European Journal of Case Reports in Internal Medicine

Not so Mutually Exclusive Diseases: A Case of Co-occurrence of Inflammatory Spondyloarthritis and Diffuse Skeletal Hyperostosis in a Young Patient

Filipa Taborda[1], Duarte André Ferreira[2], Teresa Mendonça[3,4], Fátima Farinha[4]

[1] Internal Medicine Department, Hospital de Cascais, Alcabideche, Portugal

[2] Internal Medicine Department, Centro Hospitalar do Funchal, Funchal, Portugal

[3] Internal Medicine Department, Centro Hospitalar Universitário do Porto EPE, Porto, Portugal

[4] Clinical Immunology Unit, Centro Hospitalar Universitário do Porto EPE, Porto, Portugal

Doi: 10.12890/2023_003721 - European Journal of Case Reports in Internal Medicine - © EFIM 2022

Received: 13/12/2022
Accepted: 23/12/2022
Published: 10/01/2023

How to cite this article: Taborda F, Ferreira DA, Mendonça T, Farinha F. Not so mutually exclusive diseases; a case of co-occurrence of inflammatory spondyloarthritis and diffuse skeletal hyperostosis in a young patient. *EJCRIM* 2023;**10**: doi:10.12890/2023_003721.

Conflicts of Interests: The authors declare there are no competing interests.
Patient Consent: Informed consent has been obtained from the patient.

ABSTRACT

Diffuse idiopathic skeletal hyperostosis (DISH) and axial spondyloarthritis (axial SpA) are differential diagnoses of lower back pain. While the latter is considered to be an inflammatory disease, DISH is thought to be a metabolic condition. The authors report a case of a 34-year-old man who presented with a one-year history of axial lower back pain associated to migratory polyarthritis, buttock and heel pain. Imaging revealed contiguous calcification of the anterior longitudinal ligament of the cervical segment, meeting major criteria for DISH. However, he also exhibited signs of bilateral sacroiliitis highly suggestive of axial SpA for which he initiated biological therapy.

LEARNING POINTS

- Although the most used criteria for diffuse idiopathic skeletal hyperostosis (DISH) were designed to exclude radiographic signs of spondyloarthritis (SpA), both conditions can be present simultaneously.
- There are only few case reports in the literature that demonstrate the association of the two diseases.
- Overlap and misperception of SpA and DISH could result in undertreatment of individual patients and have a negative impact on prognosis.

KEYWORDS

Diffuse idiopathic skeletal hyperostosis, DISH, ankylosing spondylitis, spondyloarthritis, SpA

INTRODUCTION

Diffuse idiopathic skeletal hyperostosis (DISH), also known as ankylosing hyperostosis and Forestier's disease, is considered a non-inflammatory condition, mainly characterised by new bone formation at spinal ligaments and entheses[1,2]. While pathogenic pathways of DISH have not been fully elucidated, the presence of metabolic derangements are hypothesised to have an important role, since there is a clear association between DISH and obesity, hypertension, type 2 diabetes, and hyperinsulinemia[3]. Also, its prevalence increases with age, being more common in elderly males[2,3]. Most patients remain asymptomatic until advanced stages of the disease, when physical limitation and pain occur[4]. Therefore, it is usually diagnosed late in its course, and treatment only targets the symptoms, not preventing further deterioration and disability[3].

European Journal
of Case Reports in
Internal Medicine

Axial spondyloarthritis (SpA) is a group of chronic systemic inflammatory diseases majorly involving the axial skeleton[5]. The most common presenting symptoms are chronic back pain – typically in young adults before the age of 45 – and spinal stiffness, but peripheral and extra-musculoskeletal manifestations also occur frequently[5,6]. Imaging is a cornerstone in the diagnosis of SpA, with radiographic sacroiliitis being a hallmark of the disease. In the last few years, there have been a lot of advances in treatment options, including biological disease-modifying anti-rheumatic drugs (DMARDs), which have proved their benefit in controlling disease activity and function[5].
Although SpA and DISH may appear to be distinct radiographic conditions, they frequently overlap in key features, resulting in diagnostic uncertainty.

