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KAD SIMPTOMI ZAVARAJU: IDIOPATSKA SKELETNA HIPEROSTOZA (DISH), AKSIJALNI SPONDILOARTRITIS (AXSPA) I DEGENERATIVNA BOLEST DISKA (DDD)

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Uvod

Bol u kralježnici i subjektivna ukočenost među najčešćim su razlozima upućivanja fizijatru. Klinički problem nastaje kada se sličan simptomatski obrazac pripiše pogrešnoj nosološkoj jedinici: difuznoj idiopatskoj skeletnoj hiperostozi (DISH), ankilozantnom spondilitisu odnosno aksijalnom spondiloartritisu (AS/axSpA) ili degenerativnoj bolesti diska (DDD). Iako se sve tri bolesti mogu manifestirati kroničnom boli, smanjenom pokretljivošću i radiološkim promjenama u kralježnici, njihova etiopatogeneza, komorbiditeti i terapijski pristup bitno se razlikuju. Cilj je ovog rada sažeto prikazati ključne razlike i područja preklapanja te istaknuti gdje anti-TNF biološki lijekovi imaju jasnu ulogu, a gdje su dokazi ograničeni ili izostaju. Etiopatogeneza AS/axSpA je imunološki posredovana bolest u kojoj je središnje mjesto zahvaćanja entezisa i sakroilijakalnih zglobova, uz genetsku podlogu (HLA-B27) i upalne osi (npr. TNF, IL-17). Tipičan patofiziološki slijed uključuje aktivnu upalu, zatim reparaciju i novostvorenu kost (sindesmofite), što dugoročno može dovesti do ankiloze. DISH je sustavna entezopatija obilježena osifikacijom ligamenata i hvatišta tetiva, osobito prednjeg uzdužnog ligamenta kralježnice. Patogeneza je multifaktorska i snažno je povezana s metaboličkim čimbenicima (pretilost, inzulinska rezistencija, DM2), a važan klinički aspekt je povećan rizik nestabilnih prijeloma u rigidnoj kralježnici. DDD primarno nastaje zbog starenja, mehaničkog opterećenja i genetske predispozicije, uz poremećaj homeostaze matriksa diska, staničnu senescenciju i lokalnu citokinsku aktivaciju. Iako se u degeneriranom disku mogu naći medijatori poput TNF-a, riječ je o lokalnom procesu bez tipične sistemske upalne slike.

Klinička slika AS/axSpA.

Najčešće počinje u mlađoj dobi i dominira inflamatorna križobolja (jutarnja ukočenost, poboljšanje kretanjem, noćna bol, izmjenična glutealna bol). Česte su izvan-koštano-zglobne manifestacije (uveitis, IBD, psorijaza), što je klinički važno i pri izboru biološke terapije. DISH. Tipično se javlja u starijoj dobi (češće muškarci) s progresivnom ukočenošću, osobito torakalno, i boli češće mehaničkog karaktera. Mogu se pojaviti disfagija, promuklost ili respiratorne tegobe zbog velikih cervikalnih osteofita te prijelomi nakon minimalne traume u krutoj kralježnici.

DDD

Bol je najčešće mehanička (pogoršanje opterećenjem, poboljšanje mirovanjem) uz moguću radikulopatiju ili neurogenu klaudikaciju kod hernijacije diska ili stenoze. Ne očekuju se sistemske manifestacije tipične za SpA.

Dijagnostika

Diferencijacija se oslanja na kombinaciju anamneze, kliničkog pregleda, laboratorija i slikovnih metoda. Laboratorijski upalni markeri (CRP/SE) i HLA-B27 mogu poduprijeti sumnju na axSpA, ali nisu sami po sebi dijagnostički. Najveća se zamjena događa u interpretaciji radiologije. Obrasci i ključne razlike DISH, AS/axSpA, DDD odnose se na dob, karakter boli, Rtg/NM promjene, B27 +/-, zahvaćenost SIZ-ova, izvanzglobne manifestacije i prisutnost/odsutnost upalnih parametara. MR sakroilijakalnih zglobova korisna je u ranoj fazi axSpA i u procjeni aktivnosti upale. Važno je znati da se na MR mogu vidjeti SpA-slične promjene i u DISH-u ili DDD-u (npr. koštani edem), što zahtijeva interpretaciju u odgovarajućem kliničkom kontekstu.

Liječenje AS/axSpA

Temelj su edukacija, redovita tjelovježba i NSAIL. Kod visoke aktivnosti bolesti uz objektivne znakove upale (CRP i/ili MR) indicirani su biološki DMARD: TNF inhibitori (TNFi) ili IL-17 inhibitori, a izbor se individualizira prema fenotipu i izvanzglobnim manifestacijama.

