Diffuse Idiopathic Skeletal Hyperostosis: Differentiation From Ankylosing Spondylitis

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Diffuse idiopathic skeletal hyperostosis (DISH) and ankylosing spondylitis (AS) share involvement of the axial skeleton and peripheral entheses. Both diseases produce bone proliferations in the later phases of their course. Although the aspect of these bone proliferations is dissimilar, confusion of radiologic differential diagnosis between the two diseases exists mostly as a consequence of a lack of awareness of their characteristic clinical and radiographic features. The confusion may extend to the clinical field because both advanced DISH and advanced AS may cause the same limitations of spinal mobility and postural abnormalities. However, the radiologic spinal findings are so different that changes due to each disease can be recognized even in patients in whom both diseases occur. This article reviews the clinical and radiologic characteristics that should help clinicians differentiate between the two diseases without much difficulty.

Introduction

Diffuse idiopathic skeletal hyperostosis (DISH), also known as ankylosing hyperostosis, is a totally different disease from ankylosing spondylitis (AS), although they share the involvement of the axial skeleton and the peripheral entheses [1,2]. Both diseases produce bone proliferation in the spine and at the extraspinal entheseal sites in the later phases of their disease course. Although the aspect of these bone proliferations is dissimilar, confusion of radiographic differential diagnosis between the two diseases exists mostly as a consequence of a lack of awareness of their characteristic features [2,3]. In fact, Khan [4] pointed out the error when a patient was reported suffering from AS when the published radiographs in a prestigious medical journal strongly supported the diagnosis of ankylosing hyperostosis.

In the past few years, it has been noted that the differential diagnosis between DISH and long-standing advanced AS is not limited to the radiologic findings and can extend to the clinical aspects because DISH patients can occasionally have severe limitation of spinal mobility, along with postural abnormalities that resemble long-standing advanced AS [5••]. Before examining the radiographic differential diagnosis of AS and DISH, it would be proper to briefly review the features of the two conditions.

Diffuse Idiopathic Skeletal Hyperostosis

DISH is characterized by calcification and ossification of soft tissues, mainly ligaments and entheses. This condition, described by Forestier and Rotes-Querol [6] more than 50 years ago, was termed *senile ankylosing hyperostosis*. The axial skeleton is often involved, particularly the thoracic spine, but involvement of peripheral entheses led to the term *DISH* [1,7]. The prevalence rates of the disease range from 2.9% in Koreans to 27.3% in Caucasian men in a European population [8–10,11•,12]. The disease is observed mostly in the elderly with a male preponderance [8–10,11•,12]. In a recent population-based study, 27.3% of men and 12.8% of women older than 50 years old were found to show evidence of DISH [12]. Its etiology is unknown, but it is associated with various metabolic disorders, especially obesity and insulin-dependent diabetes mellitus [13–16].

Spinal involvement of DISH is characterized by "flowing mantles" of ossification occurring in the anterior longitudinal ligament and to a lesser extent in the paravertebral connective tissue and the peripheral part of the annulus fibrosus (Fig. 1) [1,17,18]. The ossification may be limited to one section of the spine (ie, cervical, thoracic, or lumbar), or it may affect more than one section. The

Figure 1. Lateral view of the lumbar spine showing flowing mantles of ossification in the anterior longitudinal ligament extending from the first to the fourth vertebrae. A radiolucency (*arrow*) is visible between the anterior aspect of the fourth vertebrae and the adjacent bone proliferation.

thoracic spine, especially in the middle and lower part, is the most frequently involved section, followed by the lumbosacral spine and cervical spine [1,17,18]. Because the anterior longitudinal ligament covers the anterior, as well as the anterolateral aspects of the spine, its ossification on anteroposterior radiograph of the spine may appear as lateral ossifications and bony bridging. The lateral ossifications or bridging are usually bilateral, but in the thoracic region, they are either confined to, or are more prominent on, the right side of the spine [1,17,18]. The predominant involvement of the left side of the spine in individuals with situs inversus viscerum suggests that pulsation of the descending thoracic aorta may influence the location of ossification [19–21]. Frequently, radiolucency is noted between the new bone and the anterior aspect of the vertebral bodies on lateral view [1,6,17,18]. Radiolucent areas in the ossified bone mass may be noted at the level of the intervertebral disk space, due to displacement of disk material.

