Open Exploration

Diffuse idiopathic skeletal hyperostosis and axial spondyloarthritis—similarities and differences

David Kiefer[1,2]* , Muhammad Asim Khan[3] , Xenofon Baraliakos[1,2]

[1]Ruhr-Universität Bochum, Am Marienhospital Herne, Hölkeskampring 40, 44625 Herne, Germany
[2]Rheumazentrum Ruhrgebiet, Claudiusstrasse 45, 44649 Herne, Germany
[3]Case Western Reserve University, Cleveland, OH 44106, USA

*Correspondence: David Kiefer, Rheumazentrum Ruhrgebiet, Claudiusstrasse 45, 44649 Herne, Germany. David.kiefer@elisabethgruppe.de

Abstract

Diffuse idiopathic skeletal hyperostosis (DISH) and axial spondyloarthritis (axSpA) are diseases with inflammatory involvement of the axial skeleton that can result in new bone formation that may lead to total ankylosis of the spine and functional impairment of different extent in individual patients. In these diseases, the new bone formation may lead to total ankylosis of the spine and impaired mobility with functional impairment. This review will highlight the similarities and differences of these two conditions. In axSpA, the genetic background with the association with human leukocyte antigen-B27 (HLA-B27) is known for 50 years, while in DISH, a genetic contribution is not yet proven. The phenotype of new bone formation and its anatomic features are different between these diseases. In axSpA symmetric, thin and marginal syndesmophytes representing an ossification of enthesitic inflammation at the area of the attachment of the annulus fibrosus that may extend to the adjacent deeper layers anterior longitudinal ligament and are typical, while in DISH the so-called "chunky bridging osteophytes" grow as an additional layer on the anterior longitudinal ligament. Besides distinct anamnestic and clinical features, magnetic resonance imaging is helpful differentiating the two diseases since inflammatory changes with the typical pattern of axSpA are reliably visualized. Similar in both diseases is the high prevalence of vertebral fractures, which are mainly caused by the local osteoporosis and decreased flexibility of the affected bones, and therefore may occur even after minor traumata. The presence of extraarticular manifestations like uveitis, inflammatory bowel disease or psoriasis are only linked to axSpA. In contrast, DISH is associated with obesity, diabetes mellitus, and other metabolic diseases. Although DISH and axSpA are distinct conditions, the cooccurrence of these two diseases exists in some patients. Various therapeutic options are becoming available for axSpA, but no therapy has been approved for DISH yet.

Introduction

Diffuse idiopathic skeletal hyperostosis (DISH), initially known as ankylosing hyperostosis or Forestier's disease is characterized by excessive bone formation (hyperostosis) at entheses (where tendons and ligaments attach to bones) in the spine, and less often the ischial tuberosity, femoral trochanter, tibial tubercle and calcaneum [1–3]. The current name emphasizes that extraspinal hyperostosis may occur without appreciable spinal changes; therefore, a new name—DISH—is preferred. DISH can be confused with ankylosing spondylitis (AS) and related forms of spondyloarthritis (SpA) with involvement of the spine. There are no diagnostic criteria do not exist but imaging both with conventional radiographs or by magnetic resonance imaging (MRI) is similarly crucial for its identification. Although DISH and axial spondyloarthritis (axSpA) are distinct conditions, cooccurrence of these two diseases has been reported in some patients due to chance cooccurrence of two relatively common diseases [4, 5].

Similarities and differences in epidemiology and demographics

DISH and axSpA are two musculoskeletal disorders that have partly distinct epidemiological and demographic profiles. DISH primarily affects older individuals, while axSpA affects a younger population. DISH has a prevalence ranging from 3.8% [6] to 30% [7–15] in people aged > 50 years. The prevalence of DISH is increasing with age [16]. Still, despite that DISH is more prevalent in older patients, it has also been described in patients < 50 years [16] and even cases of DISH at the age of under 40 have been reported [17, 18] which can make it sometimes difficult to differentiate it from axSpA. While in Caucasian and Asian populations the prevalence of DISH is higher in men, this ratio seems to be more balanced in Sub-Saharan Africans and African Americans [6, 19]. AxSpA is comprising from both non-radiographic (nr-) and radiographic (r-) axSpA, with an estimated prevalence between 0.1% and 1.4% in different parts of the world [20]. AxSpA mainly starts in the third decade of life, rarely (< 5%) with an onset older than 45 years, but in 10–20% of patients even between the ages of 10 years and 20 years [21]. The male/female ratio is estimated to be 2:1 in r-axSpA, with an equal sex distribution among patients with nr-axSpA, indicating that women (for still unclear reasons) develop chronic changes later and less frequently [22, 23].

Similarities and differences in clinical features

DISH and axSpA share common clinical features, mainly back pain, but also impaired physical function, although there are also many differences in their clinical appearances and manifestations. Peripheral arthritis is very common in axSpA, but also found in DISH [24]. In both diseases, but especially in DISH, asymptomatic forms can be seen in clinical practice, being revealed by chance in performed imaging. Both DISH and axSpA can cause spinal stiffness and chronic pain, particularly in the lower back region. The pain in SpA is typically inflammatory in nature and may be accompanied by morning stiffness that improves with exercise, while DISH pain is usually mechanical and worsens with physical activity [23, 25]. While inflammatory back pain is a cardinal feature of axSpA and included in the classification criteria [26], DISH is not associated with typical inflammatory back pain [27]. Both conditions can lead to reduced spinal mobility, affecting the range of motion of the neck, back, and hips, resulting in impaired physical function [11, 28–30]. Chest expansion, typically reduced in advanced stages if axSpA, may also be reduced in up to 50% of patients with DISH [3] mainly due to the characteristic involvement of consecutive vertebral segments [31]. Peripheral manifestations like arthritis, dactylitis, and enthesitis are more common in SpA than in DISH. In both conditions, the affected joints are usually not affected by primary osteoarthritis [24, 32]. In DISH, enthesopathies at various sites including entheseal insertions of joint capsules, and tendons attachments are showing calcification and ossification [24]. Similar to axSpA, also Achilles tendon and plantar fascia are affected [2]. While in daily practice arthritis and enthesitis are more common in axSpA

than in DISH, studies with small numbers of patients demonstrated the presence of inflammatory signal on power Doppler but also presence of erosions also in DISH-associated enthesopathies [33]. In addition, typical extra-musculoskeletal manifestations of axSpA, such as uveitis, psoriasis, and inflammatory bowel disease are not found in patients diagnosed with DISH. These extra-musculoskeletal manifestations can significantly impact the patient's health-related quality of life (HRQoL), contributing to physical and psychological distress [23]. The cervical spine involvement of DISH may in rare cases develop giant osteophytes that induce dysphagia as well as other airway compressions which might result in sleep apnea, aspiration pneumonia and stridor and may lead to surgery [1, 27, 34]. Ozgocmen coined the term "DISHphagia" to describe the dysphagia observed in association with DISH [35, 36].

