CASE REPORT

A special case of lower back pain in a 3-year-old girl

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SUMMARY

We describe the case of a 3-year-old girl with a 15-day clinical history of lower back pain. We diagnosed a spondylodiscitis of vertebral bodies L5–S1 caused by *Salmonella* species group B that totally recovered with appropriate antibiotic therapy. Spondylodiscitis in children is a rare condition and *Salmonella* infection is one of the rarest aetiology. A high index of suspicion is needed for prompt diagnosis to ensure better long-term outcome. Microbiological diagnosis is essential for the appropriate choice of antibiotic treatment.

BACKGROUND

Infective spondylodiscitis in healthy individuals is a rare condition; in children it is more common between 6 months and 3 years of age.

Mycobacterium tuberculosis is the commonest cause of spinal infection worldwide and accounts for 9–46% of cases in developed countries. The other more common organisms causing spondylodiscitis are *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas*, *Streptococci* and *Klebsiella*.¹ *Salmonella* organism is a rare cause of bone diseases in immunocompetent children and spondylodiscitis have been reported to account for only 2–5% of all the cases of osteomyelitis infection.^{1–4}

In non-endemic areas, most cases have been reported in patients who were immunologically compromised by sickle-cell haemoglobinopathy,⁵ malignant lesions, collagen or vascular diseases and diabetes.⁶ Only sporadic cases of *Salmonella* spondylodiscitis in immunocompetent patients have been reported.^{7–12}

The main target bone in *Salmonella* osteomyelitis is unknown but, in general, the vertebrae are rarely infected in the paediatric age.^{3 13}

CASE PRESENTATION

A 3-year-old Italian girl was admitted to the paediatric emergency unit with a 15-day history of lower back pain exacerbated by deambulation, extended to both hips with movement difficulties, especially in sitting and keeping several postural positions. Her general conditions were compromised and associated with mild fever since 2 days before admission.

The parents correlated the onset of the pain with an accidental fall on her back 1 month prior to admission. Moreover, 15 days before the beginning of the lower back pain, the patient presented an acute episode of diarrhoea with abdominal pain and fever (peak of 38.8°C) lasting for 4 days. A bacterial gastroenteritis was suspected and a group B *Salmonella* species was isolated in the coproculture. The patient was treated only with

oral rehydration and probiotics with complete resolution of symptoms.

At hospital admission, she presented with mild fever (37.5°C) and non-specific symptoms such as irritability, fatigue, loss of appetite and lack of desire to play. Physical examination showed mild lumbar spine stiffness, gross restriction of lumbar movements and difficulty in walking. The back pain was exacerbated by movements and the patient was unable to bend over to pick up a little toy and showed irritation of the hips when held in extension (log-roll test).¹³ Neurological examination showed no signs of meningism and showed a normal lower tendon reflexes. The remaining clinical examination was normal.

INVESTIGATIONS

Initial blood test showed a mild increase in white blood cell count (WBC 12.610/mm³; neutrophils 48%, lymphocytes 41%) and platelets (557.000/microl) with normal red blood cells (RBC 4.070.000/mm³), median corpuscular volume (77 fl) and haemoglobin (11.0 g/dl). Erythrocyte sedimentation rate (ESR 65 mm/h) was increased with a normal C reactive protein (CRP 0.50 mg/dl). Peripheral blood smear showed no WBC and/or RBC abnormalities.

Tuberculin skin test and interferon- γ based release assay (QuantiFERON-TB Gold) were negative; blood culture taken on admission remained negative.

Other immunological deficiencies or collagen diseases were ruled out.

The Widal-Wright test was positive for *Salmonella typhi* H (titre 1:800).¹² Considering the previous episode of diarrhoea, the coproculture was repeated which confirmed the persistence of *Salmonella* group B species.