The ossification of the anterior longitudinal ligament may be associated with ossification of the syndesmoses connecting the laminae, spines, and transverse processes (ie, ligamenta flava and supraspinous and interspinous ligaments). These ossifications together with enthesopathies of the zygapophyseal joints can produce stenosis of the spinal canal [22]. DISH may also be associated with ossification of the posterior longitudinal ligament, especially of the cervical spine, which can further aggravate the spinal canal stenosis [23]. Some degree of ossification of the syndesmoses of the vertebral arches and of the posterior longitudinal ligament can occasionally also be observed in patients with AS without any signs of DISH [24–27].

DISH may also affect the sacroiliac joints, which can further result in being mistaken for sacroiliitis of AS. The upper (ligamentous) portion of the joint may show changes, such as vacuum phenomenon, narrowing, sclerosis, and even partial or complete bony ankylosis [2,3,28–31]. The lower two-third (synovial) part of the joint is spared. However, ossification of the joint capsule on the anterior surface of the joint may occur, resembling the obliteration of the sacroiliac joints on anteroposterior pelvic radiograph that may erroneously be interpreted as postinflammatory ankylosis of the joint [2,3,28–32]. CT can be useful in these cases by showing the normal aspect of joint space and bony margins, and presence of the anterior capsular ossifications [30,31].

Extraspinal manifestations of DISH are frequent and so characteristic to allow the recognition of the disease even in the absence of proper spinal radiographs [32,33]. Even though any entheses can be involved, features are especially common and distinctive at certain sites. On pelvis radiographs, bone proliferation is seen on the iliac crests, the ischial tuberosities, the pubis, lateral acetabulum, and the greater and lesser trochanters (Fig. 2). Ossification of the sacrotuberous and iliolumbar ligaments are further typical findings. In the foot, the calcaneal insertions of the plantar fascia, the long plantar ligament, and the Achilles tendon, and the insertions on the navicular bone, medial cuneiform, and the base of the fifth metatarsal bones are frequently involved. Additional frequent sites of bone proliferation include the attachment of quadriceps femoris to the base of the patella, the insertions of the ligamentum patellae on the patellar apex and the tubercle of the tibia, and the insertions of the humeral medial and lateral epicondyles.

In terms of clinical aspects, spinal involvement of DISH has long been considered a radiographic entity with minor and nonsignificant clinical manifestations compared with other spinal diseases. Generally, this is true. However, patients with DISH can have marked limitations of spinal mobility, and occasionally may have some spinal pain. Mata et al. [34] found more frequent reduction in spinal

Figure 2. Anteroposterior view of the pelvis showing bone proliferations of diffuse idiopathic skeletal hyperostosis (DISH) at the left lesser trochanter and around the acetabuli, more prominent in the left hip joint. A bone bridge typical of DISH is visible at the inferior part of both sacroiliac joints.

mobility and greater physical disability in patients with DISH compared with healthy subjects. A recent study from Italy and the United States reported that patients suffering from DISH may have severe limitation of spine mobility together with the typical postural abnormalities typical of long-lasting advanced AS [5••]. This report emphasized that the differential diagnosis between DISH and AS is not restricted to radiologic findings and extends to the clinical aspects. For example, peripheral enthesopathy of DISH is usually not as painful as peripheral enthesitis of spondyloarthritis. The two conditions are also often easily distinguished by painful and warm soft-tissue swelling in peripheral enthesitis of spondyloarthritis. Recently, a man presented with DISH, showing the postural abnormalities of long-standing AS together with a diffuse swelling at the insertion of the Achilles tendon resembling the typical fusiform soft-tissue swelling of Achilles enthesitis of spondyloarthritis [35]. However, palpation of the region did not reveal inflammatory findings of enthesitis, but a bony consistency of large spurs, also seen on radiographs. This observation emphasized that the clinical differential diagnosis between the two diseases extends to peripheral enthesopathy. Other clinical manifestations of DISH include dysphagia, hoarseness, stridor, myelopathy, aspiration pneumonia, sleep apnea, atlantoaxial complications, and spine fractures [36].

The diagnosis of DISH is currently based on classification criteria that require the involvement of the spinal thoracic segment. To differentiate DISH from AS and degenerative disease, Resnick et al. [1] proposed the following criteria: 1) "flowing" ossification extending over four contiguous vertebrae; 2) relative preservation of intervertebral disc height in relation to age; and 3) absence of apophyseal joint ankylosis or sacroiliac changes [7]. With regard to the last criterion, the apophyseal joints may show some narrowing, as well as hypertrophic alterations and capsular ossification on conventional radiographs, although there is no ankylosis of the joint per se in DISH. Incidentally, similar changes can also be seen in costovertebral and costotransverse joints, resulting in limitation of chest expansion in patients with advanced DISH [37]. We have already discussed the sacroiliac joint changes seen in patients with DISH.