While physical function and spinal mobility are impaired by both diseases, reports on the impairment in quality of life are more frequent for patients with axSpA, while only small studies exist for DISH patients, indicating that HRQoL in those patients is not reduced in comparison to matched patients without DISH [30]. Progressive fusion of the spinal column and altered biomechanical characteristics increase the risk of vertebral fractures in both DISH and axSpA as compared to the general population. These fractures are more frequently accompanied with a higher risk of complications such as neurological deficits due to associated spinal cord injury [37–39]. Fractures may occur after even a minor or trivial trauma [38, 40]. A retrospective analysis has shown that 15% of patients with DISH presenting to a particular neurosurgical unit had serious neurologic manifestations requiring neurosurgical intervention [41]. The ossification of the ligamentum flavum and an association of ossification of the posterior longitudinal ligament (OPLL) with DISH may explain, in part, the occasional presence of spinal stenosis, spinal root compression with posterior segment involvement, and resultant neurologic findings in patients with DISH [42].

Similarities and differences in ethiopathogenesis

While both DISH and axSpA are characterized by formation of new bone tissue in the axial skeleton, the underlying pathogenetic pathways seem to be different. In axSpA, up to 90% of the pathogenesis is genetically determined, with human leukocyte antigen-B27 (HLA-B27) being by far the most important risk factor [43, 44]. The chance of developing SpA in HLA-B27-positive individuals is about 5%, in HLA-B27-positive first-degree relatives from r-axSpA patients it is 12–27%, while in HLA-B27-negative relatives from r-axSpA patients it is less than 1% [45, 46]. The most recent reports show a very convincing evidence that HLA-B27 is directly involved in disease pathogenesis because it presents microbial peptides that act as a trigger for autoimmunity by activating CD8+ T-cells that cross-react with self-peptides and result in AS/SpA [47]. In addition, microbiomic dysbiosis, other genetic and epigenetic factors, and entheseal stress and micro-damage influence disease induction and progression.

Gut bacteria seem to be an important environmental factor, since axSpA can occur in the context of reactive arthritis, inflammatory bowel disease (IBD) and clinically relevant or subclinical colitis [23, 48]. Although its exact role has not yet been identified, there is an increasing interest to investigate the role of microbiota in the pathogenesis of SpA [49, 50].

DISH is considered a metabolic condition, as multiple associations between DISH and metabolic syndrome, cardiovascular disorders, high body mass index (BMI) and type 2 diabetes mellitus (DM) have been regularly reported [15, 51, 52]. DISH is associated with overweight and obesity [51, 53–55] in particular in patients with obesity measured by waist circumference [51, 56]. Furthermore, association between impaired glucose tolerance and/or type 2 DM and the prevalence of DISH, has been found [11, 51, 57]. While type 2 DM has been reported to be associated with DISH, such association has not been found in patients with type 1 DM [58]. In contrast to DISH, axSpA is not associated with metabolic disorders, and hence, its metabolic markers are usually within normal limits.

From the laboratory analyses, elevated C-reactive protein (CRP) levels is found in only about 60% of r-axSpA patients and in about 33% of patients with nr-axSpA [59], while a significant number of patients with axSpA have clearly inflammatory symptoms despite normal levels of acute phase reactants [60]. CRP and erythrocyte sedimentation rate (ESR) levels are not significantly different in DISH and controls [61].

Associations between DISH and dyslipidaemia or hyperuricaemia are also reported [52, 62]. In comparison, HLA-B27 plays no role in the pathogenesis of DISH [63].

Similarities and differences in imaging

DISH and axSpA are the prototypes of hyperostotic diseases of the axial skeleton [64]. The bone proliferation leads in the long term to ankylosis of the spine and functional impairment. Besides the axial skeleton, peripheral involvement of joints, entheses and ligaments with or without structural changes are common in both entities.

In axSpA, sacroiliitis, spondylitis, and spondylarthritis are the main inflammatory manifestations in the axial skeleton [65], which may lead to new bone formation occurring as syndesmophytes and ankylosis in the vertebral column and may lead to the development of a "bamboo spine" [66]. Peripheral manifestations are mainly found in the root joints, the hips and the shoulders, and frequently affect entheses such as the heel, the knee and the elbow.

In DISH, structural changes are typically characterized by calcification and ossification of ligaments and entheses. The condition usually affects the axial skeleton, in particular at the thoracic segment though also other portions of the spine are often involved. Like in axSpA, in DISH peripheral joint, tendinous and/or entheseal involvement may occur [24].

Typical for DISH are the so-called "chunky bridging" osteophytes' which grow as an additional layer on the anterior longitudinal ligament mostly starting at the thoracic spine. Interestingly, whereas the hyperostosis in the cervical spine is symmetrically distributed anterior to the vertebral bodies without a flowing pattern, the involvement in the thoracic spinal exhibits an asymmetrical flowing pattern because the vascular system (the descending aorta) acts as a natural barrier against new bone formation in DISH [67]. There is also a significant ventral displacement of the trachea and esophagus that may explain the mechanism of dysphagia and airway obstruction that can occur in some patients with DISH.

In axSpA the structural changes of the axial skeleton usually start in the sacroiliac joint (SIJ) and lumbar spine [32]. Sacroiliitis in axSpA is the key features of the disease and typically also present in early stages [68], and in later stages the frequently thin, marginal and often symmetrical syndesmophytes are characteristic [24]. In DISH, pelvic enthesopathies are considered to be highly characteristic of DISH mostly seen as an ossification or calcification of the entheses [69, 70]. Similar to axSpA, the SIJ may also be involved in DISH, with enthesopathies of the anterior and posterior ligaments and capsule, as well as bridging, fusing enthesophytes within the joints mimicking joint ankylosis of axSpA [64, 71, 72].