DISH

Liječenje je pretežno simptomatsko (analgezija/NSAIL prema potrebi, fizikalna terapija, održavanje mobilnosti) uz naglasak na liječenje komorbiditeta (pretilost, metabolički sindrom, DM2) i prevenciju komplikacija. Kirurško liječenje razmatra se kod disfagije, kompresije ili nestabilnih prijeloma.

DDD

Primarno konzervativno: aktivna rehabilitacija, edukacija, analgetska terapija, po potrebi intervencijske procedure. Kirurgija je rezervirana za jasne neurološke indikacije ili refraktornu bol uz korelaciju kliničkih i slikovnih nalaza.

Anti-TNF biološki lijekovi u DISH-u: što znamo i kada bi „eventualno" mogli doći u obzir? Za AS/axSpA, TNF inhibitori su terapija s jasnom indikacijom i dokazima učinkovitosti u aktivnoj bolesti. Nasuprot tome, za „čisti" DISH nema smjernicama utemeljene indikacije za TNFi. Razlog je to što DISH nije klasična sistemska TNF-posredovana upalna bolest, nego prvenstveno osificirajuća entezopatija povezana s metaboličkim čimbenicima. Ipak, u literaturi postoje ograničeni opservacijski podaci (konferencijski izvještaji i mali opservacijski uzorci) koji opisuju poboljšanje simptoma kod odabranih bolesnika s tzv. „klinički aktivnim" DISH-om liječenih TNFi. Autori pritom naglašavaju mogućnost da se radi o modulaciji boli, a ne o stvarnom usporavanju osifikacije, te da je potrebna rigorozna randomizirana studija.

Klinički razumna „siva zona" (izvan standarda):

TNFi bi se u praksi razmatrao gotovo isključivo ako postoji druga jasna indikacija: (1) DISH uz dokazani axSpA/AS (overlap) s objektivnom upalom (sakroiliitis na MRI/CT, povišen CRP) – tada se liječi SpA komponenta prema smjernicama; (2) DISH uz neku drugu registriranu TNF-indikaciju (npr. psorijatični artritis, reumatoidni artritis, IBD). Primjena TNFi isključivo zbog DISH-a ostaje eksperimentalna/off-label.

HLA-B27 i DISH: može li DISH biti „B27 pozitivan"?

Općenito, DISH nije povezan s HLA-B27 i to se često koristi kao diferencijalno-dijagnostički argument u odnosu na AS/axSpA. Međutim, moguće je da pojedini bolesnici imaju komorbidni/overlap fenotip DISH + AS. U klasičnom prikazu koegzistencije DISH-a i AS-a opisani su bolesnici među kojima su 2 od 3 bili HLA-B27 pozitivni, što upućuje na to da HLA-B27 pozitivnost u takvom kontekstu više govori u prilog prisutnosti SpA komponente nego „B27-DISH-u".

Povezanost s DM i metaboličkim sindromom te zahvaćanje drugih organskih sustava

DISH je najdosljednije povezan s metaboličkim sindromom (pretilost, hipertenzija, dislipidemija i DM2). Novi kohortni podaci u kardiovaskularnih bolesnika sugeriraju da je prisutnost DISH-a na rutinskoj radiografiji povezana s višom stopom incidentnog DM2, neovisno o uobičajenim rizičnim markerima, što otvara mogućnost da DISH bude „signal" za intenzivniji metabolički screening. Osim metaboličkog aspekta, DISH može zahvatiti i druge sustave posredno ili mehanički: disfagija i respiratorne tegobe (cervikalni osteofiti), te veći rizik teških prijeloma kralježnice zbog rigidnosti.

Zaključak

DISH, AS/axSpA i DDD mogu se prezentirati sličnim simptomima, ali imaju različite mehanizme bolesti i različite terapijske ciljeve. Ključ diferencijacije je prepoznati (i objektivizirati) upalu u axSpA te razlikovati entezofitnu osifikaciju DISH-a od degenerativnih promjena DDD-a. Anti-TNF terapija je standard u aktivnom axSpA, dok je u DISH-u zasad eksperimentalna i razmatra se ponajprije u slučaju preklapanja s axSpA ili druge jasne TNF-indikacije. S obzirom na snažnu povezanost DISH-a s metaboličkim sindromom, prepoznavanje DISH-a ima vrijednost i izvan lokomotornog sustava – kao poticaj za sustavno procjenjivanje i liječenje kardiometaboličkog rizika.

