2018; 34: 1947-1956.

39. Mitchell PD, Viswanath A, Obi N, Littlewood A, Latimer M. A, et al. A prospective study of screening for musculoskeletal pathology in the child with a limp or pseudoparalysis using erythrocyte sedimentation rate, C-reactive protein and MRI. J Child Orthop. 2018; 12: 398-405.

40. Wenger D, Bobechko W, Gilday D. The spectrum of intervertebral disc-space infection in children. J Bone Jt Surg Am. 1978;60: 100-108.

41. Spiegel P, Kengla K, Isaacson AS, Wilson JR JC. Intervertebral disc space inflmmation in children. J Bone Jt Surg Am. 1972; 54: 284-296.

42. Cushing AH. Diskitis in children. Clin Infect Dis. 1993; 17: 1-6.

43. M Modic MT, Feiglin DH, Piraino DW, Boumphrey FR, Weinstein MA, et al. Vertebral osteomyelitis: Assestement using MRI. Radiology. 1985; 157: 157-166.