Different imaging techniques are relevant for diagnosis, classification, assessment of disease activity and structural damage, and prognosis of patients with DISH and axSpA. Conventional radiography (CR) mainly is still the initial imaging modality and the gold standard for the assessment of structural changes in both DISH and axSpA (Figures 1 and 2). With CR, typical findings in axSpA are sclerosis, erosions, and pseudowidening joint, progressing later to ankylosis of the SIJ and spinal involvement that can result in formation of bony bridges (syndesmophytes) and spinal fusion [24, 32]. For the classification of axSpA CR of the SIJ is used to grade structural damage according the New York criteria [73]. Furthermore, CR is used in clinical trials to calculate the modified stoke AS spinal score (mSASSS), a scoring method for grading the radiographic changes in the spine [74]. CR in patients with DISH can show the characteristic flowing osteophytes along the anterior aspect of the vertebral bodies and ossification of the anterior longitudinal ligament. It may also visualize hyperostosis at the sites of entheses, such as the iliac crest and ischial tuberosity [24]. For clear identification of DISH, CR of the thoracic spine is used for the classification in order to prove the occurrence of the Resnick criteria [31].

In axSpA, computed tomography (CT) scans of the SIJ and spine have been found to be superior to CR for the detection of structural changes because of the multidimensional imaging of anatomic structures [75–77] but is mainly used for research purposes. For the diagnosis of DISH, the use of CT is superior to CR with less intra- and inter-observer error compared to CR and may also have advantages at early disease stages [16, 78].
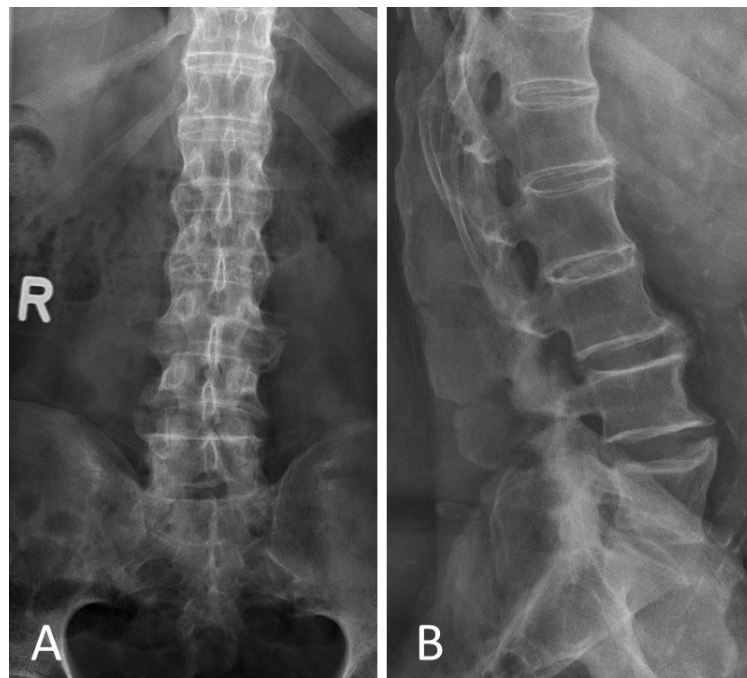
Figure 1. X-ray of a patient with AS. (A) Anterior-posterior with syndesmophytes and sacroiliitis; (B) lateral view with syndesmophytes. R: right side
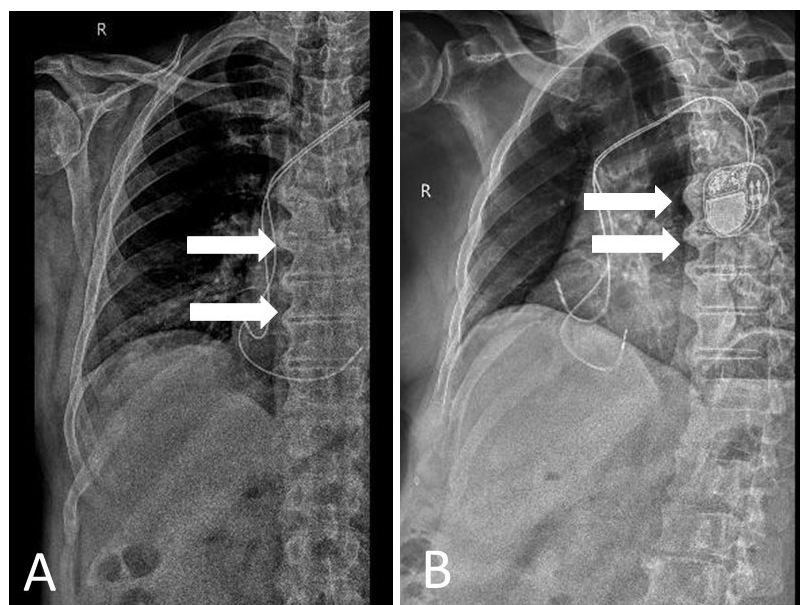

Figure 2. X-ray. (A) Anterior posterior view; (B) lateral view. Patient with DISH showing characteristic flowing osteophytes and ossification of the anterior longitudinal ligament. R: right side