Chest x-ray and abdominal ultrasound were normal. Lateral x-ray of the lumbosacral tract revealed inhomogeneous appearance of the posterior wall of the lumbar 5 (L5) vertebral body together with a posterior irregular profile of L4 spine (figure 1). The lumbosacral vertebrae MRI studies showed an inhomogeneous hyperintensity of vertebral bodies of L5 and sacral 1 (S1), particularly L5 body showed a pseudolacunar and serpiginous image in its posterior part with oedema of surrounding tissues (figure 2A). Moreover, it demonstrated an intervertebral disc height loss between L5 and S1 with a signal strength reduction (figure 2B). The MRI also confirmed the inflammatory state of the area located at the right-hand side of the intervertebral disc between L4 and L5, as well as the presence of oedema and a cuff-like thickening of paravertebral tissues with posterior

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Figure 1 X-ray of the lumbosacral spine revealed inhomogeneous appearance of the posterior wall of the L5 vertebral body with also a posterior irregular profile of L4 spine.

pressure on the dural membrane (figure 3). The contrast medium caused intense and homogenous enhancement of the aforementioned findings. To better differentiate among inflammatory and malignancy origin, the patient underwent fluorine-18 fluorodeoxyglucose positron emission tomography (18F-FDG PET) that showed mild L5–S1 hyperaccumulation of radiopharmaceutical medium with a standard uptake value maximum (SUV max) of 3 g/ml.¹⁴

The result supported mainly inflammatory nature of the bone lesion like spondylodiscitis and, given the history, a *Salmonella* infection was suspected. The aetiology could only be confirmed by a percutaneous CT-guided spinal biopsy, but considering the young age of the patient and the invasiveness of the procedure, we decided to start intravenous antibiotic therapy based on the coproculture antibiogram sensitivity and to follow-up the clinical and radiological evolution of the vertebral lesion. After antibiotic therapy was started in association to the use of a lumbar corset, the patient's clinical conditions rapidly improved. To evaluate the evolution of the inflammatory lesion and to exclude any illness progression, an MRI scan of the lumbosacral tract was repeated after 2 weeks of treatment, showing a slight improvement of the previously reported findings (figure 4). Clinical and radiological improvement convinced us to continue with the ongoing therapy without proceeding to CT-guided biopsy.

An MRI performed 4 weeks after the initiation of the treatment showed a noteworthy reduction of the vertebral lesion along with an improvement of intervertebral and paravertebral inflammatory state (figures 5 and 6).

After an intermediate MRI control at 4 months, the last MRI at a 15-month follow-up demonstrated the complete

Figure 2 T2 (A) and STIR (B) sequences of the first MRI: dishomogeneous hyperintensity of vertebral bodies L5–S1; L5 body showed pseudolacunar and serpiginous image in its posterior part together with disc height loss. STIR, short time inversion recovery.

Figure 3 MRI of the T1-weighted images: oedema and a cuff-like thickening of paravertebral tissues with a hypointense signal in T1-weighted images and hyperintense signal in STIR with posterior pressure on the durale. STIR, short time inversion recovery.

normalisation of vertebral bodies L5–S1 (figure 7) with a reduction of the intervertebral space caused by a permanent lesion of the intervertebral disc.

DIFFERENTIAL DIAGNOSIS

Spine pathologies can involve various anatomical districts: the vertebral body (osteomyelitis or tumours), the intervertebral disc

space (discitis) and the surrounding soft tissue (epidural or paraspinal abscesses). When the original illness becomes clinically symptomatic it is usually difficult to differentiate where pathology originated: generally in infections and/or in tumours all three anatomical vertebral districts that are already involved.^{1–15}

Even if the medical history along with the combination of symptoms and laboratory and radiological findings oriented the diagnosis towards a spondylodiscitis infection, we had further minimal doubts in excluding other aetiologies with a similar clinical presentation, including traumatism or neoplasm, particularly osteosarcomas.

In children, diagnosis of infective vertebral spondylodiscitis could be delayed because back pain is often related to traumatism.^{1–2–13}

In our patient diagnosis was oriented by a recent episode of diarrhoea where group B *Salmonella* was isolated in coproculture.

