Early Diagnosis of Spondyloarthropathies

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Introduction

Spondyloarthropathies are chronic inflammatory rheumatic disorders that are characterised by sacroiliitis, ascending spondylitis, enthesitis, extra-articular manifestation and genetic factor predisposition (HLA B27). They include ankylosing spondylitis (AS), psoriatic arthritis, reactive arthritis, and arthritides associated with inflammatory bowel disease.

Patients suffering from early spondyloarthropathies may not seek medical attention because of lack of awareness of their underlying conditions. Patients with advanced disease have significant restriction of movement of the trunk and neck leading to impairment in their activities of daily living. Early diagnosis can help counsel these patients and maintain spinal mobility by physiotherapy and achieve symptomatic control by the use of non-steroidal anti-inflammatory drugs. Recent advances in medical treatment using anti-tumour necrosis factor-α (anti-TNF-α) have shown significant symptomatic and radiological improvement.

Psoriatic arthropathies
Psoriasis affects 1-2% of the general population and around 10% of patients with skin psoriasis develop arthritis. The disease may start at any age. Joint involvement occasionally occurs prior to the development of psoriatic skin disease. About 70% of patients with psoriatic arthritis show evidence of nail dystrophy including pitting, ridging and onycholysis compared with only 20% of patients without arthritis.

Psoriatic arthropathies may take one of the five patterns of joint involvement: distal interphalangeal joints, oligoarticular, rheumatoid arthritis like, spondyloarthropathy and arthritis mutilans.

Reactive arthritis
This inflammatory joint disease typically follows a genitourinary or gastrointestinal infection. Gram negative bacteria including Chlamydia trachomatis, Shigella, Salmonella, Yersinia and Campylobacter have been implicated in the underlying pathogenesis. There is typically arthritis involving lower limb joints that resolves within 3-6 months. Around 40% of patients develop persistent erosive arthritis.

Enteropathic arthropathies
Approximately 10% of patients with inflammatory bowel disease develop peripheral arthritis. Arthropathies are more commonly seen in patients with Crohn’s disease than in ulcerative colitis. Oligoarticular involvement of lower limb joints may develop in some patients. AS occurs in around 5-10% of patients with Crohn’s disease.

Early Diagnostic Features Of Spondyloarthropathies

Back pain
Limited spinal mobility is a cardinal feature of spondyloarthropathies. Low back pain is one of the earliest symptoms of lumbar spondylitis. A distinction should be made in regard to the nature of pain being inflammatory or mechanical. Mechanical back pain is brought on by exercise. Inflammatory back pain should be alerted if it is of insidious onset in a patient younger than 40 years that persists for more than 3 months and is associated with morning stiffness that improves with exercise. Clinical history has been found to be useful as a screening tool for detection of patients with AS in the out-patient setting.

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Inflammatory back pain gives satisfactory sensitivity (71.4%) and specificity (77.3%) in the diagnosis of early spondyloarthropathies. The early plain radiographic abnormalities of spondylitis may appear as marginal sclerosis with shiny corners at the margin of the intervertebral disk which may best be seen in MRI. New bone along the anterior vertebral margin results in squared appearance of lumbar vertebrae. With time, the spinal ligaments ossify forming vertically oriented bony bridges between the vertebral bodies called syndesmophytes. The posterior apophyseal and costotransverse joints become fused. In advanced disease the whole spine is rigidly fused and becomes a solid block of bone and is known as ‘bamboo’ spine.

Chest wall pain and limited chest expansion
Anterior chest pain may occur as a result of arthritis of the manubriosternal, sternoclavicular and costosternal joints. Together with limited chest expansion, chest wall pain is commonly seen in thoracic spinal involvement. Reduced chest expansion, especially of less than 5 cm, represents advanced forms of spondylitis and is of limited value in differentiating normal from early cases of spondylitis.

Restricted spinal movement
The clinical course of spondyloarthropathies is characterised by ascending spondylitis with gradual sequential involvement of the lumbar, thoracic and cervical spine. Limited spinal mobility is one of diagnostic criteria for spondyloarthropathies. Ankylosis is a late feature and is a result of ossification of ligaments, vertebrocostal and sternocostal joints. This eventually forms the classical “bamboo spine”. Limitation in flexion and extension, rotation and lateral flexion of the lumbar spine may be detected in patients with early disease. However, the measurement is poorly standardised in clinical practice. Limited spinal motion appears to reflect the disease duration rather than a diagnosis of early disease.