Both for classification and diagnosis MRI has become the most important tool for axSpA. In contrast to CR and CT, MRI of the axial skeleton and peripheral joints can show active inflammation in the form bone marrow edema (BME) as a sign of osteitis. Besides BME, MRI is capable of detecting enthesitis, synovitis and capsulitis. Inflammation of the SIJ is the key feature of axSpA may be visualized with MRI (Figure 3). Typical findings of disease activity when using spinal MRI in patients with axSpA are spondylitis (Figure 4), inflammation of the facet joints and aseptic spondylodiscitis but inflammation of costosternal and costovertebral joints are also commonly seen. To increase specificity for clinical trials Assessment of SpA international Society (ASAS) recently published the definition of a positive MRI of the SIJ and spine in axSpA [79]. Furthermore, MRI is also capable for the detection of structural changes such as erosions [80]. The contextual interpretation of BME and erosions are of high relevance in differential diagnostic consideration, and also in the differentiation to DISH. To strengthen specificity for axSpA the ASAS MRI working group has recently published new definitions for MRI lesions in the SIJ and spine [81].
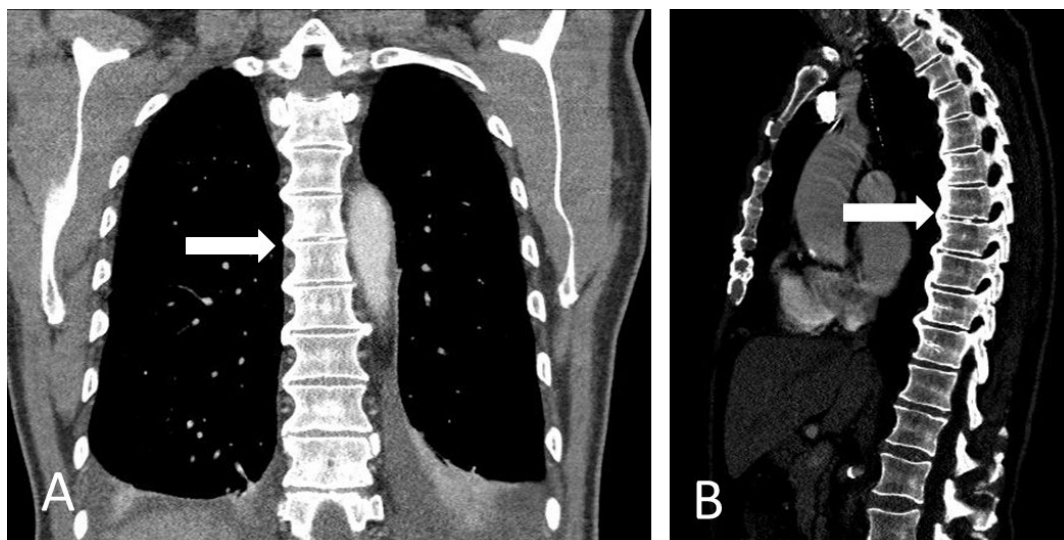
Figure 3. CT spine. (A) Coronal view; (B) sagittal view. Patient with DISH showing characteristic flowing osteophytes and ossification of the anterior longitudinal ligament
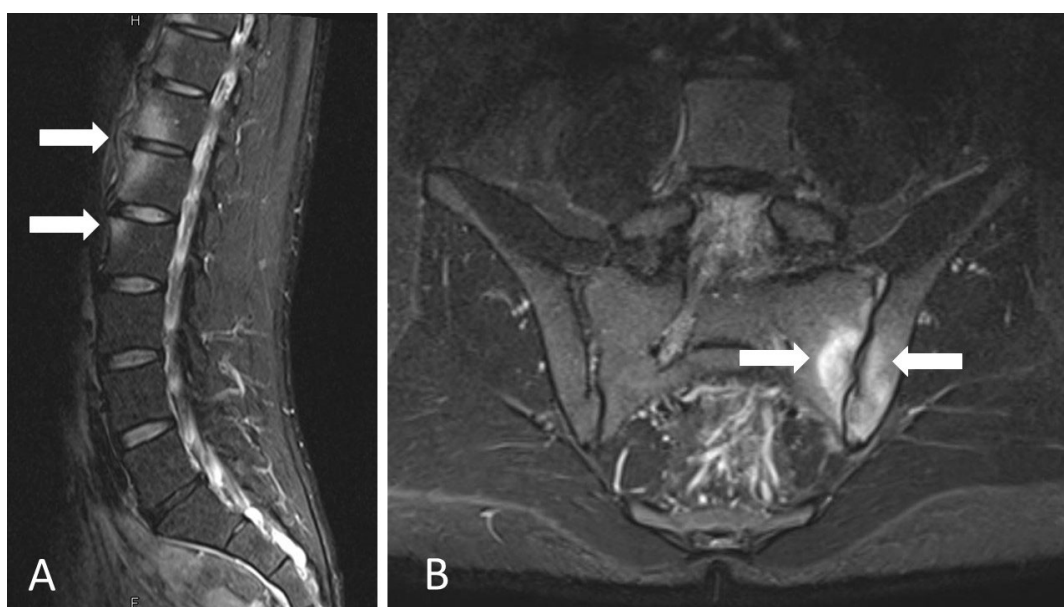
Figure 4. MRI turbo inversion recovery magnitude (TIRM) sequences. (A) Lateral view; (B) SIJs coronal view. Patient with axSpA and BME showing spondylitis and sacroiliitis

Some preliminary MRI studies have demonstrated BME in MRI of SIJ and spine MRI in patients with DISH suggesting a local inflammatory process (Figure 5) [82]. Comparing axSpA and DISH, patients with axSpA were more likely to present non-corner ankylosis, facet joint ankylosis, upper corner fat infiltration and SIJ BME, however, these features were not completely absent in DISH [83]. However, the presence of BME in DISH needs further investigation.

There is increasing evidence that mechanical stress and microtrauma of cartilage/bone at weightbearing parts of the skeleton [84] might be possibly initiating factor for the onset and progression of axSpA [85, 86]. Inflammation in the bone can be followed by new bone formation as part of a repair process. However, the complex pathogenic process between inflammation and transformation to structural changes in axSpA is still incompletely understood [87].

New bone formation and the rate of progression vertebral bony bridging is quite similar between DISH and axial SpA [64, 88]. The pathways of radiographic progression are under investigation for axSpA but so far there is no clear biologic explanation for radiographic progression in DISH.

Figure 5. MRI of a patient with DISH with BME in TIRM sequences

Similarities and differences in disease management and therapeutic options

The management of axSpA comprises pharmacological and non-pharmacological treatment options. Recently, the ASAS-European League Against Rheumatism (EULAR) recommendations for the management of axSpA has been updated [89]. Besides non-pharmacological treatments such as physiotherapy and physical activity, the first line treatment option are still non-steroidal anti-inflammatory drugs (NSAIDs) followed by biologic disease-modifying antirheumatic drugs (bDMARDs) like tumor necrosis factor inhibitors (TNFi) and interleukin-17 inhibitors (IL-17i) and targeted synthetic (ts)-disease-modifying antirheumatic drugs (DMARDs; JAK-inhibitors) [90].