According to Arlet and Mazières [18], the involvement of three contiguous vertebral bodies at the lower thoracic level is sufficient for diagnosing DISH. Julkunen et al. [37] suggested that DISH can also be diagnosed when bridging connects two vertebral bodies in at least two sites of the thoracic spine. None of these criteria considers the involvement of peripheral entheses. Another set of criteria suggested by Utsinger [38] for the diagnosis of probable DISH lowered the threshold for spinal involvement to three contiguous vertebral bodies and added the presence of peripheral enthesopathy. Currently, a new set of diagnostic criteria is needed to recognize milder forms of the disease in the spine, those sparing the thoracic segments, and those beginning with peripheral enthesopathy [39••,40]. The early recognition of the disease could allow the management of the associated metabolic diseases in an attempt to slow the progression of the disease to a more advanced state [41].

Ankylosing Spondylitis

AS is an inflammatory disorder of the axial skeleton involving the sacroiliac joints, the diskovertebral junction, the apophyseal joints, and the costovertebral and costotransverse joints [2,42]. It occurs worldwide generally in proportion to the prevalence of the HLA-B27 antigen [43].

The prevalence of AS varies between 0.10% to 0.87%, and is even higher in some countries, such as China and Turkey [44]. Symptoms usually start in the second and third decades of life and rarely after age 40. The axial distinctive radiographic findings of disease evolve over many years, with the earliest, most characteristic findings seen in the sacroiliac joints. The pathologic process within these joints evolves over months or years and the diagnostic findings on conventional plain pelvic radio-

graphs emerge only several years after the onset of the disease. In the preradiographic phase, inflammation can now be demonstrated by MRI as cartilage abnormalities and bone marrow edema [45]. The process consists of an inflammatory chondritis and subchondral osteitis involving the iliac and sacral surfaces of the synovial (inferior two-thirds) part of the joint. Inflammation also involves the ligamentous (superior one-third) of the joint. The radiographic features of sacroiliitis in the synovial portion are usually symmetric, consisting of subchondral bony erosions and sclerosis, typically more evident and severe on the iliac side because cartilage on the iliac surface of the joint is thinner than that on the sacral side. With progression of the erosions, the pelvic radiograph may show pseudo-widening of the joint space. The early inflammatory abnormalities in the upper third of the joint are not as clearly demonstrated because of absence of cartilage. With passage of time, the chondritis and ligamentous inflammation in the sacroiliac joints results in fibrosis, calcification, and ossification, finally leading to bony ankylosis of the joints. Radiographic sacroiliitis is scored in clinical practice according to the New York criteria [46].

In the spine, the inflammation at the diskovertebral junction usually occurs at the attachment of the annulus fibrosus. The subsequent adjacent subchondral osteitis is radiologically characterized by a destructive vertebral lesion and sclerosis confined to the anterior corners of the vertebral bodies ("Romanus lesion"). With the healing of these lesions, there is bony remodelling, together with adjacent periosteal reaction, that results in "squaring" of the vertebral bodies on lateral view of the spine. At the same time, the healing process continues resulting in gradual ossification in the periphery of the annulus fibrous, as well as in the formation of syndesmophytes, which are vertical bony bridges joining adjacent vertebral bodies anteriorly and laterally to form a "bamboo-spine." The inflammatory process also involves the zygapophyseal, costovertebral, and costotransverse joints, slowly resulting in their fusion and severe impairment of chest expansion and spinal mobility. The ossification of the interspinous and supraspinous ligaments can result in the formation of a vertical radio-opaque stripe in the midline on anteroposterior view of spinal radiograph, the so-called "tram-track" and "dagger" signs [47]. Presence of concomitant osteoporosis adds to the risk of development of progressive spinal kyphosis.

McEwen et al. [48] described two different forms of spondylitis. Primary AS and spondylitis associated with inflammatory bowel diseases showed bilateral sacroiliitis, symmetrical and marginal syndesmophytes, ligamentous ossification, and progression of syndesmophytes from the lumbar to the cervical spine. The spondylitis associated with psoriasis and reactive arthritis was characterized more often by asymmetrical findings both in the sacroiliac joints and the syndesmophytes, and, moreover, the syndesmophytes were mostly paramarginal rather than marginal.

