

# Spondylodiscitis in pediatric age – a diagnostic challenge

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## ABSTRACT

Spondylodiscitis is an inflammatory process of the intervertebral disc and the adjacent vertebral endplates and mainly involves the lumbar spine. Clinical suspicion is not raised in most instances, often resulting in difficult and delayed diagnosis. The onset may be insidious and clinical signs can be mild and unspecific. This is also true with laboratory tests, which often remain within the normal range. Refusal to walk and back pain are the main symptoms, and magnetic resonance imaging of the spine is the gold standard for the diagnosis. The duration and type of treatment are controversial, but the use of antimicrobial therapy together with rest and immobilization showed good results in specific cases, leading to a progressive recovery.

We describe a previously healthy two-year old boy with spondylodiscitis, in whom no direct infectious pathogen was identified. We discuss the clinical features, laboratory findings, as well as the outcome of this clinical entity based on a review of the reported cases.

**Keywords:** Back pain; discitis; spondylodiscitis; vertebral infection

## ESPONDILODISCITE EM IDADE PEDIÁTRICA – UM DESAFIO DIAGNÓSTICO

### RESUMO

A espondilodiscite é um processo inflamatório do disco intervertebral e da superfície dos corpos vertebrais com predileção pela região lombar.

Do ponto de vista clínico e laboratorial é uma doença com achados inespecíficos, o que pode resultar em dificuldades e atrasos no diagnóstico se não existir uma elevada suspeição clínica. A recusa da marcha e a dor lombar são os principais sintomas, sendo a ressonância magnética da coluna o ideal para o diagnóstico. A etiologia e o tratamento ainda não são consensuais. O uso de antibióticos, juntamente com o repouso e a imobilização da coluna vertebral têm-se associado, na maioria dos casos, a uma evolução clínica favorável.

Apresenta-se o caso de uma criança com dois anos de idade, previamente saudável, com espondilodiscite sem agente patogénico direto identificado e discute-se a apresentação clínica, as alterações nos exames laboratoriais, bem como a evolução desta entidade com base numa revisão da literatura.

**Palavras-chave:** Discite; espondilodiscite; infeção vertebral; lombalgia

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## INTRODUCTION

Pyogenic infection of the spine was first reported by Lannelongue in 1879, however spondylodiscitis was not defined as an independent entity until 1925, by Mayer.<sup>1,2</sup>

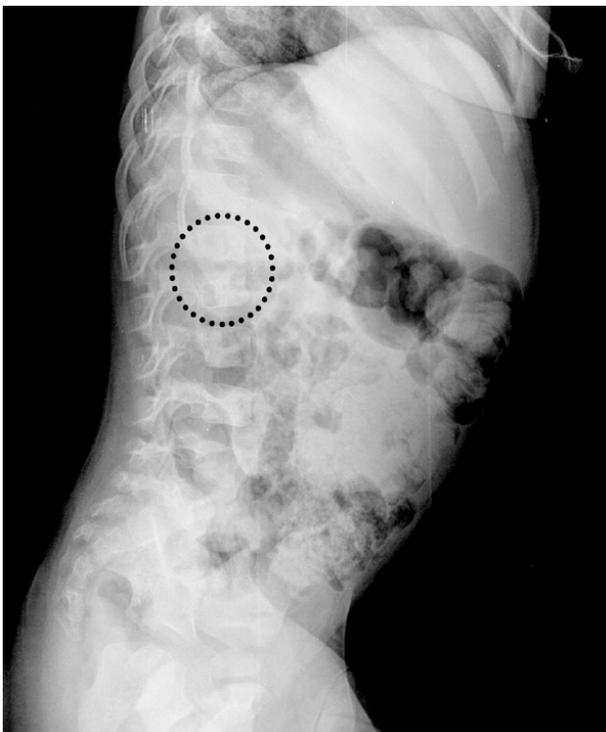
The term spondylodiscitis covers vertebral osteomyelitis, spondylitis and discitis, which are different manifestations of the same pathological process.<sup>1-5</sup> It is an uncommon disorder with an estimated incidence ranging from one to two cases per 32.500 pediatric hospital evaluations per year.<sup>1-6</sup> The average age for the diagnosis in children is approximately two to eight years, although some cases can occur in adolescence.<sup>1,7-9</sup> The etiology is still debated in literature and various pathogenic factors have been identified.<sup>1-5,10,11</sup> From a clinical point of view, it is a disease with unspecific signs and symptoms, sometimes resulting in a difficult and delayed diagnosis. In addition, laboratory investigations are often unhelpful and blood cultures are negative in approximately 50% of patients.<sup>12</sup> The long-term outcome usually is good.<sup>1,3,7,13</sup>

The authors report a child affected by spondylodiscitis who was successfully treated with antimicrobial therapy. This clinical report reinforces the need to consider this diagnosis when a child refuses to walk.