Due to the lack knowledge about underlying pathologies and the lack of clinical trials, there are no recommendations or guidelines for non-pharmacological and pharmacological treatment of DISH [91]. Although there is no evidence for the efficacy of NSAIDs, they might be used for back pain or for symptomatic peripheral enthesopathies. So far, no further treatment options like the use of DMARDs, biologic- or ts-DMARDs are approved for the management of DISH.

Conclusions

DISH and axSpA have distinct epidemiological and demographic profiles. Both diseases share some clinical features, such as spinal stiffness and chronic pain, but differ in their underlying pathology and age of onset. DISH and axSpA are diseases defined by osteoblastic features of the axial skeleton that may lead to ankylosis and functional impairment, DISH typically is first to be detected in the thoracic spine while axSpA starts in the SIJ and lumbar spine. While both diseases may present peripheral manifestations, extraarticular manifestations like uveitis, IBD or psoriasis are only linked to axSpA. In contrast to axSpA, DISH is associated with obesity, DM and other metabolic diseases. In axSpA, there are various treatment options in the management in axSpA while no therapy has been approved for DISH yet.

Abbreviations

AS: ankylosing spondylitis

ASAS: Assessment of SpondyloArthritis international Society

axSpA: axial spondyloarthritis

BME: bone marrow edema

CR: conventional radiography

CT: computed tomography

DISH: diffuse idiopathic skeletal hyperostosis

DM: diabetes mellitus

DMARDs: disease-modifying antirheumatic drugs

HLA-B27: human leukocyte antigen-B27

MRI: magnetic resonance imaging

nr-: non-radiographic

r-: radiographic

SIJ: sacroiliac joint

SpA: spondyloarthritis

Declarations

Author contributions

DK, MAK and XB: Writing—original draft, Writing—review & editing.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical approval

The manuscript does not require ethical approval in accordance with the Article 15 of the Professional Code of Conduct for Physicians of the Westphalia-Lippe Medical Association.

Consent to participate

Informed consent to participate in the study was obtained from all participants.

Consent to publication

Not applicable.

Availability of data and materials

Not applicable.

Funding

Not applicable.

Copyright

© The Author(s) 2023.

References

1.   Mader R. Clinical manifestations of diffuse idiopathic skeletal hyperostosis of the cervical spine. Semin Arthritis Rheum. 2002;32:130–5.

2.   Mader R, Sarzi-Puttini P, Atzeni F, Olivieri I, Pappone N, Verlaan JJ, et al. Extraspinal manifestations of diffuse idiopathic skeletal hyperostosis. Rheumatology (Oxford). 2009;48:1478–81.

3.   Resnick D, Shapiro RF, Wiesner KB, Niwayama G, Utsinger PD, Shaul SR. Diffuse idiopathic skeletal hyperostosis (DISH) [ankylosing hyperostosis of forestier and Rotes-Querol]. Semin Arthritis Rheum. 1978;7:153–87.

4.   Kuperus JS, Waalwijk JF, Regan EA, van der Horst-Bruinsma IE, Oner FC, de Jong PA, et al. Simultaneous occurrence of ankylosing spondylitis and diffuse idiopathic skeletal hyperostosis: a systematic review. Rheumatology (Oxford). 2018;57:2120–8.

5.   Moreno AC, Gonzalez ML, Duffin M, López-Longo FJ, Carreño L, Forrester DM. Simultaneous occurrence of diffuse idiopathic skeletal hyperostosis and ankylosing spondylitis. Rev Rhum Engl Ed. 1996;63:292–5.

6.   Cassim B, Mody GM, Rubin DL. The prevalence of diffuse idiopathic skeletal hyperostosis in African blacks. Br J Rheumatol. 1990;29:131–2.

7.   Yamada K, Satoh S, Hashizume H, Yoshimura N, Kagotani R, Ishimoto Y, et al. Diffuse idiopathic skeletal hyperostosis is associated with lumbar spinal stenosis requiring surgery. J Bone Miner Metab. 2019;37:118–24.

8.   Weinfeld RM, Olson PN, Maki DD, Griffiths HJ. The prevalence of diffuse idiopathic skeletal hyperostosis (DISH) in two large American Midwest metropolitan hospital populations. Skeletal Radiol. 1997;26:222–5.

9.   Zincarelli C, Iervolino S, Di Minno MN, Miniero E, Rengo C, Di Gioia L, et al. Diffuse idiopathic skeletal hyperostosis prevalence in subjects with severe atherosclerotic cardiovascular diseases. Arthritis Care Res (Hoboken). 2012;64:1765–9.

10.   Hiyama A, Katoh H, Sakai D, Sato M, Tanaka M, Watanabe M. Prevalence of diffuse idiopathic skeletal hyperostosis (DISH) assessed with whole-spine computed tomography in 1479 subjects. BMC Musculoskelet Disord. 2018;19:178.

11.   Katzman WB, Huang MH, Kritz-Silverstein D, Barrett-Connor E, Kado DM. Diffuse idiopathic skeletal hyperostosis (DISH) and impaired physical function: the Rancho Bernardo Study. J Am Geriatr Soc. 2017;65:1476–81.

12.   Kiss C, O'Neill TW, Mituszova M, Szilágyi M, Poór G. The prevalence of diffuse idiopathic skeletal hyperostosis in a population-based study in Hungary. Scand J Rheumatol. 2002;31:226–9.

13.   Ciaffi J, Borlandelli E, Visani G, Facchini G, Miceli M, Ruscitti P, et al. Prevalence and characteristics of diffuse idiopathic skeletal hyperostosis (DISH) in Italy. Radiol Med. 2022;127:1159–69.

14.   Ikuma H, Hirose T, Nakamura D, Yamashita K, Ueda M, Sasaki K, et al. The prevalence and characteristics of diffuse idiopathic skeletal hyperostosis (DISH): a cross-sectional study of 1519 Japanese individuals. Diagnostics (Basel). 2022;12:1088.

15.   Auðunsson AB, Elíasson GJ, Steingrímsson E, Aspelund T, Sigurdsson S, Launer L, et al. Diffuse idiopathic skeletal hyperostosis in elderly Icelanders and its association with the metabolic syndrome: the AGES-Reykjavik Study. Scand J Rheumatol. 2021;50:314–8.