Ključne riječi

bol, DDD, hiperostoza, kralježnica, spondiloartritis, ukočenost

WHEN SYMPTOMS MISLEAD: DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS (DISH), AXIAL SPONDYLOARTHRITIS (AXSPA), AND DEGENERATIVE DISC DISEASE (DDD)

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Introduction

Spinal pain and patients perceived stiffness are among the most common reasons for referral to a physiatrist. A clinical problem arises when a similar symptomatic pattern is attributed to the wrong nosological entity: diffuse idiopathic skeletal hyperostosis (DISH), ankylosing spondylitis/axial spondyloarthritis (AS/axSpA), or degenerative disc disease (DDD). Although all three conditions may present with chronic pain, reduced mobility, and radiological changes in the spine, their etiopathogenesis, comorbidities, and therapeutic approaches differ substantially. The aim of this paper is to concisely present the key differences and areas of overlap, and to highlight where anti-TNF biologic agents have a clear role and where evidence is limited or lacking. Etiopathogenesis AS/axSpA is an immune-mediated disease in which the central site of involvement is the enthesis and the sacroiliac joints, with a genetic background (HLA-B27) and inflammatory pathways (e.g., TNF, IL-17). A typical pathophysiological sequence includes active inflammation followed by repair and new bone formation (syndesmophytes), which over time may lead to ankylosis. DISH is a systemic enthesopathy characterized by ossification of ligaments and tendon insertions, particularly the anterior longitudinal ligament of the spine. Its pathogenesis is multifactorial and strongly associated with metabolic factors (obesity, insulin resistance, type 2 diabetes mellitus). An important clinical aspect is the increased risk of unstable fractures in a rigid spine. DDD primarily results from aging, mechanical loading, and genetic predisposition, involving disturbed disc matrix homeostasis, cellular senescence, and local cytokine activation. Although mediators such as TNF can be found in a degenerated disc, this is a local process without a typical systemic inflammatory picture. Clinical presentation AS/axSpA. It most often begins at a younger age, with the dominant symptom of inflammatory low back pain. Extra-musculoskeletal manifestations are common (uveitis, inflammatory bowel disease, psoriasis), which is clinically important when selecting biologic therapy. DISH. It typically occurs at an older age (more often in men) with progressive stiffness—especially in the thoracic spine—and pain that is more often mechanical in character. Dysphagia, hoarseness, or respiratory symptoms may occur due to large cervical osteophytes, as well as fractures after minimal trauma in a stiff spine. DDD. The pain is most often mechanical (worse with loading, better with rest), with possible radiculopathy or neurogenic claudication in cases of disc herniation or spinal stenosis. Systemic manifestations typical of SpA are not expected. Diagnostics Differentiation relies on a combination of history, physical examination, laboratory testing, and imaging. Inflammatory markers (CRP/ESR) and HLA-B27 can support suspicion of axSpA, but are not diagnostic on their own. The greatest diagnostic confusion occurs in radiologic interpretation. MRI of the sacroiliac joints is useful in

the early stage of axSpA and for assessing inflammatory activity. It is important to recognize that MRI can also show SpA-like changes in DISH or DDD (e.g., bone marrow edema), which requires interpretation within the appropriate clinical context. Treatment The cornerstone therapy for all three entities consists of patient education, regular exercise, and NSAIDs. AS/axSpA. In cases of high disease activity with objective signs of inflammation (CRP and/or MRI), biologic DMARDs are indicated: TNF inhibitors (TNFi) or IL-17 inhibitors, with the choice individualized according to phenotype and extra-musculoskeletal manifestations. DISH. Treatment is predominantly symptomatic with emphasis on managing comorbidities (obesity, metabolic syndrome, type 2 diabetes) and preventing complications. Surgical treatment is considered in cases of dysphagia, compression, or unstable fractures. DDD. Primarily conservative management and—when appropriate—interventional procedures. Surgery is reserved for clear neurological indications or refractory pain with concordant clinical and imaging findings. Anti-TNF biologics in DISH: what do we know, and when might they "possibly" be considered? For AS/axSpA, TNF inhibitors have a clear indication and strong evidence of efficacy in active disease. In contrast, for "pure" DISH, there is no guideline-based indication for TNFi. This is because DISH is not a classic systemic TNF-mediated inflammatory disease, but rather a primarily ossifying enthesopathy associated with metabolic factors. Nevertheless, the literature contains limited observational data describing symptom improvement in selected patients with so-called "clinically active" DISH treated with TNFi. The authors emphasize the possibility that this reflects modulation of pain rather than a true slowing of ossification, and that a rigorous randomized trial is needed. A clinically reasonable "gray zone" (outside standard practice) In practice, TNFi would be considered almost exclusively when there is another clear indication: DISH with confirmed axSpA/AS overlap and objective inflammation (sacroiliitis on MRI/CT, elevated CRP)—in that case, the SpA component is treated according to guidelines; DISH with another approved TNF indication (e.g., psoriatic arthritis, rheumatoid arthritis, inflammatory bowel disease). Use of TNFi solely for DISH remains experimental/off-label. HLA-B27 and DISH: can DISH be "B27 positive"? In general, DISH is not associated with HLA-B27, which is often used as a differential diagnostic argument compared with AS/axSpA. However, some patients may have a comorbid/overlap phenotype of DISH + AS. In a classic report describing co-existence of DISH were HLA-B27 positive, suggesting that HLA-B27 positivity in this context supports the presence of an SpA component rather than "B27-DISH." Association with diabetes/metabolic syndrome and involvement of other organ systems DISH is most consistently associated with metabolic syndrome. New cohort data in cardiovascular patients suggest that the presence of DISH on routine radiography is associated with a higher rate of incident type 2 diabetes, independent of usual risk markers—raising the possibility that DISH may serve as a "signal" for more intensive metabolic screening. Beyond the metabolic aspect, DISH can also affect other systems indirectly or mechanically: dysphagia and respiratory symptoms (cervical osteophytes), and a risk of spinal fractures. Conclusion DISH, AS/axSpA, and DDD can present with similar symptoms, but

