DIFFERENCES OF MRI FEATURES BETWEEN TUBERCULOUS AND BACTERIAL SPONDYLITIS IN A TB-ENDEMIC AREA

Jureerat Thammaroj[1], Amnat Kitkuandee[2] and Kittisak Sawanyawisuth[3,4]

Departments of [1]Radiology, [2]Surgery, [3]Medicine, Faculty of Medicine, Srinagarind Hospital, Khon Kaen; [4]Research Center in Back, Neck Other Joint Pain and Human Performance (BNOJPH), Khon Kaen University, Khon Kaen, Thailand

Abstract. Pyogenic and tuberculous spondylitis are common causes of infectious spondylitis. The purpose of this study was to determine the specific MRI findings that can differentiate these two types of infectious spondylitis. This study retrospectively analyzed MRIs in patients diagnosed with infectious spondylitis from January 1, 2005 to December 31, 2009. Tuberculous spondylitis was diagnosed by histopathological findings of caseous granuloma, while pyogenic spondylitis was diagnosed by positive cultures of tissue, fluid, or blood. Locations and extents of the lesions, and the findings using individual imaging criteria were recorded. Statistical analysis was performed with the Fisher's exact test. A significant difference was considered at $p < 0.05$. During the study period, 33 patients met the criteria. Of those, 24 patients had tuberculous spondylitis and nine had pyogenic spondylitis. Two suggestive findings for tuberculous spondylitis were abscesses with thin and smooth walls (75% in tuberculous spondylitis *vs* 0% in pyogenic spondylitis, $p < 0.001$) and well-defined paraspinal soft tissue (66.7% in tuberculous *vs* 11.1% in pyogenic spondylitis, $p = 0.007$). These two MRI findings may be helpful for differentiating between tuberculous and pyogenic spondylitis.

Keywords: pyogenic spondylitis, tuberculous spondylitis, MRI, endemic area

INTRODUCTION

Infectious spondylitis is an infection of one or more components of the spine including vertebrae, paravertebral soft tissue, intervertebral discs and epidural space (Sharif *et al*, 1995). It accounts for 2% - 4% of osteomyelitis cases and occurs most commonly in males and in the 50-60 year age group (Smith and Blaser, 1991).

Staphylococcus aureus is the most common cause of spinal infection (15%-84%). Other pathogens that have been isolated include gram-positive cocci such as *Streptococcus* and *Enterococcus* species (Khan *et al*, 1999). Fungal infections due to *Candida albicans* or *Aspergillus* species are rare causes of infectious spondylitis; less than 1% (Friedman *et al*, 2002). In particular countries, unusual pathogens may be found. In northeastern Thailand, *Burkholderia pseudomallii* is another pathogen possibly causing spinal infection and may mimic tuberculous spondylitis

Correspondence: Dr Jureerat Thammaroj, Department of Radiology, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.
Tel: +66 (0) 43 363178; Fax: +66 (0) 43 363178
E-mail: drjureeratt@gmail.com

(Chaowagul *et al*, 1989; Vidyalakshmi *et al*, 2008). *Brucella* was isolated from 4 out of 18 patients with spondylitis in Italy and 105 out of 219 patients in Spain (Colmenero *et al*, 1997).

Mycobacterium tuberculosis spondylitis is also common in developing countries. Risk factors for tuberculous spondylitis are immunocompromised status and intravenous drug use. It is crucial to be able to differentiate between bacterial and tuberculous spondylitis. Correct diagnosis and treatment improve functional outcomes in patients with infectious spondylitis (Moore and Rafii, 2001).

Magnetic resonance imaging (MRI) is currently a modality of choice for the evaluation of spinal infection. Having high sensitivity in detecting subtle changes in the water and fat content of medullary bone, MRI should be sensitive to the disc and marrow changes in infectious spondylitis. Use of MRI, however, is controversial for differentiating TB spondylitis from pyogenic spondylitis (Jung *et al*, 2004; Chang *et al*, 2006; Harada *et al*, 2008). The objective of this study was to seek differences in MRI findings between these conditions in Thailand, where tuberculosis is endemic.