16.   Hirasawa A, Wakao N, Kamiya M, Takeuchi M, Kawanami K, Murotani K, et al. The prevalence of diffuse idiopathic skeletal hyperostosis in Japan – the first report of measurement by CT and review of the literature. J Orthop Sci. 2016;21:287–90.

17.   Chitten JJ, James B. Diffuse idiopathic skeletal hyperostosis in a 33-year-old woman with PCOS and metabolic syndrome: a rare scenario. BMJ Case Rep. 2019;12:e223740.

18.   Ibáñez Barceló M, Estremera Rodrigo A, Ros Vilamajó I, Juan Mas A. Diffuse idiopathic skeletal hyperostosis in a young woman treated with isotretinoin. Reumatol Clin (Engl Ed). 2022;18:184–5.

19. Yoshihara H, Nadarajah V, Horowitz E. Prevalence and characteristics of thoracic diffuse idiopathic skeletal hyperostosis in 3299 black patients. Sci Rep. 2021;11:22181.

20. van Tubergen A. The changing clinical picture and epidemiology of spondyloarthritis. Nat Rev Rheumatol. 2015;11:110–8.

21. Feldtkeller E, Khan MA, van der Heijde D, van der Linden S, Braun J. Age at disease onset and diagnosis delay in HLA-B27 negative *vs.* positive patients with ankylosing spondylitis. Rheumatol Int. 2003;23: 61–6.

22. Kiltz U, Baraliakos X, Karakostas P, Igelmann M, Kalthoff L, Klink C, et al. Do patients with non-radiographic axial spondylarthritis differ from patients with ankylosing spondylitis? Arthritis Care Res (Hoboken). 2012;64:1415–22.

23. Sieper J, Poddubnyy D. Axial spondyloarthritis. Lancet. 2017;390:73–84.

24. Mader R, Baraliakos X, Eshed I, Novofastovski I, Bieber A, Verlaan JJ, et al. Imaging of diffuse idiopathic skeletal hyperostosis (DISH). RMD Open. 2020;6:e001151. Erratum in: RMD Open. 2020 Mar;6: e001151corr1.

25. Mader R, Verlaan JJ, Buskila D. Diffuse idiopathic skeletal hyperostosis: clinical features and pathogenic mechanisms. Nat Rev Rheumatol. 2013;9:741–50.

26. Sieper J, van der Heijde D, Landewé R, Brandt J, Burgos-Vagas R, Collantes-Estevez E, et al. New criteria for inflammatory back pain in patients with chronic back pain: a real patient exercise by experts from the Assessment of SpondyloArthritis international Society (ASAS). Ann Rheum Dis. 2009;68:784–8.

27. Bieber A, Masala IF, Mader R, Atzeni F. Differences between diffuse idiopathic skeletal hyperostosis and spondyloarthritis. Immunotherapy. 2020;12:749–56.

28. Machado P, Landewé R, Braun J, Hermann KG, Baker D, van der Heijde D. Both structural damage and inflammation of the spine contribute to impairment of spinal mobility in patients with ankylosing spondylitis. Ann Rheum Dis. 2010;69:1465–70.

29. Kiefer D, Baraliakos X, Adolf D, Chatzistefanidi V, Schwarze I, Lange U, et al. Successful evaluation of spinal mobility measurements with the Epionics SPINE device in patients with axial spondyloarthritis compared to controls. J Rheumatol. 2022;49:44–52.

30. Banno T, Togawa D, Hasegawa T, Yamato Y, Yoshida G, Kobayashi S, et al. The controlled study of diffuse idiopathic skeletal hyperostosis for the assessment of physical function in elderly populations. J Orthop Sci. 2018;23:929–34.

31. Resnick D, Niwayama G. Radiographic and pathologic features of spinal involvement in diffuse idiopathic skeletal hyperostosis (DISH). Radiology. 1976;119:559–68.

32. Kiefer D, Baraliakos X. Bildgebung bei axialer spondyloarthritis – Herausforderungen und limitationen. Aktuel Rheumatol. 2019;44:321–31.

33. Mader R, Novofastovski I, Iervolino S, Pavlov A, Chervinsky L, Schwartz N, et al. Ultrasonography of peripheral entheses in the diagnosis and understanding of diffuse idiopathic skeletal hyperostosis (DISH). Rheumatol Int. 2015;35:493–7.

34. Liawrungrueang W, Sarasombath P, Maihom T, Tantivorawit W, Sugandhavesa N, Bunmaprasert T. Anterior cervical spine surgery for treatment of secondary dysphagia associated with cervical myelopathy in patient with Forestier's disease. Ann Med Surg (Lond). 2021;72:103120.

35. Ozgocmen S. Diffuse idiopathic skeletal hyperostosis-induced dysphagia or DISHphagia. APLAR J Rheum. 2005;8:128–30.

36. Kaffel D, Kchir H. Dysphagia related to diffuse idiopathic skeletal hyperostosis (DISHphagia). Clin Case Rep. 2019;7:2265–6.

37. Buehring B, Al-Azem N, Kiltz U, Fruth M, Andreica I, Kiefer D, et al. High prevalence of foot insufficiency fractures in patients with inflammatory rheumatic musculoskeletal diseases. J Rheumatol. 2023;50:1071–7.

38. Westerveld LA, van Bemmel JC, Dhert WJ, Oner FC, Verlaan JJ. Clinical outcome after traumatic spinal fractures in patients with ankylosing spinal disorders compared with control patients. Spine J. 2014; 14:729–40.

39. Teunissen FR, Verbeek BM, Cha TD, Schwab JH. Spinal cord injury after traumatic spine fracture in patients with ankylosing spinal disorders. J Neurosurg Spine. 2017;27:709–16.

40. Taljanovic MS, Hunter TB, Wisneski RJ, Seeger JF, Friend CJ, Schwartz SA, et al. Imaging characteristics of diffuse idiopathic skeletal hyperostosis with an emphasis on acute spinal fractures: *review*. AJR Am J Roentgenol. 2009;193:S10–9.