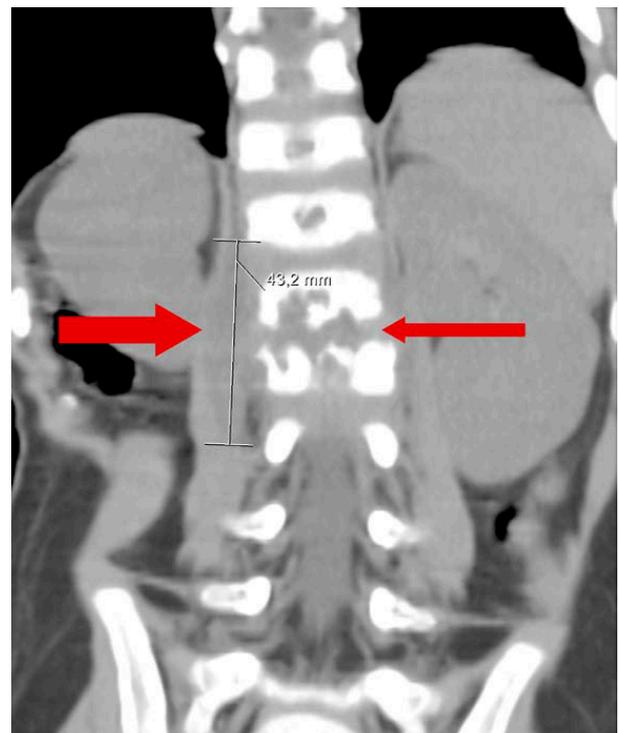
## CASE REPORT

A two-year old boy was born at term after an uncomplicated pregnancy and a normal delivery. The family history was unremarkable. He was brought to the emergency department with a two-day history of irritability, abdominal pain and a

reluctance to sit and walk. The parents stated that about two months before admission the boy has had a foot sprain at school (the level of injury was unclear) which was treated at home with rest and paracetamol. A week before the admission, the boy started nasal congestion, cough and decreased appetite. On physical examination, the infant had refusal to flex the spine. He was afebrile with normal vital signs and had no neurological dysfunction. No lumbar lesions or regional lymphadenopathy were appreciated. A complete blood count revealed 10200 white blood cells (WBCs)/uL with 30,2% neutrophils, 61,1% lymphocytes, 1,3% eosinophils and 6,8% monocytes; hemoglobin level at 10,6 g/dL; and platelet count at 587000/uL. Hepatic function panel and urine analysis were normal. Erythrocyte sedimentation rate (ESR) was increased at 32mm/hour (reference values between 0-10mm/hour). The other laboratory tests, including C-reactive protein (CRP) serum concentration were within normal range. Chest radiography was normal. Lumbosacral spine radiography showed a reduction of disc space with erosions of adjacent vertebral endplates at L1-L2 (Figure 1). He was hospitalized for further etiological investigation and treatment after suspicion of spondylodiscitis diagnosis. Computed tomography (CT) (Figure 2) and magnetic



**Figure 1** - X-rays showing L1-L2 narrowing space with erosion of adjacent vertebral endplates, lateral view.



**Figure 2** - CT of lumbar spine: Narrowing of L1-L2 intervertebral space associated with marked erosion and irregularity of adjacent vertebral endplate that extends to the right pedicles, suggesting spondylodiscitis (small arrow). In addition, there is evidence of marked thickening of adjacent soft tissues, accompanied by formation of paravertebral abscess with extension to the right psoas muscle in a 43.2 mm extension (large arrow).

resonance imaging (MRI) of the spine (Figure 3) showed diffuse L1-L2 intervertebral disc and the adjacent vertebral body infiltration consistent with spondylodiscitis, accompanied by formation of paravertebral abscess with extension to the right psoas muscle. Empirical treatment with intravenous ceftriaxone and flucloxaciline was started.