Ewing sarcoma is a condition that must be excluded in children with back pain and radiological alterations.¹⁶ Like in spondylodiscitis, vertebral involvement is very rare and generally, when symptomatic, its advancement stage is not surgically treatable, especially for vertebral localisations.^{14–16}

The symptoms of spondylodiscitis are not specific: back pain is very common, but up to 15% of patients may be pain free. In this patient the presence of progressive back pain and grossly restrictions of movements oriented for spine pathologies.^{1–8–17}

We also found elevated ESR and leucocytes count, but with negative CRP.

Blood culture was negative but we found repeated positivity for group B *Salmonella* species in the patient's coproculture before and after the hospital admission.

It is well known that in almost half of the cases of spondylodiscitis a distant focus of infection has been identified and thus we began the antibiotic therapy on the basis of antibiogram susceptibility without performing a percutaneous CT-guided biopsy.¹⁸

Figure 4 MRI in sequences of T2-weighted images (A) and STIR (B) after 2 weeks: dishomogeneous hyperintensity of vertebral bodies L5 and S1 was diminished. STIR, short time inversion recovery.

Figure 5 MRI of the T1-weighted images at 4 weeks showed strong reduction of the inflammatory state at the right-hand side of the intervertebral disc between L4 and L5 together with the hyperintensity reduction of the paravertebral tissues cuff-like effect.

As in our patient, plain radiography is frequently used as a screening test. It may reveal some early changes of vertebral bodies and relative spines: subchondral radiolucency, loss of definition of the endplate and loss of disc height. Later, the changes include destruction of the endplate, loss of vertebral height and paravertebral soft tissue mass.^{17 19}

A CT is the gold-standard for bony abnormalities, but it is inferior to MRI in defining neural damaging, disc appearance and epidural abscesses. At MRI this patient showed diffuse involvement of all the three anatomical districts of the lumbar vertebrae: disc, bone and paravertebral soft tissues.^{13 20}

The combination of positive coproculture with MRI suggested us to begin the antibiotic therapy because of the high probability of *Salmonella* group B spondylodiscitis. Nevertheless, we had further minimal doubts in excluding osteosarcomas. PET is a non-invasive method that can help in differentiating among inflammatory and malignancy origin. A variety of tracers have been used in the radionuclide imaging of spondylodiscitis with different sensibility and specificity.^{19 21} Among them a recent technique using 18F-FDG PET seems to offer some advantages. In fact it offers the opportunity to distinguish infections from degenerative changes and/or neoplasm.^{22 23} There is a direct correlation between tumoural mitotic count and SUV max. In this patient SUV max was 3 g/ml which was a value low enough to exclude Ewing sarcoma and osteosarcoma. SUV max in Ewing sarcoma ranged from 1.6 to 9.2 g/ml and in osteosarcoma it is 3.5–20.4 g/ml. The SUV max values of all inflammatory bone lesions at 30 min ranged from 0.5 to 3.5 g/ml.²⁴

The clinical course of the patient improved rapidly after the beginning of the antibiotic therapy and a second MRI did not reveal any worsening of the imaging. For this reason we did not perform CT-guided biopsy.

TREATMENT

Following the antibiotic sensitivity reported on coproculture we started piperacillin/tazobactam therapy (0.2 g/kg/die divided in four doses) with the purpose of extending treatment to the wide range of possible spondylodiscitis aetiologies including mainly *S aureus*.¹

This treatment generated a rapid clinical improvement. Further improvement of symptomatology was reached with the application of a lumbar corset as prescribed by the orthopaedic consultant.

After 23 days of therapy the coproculture was still positive for *Salmonella* group B species and antibiogram demonstrated in vitro resistance to piperacillin/tazobactam but was susceptible to ceftazidime; the antibiotic therapy was then switched to

Figure 6 MRI after 4 weeks: further great decrease of the signal alteration of vertebral bodies L5 and S1 (A); the contrast medium technique did not show pathological enhancement (B).