CASE DESCRIPTION

A 34-year-old man presented to the outpatient clinic with a one-year history of crippling, non-radiating, lower back pain. The pain had had an insidious onset, and typically got worse after exercise but had little or no improvement with rest and would persist during the night. It was associated with buttock pain, usually unilateral. Both complaints were partly relieved with non-steroidal anti-inflammatory drugs (NSAIDs). Seven years before he had experienced peripheral asymmetric arthritis, affecting knees and feet, as well as heel pain and swelling, demanding a physician's evaluation and treatment with short courses of NSAIDs and corticosteroids. He had a prior surgical resection of anterior cervical osteophytes, from vertebrae C3 to C4, which caused dysphagia and were thought to be a result of a previous road accident. There was known history of hyperuricaemia, overweight, elevated blood pressure, and high levels of low-density lipoprotein cholesterol with an abdominal ultrasound already revealing hepatic steatosis. He was a smoker and had moderate alcohol consumption. He had been under treatment with isotretinoin for one year and four months, prescribed for severe acne. He denied the presence or a history of oral aphthous ulcers, genital ulceration, gastrointestinal and urinary symptoms, or eye disturbances. Family history was irrelevant. At physical examination he presented a tenuous desquamative rash on forearms and elbows, as well as lumbar side flexion and cervical rotation limitation, scoring 1.5 on the Bath Ankylosing Spondylitis Metrology Index (BASMI). The Ankylosing Spondylitis Disease Activity Score using C-reactive protein (ASDAS-CRP) was 3.3, compatible with high disease activity. The Faber test was positive when testing right hip and sacroiliac joints. There were no signs of peripheral arthritis, enthesitis, or dactylitis. The remainder of the musculoskeletal examination was unremarkable. The blood tests performed did not show any relevant abnormalities, with a negative immunological panel, including antinuclear antibodies (ANA) and rheumatoid factor (RF). Human leukocyte antigen (HLA) typing revealed the presence of HLA-B*51, C*06:02 and DRB1*04, being HLA-B27 negative (*Table 1*). Cervical X-ray exhibited continuous calcification of the anterior longitudinal ligament, from the vertebral body of C3 to C6, with preserved intervertebral disc height (*Fig. 1*). Plain radiographs of the sacroiliac joints showed loss of definition of the edge and areas of sclerosis of both surfaces of the joints (*Fig. 2*).

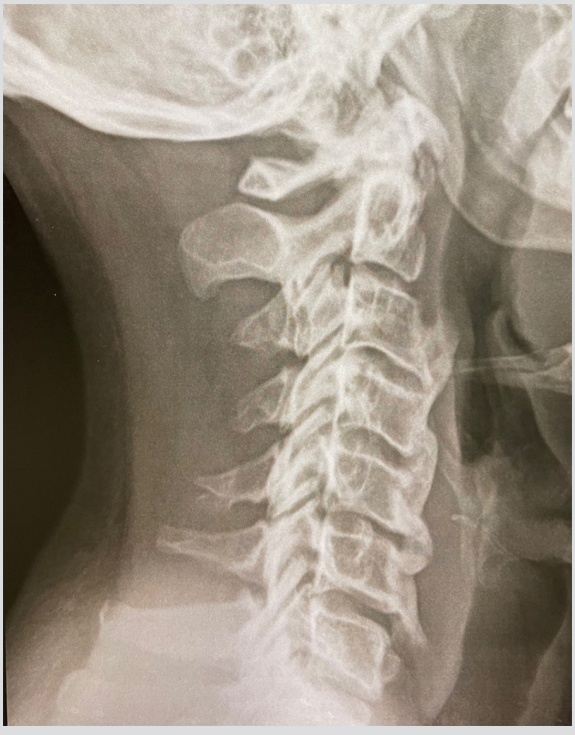

Figure 1. Cervical X-ray presenting flowing calcification of the anterior ligament from the vertebral body of C3 to C6

European Journal
of Case Reports in
Internal Medicine

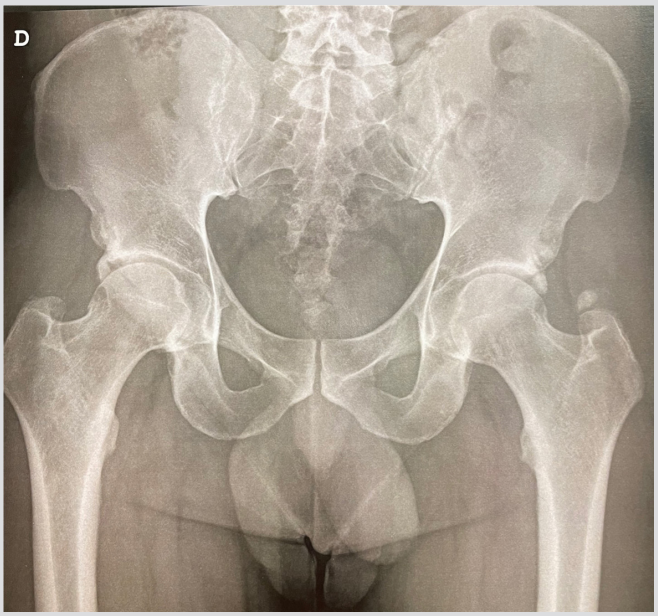

Figure 2. Plain X-ray of the sacroiliac joints showing signs of sacroiliitis grade 2