MATERIALS AND METHODS

MRIs from patients diagnosed with infectious spondylitis at Khon Kaen University, Thailand were retrospectively analyzed. The study period was between January 1, 2005 and December 31, 2009. The diagnosis of tuberculous spondylitis was made by histopathological detection of caseous granulomas and/or positive tissue cultures for *M. tuberculosis* or positive tissue acid-fast staining. Pyogenic spondylitis was diagnosed by positive tissue culture, fluid culture, or blood culture from patients clinically diagnosed with infectious spondylitis. The study protocol was approved by the Khon Kaen University review board for human research (HE 531416).

All MRIs had been obtained using a 1.5T machine (GE; Signa Horizon). Pulse sequences included fast spin-echo T1-weighted imaging (TR/TE = 580-800/8.0 -10.3) in axial and sagittal planes, fast spin-echo T2-weighted imaging (TR/TE = 3000-5360/82-110) in axial and sagittal planes, Proton-density imaging (TR/TE = 3000/9.9-11.4) in the sagittal plane and contrast-enhancing (0.2 mmol per kilogram of body weight) fat-suppressed fast spin-echo T1-weighted imaging (TR/TE = 400-800/7.6-9.4) in axial and sagittal planes. Section thicknesses were about 4 mm and 5 mm in sagittal and axial images.

All MRIs were evaluated by an experienced (13 years) neurological radiologist. Locations and extent of the lesions, and the findings using individual imaging criteria were recorded. Thoracic spine involvement, multiple vertebral body involvement, skip lesion appearance, collapse of vertebral body, vertebral enhancement, the abscess wall, presentation of intraosseous abscess, margin of paravertebral soft tissue, intervertebral disc space, extent of subligamentous spreading and presence of epidural extension were evaluated. The signal intensities in the bone marrows of abnormal vertebrae were considered abnormal by comparison to normal vertebrae in the same patient.

Operational definitions were defined as follows: "thin and smooth-walled abscess" refers to paraspinal abscesses with wall enhancement after Gadolinium injection; "well-defined paraspinal soft tissue" refers to well-defined margin of abnormal paraspinal signal in T1-weighted images. Statistical analysis was performed using

Table 1
Distribution of lesions in tuberculous and pyogenic spondylitis.

Findings	Tuberculous group	Pyogenic group
Level of involvement	6	1
Cervical spine	12	2
Thoracic spine	11	5
Lumbar spine	3	3
Sacral spine		
Number of involved vertebrae		
1	2	0
2	5	4
3	10	1
4 or more	7	4

Table 2
MRI features of tuberculous and pyogenic spondylitis.

MRI findings	No. (%)		*p*-value
	Tuberculous (*n*=24)	Pyogenic (*n*=9)	
Thin and smooth abscess walls	18 (75)	0	<0.001
Thoracic spine involvement	12 (50)	2 (22.2)	0.24
Multiple level involvement	17 (70.8)	5 (55.6)	0.44
Skip lesions	5 (20.8)	1 (11.1)	0.99
Collapsed vertebral bodies > 50%	10 (41.7)	1 (11.1)	0.21
Diffuse vertebral enhancement	16 (66.7)	8 (88.9)	0.39
Intraosseous abscess	13 (54.2)	3 (33.3)	0.44
Intervertebral disc spaces narrowing	12 (50)	7 (77.8)	0.27
Well-defined paraspinal soft tissue	16 (66.7)	1 (11.1)	0.007
Epidural extension	20 (83.3)	6 (66.7)	0.36
Subligamentous spreading > 2 levels	16 (66.7)	4 (44.4)	0.43

the Fisher's exact test. Significant difference was considered at $p < 0.05$.

RESULTS

During the study period, 33 patients were diagnosed with infectious spondylitis (pyogenic spondylitis in nine and tuberculous spondylitis in 24). Twenty-three patients (69.7%) were male. The median duration (first and third quartile values) of back pain prior to presentation was 30 days (14, 60) in the pyogenic group, and 30 days (15.75, 60) in the tuberculous group. There was no statistical difference between the groups (p=0.956).

