DISH is a condition characterized by calcification and/or ossification of soft tissues, mainly entheses, ligaments and joint capsules. Its prevalence increases with age and, therefore, DISH is a relatively common entity in the elderly. The classical site of involvement is the spinal column with right anterolateral soft tissue ossification being the most characteristic feature. However, DISH is not limited to the spine, and may affect multiple peripheral sites independently. Extraspinal entheseal ossifications are common and observing their isolated presence may lead to the diagnosis of DISH. Furthermore, hypertrophic or atypical OA observed in joints usually not affected by primary OA has frequently been reported in DISH.

Several metabolic derangements and concomitant diseases have been suggested to be associated with DISH including obesity, increased waist circumference, hypertension, dyslipidaemia, diabetes mellitus (DM), hyperuricaemia, metabolic syndrome and an increased risk for cardiovascular diseases. Witnessing the present increase in lifespan, obesity, DM and metabolic syndrome in the Western population, the prevalence of DISH should be expected to rise. In order to increase the awareness for DISH, this review focuses on the extraspinal features of the condition.

**Key words:** DISH, Enthesopathy, Osteoarthritis, Calcification, Metabolic syndrome.

**Introduction**

DISH is a condition characterized by calcification and ossification of enthesal sites. At present, ossification and calcification of the anterolateral aspect of the thoracic spine is considered to be the hallmark of the disease [1, 2]. The most commonly used classification criteria were defined by Resnick and Niwayama [3], and require involvement of at least four contiguous thoracic vertebral segments, preservation of intervertebral disc spaces and the absence of apophyseal joint degeneration or sacroiliac inflammatory changes. DISH is probably an asymptomatic condition in many affected individuals, although numerous clinical symptoms have been described including pain, limited range of spinal motion and increased susceptibility to unstable spinal fractures after trivial trauma. Cervical and lumbar segments of the spine are also frequently affected by DISH, and clinical manifestations include dysphagia and airway obstruction at cervical levels and radiculopathy and painful stiffness at lumbar levels.

DISH is, however, not limited to the spinal column and has often been reported to involve peripheral sites as well. This finding was reflected by the newer definition of Utsinger [4], who lowered the threshold for spinal involvement to three contiguous vertebral bodies, but required the presence of peripheral enthesopathies to the diagnostic parameters to establish a (high probability of) DISH. Additionally, various constitutional and metabolic abnormalities have been reported to be associated with DISH in varying degrees, although their presence is currently not mandatory to establish a formal diagnosis of DISH. Recognizing the present shortcomings to comprehensively describe the full phenotype of DISH, the current review will focus on the extraspinal manifestations of DISH.

**Peripheral involvement**

Peripheral involvement in DISH is characterized by several distinctive features, as given below:

1. involvement of joints usually unaffected by primary OA;
2. increased hypertrophic changes compared with primary OA;
3. prominent enthesopathies at various sites adjacent to peripheral joints; and
4. calcification and ossification of entheses in sites other than joints.

In their secular work, Resnick et al. [5] showed that the majority of the patients with DISH also showed clinical and radiographic abnormalities at locations other than the classical OA sites including elbows, wrists, ankles and shoulders. The main radiological findings consisted of hyperostosis of joints involved. It was suggested that the radiographic appearance in the peripheral skeleton might be distinctive enough to suggest the diagnosis of DISH, even in the absence of axial radiographs. It should be noted, though, that large discrepancies between radiological and clinical findings may exist. In fact, hyperostosis of the shoulder has been often associated with shoulder pain [6]. On the other hand, the association of hyperostosis of the elbow and pain was found to be dubious in the study by Beyeler et al. [7]. MCP joint involvement is uncommon in OA, and in recent imaging studies (radiographs and/or ultrasonography), these joints were affected in up to 10% of the populations studied [8, 9]. Contrasting these data, the reported prevalence of MCP involvement in patients affected by DISH was 56% in a radiological study without clinical endpoints [10] (Fig. 1). In a study that evaluated the radiographic appearance of the sternomanubrial joint in various inflammatory joint diseases, the most remarkable changes were seen in patients with DISH. It was shown that the juxta-articular bone was often affected with sparing of the joint surfaces [11].