A magnetic resonance imaging (MRI) of the spine and sacroiliac joints was then performed, showing anterior osteophytes of the cervical and thoracic segments as well as unequivocal signs of active sacroiliitis with multiple areas of bone marrow oedema but no bone erosions (*Fig. 3*). Extraspinal involvement was also detected, characterised by osteophytes at the dorsal surface of the talus and tibial tuberosity, and enthesopathic calcifications of Achilles tendons. Finally, a body scintigraphy revealed high uptake in the spine, sacroiliac, tibiotarsal, and tibiofibular joints consistent with areas of inflammation (*Fig. 4*). In light of these findings, the patient not only met the major DISH criteria but also had evidence of an inflammatory component, and the concurrent diagnosis of SpA was made. Since he had an insufficient response to NSAIDs, with a high activity disease, it was decided to initiate biological therapy with tumour necrosis factor (TNF) inhibitor. Under this treatment, the patient showed a significant clinical improvement, with no need for analgesic therapy.

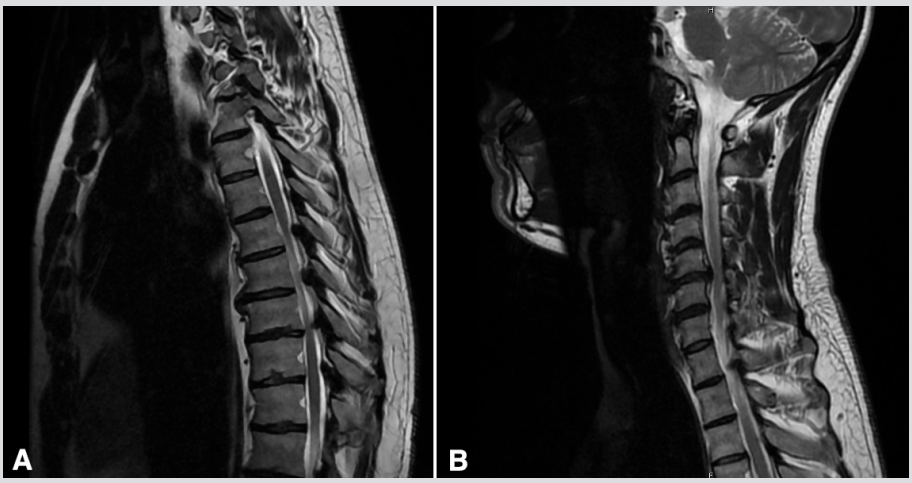

Figure 3. MRI of the cervical and dorsal spine showing anterior osteophytes

DISCUSSION

Even though SpA and DISH have different clinical expressions and characteristic radiological patterns, this case report highlights the exceptional coexistence of abnormalities suggestive of both conditions in the same patient[2,7].

Only few case reports regarding the simultaneous occurrence of both diseases are described in the medical literature. All these cases have been questioning the validity of the most accepted criteria for DISH, by Resnick and Niwayama, which foresee that radiologic signs of sacroiliitis have to be excluded.