Serum antibodies, anti-Herpes Simplex Virus 1 and 2, Adenovirus, Cytomegalovirus, *Mycoplasma pneumoniae*, *Borrelia burgdorferi*, *Brucella melitensis* and Epstein-Barr virus and blood culture results (obtained from two samples) were negative.

Mantoux tuberculin skin test and Interferon-Gamma Release Assays (IGRA) blood test for tuberculosis were equivocal (first one was nonreactive and second one was indeterminate). Polymerase chain reaction (PCR) for *M. tuberculosis* from early morning gastric washing samples was negative. Pathology staining for acid-fast bacilli and cultures for mycobacteria were also reported as negative.

After the first week of treatment the child had no abdominal or spinal pain and laboratory tests showed a decrease in the ESR value to 3mm/hour, with the level of WBC count and CRP remaining within normal range. Two weeks later the patient began to sit and to walk. After three weeks he had a full clinical recovery, the inflammatory markers were normal and intravenous treatment was then switched to oral for another three weeks. Bed rest was carried out and combined with the administration of antibiotics until evidence of clinical and laboratory resolution of the condition.

At the first month follow-up, IGRA test was repeated with negative result. At the two-month follow-up, a new spinal MRI showed a reduction of the signal changes in both L1 and L2 vertebral bodies and intervertebral disc, despite the persistence of somatic vertebral morphostructural modifications (Figure 4). X-rays taken after two-years showed persistence of segmental reduction at L1-L2 but with no functional significance (Figure 5). The child asymptomatic and presents a normal neurological examination.

## DISCUSSION

This case highlights the importance of clinical suspicion in the early diagnosis of spondylodiscitis an insidious disorder, not always accompanied by specific laboratory findings. However it is important to reinforce the need to consider the diagnosis every time a child suddenly refuses to walk, crawl or stand up. In fact, Brown *et al* reported a series of 11 consecutive cases where those signs were present in 63% of patients.<sup>14</sup> Back pain is also often reported. Fever is usually low grade or absent and abdominal pain may be the predominant complaint in lesions involving L1, as occurred in this case.<sup>12,15,16</sup> When the cervical spine is affected, manifestations may include dysphagia and stiff neck.<sup>16</sup> Contracture and spasm of paravertebral and psoas muscles occur with limited mobility of the spine, which can be extremely painful and cause loss of the lumbar lordosis.<sup>3,10,12,14,16,17</sup> Other findings may include percussion tenderness over the involved spine, decreased muscle strength or reflexes or ileus (with high lesions: T8-L1). Unspecific symptoms are also



**Figure 3** - MRI study with gadolinium enhancement showing a hypersignal at L1-L2 intervertebral disc and the adjacent vertebral body, on T2-weighted images. (a) Sagittal image. (b) Coronal image.



**Figure 4** - MRI study with gadolinium enhancement at two-month follow-up showing reduction of the signal changes in both L1 and L2 vertebral bodies and intervertebral disc. Persistence of somatic vertebral morphostructural modifications. T2-weighted images.



**Figure 5** - X-rays after two-years showing persistence of L1-L2 narrowing space and erosions of adjacent vertebral endplates (arrow), lateral view.

common such as fatigue, irritability, loss of appetite, and a lack of desire to play.<sup>13,16</sup> Table 1 shows other causes of back pain in children, which have different implications for treatment or prognosis, and must also be considered. A review of the literature of spondylodiscitis in children suggests that it has a biphasic age distribution primarily affecting the young toddler, with a second peak in adolescence.<sup>9,15</sup> The pathophysiology of the condition has not been clearly established. Trauma, inflammation and infection have all been implicated.<sup>3,18,19</sup> The pathogens can infect the spine from three sources: by haematogenous spread (arterial or venous), by external direct inoculation, or by contiguous spread from adjacent tissues. The predominant form is blood haematogenous. Unlike adults, the intervertebral disc in young children is vascularized.<sup>13,20</sup> Vascularization in children is made up of vessels across the cartilaginous vertebral plate and into the ring; after eight years of age, these vessels disappear, but a rich anastomotic network of vessels remains in the periphery of the disc. The vascularized nature of the intervertebral disc in children explains the higher incidence of this disease in this age group. According to various studies, this fact explains the hypothesis of bacterial etiology, and also the satisfactory response to treatment with antibiotics.<sup>7,12,18,20,21</sup> In tuberculosis, the destruction starts with the vertebral body and spreads to the adjacent vertebra through the ligaments. Extensive bone infarcts