Because DISH and OA affect similar age groups, these conditions might (and probably do) coexist. Due to the hypertrophic nature of DISH, joints affected by both OA and DISH are typically more hypertrophic compared with joints with OA but...
without concomitant DISH. Moreover, the frequency of Heberden’s and Bouchard’s nodes was found to be doubled in patients with spinal DISH compared with controls; therefore, it was suggested that DISH should be considered as an independent risk factor for the development of palpable finger joint nodules [12].

Hyperostoses, in the form of enthesopathies affecting structures adjacent to joints, have been reported to occur in many locations such as the elbows, hips, shoulders, knees and ankles (Fig. 2). These changes may probably be responsible for a reduced range of motion in these joints and possibly also for the subsequent development of OA changes [4, 5, 13]. Stiffening of the capsules and adjacent ligaments, as a result of calcification and/or ossification, may play a role in the more hypertrophic and destructive nature of OA processes, due to increased IA pressure [14]. Peripheral enthesopathies, which often are ossified, are common findings in DISH. Typically they are large, symmetrical, showing a distinct cortex and have been reported to be present in the tibial spine, heel, patella and olecranon [15] (Fig. 3). Particular attention has been paid to enthesopathies of the pelvis and, although hampered by sample size, a study identified sites of ossifications highly characteristic for DISH, such as the sacrotuberous ligament, iliolumbar ligament, ligamentous upper portion of the sacroiliac joint and insertion of the iliopsoas muscle into the lesser trochanter [13]. These studies suggest, independently, that peripheral enthesopathies should be considered into the full set of criteria defining DISH.

The propensity for new bone formation in patients with DISH has emerged in descriptions of large sesamoid bones, thickened cortical bone, enlarged fingers’ distal tufts, hyperostosis of ribs and the tendency for heterotopic ossifications following orthopaedic surgery [10, 16–18]. Concomitant chondrocalcinosis, ectopic enthesal calcifications or nephrolithiasis have been reported in familial cases of DISH [19]. This information suggests that the same, yet unknown, pathogenetic factors operating in DISH might influence structures other than bone. Because arterial and cartilage calcification might share similar pathogenetic mechanisms, the association of DISH with calcification and/or ossification in soft tissues other than the musculoskeletal system, such as arterial walls, deserves further investigations [20]. Although DISH may coexist with OA, the distinct clinical and radiological features as described above could allow for a separate and more accurate definition of DISH [21].

It should be taken into consideration, though, that the large body of data has mainly been based on imaging studies; only a few studies addressed the relationships between radiological findings and clinical manifestations. The clinical impacts of these radiographic findings have not been extensively studied, and therefore need further investigations.

It is evident that there is a need to incorporate the musculoskeletal extraspinal manifestations into a future classification for DISH. Within this context, a better characterization of the musculoskeletal clinical manifestations of DISH is needed in order to generate a practical clinical–radiological classification rather than a radiological-only classification.

Other extraskeletal associations

Beyond the musculoskeletal manifestations of DISH, other conditions have been reported to be closely associated with the disease. Some of these conditions have persistently been found in patients with DISH and might, therefore, be considered as integral components of the clinical spectrum of the disease. Obesity, a large waist circumference (WC), hypertension, diabetes mellitus

**Fig. 1.** Joint space narrowing and hypertrophic exuberant new bone formation of the metacarpals (1). New bone formation of the distal tufts (2).

**Fig. 2.** Elbow enthesopathies involving the olecranon (1) and both epicondyles (2).

**Fig. 3.** Ossified patellar and tibial tuberosity enthesopathies.
(DM), hyperinsulinaemia, dyslipidaemia and hyperuricaemia have all been reported in patients with DISH [23–29].

A robust body build in patients with DISH compared with non-DISH patients, expressed by either higher BMI or WC, is a well-known feature, since the early descriptions by Forestier and others [22, 30, 31] were reiterated recently. This finding has been consistent across many studies and should be regarded as a significant health risk in patients with DISH.

