SPONDYLODISCITIS DESEASE EVALUATION IN PATIENTS WITH SERONEGATIVESPONDYLOARTHROPATHIES

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Abstract

Spondylodiscitis (SD) is a destructive discovertebral lesion which is uncommon, but well recognised as a complication of Ankylosing Spondylitis (AS), and also called the Andersson lesion. This prospective study described 24 cases of AS, 12 of them with SD with variable clinical presentation and radiological appearance (SD). Two had multiple lesions, in one patient spondylodiscitis was the presenting symptom of AS. None had a history of even a minor trauma and radiological appearance of Andersson lesion in AS.

In a prospective analysis of 24 patients with ankylosing spondylitis (AS) with multiple nationalities, 12 individuals (50%) had spondylodiscitis, affecting the spine at various levels, we described the demographic data, full medical history, clinical examination and radiological findings including thoracolumbar spinal magnetic resonance imaging (MRI) in all patients diagnosed as SD with AS admitted to our department. All patients were fulfilling the modified New York criteria and ASAS criteria for AS.

The results showed that the mean age of patients was 43 ± 10.8 yrs, 16 (66.667%) were males. Half of the 12 patients had multiple lesions (between two and six levels). Mean disease duration were 11±8.7. The most common site of lesion was the thoracic spine

The prognosis was good with conservative treatment including NSAID's, rest, and physiotherapy. The literature was reviewed regarding the mechanisms that may contribute to these lesions: mainly inflammatory like increasing enthesopathy or mainly mechanical like pseudo-arthrosis about a fracture site. It might be that both mechanisms could result in similar destructive intervertebral disc lesions.

Keywords: Spondylodiscitis, Andersson lesion, Ankylosing Spondylitis, Radiograghs, MRI.

Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease primarily affecting the spine and sacroiliac joints, causing pain, stiffness and progressive thoracolumbar kyphotic deformity (Bron *et al,* 2009).

Late in the disease, the spine shows progressive ossification of the annulus fibrosis, anterior longitudinal ligament, apophyseal joints, interspinous and flaval ligaments ligament resulting in a complete ankylosed spine, often referred to as a bamboo spine (McGonagle *et al,* 2006).

A well-known complication is the development of a localized vertebral or discovertebral lesions of the spine, first described by Andersson (1937). The exact prevalence of discovertebral lesions complicating AS in literature is unknown, but reported prevalences range from 1.5% to over 28% (Rasker *et al,* 1996; Kabasakal *et al,* 1996; Langlois *et al,* 2005). The etiology of AL is either aseptic inflammation or mechanical factors (stress fractures). Diffe-rent terms used to refer to the lesions include Discovertebral lesion, vertebral lesion, destructive vertebral lesion, spondylodiscitis, discitis, diskitis, sterile diskitis, pseudoarthrosis or (stress) fracture. The lesions can be either localized or extensive. Radiologically lesions may be pseudodystrophic, pseudotuberculuos, extensive erosions, bone condensation or isolated narrowing of inter-vertebral spaces. Anderson lesion usually involves only one single spinal level with thoracolumbar junction being the most common affected site, often mis-diagnosed as tuberculous lesion (Dave *et al,* 2011).

The SD on MRI simulates a malignant lesion. In case of metastatic spinal lesions intervertebral disc height is usually preserved but this may be affected in lymphoma and multiple myeloma. Vertebral endplates are also distinct and usually regular. The posterior vertebral segments are more extensively affected early in malignant lesions. An acute presentation, no prior diagnosis of AS, appearance of lesion on MRI suggestive of infection, high prevalence of Pott's spine in endemic areas (suspicion bias) and lack of awareness about the SD, can account for misdiagnosis at various levels. Misdiagnosis leads to unnecessary financial and psychological burden in form of unwanted investigations, biopsy, treatment with antibiotics, ATT and surgical intervention (Dhakad *et al,* 2013). Localized vertebral/discovertebral lesions in an ankylosed spine on x-ray are characteristic of SD. Although the diagnosis of SD can be well established by x-ray spine, yet CT or MRI may provide greater details of the lesion. Biopsy is not required for diagnosis of SD in a typical case scenario. Conservative management was mainstay of treatment and surgical intervention was only required for progression of symptoms, unbearable pain, kyphotic deformity or neurological symptoms (Bron *et al,* 2009).