European Journal
of Case Reports in
Internal Medicine

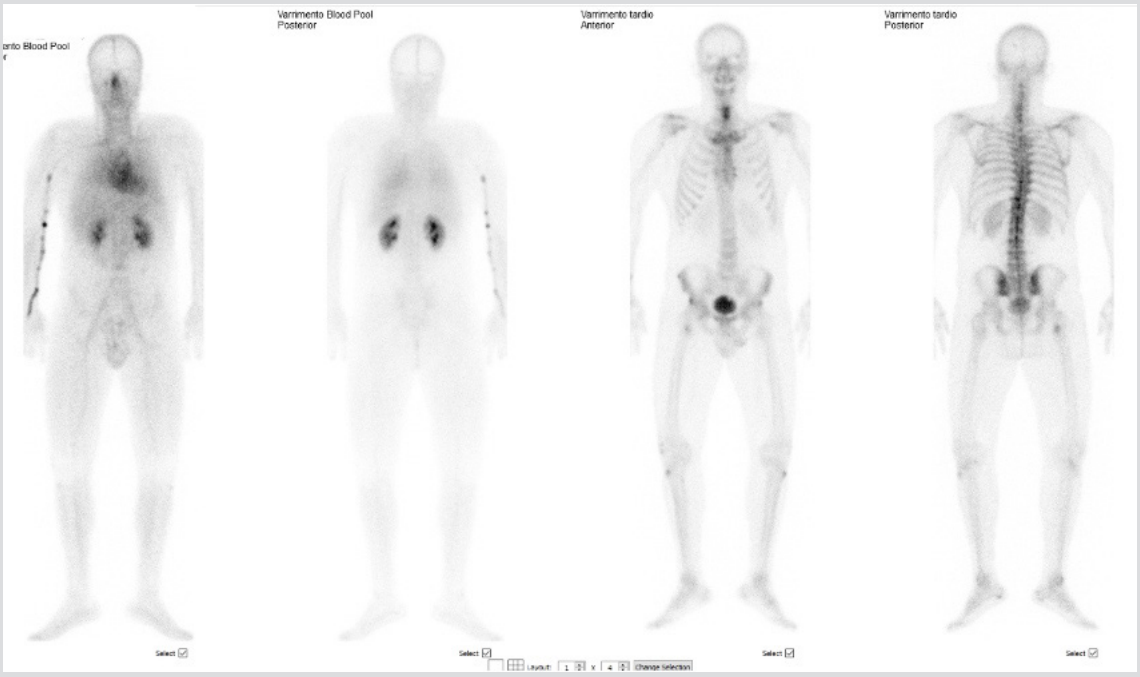

Figure 4. Whole body scintigraphy scan showing areas of high uptake of radionuclide

When evaluating a young patient with complaints of inflammatory back pain for more than three months, it is mandatory to assess the presence of other SpA features to support or exclude this diagnosis.

In this case, the diagnosis of SpA, even in the absence of HLA-B27, could be made by the presence of radiographic sacroiliitis with active inflammation on MRI, as well as the history of peripheral arthritis, enthesitis, and a good response to NSAIDs. Although the patient described that the pain was triggered by exercise, it showed a predominantly inflammatory pattern, being present at night with improvement upon rising. Furthermore, the patient showed skin lesions evocative of psoriasis although he did not have a formal diagnosis.

Spinal involvement of SpA and DISH is described as radically opposed[8]. In the first one – especially in ankylosing spondylitis – thin, delicate vertically oriented syndesmophytes are distinctive, associated with loss of height of intervertebral discs, vertebral squaring resembling a "bamboo spine", and fusion of facet joints[2,3,8,9]. DISH is characterised by coarse and thick bony bridges from along the anterior longitudinal ligament in a more horizontal orientation and mainly on the right side, showing a "dripping candle wax" appearance[2,9].

It was the axial radiography and MRI that raised the suspicion of DISH, reporting flowing calcification of the anterior ligament of four contiguous vertebral bodies which, even though it is not pathognomonic sign, meets the major criterion of Resnick and Niwayama for this entity and is one of the radiological hallmarks of the disease. The presence of localised anterior osteophytes as well as peripheral enthesopathy would also be explained by DISH. The patient's past medical history of hyperuricemia, dyslipidemia, overweight, and hypertension supports this clinical diagnosis, although it is considered to be rare in patients younger than 40. Furthermore, he had an additional risk factor which was the exposure to isotretinoin, a vitamin A derivative, which is associated with hyperostotic changes in the spine[10].

Considering his age, DISH was an unlikely diagnosis but axial radiographic changes were highly suggestive of it. On the other hand, the sacroiliac joint involvement was inconsistent with the diagnostic criteria.

The conflicting findings, in these two theoretically mutually exclusive diseases, raised a multidisciplinary discussion to offer the best treatment available for the patient. It was the recognition of both conditions that led the patient to start a DMARD that not only improved the symptoms but will unequivocally modify the prognosis.