41. Sharma RR, Mahapatra A, Pawar SJ, Sousa J, Lad SD, Athale SD. Spinal cord and cauda equina compression in 'DISH'. Neurol India. 2001;49:148–52.

42. Hukuda S, Mochizuki T, Ogata M, Shichikawa K. The pattern of spinal and extraspinal hyperostosis in patients with ossification of the posterior longitudinal ligament and the ligamentum flavum causing myelopathy. Skeletal Radiol. 1983;10:79–85.

43. Brown MA, Kennedy LG, MacGregor AJ, Darke C, Duncan E, Shatford JL, et al. Susceptibility to ankylosing spondylitis in twins: the role of genes, HLA, and the environment. Arthritis Rheum. 1997; 40:1823–8.

44. Li Z, van der Linden SM, Khan MA, Baumberger H, Zandwijk HV, Khan MK, et al. Heterogeneity of axial spondyloarthritis: genetics, sex and structural damage matter. RMD Open. 2022;8:e002302.

45. Brown MA, Laval SH, Brophy S, Calin A. Recurrence risk modelling of the genetic susceptibility to ankylosing spondylitis. Ann Rheum Dis. 2000;59:883–6.

46. van der Linden SM, Khan MA, Li Z, Baumberger H, Zandwijk HV, Khan MK, et al. Recurrence of axial spondyloarthritis among first-degree relatives in a prospective 35-year-follow-up family study. RMD Open. 2022;8:e002208.

47. Yang X, Garner LI, Zvyagin IV, Paley MA, Komech EA, Jude KM, et al. Autoimmunity-associated T cell receptors recognize HLA-B*27-bound peptides. Nature. 2022;612:771–7.

48. Mielants H, Veys EM, Cuvelier C, De Vos M, Goemaere S, De Clercq L, et al. The evolution of spondyloarthropathies in relation to gut histology. III. Relation between gut and joint. J Rheumatol. 1995;22:2279–84.

49. Costello ME, Ciccia F, Willner D, Warrington N, Robinson PC, Gardiner B, et al. Brief report: intestinal dysbiosis in ankylosing spondylitis. Arthritis Rheumatol. 2015;67:686–91.

50. Breban M, Tap J, Leboime A, Said-Nahal R, Langella P, Chiocchia G, et al. Faecal microbiota study reveals specific dysbiosis in spondyloarthritis. Ann Rheum Dis. 2017;76:1614–22.

51. Mader R, Novofestovski I, Adawi M, Lavi I. Metabolic syndrome and cardiovascular risk in patients with diffuse idiopathic skeletal hyperostosis. Semin Arthritis Rheum. 2009;38:361–5.

52. Vezyroglou G, Mitropoulos A, Antoniadis C. A metabolic syndrome in diffuse idiopathic skeletal hyperostosis. A controlled study. J Rheumatol. 1996;23:672–6. Erratum in: J Rheumatol. 1997;24: 1665.

53. Dan Lantsman C, Herman A, Verlaan JJ, Stern M, Mader R, Eshed I. Abdominal fat distribution in diffuse idiopathic skeletal hyperostosis and ankylosing spondylitis patients compared to controls. Clin Radiol. 2018;73:910.e15–20.

54. Mader R. Diffuse idiopathic skeletal hyperostosis: a distinct clinical entity. Isr Med Assoc J. 2003;5: 506–8.

55. Mata S, Fortin PR, Fitzcharles MA, Starr MR, Joseph L, Watts CS, et al. A controlled study of diffuse idiopathic skeletal hyperostosis. Clinical features and functional status. Medicine (Baltimore). 1997; 76:104–17.

56. Okada E, Ishihara S, Azuma K, Michikawa T, Suzuki S, Tsuji O, et al. Metabolic syndrome is a predisposing factor for diffuse idiopathic skeletal hyperostosis. Neurospine. 2021;18:109–16.

57. Nardo L, Lane NE, Parimi N, Cawthon PM, Fan B, Shepherd J, et al. Diffuse idiopathic skeletal hyperostosis association with thoracic spine kyphosis: a cross-sectional study for the Health Aging and Body Composition Study. Spine (Phila Pa 1976). 2014;39:E1418–24.

58. Pillai S, Littlejohn G. Metabolic factors in diffuse idiopathic skeletal hyperostosis – a review of clinical data. Open Rheumatol J. 2014;8:116–28.

59. Rudwaleit M, Haibel H, Baraliakos X, Listing J, Märker-Hermann E, Zeidler H, et al. The early disease stage in axial spondylarthritis: results from the German Spondyloarthritis Inception Cohort. Arthritis Rheum. 2009;60:717–27.

60. Spoorenberg A, van der Heijde D, de Klerk E, Dougados M, de Vlam K, Mielants H, et al. Relative value of erythrocyte sedimentation rate and C-reactive protein in assessment of disease activity in ankylosing spondylitis. J Rheumatol. 1999;26:980–4.

61. Mader R, Pappone N, Baraliakos X, Eshed I, Sarzi-Puttini P, Atzeni F, et al. Diffuse idiopathic skeletal hyperostosis (DISH) and a possible inflammatory component. Curr Rheumatol Rep. 2021;23:6.

62. Miyazawa N, Akiyama I. Diffuse idiopathic skeletal hyperostosis associated with risk factors for stroke: a case-control study. Spine (Phila Pa 1976). 2006;31:E225–9.

63. Couto AR, Parreira B, Power DM, Pinheiro L, Madruga Dias J, Novofastovski I, et al. Evidence for a genetic contribution to the ossification of spinal ligaments in ossification of posterior longitudinal ligament and diffuse idiopathic skeletal hyperostosis: a narrative review. Front Genet. 2022;13: 987867.

64. Baraliakos X, Listing J, Buschmann J, von der Recke A, Braun J. A comparison of new bone formation in patients with ankylosing spondylitis and patients with diffuse idiopathic skeletal hyperostosis: a retrospective cohort study over six years. Arthritis Rheum. 2012;64:1127–33.

65. Braun J, Bollow M, Sieper J. Radiologic diagnosis and pathology of the spondyloarthropathies. Rheum Dis Clin North Am. 1998;24:697–735.

66. Baraliakos X, Listing J, Rudwaleit M, Haibel H, Brandt J, Sieper J, et al. Progression of radiographic damage in patients with ankylosing spondylitis: defining the central role of syndesmophytes. Ann Rheum Dis. 2007;66:910–5.