The objective of the study was to assess the variable clinical presentation and radiological appearance of SD in AS and to differentiate it from radiological findings of malignant, tuberculosis lesions that affect the spines.

Subjects, Materials and Methods

Research question: The research question for the purpose of this study is: 'What are the main radiological features for the diagnosis of SD in patients with AS?"

Research method and design: This was a prospective study carried out at Department of Rheumatology at El-Tahrir Medical Center in Doha - Qatar, from October 2012 till December 2015, AS patients were derived from the outpatient clinics.

Study sample: The study population comprised 24 patients diagnosed as AS proven to fulfill the modified New York criteria according to international ASAS consensus statement (Braun *et al,* 2006) were included, patients were considered to have an active disease as defined by a bath ankylosing spondylitis disease activity index (BASDAI) of ≥4 (scale 0–10) after Garrett *et al*. (1994).

Patients were enrolled consecutively, but mainly because of limited availability of the MR scanner, several patients were not included. Furthermore, one patient did not fit into the scanner due to severe kyphosis, and several patients suffered from claustrophobia.

The study participants were recruited from the outpatient clinic, with mean age of patients was 43±10.8yrs. All the patients received adequate information about the study and written consents were obtained before enrollment. The protocol was approved by the ethics committee of the hospital.

The eligibility criteria were: Patients diagnosed with AS on the basis of ASAS diagnostic criteria and whose lumbar MRIs confirmed the presence of AS were included in the study.

Exclusion criteria were 1- Patients with history of DM, 2- Patients with history of hypercholesterolemia, 3- Patients with history of hypertriglyceridemia, 4- Patients with history of kidney failure, 5- Patients with vertebral fracture, spinal tumor, severe kyphosis, and spondylodiscitis and with degenerative air or calcification in the disc space at radiography or MRI, 6- Cigarette smokers and/or 7- Patients using TNF-α blockers.

The patients were subjected to a detailed history taking, a thorough physical examination and Laboratory examination: Erythrocyte sedimentation rate (ESR), C reactive protein (CRP) and Bath Ankylosing Spondylitis Activity Index (BASDAI) which measures disease activity, and the Bath Ankylosing Spondylitis Functional Index (BASFI), which measures functional status,

in patients with AS were determined. Body mass index (BMI) was calculated in patients with AS using the formula weight divided by height squared (kg/m2).

Radiology study: Standing anteroposterior and lateral full-length plain films and MRI of the whole spine were performed, starting from the third cervical vertebra (C3) and downwards. The conventional radio-graphs were analyzed followed by an assessment of the MRI to provide better definition of the spinal lesions and to show the extent of the inflammatory process. Spondylodiscitis was defined by destructive or sclerotic changes with or without reduction of height of the vertebral body and a narrowed disc space.

Statistical analysis: Data were computerized and analyzed by the SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) release 15 for Microsoft Windows (2006). Description of quantitative variables as mean and SD and range: A- Description of qualitative variables as number and %. B- Continuous variables were reported as the M±SD or, if skewed, as the median (range). Categorical variables were calculated as frequencies and percentages. C- Correlation co-efficient test was used to rank variables against each other positively or inversely. The P value>0.05 was insignificant, P<0.05 significant* & P<0.01 highly significant**.

Ethical Aspects: The protocol for the study was approved by the Ethical and Research Committee of Al-Azhar University's Hosp-itals. The purpose of this research study was explained to the participants. The data were collected only after the informed consent had been signed by all patients.