European Journal of Case Reports in Internal Medicine

		Reference Values
Haemoglobin	15.2 g/dL	13-17 g/dl
WBC count	5,97x10^3/µL	4,00 - 11,00 x10^3/µL
Platelet count	245x10^3/µL	150-400 x10^3/µL
Erythrocyte sedimentation rate	10 mm/h	0-10 mm/h
Urea	36 mg/dL	10-50 mg/dL
Creatinine	0.86 mg/dL	0.7 -1.3 mg/dL
Aspartate aminotransferase	38 U/L	10-34 U/L
Alanine transaminase	80 U/L	10-44 U/L
Alkaline phosphatase	85 U/L	20-129 U/L
Creatine kinase	152.9 U/L	24-204 U/L
Glycosylated haemoglobin	5.5%	4.0-6.0%
Total cholesterol	203 mg/dL	0-200 mg/dL
LDL-cholesterol	144/mg/dL	0-130 mg/dL
Vitamin A	2.64 µmol/L	1.05-2.45 µmol/L
Uric acid	7.2 mg/dL	3.4-7.0 mg/dL
Ferritin	702 ng/mL	12.80-454 ng/mL
C3	149.8 mg/dL	81.0-167.0 mg/dL
C4	21.7 mg/dL	11.0-42.0 mg/dL
Antinuclear antibodies (ANA)	Negative (AC-0)	
Rheumatoid factor	<10 IU/mL	<14 IU/mL
Anti-citrullinated protein antibodies	2.6 U/mL	<10 IU/mL
Anti-SSA	0.4 U/mL	<10.0 IU/mL
Anti-SSB	0.3	<10.0
Anti-Proteinase 3 (PR3)	<2.3 UQ	<20.0 UQ
Anti-myeloperoxidase (MPO)	<3.2 UQ	<20.0 UQ
Anti-cardiolipin IgG/IgM	5.9/11 UQ	<20.0 UQ
Beta-2-glycoprotein IgG/IgM	<6.4/< 1.1 UQ	<20.0 UQ
Lupus anticoagulant	Negative	
HLAB27 (flow cytometry)	Negative	
HLA typing	HLA-A*03; HLA-A*68:01 HLA-B*45; HLA-B*51 HLA-C*02:02; HLA-C*06:02 HLA-DRB1*03; HLA-DRB1*04 HLA-DRB3+; HLA-DRB4+	
Interferon-Gamma Release Assay (IGRA)	Negative	

Table 1. Laboratory values

DOI: 10.12890/2023_003721

European Journal
of Case Reports in
Internal Medicine

REFERENCES

1. 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.
2. Kuperus JS, Waalwijk JF, Regan EA, van der Horst-Bruinsma, Cumhur Oner F, de Jong PA, et al. Simultaneous occurrence of ankylosing spondylitis and diffuse idiopathic skeletal hyperostosis: A systematic review. *Rheumatology (Oxford).* 2018;**57**:2120-2128.
3. Mader R, Verlaan J-J, Eshed I, Bruges-Armas J, Sarzi Puttini P, Atzeni F, et al. Diffuse idiopathic skeletal hyperostosis (DISH): Where are we now and where to go next. *RMD Open.* 2017;**3**:e000472.
4. Quintero-Gonzalez DC, Arbeláez-Cortés Á, Rueda JM. Clinical and radiological characteristics of diffuse idiopathic skeletal hyperostosis in two medical centers in Cali, Colombia: Report of 24 cases. *Rev Colomb Reumatol.* 2020;**27**:80–87.
5. Ritchlin C, Adamopoulos IE. Axial spondyloarthritis: New advances in diagnosis and management. *BMJ* 2021;372:m4447.
6. Navarro-Compán V, Sepriano A, El-Zorkany B, van der Heijde D. Axial spondyloarthritis. Ann Rheum Dis. 2021;80:1511-1521.
7. Kozanoglu E, Guzel R, Guler-Uysal F, Goncu K. Coexistence of diffuse idiopathic skeletal hyperostosis and ankylosing spondylitis: A case report. *Clin Rhematol.* 2002;**21**:258-260.
8. Latourte A, Charlon S, Etcheto A, Feydy A, Allanore Y, Dougados M, et al. Imaging findings suggestive of axial spondyloarthritis in diffuse idiopathic skeletal hyperostosis. *Arthritis Care Res (Holboken).* 2018;**70**:145-152.
9. Betsinger TK, Scott AB. Back-to-back: The co-occurrence of DISH and ankylosing spondylitis from early modern Poland. *Int J Paleopathol.* 2022; **40**:1-6.
10. DiGiovanna JJ. Isotretinoin effects on bone. *J Am Acad Dermatol.* 2001;**45**:S176-S182.