67. Bakker JT, Kuperus JS, Kuijf HJ, Oner FC, de Jong PA, Verlaan JJ. Morphological characteristics of diffuse idiopathic skeletal hyperostosis in the cervical spine. PLoS One. 2017;12:e0188414.

68. Bennett AN, McGonagle D, O'Connor P, Hensor EM, Sivera F, Coates LC, et al. Severity of baseline magnetic resonance imaging-evident sacroiliitis and HLA-B27 status in early inflammatory back pain predict radiographically evident ankylosing spondylitis at eight years. Arthritis Rheum. 2008;58: 3413–8.

69. Haller J, Resnick D, Miller CW, Schils JP, Kerr R, Bielecki D, et al. Diffuse idiopathic skeletal hyperostosis: diagnostic significance of radiographic abnormalities of the pelvis. Radiology. 1989;172: 835–9.

70. Leibushor N, Slonimsky E, Aharoni D, Lidar M, Eshed I. CT abnormalities in the sacroiliac joints of patients with diffuse idiopathic skeletal hyperostosis. AJR Am J Roentgenol. 2017;208:834–7.

71. Yagan R, Khan MA. Confusion of roentgenographic differential diagnosis between ankylosing hyperostosis (Forestier's disease) and ankylosing spondylitis. Clin Rheumatol. 1983;2:285–92.

72. Khan MA, Yagan R. Sacroiliac abnormalities in dish. J Rheumatol. 1989;16:1399.

73. van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum. 1984;27:361–8.

74. van der Heijde D, Braun J, Deodhar A, Baraliakos X, Landewé R, Richards HB, et al. Modified stoke ankylosing spondylitis spinal score as an outcome measure to assess the impact of treatment on structural progression in ankylosing spondylitis. Rheumatology (Oxford). 2019;58:388–400.

75. Lawson TL, Foley WD, Carrera GF, Berland LL. The sacroiliac joints: anatomic, plain roentgenographic, and computed tomographic analysis. J Comput Assist Tomogr. 1982;6:307–14.

76. Ryan LM, Carrera GF, Lightfoot RW Jr, Hoffman RG, Kozin F. The radiographic diagnosis of sacroiliitis. A comparison of different views with computed tomograms of the sacroiliac joint. Arthritis Rheum. 1983;26:760–3.

77. Fam AG, Rubenstein JD, Chin-Sang H, Leung FY. Computed tomography in the diagnosis of early ankylosing spondylitis. Arthritis Rheum. 1985;28:930–7.

78. Kuperus JS, Buckens CF, Šprem J, Oner FC, de Jong PA, Verlaan JJ. The natural course of diffuse idiopathic skeletal hyperostosis in the thoracic spine of adult males. J Rheumatol. 2018;45:1116–23.

79. Hermann KG, Baraliakos X, van der Heijde DM, Jurik AG, Landewé R, Marzo-Ortega H, et al.; Assessment in SpondyloArthritis international Society (ASAS). Descriptions of spinal MRI lesions and definition of a positive MRI of the spine in axial spondyloarthritis: a consensual approach by the ASAS/OMERACT MRI study group. Ann Rheum Dis. 2012;71:1278–88.

80. Diekhoff T, Greese J, Sieper J, Poddubnyy D, Hamm B, Hermann KA. Improved detection of erosions in the sacroiliac joints on MRI with volumetric interpolated breath-hold examination (VIBE): results from the SIMACT study. Ann Rheum Dis. 2018;77:1585–9.

81. Maksymowych WP, Lambert RG, Østergaard M, Pedersen SJ, Machado PM, Weber U, et al. MRI lesions in the sacroiliac joints of patients with spondyloarthritis: an update of definitions and validation by the ASAS MRI working group. Ann Rheum Dis. 2019;78:1550–8.

82. Arad U, Elkayam O, Eshed I. Magnetic resonance imaging in diffuse idiopathic skeletal hyperostosis: similarities to axial spondyloarthritis. Clin Rheumatol. 2017;36:1545–9.

83. Weiss BG, Bachmann LM, Pfirrmann CW, Kissling RO, Zubler V. Whole body magnetic resonance imaging features in diffuse idiopathic skeletal hyperostosis in conjunction with clinical variables to whole body MRI and clinical variables in ankylosing spondylitis. J Rheumatol. 2016;43:335–42.

84. Cambré I, Gaublomme D, Burssens A, Jacques P, Schryvers N, De Muynck A, et al. Mechanical strain determines the site-specific localization of inflammation and tissue damage in arthritis. Nat Commun. 2018;9:4613.

85. Ansell RC, Shuto T, Busquets-Perez N, Hensor EM, Marzo-Ortega H, McGonagle D. The role of biomechanical factors in ankylosing spondylitis: the patient's perspective. Reumatismo. 2015;67: 91–6.

86. Ramiro S, Landewé R, van Tubergen A, Boonen A, Stolwijk C, Dougados M, et al. Lifestyle factors may modify the effect of disease activity on radiographic progression in patients with ankylosing spondylitis: a longitudinal analysis. RMD Open. 2015;1:e000153.

87. Braun J, van der Heijde D. Imaging and scoring in ankylosing spondylitis. Best Pract Res Clin Rheumatol. 2002;16:573–604.

88. Olivieri I, D'Angelo S, Cutro MS, Padula A, Peruz G, Montaruli M, et al. Diffuse idiopathic skeletal hyperostosis may give the typical postural abnormalities of advanced ankylosing spondylitis. Rheumatology (Oxford). 2007;46:1709–11.

89. Ramiro S, Nikiphorou E, Sepriano A, Ortolan A, Webers C, Baraliakos X, et al. ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update. Ann Rheum Dis. 2023; 82:19–34.

90. Baraliakos X, Kiltz U, Kononenko I, Ciurea A. Treatment overview of axial spondyloarthritis in 2023. Best Pract Res Clin Rheumatol. 2023; 2023;[Epub ahead of print].

91. Al-Herz A, Snip JP, Clark B, Esdaile JM. Exercise therapy for patients with diffuse idiopathic skeletal hyperostosis. Clin Rheumatol. 2008;27:207–10.