Results

The study population comprised 24 cases of AS with multiple nationalities, 12 of them with SD recruited were selected from the outpatient clinic. Data collected from the patients were the age, disease duration and symptom duration as well as full detailed history for detection of any diseases. Also past surgical and medical history were taken. Mean age was 43±10.8yrs, 16 (66.667%) were males. 12 individuals (21.429%) had spondylodiscitis, ages of 12 spondylodiscitis cases at the time of radiographic evaluation ranged from 31 to 72yr (mean age 49.1±12.7yrs). Six patients had multiple lesions (between two and six levels). Mean disease duration were 11±8.7.

As evident, the commonest site of lesion was thoracic 7 (58.333%) cases and only 3 (25%) in the cervical region. Sacroiliac involvement was only observed in the patient with chronic recurrent multifocal osteomyelitis (case 6). Other joint and bone conditions consisted of knee arthritis in one patient (case 2), anterior chest wall involvement in four patients (cases 1, 2, 7, & 8) three with sternoclavicular arthritis and one with sternocostoclavicular hyperostosis), proximal interphalangeal joint arthritis in one patient (case 1), and tibial aseptic osteomyelitis in one patient (case 7).

Table 1: Baseline characteristics of study subjects; (*n*: 24).

	Mean ± SD	Range
Number	24	
Age (in years)	43 ± 10.8	22–73
Male (%)	16	68 %
Disease duration (in years)[a]	11 ± 8.7	1–41
Symptom duration (in years)[b]	21 ± 11.3	1–49
BASDAI (0–10)[c]	6.4 ± 1.4	4.0–9.7
Tragus-to-wall distance (cm; normal, <15 cm)	16 ± 6.0	11–44
Lumbar flexion index (cm; normal, >5 cm)	2.5 ± 1.2	0.3–5
Lumbar side flexion (cm; normal, >10 cm)	10 ± 4.9	3.8–19
Chest expansion (cm; normal, >5 cm)	3.4 ± 1.5	0.5–7

a= Disease duration: mean time between diagnosis and baseline, b= Symptom duration: mean time between first symptoms and baseline, c= BASDAI: bath ankylosing spondylitis disease activity index; mean value, 11

Table 2: Clinical features and HLA B antigens

Patient	Location of back pain	Clinical measures	Other bone and/or joint involvement
1	Thoracic	Chest expansion: + 4 cm	Sternoclavicular and interphalangeal joint arthritis
2	Thoracic and lumbar	Schober's score: + 1 cm	Knee and sternoclavicular arthritis
3	Cervical	Cervical spine range of movement: limited in all range of motion	None
4	Lumbar	Schober's score: + 0 cm	None
5	Thoracic	Chest expansion: + 4 cm	None
6	Lumbar and sacral	Schober's score: 0 cm	Sacroiliac joints
7	Thoracic	Chest expansion: + 4 cm	Sternocosto-clavicular hyperostosis and tibial osteomyelitis
8	Thoracic	Schober's score: + 3 cm	Sternocosto-clavicular arthritis
9-12	Thoracic	Schober's score: + 3 cm	Sternocosto-clavicular arthritis

These patients complained of backache, with fever, which occurred only in one patient (case 2, 37.8°C). A reduced spine movement range at the level of spine involvement was observed for each patient with spondylodiscitis (Tab. 2)

Table 3: Radiological, and MRI features

Patient	Spinal radiography	Magnetic resonance imaging
1	Spondylodiscitis T7-T8	T1: Decreased signal T6,T7,T8, T1 + gado: increased signal T6,T7,T8
2	Spondylodiscitis L1-L2, Spondylodiscitis T9-T10	ND
3	Spondylodiscitis C6-C7-T1 then C5-C6-C7-T1	T1: Decreased signal C7-T2: Increased signal C5,C6 +disc spaces C6-C7,C7-T1
4	Spondylodiscitis L4-L5	T1 and T2: Spondylodiscitis sequelae. No increased signal
5	Spondylodiscitis T8-T9	ND
6	Spondylodiscitis L3,L4,L5	ND
7	Spondylodiscitis T9-T10	ND
8	Spondylodiscitis T6-T7 L4-L5	T1 and T2: Spondylodiscitis sequelae. No enhanced signal
9-12	Spondylodiscitis T6-T7	T1 and T2: Spondylodiscitis sequelae. No enhanced signal