In the pyogenic spondylitis group, six patients (66.7%) were male with a mean age of 55.5 years (range 3 months to 70 years). The mean age of tuberculous spondylitis patients was 47.8 years

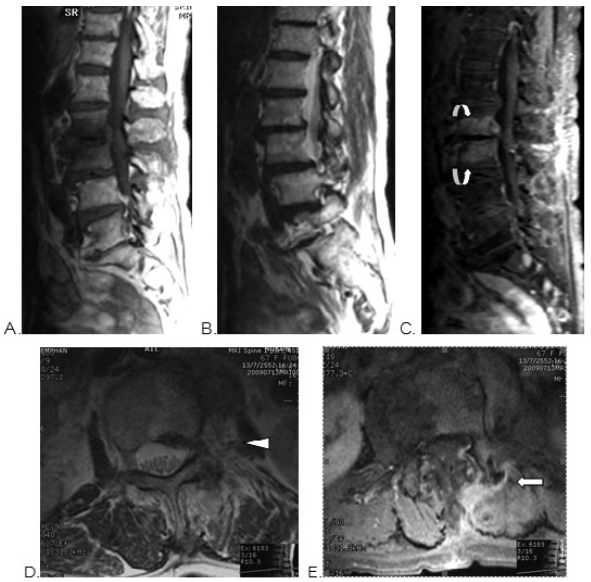

Fig 1–Pyogenic spondylitis caused by *Burkholderia pseudomallei* in a 68-year-old woman. (A) T1-weighted sagittal image (TR/TE=680/8.2) shows low signal intensity from L2-L3 vertebrae and exhibits high signal intensity in (B) a T2-weighted image (TR/TE=3000/92.7). Vertebral destruction less than 50% is also seen. (C) Fat-suppressed CE T1-weighted sagittal image (TR/TE=420/8.3) shows homogeneous enhancement of vertebral bodies (curved arrow). (D) T2-weighted axial image (TR/TE=3040/86.7) and (E) Fat-suppressed CE T1-weighted axial image (TR/TE=500/8.5) show ill-defined paraspinal soft tissue (arrowhead) and a thick irregular abscess wall (white arrow).

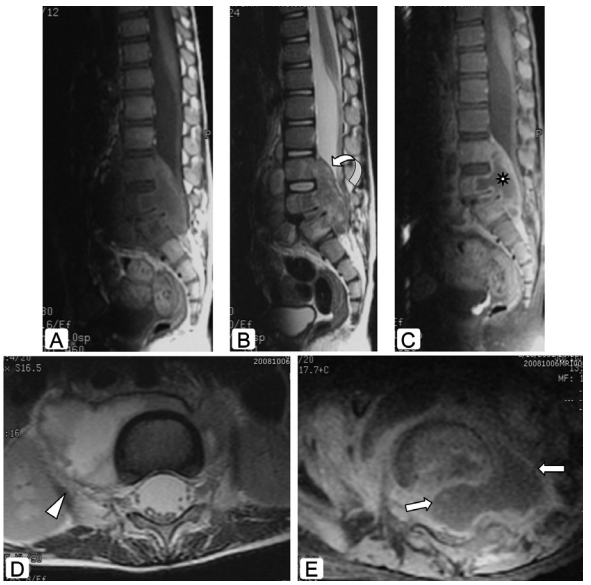

Fig 2–Tuberculous spondylitis in a three-year-old boy (A) T1-weighted sagittal image (TR/TE=580/8.6) and (B) T2-weighted sagittal image (TR/TE=3000/95) show heterogeneous abnormal signal intensity from L3-L5 vertebrae; also note large epidural extension and subligamentous spreading from L3 – S2 level (curved arrow). Preservation of L3/4 disc but narrowing of L4/5 disc is seen. (C) Fat-suppressed CE T1-weighted sagittal image (TR/TE=800/8.6) shows thin and smooth intraosseous abscess wall (asterisk) at L4 vertebral body. (D) T2-weighted axial image (TR/TE=5360/85.5) shows well-defined parasinal soft tissue (arrowhead). (E) Fat-suppressed CE T1-weighted axial image (TR/TE=680/7.6) shows thin and smooth abscess wall with epidural extension (white arrows).

(range 3-80 years) and 17 (70.8%) were male. The causative pathogens in pyogenic spondylitis were *Burkholderia pseudomallei* (two patients), *Burkholderia pseudomallei* and Group D *Streptococcus* (one patient), Group B *Streptococcus* (two patients), Group A *Streptococcus* (one patient), Group D *Streptococcus* (one patient), *Staphylococcus aureus* (one patient) and *Salmonella* sp (one patient).