Sacroilitis
Unilateral or bilateral buttock pain is one of the earliest symptoms of sacroilitis. The pattern of involvement of the SI joints being unilateral or bilateral may also give a clue to the underlying diagnosis. AS typically involves both SI joints whereas unilateral sacroilitis is more usually found in psoriatic spondyloarthropathy, Reiter’s disease and enteropathic spondyloarthropathies. There may be tenderness over one or both SI joints on palpation but radiological imaging offers higher sensitivity for detection. Plain X-ray of the SI joints is simple to perform. Despite the high specificity, it showed a poor sensitivity in diagnosing spondyloarthritides. Radiological changes usually take three to seven years to develop and are the characteristics of advanced disease. A grading system has been devised depending on the chronic radiographic changes (Table 1). The earliest radiological change (Grade I) involve irregular fuzzy outlines of the joint margins that can be non-specific and may be difficult to differentiate from degenerative and infective changes of the SI joints. Grade 2 lesions show up as early erosion with sclerosis of the joint but may take years to develop. Eventually the process leads to obliteration of the joint space (Grade 4).

Computerized Tomography (CT) of the SI joints may allow detection of structural changes and is superior to conventional radiography for detecting bony changes related to sacroilitis. Magnetic resonance imaging (MRI) can detect bone oedema and fatty conversion in the subchondral marrow, features of early sacroilitis. It can also demonstrate joint inflammation in the synovial joint. However, the MRI grading has not been standardised and their role in diagnosis is still under investigation. There is no firm consensus on the relative merits of CT versus MRI in the diagnosis of sacroilitis. MRI is superior in the detection of both cartilage abnormalities and erosions whereas CT is superior to MRI in the detection of new bone formation and ankylosis. Scintigraphy is an alternative method to detect sacroilitis but the sensitivity and specificity is lower than with other imaging techniques. Areas of increased uptake of radioisotope may suggest pseudoarthrosis or fractures that may complicate the clinical course in patients with advanced disease.

Family history
The development of spondyloarthropathies is strongly linked to HLA B27 haplotype. The haplotype is prevalent in all forms of spondyloarthropathies especially AS and is inherited in an autosomal co-dominant fashion. The risk of developing AS in a person with positive family history is 20 to 40 times higher than the general population. Fifty percent of first degree relatives of HLA-B27 positive individuals possess the antigen. The prevalence of HLA B27 among spondyloarthropathies and general population is shown in Table 2. HLA B27 is present in around 10% of normal population but in 90% of patients with AS. It has a high negative predictive value and is useful in early screening of the disease. The presence of HLA B27 and/or family history of spondyloarthropathies show high specificity in diagnosis when associated with inflammatory back pain.

Enthesitis
Inflammation of the entheses, the sites of ligamentous attachment to bones, is one of the prominent features of spondyloarthropathies. Patients commonly complain of pain over the heel or the sole of the foot on walking. Tenderness can be elicited on the Achilles tendon and plantar fascia for detection of enthesitis at these sites. Clinical examination has only low sensitivity in detecting enthesitis. The role of MRI and ultrasonography as a more accurate tool in detecting enthesitis is currently under evaluation.

Peripheral arthritis
Some patients with spondyloarthropathies also have peripheral arthritis and may present with dactylitis, asymmetrical monoarthritides, oligoarthritis or a pattern simulating rheumatoid arthritis. There is usually a predominant involvement of joints of the lower limbs. In Reiter’s disease, few joints are involved and there may be calcaneal erosions with spur formation that can be detected on Xray.

Extra-articular features
Extra-articular manifestations of spondyloarthropathies include inflammatory bowel disease, psoriasis, urethritis and anterior uveitis. These specific features
help to differentiate the particular sub-types of spondyloarthropathies. For example, anterior uveitis is more common in patients with AS (a prevalence of 40%) and skin psoriasis and nail dystrophy suggest psoriatic arthropathy. Other features such as fibrosing alveolitis, aortic incompetence, amyloidosis, balanitis and iritis may aid in diagnosis of spondyloarthropathies.

Conclusion

With the development of new therapies, there is a need to recognise patients with early disease who have worse prognosis. The inflammatory nature of back pain obtained from clinical history is helpful in the early diagnosis of spondyloarthropathies. Clinical sacroiliitis lacks the specificity and radiological sacroiliitis is too insensitive to be useful in early diagnosis. The emerging technique of ultrasound and MRI are future tools in assisting early diagnosis. Other useful information includes tissue-typing and family history. Particular extra-articular features help to differentiate the sub-types of spondyloarthropathies.

With the development of new biologic therapies, early recognition of patients with early stage of disease, together with information from future researches on identifying patients with worse prognosis and better response to treatment for earlier therapy will be of great benefit.