ND, not determined; gado, gadolinium

This table showed that the destructive and sclerotic changes of lumbar vertebral bodies without narrowing of disc spaces were observed in the patient with chronic recurrent multifocal osteomyelitis (case 6) and this corresponded more to a spondylitis than a spondylodiscitis Other patients presented one or more examples of spondylodiscitis on x ray (one patient in the cervical spine: case 3; five patients in the thoracic spine: cases 1, 2, 5, 7, and 8; and three patients in the lumbar spine: cases 2, 4, and 8), with narrowed disc space and erosive and sclerotic remodelling in the opposite regions of the vertebral bodies .

In six patients (cases 2, 8, 9, 10, 11 &12), destruction of the entire vertebral junction (T9-T10 and T6-T7 respectively) was observed. No infectious lesion such as abscess was shown.

The MRI showed decreased signal intensity on T1 weighted sequence in thoracic vertebral bodies enhanced after injection of gadolinium (case1), while the disc spaces showed no increased signal. In the cervical spondylitis (case 3), similar signal abnormalities were observed in the cervical vertebral bodies. However, an intense signal was observed in the C6-C7 and C7-T1 disc spaces, corresponding to discitis associated with contiguous spondylitis. However, neither abscesses nor epiduritis were recorded.

Table 4: Mean values of Bath ankylosing spinal functional index † and
t Bath ankylosing spondylitis disease activity index ††:

BASFI †	P-value
6.0±1.9	0.45
BASDAI ††	P-value
5.9±2.0	0.53

Bath ankylosing spinal functional index † and the Bath ankylosing spondylitis disease activity index ††
not significantly correlated to t disease activity.

Discussion

Spondylodiscitis is rare and, with nonspecific initial signs and symptoms, a delay before diagnosis and treatment often occurs.

The average duration between the first symptoms and diagnosis is reported to be between two and six months (Zarghooni *et al,* 2012). Spondylodiscitis refers to the primary infection of the intervertebral disc by a pathogen and secondary osteomyelitis of the adjacent end-plates, usually occurring in the conjunction with one another. The incidence of spondylodiscitis varies in the developed countries between 1:100,000 and 1:250,000 (Butler *et al,* 2006) and considered the main manifestation of haematogenous osteomyelitis in patients aged over 50 years and represents around 3-5% of all cases of osteomyelitis (Sobottke *et al,* 2008) yet it occurs as a late non-inflammatory sequel in ankylosing spondylitis (Dave *et al,* 2011).

The presenting symptoms in cases of SD were mechanical pain, deformity, and occasional neurological deficit (Mundwiler *et al,* 2008). In case of longstanding ankylosing spondylitis, the physicians tend to ignore the symptom of pain. Unfortunately, it has been shown that in a large percentage of cases, the correct diagnosis is not established until after the patient has already experienced a decline in neurologic function.

In the present study, recruited 24 AS patients from Department of Rheumatology El-Tahrir Medical Center in Doha, Qatar, 16 were males (66.667%) from the outpatient clinic, without significant difference between the patients with AS regards sex. The mean disease duration was 11±8.7. The AS duration at the time of spondylodiscitis diagnosis ranged from 20 to 30yr (mean 20 yr)

as confirmed by other authors (Cawley *et al,* 1972; Litde *et al*, 1978). This result agreed with the present study findings. By radiographic evaluation 12 individuals (21.429%) had spondylodiscitis, and MRI had proven to have primary spondylodiscitic lesions at multiple levels, in absence of classical spinal syndesmophytosis. These latter findings, together with the tendency for intervertebral bony bridges to form, have suggested a different pathogenetic mechanism for this particular type of spondylodiscitis. In our 12 patients some clinical and radiological and MRI findings display peculiar features which distinguish them from classical AS. Radiological findings consisted of erosive or sclerosing remodelling of endplates with a narrowed disc space; a reduced height of the vertebral body was also observed in some cases. These spinal lesions occurred in the three vertebral segments. Multiple sites of spondylodiscitis in the same patient were common. MRI was useful for excluding the presence of infection. Enhanced signals on T2 weighted sequence or after injection of gadolinium were often observed. Chest wall involvement was observed in four cases and sacroiliac joint lesions only in the case with osteomyelitis.