Regarding pre-existing diseases, two patients in each group were diabetic, one patient in the pyogenic spondylitis group was cirrhotic and another was on steroid

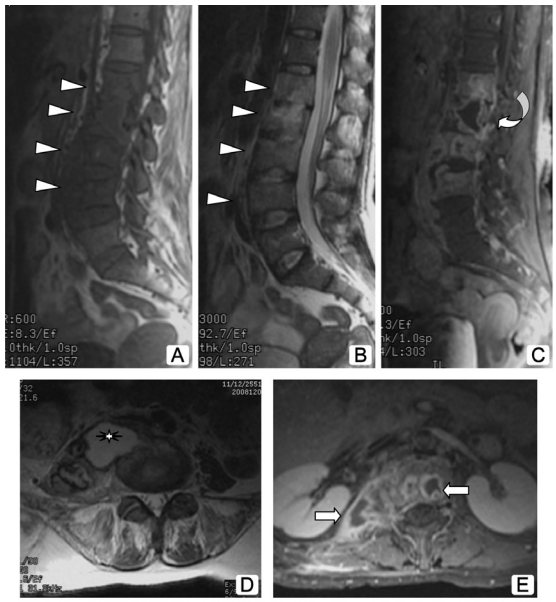

Fig 3–Tuberculous spondylitis in a 52-year-old woman. (A) T1-weighted sagittal image (TR/TE=600/8.3) and (B) T2-weighted sagittal image (TR/TE=3000/92.7) show heterogeneous abnormal signal intensity from L1-L4 vertebrae (arrowheads). (C) Fat-suppressed CE T1-weighted sagittal image (TR/TE=400/8.3) shows smooth-walled intraosseous abscess extending through the intervertebral disc at L1/2 and L2/3 (D) T2-weighted axial image (TR/TE=4421/92.1) shows well-defined paraspinal soft tissue (asterisk). (E) Fat-suppressed CE T1-weighted axial image (TR/TE=519/8.1) shows multiple thin and smooth abscess walls with epidural extensions (white arrows).

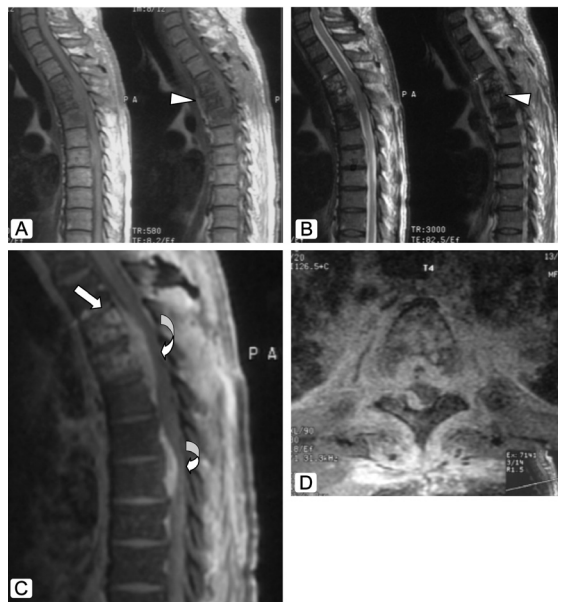

Fig 4–Another case of mellioid spondylitis in a 68 year-old woman with underlying polyarthritis treated with steroid therapy. (A) T1-weighted sagittal images (TR/TE=580/8.2) and (B) T2-weighted sagittal images (TR/TE=3000/82.5) show heterogeneous abnormal signal intensity from T3-4 vertebrae with vertebral endplate destruction (arrowhead). Epidural extension is also evident. (C) and (D) fat-suppressed CE T1-weighted sagittal and axial images (TR/TE=800/8.2 and 400/8.8) show multiple intraosseous microabscesses in T3 and T4 vertebral bodies (white arrow). Subligamentous spreading along the posterior longitudinal ligament with epidural extension from T3 to T7 was found (curved arrows). Poorly defined paraspinal soft tissue enhancement is demonstrated on the left side (D).

therapy for connective tissue disease. None of the patients was positive for HIV.

The results of MRI findings for tuberculous spondylitis and pyogenic spondylitis are summarized in Tables 1 and 2 and Figs 1-5. Tuberculous spondylitis was more common in thoracic or lumbar regions and had three or more vertebral spine involvements (Table 1). There was no common area or numbers of vertebral spine involvements in pyogenic spondylitis. When compared with pyogenic spon-