Figure 7 MRI of the T1-weighted images after 15 months: resolution of the inflammatory state of L4 and L5 vertebral bodies (A), together with the normalisation of paravertebral district (B).

intravenous ceftazidime (0.1 g/kg/die divided in three doses). Intravenous antibiotic therapy was continued for a total of 5 weeks.

After discharge, the treatment was continued for two more weeks with oral sulfamethoxazole/trimethoprim, on the basis of the last *Salmonella*'s susceptibility antibiogram.

Body corset therapy has been continued for 4 months after MRI demonstrated almost complete resolution of the vertebral body lesions.

The patient continued physiotherapy exercises for a total of 12 months with complete resolution of symptomatology.

OUTCOME AND FOLLOW-UP

Clinical conditions of the child improved gradually after the beginning of intravenous antibiotic therapy.

After 6 weeks of antibiotic therapy she walked without difficulties and her lower back movements were almost normal.

She continued with physiotherapy and with lumbar support corset for several months.

An MRI of the lumbosacral vertebrae was performed at 0, 2, 4 and 16 weeks that showed a progressive improvement of the lesions up to a total resolution.

The only negative outcome was the complete degeneration of L5–S1 disc demonstrated with a loss of height of the intervertebral space in the last MRI, at 15 months follow-up.

DISCUSSION

Vertebral infective spondylodiscitis is uncommon in children and accounts for only 2–5% of all osteomyelitis.^{1 2}

The main documented pathogens are *Mycobacterium tuberculosis* and, among pyogenic infections, *S aureus*.¹

The two greatest retrospective paediatric studies described 16 and 18 children, respectively, none of them affected by *Salmonella*.^{18 25} This infectious aetiology is a rare condition in immunologically normal children and it is described mainly in the case reports.^{7 9–11} Also, in adults, it is a very rare condition presented in the literature in few retrospective studies.^{2 4 12}

Pathogens can infect the spine from three main sources: by haematogenous spread (arterial and venous), by contiguous spread and by external inoculation.

In children, different from adults, the intervertebral disc is vascularised with a lot of anastomotic vessels directly communicating with the metaphyseal ring of the above and below two adjacent vertebrae.^{1 13} This vascular distribution explains the higher incidence of spondylodiscitis in children and the findings of clinical and imaging examinations. The main step of the antimicrobial therapy is the cultural isolation of the pathogens causing spondylodiscitis.

A distant focus of the infection has been identified in almost half the cases of spondylodiscitis: genitourinary tract (17%), skin and soft tissues (11%), gastrointestinal tract (9%), intravascular devices (5%) and respiratory tract (2%).²⁶

As a complication of spondylodiscitis, an endocarditis was reported in 12% of affected patients.¹ For these reasons and before antibiotic use, multiple cultures from various anatomical districts should be taken.

Since spondylodiscitis is mainly monomicrobial and often has a haematogenous source, blood cultures are reported to be positive in a range between 40 and 60% of the patients.^{1 13}

A CT-guided biopsy is also another important tool used in identifying various pathogens affecting spine districts. Till now the mandatory role of biopsy in children is debated on the basis of the risk–benefit analysis and on the fact that as many as 40% of them are negative even before antibiotic use, as described by Karadimas *et al.*²

In this case an anti-*Salmonella* antibiotic therapy was oriented by the following main points: a repeated positive coproculture, a clinical history of diarrhoea, a high Widal titre and the MRI.