they involve different disease mechanisms and different therapeutic targets. The key to differentiation is recognizing (and objectifying) inflammation in axSpA and distinguishing DISH-related enthesophyte ossification from degenerative changes of DDD. Anti-TNF therapy is the standard of care in active axSpA, whereas in DISH it remains experimental and is considered primarily in cases of overlap with axSpA or another clear TNF indication. Given the strong association between DISH and metabolic syndrome, identifying DISH has value beyond the musculoskeletal system—as a prompt for systematic assessment and management of cardiometabolic risk.

Keywords

DDD, hyperostosis, pain, spine, stiffness, spondyloarthritis

References

1. Ramiro S, Nikiphorou E, Sepriano A et al. ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update. Ann Rheum Dis. 2023;82(1):19-34. doi:10.1136/ard-2022-223296.
2. Mader R, Verlaan JJ, Eshed I et al. Diffuse idiopathic skeletal hyperostosis (DISH): where we are now and where to go next. RMD Open. 2017;3(1):e000472. doi:10.1136/rmdopen-2017-000472.
3. Mader R, Pappone N, Baraliakos X et al. Diffuse idiopathic skeletal hyperostosis (DISH) and a possible inflammatory component. Curr Rheumatol Rep. 2021;23(1):6. doi:10.1007/s11926-020-00972-x.
4. Kuperus JS, Mohamed Hoesein FAA, de Jong PA, Verlaan JJ. Diffuse idiopathic skeletal hyperostosis: etiology and clinical relevance. Best Pract Res Clin Rheumatol. 2020;34(3):101527. doi:10.1016/j.berh.2020.101527.
5. Harlianto NI, Foppen W, Mohamed Hoesein FAA, Hol ME, Verlaan JJ, de Jong PA, Westerink J, UCC-SMART Study group. DISH as a marker for incident diabetes mellitus in cardiovascular disease patients. Rheumatology (Oxford). 2025;64(10):5287-5294. doi:10.1093/rheumatology/keaf268.
6. Takahashi T, Yoshii T, Mori K et al. Comparison of radiological characteristics between diffuse idiopathic skeletal hyperostosis and ankylosing spondylitis: a multicenter study. Sci Rep. 2023;13(1):1849. doi:10.1038/s41598-023-28946-w.
7. Ziade N, Udod M, Kougkas N, Tsiami S, Baraliakos X. Significant overlap of inflammatory and degenerative features on imaging among patients with degenerative disc disease, diffuse idiopathic skeletal hyperostosis and axial spondyloarthritis: a real-life cohort study. Arthritis Res Ther. 2024;26(1):147. doi:10.1186/s13075-024-03359-w.
8. Gradisnik L, Kocivnik J, et al. Degenerative disease of intervertebral disc: a narrative review of pathogenesis, clinical implications and therapies. Bioengineering. 2025;13(1):40. doi:10.3390/bioengineering13010040.
9. Kiefer D, Khan MA, Baraliakos X. Diffuse idiopathic skeletal hyperostosis (DISH) and axial spondyloarthritis (axSpA) - similarities and differences. Explor Musculoskeletal Dis. 2023;1:194-206. doi:10.37349/emd.2023.00022.