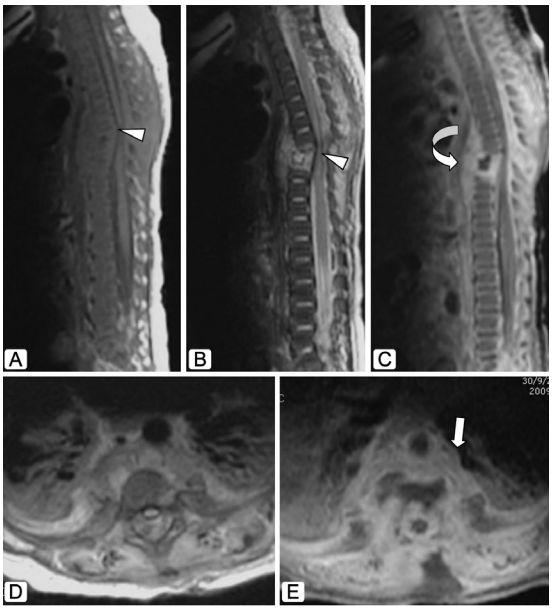

Fig 5–Staphylococcal spondylitis in a three-month-old girl. (A) T1-weighted sagittal image (TR/TE=720/8.5) and (B) T2-weighted sagittal image (TR/TE=3000/112) show severe T7-9 vertebral destruction with kyphosis (arrowhead). (C) Fat-suppressed CE T1-weighted sagittal image (TR/TE=540/8.5) shows subligamentous spreading along anterior longitudinal ligament from T5-T10 level (curved arrow); also noted is multilevel epidural soft tissue enhancement posterior to dural sac. (D) T2-weighted axial image (TR/TE=4360/86) shows ill-defined paraspinal soft tissue. (E) Fat-suppressed CE T1-weighted axial image (TR/TE=540/8.4) shows formation of an abscess with thick and irregular walls (white arrow) with epidural extension. Heterogeneous enhancement of paraspinal muscles is seen.

dylitis, tuberculous spondylitis was more common in the thoracic and lumbar spine and had more than 3 involved vertebrae (p= 0.01 for both factors).

Two significant findings differentiating tuberculous and pyogenic spondylitis were thin and smooth abscess walls (Fig 2C, $p < 0.001$) and well-defined paraspinal soft tissue (Fig 2D, $p = 0.007$). Both findings were much more frequent in tuberculous than pyogenic spondylitis; 75% thin and smooth paraspinal abscess walls in tuberculous spondylitis *vs* 0% in pyogenic spondylitis and well defined paraspinal soft tissue, 66.7% in tuberculous *vs* 11.1% in pyogenic spondylitis.

DISCUSSION

The symptoms and clinical findings in patients with spinal infection are often non-specific and vary depending on the site, extent, and severity of the pathological process (Trush and Enzmann, 1990). In tuberculous spondylitis, the infection usually begins within the anterior subchondral part of the vertebral body and may spread through the disc space into the adjacent vertebrae. Secondary subligamentous spreading in tuberculous spondylitis is frequent, usually beneath the anterior longitudinal ligament. However, spreading beneath the posterior longitudinal ligament can also be found. Epidural extension may cause a neural compromise (Jevtic, 2004). Due to lack of proteolytic enzymes in *Mycobacerium* spp, relative preservation of the intervertebral disc is proposed (Vidyalakshmi *et al*, 2008).

In pyogenic spondylitis, the common organisms are *Staphylococus aureus*, enterobacter, *Salmonella*, *Klebsiella*, *Pseudomonas* and *Serratia* spp. These organisms can produce enzymes, including hyaluronidase, resulting in lysis of the intervertebral disc (Jinkins *et al*, 1996). The source may be a urinary tract, pulmonary, pelvic or cutaneous infection, IV injection and, rarely, cellulitis, fasciitis, subcutaneous abscess or pyomyositis. Predisposing factors include

Table 3
MR features suggesting tuberculous spondylitis from previous studies and the present study.

Chang *et al* (2006)	Harada *et al* (2008)	Jung *et al* (2004)	Present study
Bone destruction grade 3 or more.	Well-defined paraspinal abnormal signal.	Well-defined paraspinal abnormal signal.	Well-defined paraspinal soft tissues.
Normal or mild disc destruction.	Thin and smooth abscess wall.	Thin and smooth abscess wall.	Thin and smooth abscess walls.
Well-defined post contrast paraspinal abnormal margin.	Presence of paraspinal or intraspinal abscess.	Presence of paraspinal or intraspinal abscess.	
Vertebral intraosseous abscess with rim enhancement.	Thoracic spine involvement.	Thoracic spine involvement.	
Heterogeneous and focal enhancement of vertebral body.			

diabetes mellitus, chronic renal failure, being immunocompromised by AIDS or an immunosuppressant, aging, alcohol abuse and IV drug addiction (Tali, 2004).