Table 1. Modified New York criteria for ankylosing spondylitis.

<table>
<thead>
<tr>
<th>Clinical criteria</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low back pain and stiffness for &gt;6 months that improves with exercise but is not relieved by rest</td>
<td>Grade II bilateral sacroiliitis</td>
</tr>
<tr>
<td>Limitation of motion of the lumbar spine in both sagittal and frontal planes</td>
<td>Grade III or IV sacroiliitis unilaterally</td>
</tr>
<tr>
<td>Limitation of chest expansion relative to normal values for age and sex</td>
<td></td>
</tr>
<tr>
<td>Radiological criteria</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Grading of chronic radiographic changes of the sacroiliac joint in ankylosing spondylitis.

<table>
<thead>
<tr>
<th>Grade</th>
<th>X-ray findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal</td>
</tr>
<tr>
<td>1</td>
<td>Suspicious</td>
</tr>
<tr>
<td>2</td>
<td>Sclerosis, some erosion</td>
</tr>
<tr>
<td>3</td>
<td>Severe erosion, widening of joint space, minor ankylosis</td>
</tr>
<tr>
<td>4</td>
<td>Complete ankylosis</td>
</tr>
</tbody>
</table>

Table 3. Prevalence of HLA B27 haplotypes in various spondyloarthropathies

<table>
<thead>
<tr>
<th>Spondyloarthropathies</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ankylosing spondylitis</td>
<td>90</td>
</tr>
<tr>
<td>Reactive arthritis</td>
<td>75</td>
</tr>
<tr>
<td>Psoriatic arthropathy</td>
<td>50</td>
</tr>
<tr>
<td>Enteropathic arthropathy</td>
<td>50</td>
</tr>
<tr>
<td>General population</td>
<td>10</td>
</tr>
</tbody>
</table>

References

1. Peloso PM, Braun J. Expanding the armamentarium for the spondyloarthropathies. *Arthritis Res Ther* 2004; Suppl 2: 36-43

MCHK CME Programme Self-assessment Questions

Please read the article entitled “Early diagnosis of spondyloarthropathies” by Dr Ho-yin Chung, Dr. Mo-yin Mok and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded 1 CME credit under the Programme for returning completed answer sheet via fax (2865 0345) or by mail to the Federation Secretariat on or before 30 November 2006. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Questions 1-10: Please choose the best answer.

1. Which of the following diseases do not belong to spondyloarthropathies?
   a. Ankylosing spondylitis
   b. Rheumatoid arthritis
   c. Psoriatic arthropathy
   d. Inflammatory bowel disease related arthritis

2. What of the following is not a pathological characteristic of spondyloarthropathies?
   a. Sacroiliitis
   b. Enthesitis
   c. Osteoarthritis
   d. Spondylitis

3. Which of the following is not an early symptom of presentation of spondyloarthropathy?
   a. Neck pain
   b. Back pain
   c. Buttock pain
   d. Back stiffness
4. Which of the following is most sensitive in the detection of early sacroiliitis?
   a. Plain X-ray
   b. Magnetic Resonance Imaging
   c. Scintigraphy
   d. Tenderness on sacroiliac joint

5. Which of the following pattern of peripheral arthritis is seen in spondyloarthropathies?
   a. Oligoarticular
   b. Rheumatoid arthritis-like
   c. Monoarticular
   d. All of the above

6. Which of the following are predictive of psoriatic arthritis in a patient with skin psoriasis?
   a. Nail dystrophy
   b. Extensive psoriatic skin plaques
   c. Erythroderma type of skin psoriasis
   d. Family history of skin psoriasis

7. Which of the following is not an extra-articular manifestation of spondyloarthropathies?
   a. Cardiac valvular defect of aortic regurgitation
   b. Uveitis
   c. Generalised lymphadenopathies
   d. Apical lung fibrosis

8. Which of the following is poor prognostic factor in spondyloarthropathies?
   a. Male
   b. Female
   c. Hip involvement
   d. Family history

9. Which of the following is compatible with advanced spondyloarthropathies?
   a. Restricted movement of the neck
   b. Limited chest expansion
   c. Bamboo spine on X-ray of the lumbosacral spine
   d. All of the above

10. What is the biologic treatment that has currently been shown to be efficacious in the treatment of ankylosing spondylitis?
    a. Anti-CD20 antibody
    b. Anti-tumour necrosis factor-alpha therapy
    c. Methotrexate
    d. Mycophenolate mofetil

Please return the completed answer sheet to the Federation Secretariat on or before 30 November 2006 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

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Answers to October 2006 issue

Endocrine Hypertension-Strategy for Screening and Workup