Many radiologically detected alterations can also be found at sites other than the sacroiliac joints and the spine. These sites comprise sclerosis, erosion, and ankylosis of the cartilaginous joints (ie, symphysis pubis, manubriosternal joint, and costosternal joints); erosion, joint space narrowing, and bony ankylosis in the hip and shoulder joints (peripheral joints are less frequently involved, especially in primary AS in developed countries); ossification of different ligaments, including coracoclavicular, iliolumbar, sacrospinous, and sacrotuberous; and erosion and new bone proliferation at different entheseal sites, more often in the lower extremities, especially the heels [49••]. In general, the bone proliferative changes of enthesitis of spondyloarthritis are ill-defined, finely speculated, and differ from the coarse and well-marginated noninflammatory bony outgrowths of DISH [50]. The inflammation of the entheses can be shown by MRI and ultrasonography combined with power Doppler, and they can demonstrate response to therapy [49••].

Differentiating Features

AS and DISH are two different diseases that could usually be differentiated for several clinical features. Symptoms of AS begin at a young age, usually late adolescence and early adulthood, and consist of inflammatory spinal pain and stiffness and decreasing range of spinal motion [42]. After many years, the illness can result in characteristic postural abnormalities (eg, Bechterew stoop). In contrast, DISH affects middle-aged and elderly persons and is often asymptomatic, or is associated with mild dorsolumbar pain and some restriction of spinal mobility [34].

From a radiologic point of view, the differential diagnosis between DISH and AS occurs when the two diseases are in their later phases of evolution. Radiographs can demonstrate erosive sacroiliitis, together with Romanus lesion and squaring of vertebral bodies characteristic of patients with AS. Differentiation between the two diseases has become more important recently because of the marked efficacy of anti–tumor necrosis factor–α (TNF-α) therapy in patients with symptomatic AS, even in an advanced state of the disease. Patients with DISH, especially those with impaired spinal mobility and postural abnormalities, and ligamentous ossification resembling bamboo spine, together with narrowing and sclerosis in the upper ligamentous portion of the sacroiliac joint and the capsular bridging obscuring the joint space of the synovial part, can be erroneously diagnosed as AS. Conversely, some AS patients with syndesmophytes, mainly of paramarginal type, and some ossification of the anterior longitudinal ligament, may be misdiagnosed as suffering from DISH if the sacroiliac joint abnormalities are not characteristically evident [2]. However, additional analysis of the clinical and radiologic characteristics helps differentiate the two diseases without much difficulty (Table 1).

In the later phases of AS, both the ligamentous and synovial parts of the sacroiliac joints show sclerosis, joint space

Table 1. Distinguishing features of DISH and AS

	DISH	AS
Usual age of onset	> 50 y	< 40 y
Dorsal kyphosis	Frequent	Very frequent
Limitation of spinal mobility	Frequent	Very frequent
Pain	Unusual	Very frequent
Limitation of chest expansion	Frequent	Very frequent
Roentgenography		
Hyperostosis	Very frequent	Frequent
SI joint erosion	Absent	Very frequent
SI joint (synovial) obliteration	Unusual	Very frequent
SI joint (ligamentous) obliteration	Frequent	Very frequent
Apophyseal joint obliteration	Absent	Very frequent
ALL ossification	Very frequent	Unusual
PLL ossification	Very frequent	Frequent
Syndesmophytes	Absent	Unusual
Enthesopathies (whiskering) with erosions	Absent	Very frequent
Enthesopathies (whiskering) without erosions	Very frequent	Frequent
HLA-B27 (European "whites") [63,64]	About 8%	About 90%
HLA-B27 (African Americans) [63,64]	About 2%	About 50%

ALL—anterior longitudinal ligament; AS—ankylosing spondylitis; DISH—diffuse idiopathic skeletal hyperostosis; PLL—posterior longitudinal ligament; SI—sacroiliac.

narrowing, erosion, or fusion. In contrast, in DISH, only the obliteration of the ligamentous portion and a mild narrowing of the synovial part can occur, but erosions and bony ankylosis are not observed. CT can easily demonstrate the apparent obliteration of the synovial part on pelvic radiograph due to capsular ossification in DISH [30,31].