Hermann *et al*. (2005) compared MRI and conventional radiography of spinal changes in patients with spondylodiscitis. They concluded that the best way to detect syndesmophytes was through radiography; ankylosis was detected equally well by both radiography and MRI, but for all other lesions, MRI was the preferred method.

A disadvantage of conventional radiographs of the spine is the difficult analysis of the vertebrae of thoracic segment because of

the over-imposed of the lung tissue (Braun et al, 2004).

In the present study, most disorders of the discovertebral junction occurred in the lower part of the thoracic and upper parts of the lumbar spine, which comes in agreement with others (Baraliakos et al, 2005; Braun et al, 2002).

Some MRIs in the present study showed features of severe degenerative disk disease, specifically in thoracic regions. The MRI features of these degenerative abnormalities were sometimes difficult to distinguish from destructive discovertebral lesions as was described that the appearance of an SD can resemble Modic type III degenerative lesion (Jevtic et al, 2000).

One point to differentiate between SD and degenerative disk disease in AS was the fact that SD occurs as a result of inflammation in combination with mechanical stress of the ankylosed spine. The second point is that AL differs from degenerative disk disease in the localization, because most AL lesions occur at the level of the cervical and thoracolumbar spine, whereas the degenerative disk disease predominates at the lumbosacral level (Bron et al, 2009).

Also, in the present study, in cases of the BASDAI was higher than 4 points, the control of the disease activity was not appropriate, and thus they could be considered as cases requiring the consideration of the change of therapeutics.

This could be thought to be due to first, the BASFI was a visual analogue scale measurement instrument; on the other hand, the BASFI is an evaluation that assesses whether specific activity could be performed in ankylosing spondylitis patients (Park et al, 2011). This was also not surprising, since disc degeneration is a progressive process and BASDAI reflects disease activation in the most recent period. Additionally, these findings proved a worsening in BASFI while BASDAI remained relatively stable in a five year follow-up of patients with AS (Robertson and Davis, 2004).

The role of laboratory tests was limited. Both erythrocytes sedimentation rate and C-reactive protein levels may be elevated in patients with SDs, but this is of little diagnostic value (Langlois et al, 2005; Finkelstein et al, 1999; Unsal et al, 2002). Both parameters were usually more associated with the involvement of peripheral joints (Ozgocmen et al, 2007) White blood count and blood cultures are of no additional diagnostic value (Bron et al, 2009).

Conclusion

The outcome results showed 1- Spondylodiscitis may occur in patients with AS, 2- these patients have early onset of disease, 3- multiple-level lesions in the spine are not uncommon among those with spondylodiscitis and 4- lesions are usually asymptomatic.

Spondylodiscitis was documented in patients with AS. Some authors suggest that this could be a possible late complication of the classical AS, following a known or suspected trauma upon an ankylosed spine. Others think that these unusual signs might be related to the same inflammatory mechanism of the primary disease, yet the exact mechanism needs further studies.

High index of suspicion was required in patients of late AS presenting with recent onset new pain. Thorough clinical and radiological assessment should be performed, yet MRI was considered a valuable tool to characterize SD.

Recommendations

Future studies are ongoing to evaluate the role of HLA typing particularly B27 in the etiology of SD, yielding an opportunity to improve the disease outcome. Randomized trials with adequate power are needed to assess the role of MRI in assessing the degree of affection for postulating the effective treatment. More research with a long-term follow-up of SD in AS patients is ongoing to clarify the evolution of these lesions.

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