**Table 1** - Causes of back pain in children<sup>3</sup>

<b>Infectious</b>
Discitis
Vertebral osteomyelitis, including tuberculosis (Pott disease)
Epidural abscess
Sacroiliac joint infection
<b>Inflammatory</b>
Ankylosing spondylitis
Psoriatic arthritis
IBD-associated arthritis
Reactive arthritis
<b>Musculoskeletal</b>
Spondylolysis/spondylolisthesis
Scoliosis
Scheuermann disease
Disc degeneration and/or prolapse
<b>Neoplastic</b>
Osteoid osteoma
Leukemia or lymphoma
Solid malignancy, primary or metastatic
Neurofibroma
Vascular malformation

IBD: Inflammatory bowel disease

lead to the formation of cavitation and compression fractures. Failure to control the infection can cause paravertebral, psoas or epidural abscess.<sup>16</sup> Pyogenic spondylodiscitis from the haematogenous source particularly affects the lumbar spine, followed by the thoracic and cervical spine, reflecting the volume of blood flow.<sup>3,6,22</sup> In tuberculosis, we observed involvement of the thoracic spine.<sup>16</sup>

We noticed that the patient had an episode of trauma two months before the development of spondylodiscitis which could have been implicated in the etiology for the condition as well as explain the presence of spinal radiographic changes at the time of the diagnosis (usually not seen until second or third week of onset of the disease). On the other hand, the presence of a prodromal illness one week before the admission to the hospital could lead to believe in the infectious nature for the process. The absence of a marked systemic response could have simply reflected an appropriate local host response to a pathogen of low virulence, such as *Kingella kingae*.

When reviewing the laboratory investigations, we found that the WBCs and CRP values were normal, but ESR had increased above 30mm/hour. In fact, ESR is usually elevated in  $\geq 90$  percent of patients.<sup>1,4,15,23</sup>

As seen in other reported cases, blood cultures were negative and thus unable to provide sufficient etiologic information. In series where positive cultures were present, *Staphylococcus aureus* was the most common isolated organism.<sup>1,6,22,24</sup> Recently the reported number of cases of *K. kingae* infection has markedly increased. Many studies have demonstrated that this pathogen has become the leading cause of spondylodiscitis in children aged between 6 and 48 months and the microorganism is currently recognized to account for 30% to 93.8% of all culture-positive osteoarticular infection.<sup>24,27</sup> The high rate of sterile blood cultures and the frequent failure to identify the causative pathogen, even on disk or vertebral aspiration, is another very suggestive argument that most cases of the infantile form of spondylodiscitis are due to *K. kingae*. In fact, the recovery of *K. kingae* from purulent specimens seeded onto solid culture media is suboptimal and results are negative in a frustrating proportion of cases.<sup>23</sup> Thus sterile blood cultures can be interpreted as false-negative results correlated to inappropriate techniques of *K. kingae* identification in spondylodiscitis. In our case, we could not prove that the spondylodiscitis was actually caused by *K. kingae*, as we did not make specific culture nor used molecular detection methods. We also did not perform any biopsies or needle aspirations for diagnostic purposes which reflected our risk/benefit analysis based on the low rate (less than 50%) of positive cultures reported in previous series.<sup>7,9</sup> According to some authors, this procedure should be reserved for children not responding to intravenous antibiotics.<sup>7</sup>

*Mycobacterium* and *Brucella* infection were also investigated. Brucellosis still has a high incidence in many parts of the world, including the Mediterranean littoral and remains an important cause of granulomatous spondylodiscitis.<sup>25,26</sup> It should be noted that in the early stages, the differential diagnosis between

unspecific infection (pyogenic discitis) and granulomatous infection (spinal tuberculosis or brucellosis) can be difficult. In this case, patient's clinical improvement with empiric antibiotic therapy led us to exclude the tuberculosis hypothesis.