Syndesmophytes of AS represent ossification of the peripheral layers of the annulus fibrosus. They connect the angles of adjacent vertebral bodies and are usually fine and marginal. In psoriatic spondylitis and spondylitis associated with reactive arthritis, syndesmophytes can be paramarginal. In contrast, spinal outgrowths of DISH result from an ossification process involving the anterior longitudinal ligament (Fig. 1). They are large and run along the edges of the vertebral bodies and disc spaces. A radiolucent line usually separates the ossified anterior longitudinal ligament from the anterior aspect of the adjacent vertebral bodies.

Several other spinal radiographic changes are useful in the differentiation of the two diseases. Although ossification of the posterior longitudinal ligament has been described in AS [24–27], it is much more frequent in DISH [23]. Apophyseal joint alteration—involving partial or complete ankylosis of the zygapophyseal, costovertebral, and costotransverse joints—is typically present in advanced AS, whereas only some narrowing with hypertrophic alterations and capsular ossification can be observed in these joints in DISH. The ossification of interspinous ligaments is also frequently seen in advanced AS, whereas it only occasionally appears in DISH. Involvement of symphysis pubis, marked by erosion, sclerosis, and bony ankylosis similar to that observed in the sacroiliac joints, can be seen in AS, whereas usually only bony bridging occurs in DISH. Pelvic enthesopathy appearance can also differentiate between the two diseases, with hypertrophic whiskerings in DISH, whereas in AS the bone proliferation is less evident and associated with bony erosion and sclerosis. These differences also extend to peripheral enthesis involvement. The hip joints are also frequently involved in AS, with concentric joint space narrowing, erosion, and bony ankylosis. In DISH, only prominent enthesophytes, often limiting joint mobility, are observed.

Coexisting Diffuse Idiopathic Skeletal Hyperostosis and Ankylosing Spondylitis

As DISH and AS are not rare diseases, they can occur in the same individual by chance [8–10,11•,12,44]. So far, only 16 patients with the coexistence of the two diseases have been reported in the English literature [51–62]. The radiologic findings of axial involvement of AS and DISH are so different that, in patients with this coexistence, it is possible for experts to recognize changes caused by each of the two diseases at any level. For example, one of the patients reported by Rillo et al. [54] and one by Olivieri et al. [58] showed concomitant findings typical of AS

(sacroiliac joint erosions, joint space narrowing, sclerosis, and ankylosis) and DISH (anterior capsular bridging) on CT scans of the sacroiliac joints. Lastly, it is important to point out that, unlike in AS, there is no association of HLA-B27 with DISH (Table 1) [2,63,64].

Conclusions

DISH and AS are two completely different diseases that happen to share the involvement of the axial skeleton and the peripheral entheses, resulting in bone proliferations in the spine and at the extraspinal entheseal sites in the later phases of their course. Although the aspect of these bone proliferations is dissimilar, confusion of radiologic differential diagnosis between the two diseases exists mostly as a consequence of a lack of awareness of their characteristic clinical and radiographic features. The confusion may extend to the clinical field because advanced DISH can present the same limitation of spinal mobility and postural abnormalities as those seen in patients with advanced AS. However, the radiologic findings of axial involvement of the two diseases are so different that it is possible to recognize changes caused by each disease at any level, even in patients in whom they may co-occur.

Correct diagnosing of a disease is the primary goal in medicine. It is a *conditio sine qua non* for properly treating patients, and avoiding ineffective, unnecessary, and risky therapies. The management of AS is vastly different from that of DISH. The differentiation between the two diseases has become even more important these days because of the marked efficacy of anti–TNF-α therapy in patients with symptomatic AS, even in an advanced state of the disease. Conversely, anti–TNF-α therapy has no role in the management of patients with DISH. Nevertheless, some of us have been referred patients diagnosed as having AS because they failed to respond to anti–TNF-α therapy, when in fact they were suffering from DISH.

DISH, especially in those patients with impaired spinal mobility and postural abnormalities, and ligamentous ossification resembling bamboo spine, together with narrowing and sclerosis in the upper ligamentous portion of the sacroiliac joint and capsular bridging obscuring the joint space of the synovial part, can be erroneously diagnosed as AS. Conversely, some cases of AS in patients with syndesmophytes, mostly of paramarginal type seen mainly in psoriatic spondylitis, with some ossification of the anterior longitudinal ligament, may be misdiagnosed as DISH if the sacroiliac joint abnormalities are not characteristically evident [2]. However, additional analysis of the clinical and radiologic characteristics, as discussed in this review, should help clinicians differentiate the two diseases without much difficulty.

Disclosure

No potential conflicts of interest relevant to this article were reported.

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