Glucose intolerance, DM and hyperinsulinaemia have been often reported in patients with DISH. However, this notion is not accepted by all and was again questioned recently [26, 32]. The difference in results could be derived from the fact that most studies measured fasting glucose and insulin, rather than performing these laboratory tests after glucose challenge [23]. Although many patients with DISH are also affected by DM, this association and the presumed association of DISH with hypertension and hyperuricaemia need further controlled studies.

Hyperlipidaemia has been reported in DISH patients by some authors. However, other studies showed that elevated total cholesterol or triglyceride levels did not differ between non-diabetic patients with and without DISH. It should be noted that the cut-off values for the definition of dyslipidaemia and DM were different than current more modern definitions, and the authors did not consider high-density and low-density lipoprotein separately. Furthermore, the use of lipid-lowering agents was not accounted for, as was previous cardiovascular morbidity [26, 28]. Therefore, at present, the association between DISH and hyperlipidaemia is questionable. The inconsistencies of reporting metabolic abnormalities in relation to DISH could be derived from a lack of standardization in clinical or laboratory measurements, selection bias or insufficient sample size.

From the large body of literature dealing with the constitutional and metabolic derangements in DISH, it could be expected that patients with this condition are at risk for the metabolic syndrome and cardiovascular risks. Two recent studies [33, 34] showed these patients to have a higher incidence of risk factors than their counterparts. Based on these data, it is suggested that DISH should no longer be regarded as an isolated spinal condition, but rather as a systemic disease. DISH should be considered as an extensive health risk in patients with DISH.

**Therapeutic considerations**

The pathogenesis of the disease is not clear, and therefore the current therapeutic interventions are empirical. Treatment should be aimed at symptomatic relief of pain and stiffness, and measures similar to those employed in the treatment of OA, such as analgesics, NSAIDs, local applications and physiotherapy, might also prove to be useful in patients with DISH. Control of associated constitutional and metabolic disorders, including obesity, hypertension, hyperinsulinaemia (with or without hyperglycaemia), dyslipidaemia, hypertriglyceridaemia and hyperuricaemia, may reduce the morbidity associated with these disorders, may retard future cardiovascular disease and possibly slow down the progression of soft tissue ossification. Therapeutic interventions should also aim at a reduction of insulin secretion and insulin resistance. In patients with non-insulin-dependent DM, the use of biguanides, which induce a better usage of insulin, may offer an advantage over the use of sulphnylureas, which increase insulin secretion. When coexisting hypertension is treated, the choice of drugs that might improve insulin resistance such as angiotensin-converting enzyme inhibitors, Ca\(^{2+}\) channel blockers and \(\alpha\)-blockers should be preferred over drugs that might worsen insulin resistance, such as thiazide diuretics and \(\beta\)-blockers.

Prevention of possible complications such as spinal fractures and heterotopic ossification following orthopaedic surgical procedures deserves further attention. Some therapeutic options are summarized in Fig. 4 [35].

**Conclusions**

DISH is a clinical–radiological entity usually diagnosed on radiographic grounds only. The clinical manifestations of the disease, in particular those related to the peripheral sites of involvement, have not yet been characterized but deserve particular attention. The role played by the metabolic and constitutional derangements as well as its impact on the diagnosis of DISH awaits further studies. Based on these data, it is suggested that DISH should not be regarded as an isolated spinal condition, but rather as a systemic disease. DISH should be considered as an extensive health risk in patients with DISH.

**Prevention of complications**

- Interventions at molecular level to inhibit factors that might promote mesenchymal differentiation into osteoblasts:
  - NF-\(\kappa\)-B, PDGF-BB, TGF-\(\beta\)-1, PGI\(_2\) and BMP-2

**Future perspectives**

**Fig. 4.** Therapeutic options in DISH. ACE: angiotensin-converting enzyme; NF-\(\kappa\)-B: nuclear factor-\(\kappa\)-B (reproduced with permission from Mader [35]).
proliferative musculoskeletal disease with clinical and metabolic derangements, and that the expected worldwide increase in obesity and diabetes urgently needs further investigations. Large-scale controlled studies are needed in order to delineate the entire spectrum of this condition.

Rheumatology key messages

- Musculoskeletal manifestations of DISH are not limited to the spine and often affect peripheral sites.
- DISH is often associated with metabolic and constitutional derangements, leading to an increased cardiovascular risk.

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References