We used CT and MRI to establish the diagnosis. MRI has high sensitivity (96%) and specificity (94%), and remains the gold standard complementary imaging method for the investigation of pyogenic infection of the spine, particularly in the early stages.<sup>1,7,15,17,22,26</sup> MRI can also exclude alternative diagnoses such as vertebral osteomyelitis and tumors.<sup>1,22</sup>

In our case, changes such as reduced disc space and erosion of the end-plate were evident in spine radiography, suggesting that the disease had been present for at least two to three weeks (Figure 1).<sup>7,9</sup>

Bone scintigraphy with technetium-99m pyrophosphate shows positive signs within one to two days of the onset of the infection. The drawbacks of the technique however include low specificity and insufficient spatial resolution of the affected site. Moreover, the high accuracy of the MRI has led to scintigraphy falling into disuse.<sup>10,13,27</sup> Computed tomography (CT) scan is easy to perform, faster and more affordable than MRI. The areas of erosion of the endplates that appear early in the affected vertebral levels are easier to detect by CT scan than by the images from plain radiographs.<sup>10,13,27</sup>

Management for spondylodiscitis is not standardized. Some retrospective data suggests that initial treatment with intravenous antibiotics until the child shows clinical improvement followed by oral antibiotics is associated with a somewhat earlier response and fewer relapses than treatment with analgesia alone.<sup>1,4</sup> Due to this, our hospital routinely prescribe antibiotics as a first-line treatment for the condition. The recommended empiric antibiotic therapy is a combination of a third-generation cephalosporin combined with an antistaphylococcal agent.<sup>1,14,21</sup> Immobilization, either through bed rest, or occasionally, bracing or casting, may assist with pain control. In our case we favor immobilization through bed rest; no body plaster or orthosis was used. Restricted activities should be maintained for 10–12 weeks, or until evidence of clinical and laboratory resolution.<sup>6,12</sup> Treatment with antibiotics and rest was efficacious in this case leading to clinical resolution and recovery in a few weeks.

Recommendations regarding the duration of treatment, varies between institutions, ranging from one week to three weeks intravenously, followed by supplementary oral therapy until resolution of the inflammation and clinical improvement.<sup>3,4,12,15,16,27</sup> The total treatment can last from two weeks to six months, according to the patient's response.<sup>3,7,10,14,21</sup> In our case we used a combination of regular clinical assessment and serial measurement of inflammatory markers as a guide to the duration of treatment. The criteria for the discontinuation of the antimicrobial treatment included resolution of the symptoms and normalization of ESR e CRP. The ESR usually increases during the first few days of treatment and then declines slowly in the follow weeks. CRP returns to normal much more rapidly than ESR and it has been proposed that a weekly reduction of 50% in CRP represents

favorable evolution.<sup>3,10,16,27</sup> We also used MRI for monitoring the therapeutic response during the course of spinal infection, however we recognize that MRI scans ordered in patients responding well clinically often gives conflicting results and that we should be cautious in interpreting follow-up MRI images.<sup>24</sup> Persistent or increased gadolinium enhancement seen in the context of clinical improvement does not necessarily represent deterioration or treatment failure, as seen in this case.

Surgery is rarely indicated for disc infection in children. It may be necessary in cases of neurological deficit due to medullary or root compression, major destruction of the vertebral bodies, progressing to rapid transformation of the deformity into kyphosis, spinal instability, or failure of conservative treatment.<sup>9,12,14,16,20</sup>

The outcome is usually good, although anomalies of the disc space and adjacent vertebrae (often asymptomatic) are common findings, as reported in 50 out of 55 patients in two series.<sup>1</sup> In our case, radiographic assessment at two years follow-up, showed persistent abnormalities but no restriction of spinal movements. As a result, we believe that long-term follow-up is necessary for all children with this disorder.

## CONCLUSION

In summary, spondylodiscitis in children is an uncommon disorder and diagnosis is challenging since symptoms and signs are often insidious and nonspecific; refusal to walk and back pain are the most common.<sup>2</sup> The etiology and the best treatment are still under debate. Blood cultures are usually negative, and identification of the causative pathogen can be challenging.<sup>6</sup> Radiographic changes may only be seen within two to three weeks after the onset of the disease and spine MRI remains the gold standard to confirm the diagnosis.<sup>7-9,15,16,29</sup> This case highlights the importance of clinical suspicion and early diagnosis to reduce the risk of negative outcomes.

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