The two MRI findings indicative of tuberculous spondylitis in this study were abscesses with thin and smooth walls, and well defined paraspinal soft tissue. Previous studies also found that such abscesses were specific for tuberculous spondylitis (Jung *et al*, 2004; Chang *et al*, 2006; Harada *et al*, 2008). Five distinctive MR features for tuberculous spondylitis were bone destruction grade 3 or more; normal or mild disc destruction; well-defined post contrast paraspinal abnormal margin; vertebral intraosseous abscess with rim enhancement; and heterogeneous and focal enhancement of vertebral body (Chang *et al*, 2006). The other two studies listed above reported similar differentiating features (Table 3). Abscesses with thin and smooth walls and well-defined paraspinal soft tissues were the two compatible MR features among the four studies in various different Asian countries.

Unlike the situation in pyogenic infections, lack of proteolytic enzymes in *Mycobacterium* may spare intervertebral discs from destruction (Arizono *et al*, 1995). As mentioned earlier, tuberculous spondylitis commonly develops subligamentous spreading (Trush and Enzmann, 1990). Paraspinal soft tissue therefore is another significant MR feature for tuberculous spondylitis.

The sensitivity and specificity of these two MR features for differentiating between tuberculous and pyogenic spondylitis are calculated based on results in Table 2 (Table 4). Both MR features had fair sensitivity but quite high specificity and positive predictive values, implying that their simultaneous presence in patients with spondylitis indicates a tubercular

Table 4
Diagnostic properties of two significant MR features for differentiating between tuberculous and pyogenic spondylitis.

MR features	Sensitivity	Specificity	PPV	NPV
Thin and smooth abscess wall	75%	100%	100%	60%
Well-defined paraspinal soft tissues	66.70%	88.90%	94.10%	50%

PPV, positive predictive value; NPV, negative predictive value.

origin of the disease. The results of the present study are compatible with previous reports. Even though tuberculosis is a slow, progressive disease, the duration of symptoms prior to presentation between tuberculous and pyogenic spondylitis was comparable (p=0.956). MRI is therefore a crucial diagnostic tool for both diseases.

Several studies reported MRI findings such as thoracic spine involvement, multiple level involvements, collapse of vertebral bodies to less than 50% of their initial mass, intraosseous abscesses, epidural extension and subligamentous spreading more than three levels higher in tuberculous spondylitis (Jung *et al*, 2004; Chang *et al*, 2006; Harada *et al*, 2008). In the pyogenic groups, there were higher incidences of intervertebral disc destruction, homogeneous enhancement of the vertebrae and involvement of fewer than three vertebral bodies (Jung *et al*, 2004; Chang *et al*, 2006; Harada *et al*, 2008). Unlike these previous studies, we did not find significant differences in these MR features between tuberculous and pyogenic spondylitis in the present study (Table 2).

Melioidosis cases can mimick tuberculosis in several conditions such as pulmonary melioidosis, arthritis, spondylitis, lymphadenitis, splenic abscesses, pericarditis and parotid abscesses. In cases of melioid spondylitis, the patients had prolonged clinical symptoms with similar radiographic and MRI findings to tuberculous spondylitis (Vidyalakshmi *et al*, 2008). In the current study, there were two cases of isolated melioidosis in the pyogenic group. One case had multiple intraosseous microabscesses with a three-level involvement, which mimics tuberculous spondylitis (Fig 1), while the other case lacked these features.

Unusual forms of spinal TB have been described as isolated posterior element involvement, solitary vertebral body destruction, skip lesions, extradural lesions without vertebral body involvement, destructive lesions of the sacrum with pelvic mass, vertebral osteomyelitis forms and body destruction with intramedullary involvement (Shanley, 1995; Tali, 2004). In the present study, there were five cases (20.8%) of skip lesions in the tuberculous spondylitis group and one in the case of staphylococcal pyogenic spondylitis.

The strength of this study is it is from an area endemic for tuberculosis. Data regarding MR features in tuberculous and bacterial spondylitis in the literature are limited.

In conclusion, thin and smooth abscess walls, and well-defined paraspinal soft tissues were two MRI findings that may be helpful for differentiating between tuberculous and pyogenic spondylitis.

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