Generally, in paediatric patients the antibiotic therapy is accepted when a pathogen is isolated and demonstrated the focus-source infection. A CT biopsy is mandatory when the initial response to therapy is poor and/or the presence of atypical microorganism is suspected.^{1 18}

The frequency of performing biopsies varied among spondylodiscitis studies (19–100%) and the positivity of culture-samples ranges from 43 to 78% of the cases.^{1–3}

Symptoms in children with vertebral spondylodiscitis are variable and they depend on the gravity-stage of the infection and the age of the patient. A high-grade fever with back pain and refusal to crawl, sit or walk is usually present in older children, whereas in younger ones may predominate subtly with non-specific symptoms like low-grade fever, malaise, weight loss and irritability.^{3 8 17 20}

The aim of the treatment consists of an antimicrobial therapy together with physiotherapy and immobilisation with a lumbar corset. These support treatments are used to alleviate back pain, to reduce intradiscal pressure and to support lumbar vertebrae.^{11 27}

In this patient we started antibiotic therapy with piperacillin/tazobactam according to antibiogram. After 2 weeks we switched to antibiotic treatment from piperacillin/tazobactam to ceftazidime because of a developed in vitro resistance to our *Salmonella* strain.

In *Salmonella*'s spondylodiscitis the response to antimicrobial treatment may vary with age, antibiotic used, antibiotic sensibility, immunocompromised conditions, illness severity and duration of diarrhoea before the starting of antibiotic treatment. One of the potential risks of intestinal salmonellosis in young infants is an extraintestinal infection, but it is not known if antibiotics have a significant impact in preventing the risk of extraintestinal infections in children.^{28–30}

Many authors describe different treatment lengths, but there is a significantly increased risk of therapy failure in patients treated for less than 4 weeks instead of longer periods.^{13 31}

Several authors demonstrated that intravenous antibiotic therapy should be administered for 2–3 weeks and after that it is possible to switch to oral administration.²⁸

There is a general agreement that antibiotic treatment should be prolonged, at least, for 4 weeks, but data specifically related to paediatric *Salmonella* spondylodiscitis are very limited.¹³

The diagnosis of infective spondylodiscitis in children remains a medical challenge and it is often delayed owing to the rarity of the disease and the insidious onset of symptoms.

In the early stage of unspecified spondylodiscitis, x-rays have very low sensitivity and specificity. It is frequently employed as a screening test in patients with lumbar pain and may occasionally reveal early changes like in our patient. In fact MRI is the most useful method for the investigation of the spine infections, especially in the early stages of the illness. MRI has high sensitivity (96%) and specificity (94%). It is not invasive and it does not use radiations, which is especially important in children. It gives many advantages if compared with CT because it can also explore the disc spaces and soft and neural tissues.^{1 13 19} There does not exist a general agreement about the timing of repeated MRI to follow-up the illness evolution. Probably in this case the time for MRI follow-up was too short, but this was because of some imaging doubts on the benignity of our patient's lesions. However, the second MRI showed a light involution of the spinal lesions and confirmed the exclusion of the malignancies.

Sometimes, at the onset of the spondylodiscitis, MRI could be inconclusive in distinguishing infections from degenerative illnesses like osteosarcoma.²³

Recently, some evidences emerged on 18F-FDG PET as an important tool in evaluating the aetiology of various spine disorders including differential diagnosis with some malignancies, even if it shows a low specificity for neoplasm.^{13 22} In fact, there are many overlapping values of SUV max in Ewing sarcoma (1.6–9.2 g/ml) if compared with osteosarcoma (3.5–20.4 g/ml).¹³ The 18F-FDG PET has a direct positive correlation between the tumoural mitotic count and the SUV max.²²

Spondylodiscitis in children remains rare and *Salmonella* infection is one of the rarest aetiology. Its diagnosis is actually easier because of the availability of more effective diagnostic tools. A high index of suspicion is needed for prompt diagnosis to ensure improved long-term outcomes. Microbiological diagnosis is essential for the appropriate choice of antibiotic treatment.

Learning points

- Spondylodiscitis is a rare pathology in children: *Salmonella* infection should also be considered in immunocompetent patients.
- Cultural isolation from various anatomical districts is an important guide to begin antibiotic therapy.
- A CT-guided needle biopsy should be considered when no organism can be identified by less-invasive techniques or when malignant lesions are highly suspected.
- Only repeated MRI gives the opportunity to follow-up strictly the illness evolution until complete resolution.

Patient consent Obtained.

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