RHEUMATOLOGY

Rheumatology 2014;53:1951–1957
doi:10.1093/rheumatology/ket335
Advance Access publication 23 October 2013

Original article

The natural course of bridging osteophyte formation in diffuse idiopathic skeletal hyperostosis: retrospective analysis of consecutive CT examinations over 10 years

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Abstract

Objective. The aim of this study was to evaluate the natural progression of bridging osteophyte formation in diffuse idiopathic skeletal hyperostosis (DISH) on CT by a newly proposed scoring system.

Methods. CT examinations of the thoracic/lumbar spine of DISH patients (Resnick criteria) obtained at two or more time points within a minimum of 3 years were evaluated. Twenty-six patients (mean age at first CT 57 years, 21 males) fulfilled the entry criteria. A semi-quantitative scoring system for osteophyte progression was evaluated for intra- and interreader reliability on 68 vertebral units (VUs) in five patients. CT sagittal reformates of all 26 study patients were scored by two readers in consensus.

Results. Scoring intra- and interobserver intraclass correlation coefficient values were high (0.971 and 0.893, respectively). The average time points per patient was 3.6 in 398 VUs analysed for 93 time points. The average time between the first and last scans was 5.6 years (range 3–10). The scores of six patients were unchanged. The scores of 20 patients increased by 3 units in 48 VUs over 5.6 (S.D. 3.1) years. The time for a DISH score to increase by 1 scoring unit was 1.6 (S.D. 0.4) years. Two bridging patterns were observed: osteophyte fusion associated with a calcified anterior longitudinal ligament (ALL, 66%) and osteophyte fusion without apparent ALL calcification (33%). Both patterns were observed concomitantly in 15 patients.

Conclusion. The new scoring system may enable earlier diagnosis and help predict disease progression into its final confluent osteophyte form. The two described patterns may indicate an underlying inflammatory rather than a degenerative pathogenesis.

Key words: DISH, CT, osteophyte, radiographic progression.

Introduction

Diffuse idiopathic skeletal hyperostosis (DISH) is a common disease characterized by ossification of paravertebral ligaments and peripheral entheses [1]. The appearance of DISH depends on the spinal level in which it develops, and the occurrence of distinctive flowing linear ossification is most prominent between thoracic vertebrae [1, 2]. The classification criteria formulated by Resnick and Niwayama [1] are based on the analysis of plain radiographs and require flowing osteophytes in at least four contiguous vertebrae of the thoracic spine, preservation of the intervertebral disc space, as well as the absence of apophyseal joints or sacroiliac inflammatory changes. Although DISH was initially considered a radiographic rather than a clinical entity, and one that may not be infrequently diagnosed in asymptomatic individuals, it has become increasingly recognized that clinical complaints are prevalent among affected individuals.

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Submitted 20 February 2013; revised version accepted 28 August 2013.

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Clinical presentation may mimic long-standing advanced AS with severe spinal limitation and postural abnormalities [3]. Also similar to AS, DISH increases susceptibility to unstable spinal fractures [4]. Moreover, the majority of DISH patients complain of morning stiffness, an indication of underlying inflammation [5].

The aetiology and pathogenesis of AS has been extensively studied [6][8], but the origin of DISH remains obscure[9]. A lowered threshold for the extent of spinal involvement in the diagnosis of DISH was suggested in which only two contiguous vertebral bodies accompanied by multiple peripheral enthesopathies would suffice to establish the diagnosis [5]. Also the natural radiological progression of spinal DISH has yet to be studied in depth.

Most studies that have described and evaluated DISH were based on X-rays [1, 2, 7–11]. CT is an imaging modality that is superior to plain films due to its higher spatial resolution and three-dimensional imaging information. The aim of this study was to evaluate the natural progression and dynamics of the radiographic course of bridging osteophyte formation of DISH on CT by means of a scoring system designed for this setting.

Materials and methods

Institutional review board approval was given by the ethics committee of the Sheba Medical Center for the retrospective analysis of the CT scans and for reviewing patients' medical records between 2000 and 2012. Patient consent was waived by the ethics committee due to the retrospective nature of the study.

Population

Archival records of 157 patients with radiologically diagnosed DISH were used as the primary cohort of the study. The institution's picture computerized archive system (PACS) was searched for the presence of spinal CT studies performed on these patients. Those studies were reviewed and only those of patients who fulfilled the Resnick criteria, i.e. had at least four consecutive flowing osteophytes at either the cervical, thoracic or lumbar spine and who had undergone at least two CT examinations of the same involved spinal part with a minimum interval of 3 years between examinations, were included in this investigation. Since not all patients had CT scans of the sacroiliac joint, Resnick's criterion regarding involvement of the sacroiliac joint was not evaluated in the current study. Low-resolution CT scans or CT scans with poor quality (e.g. due to patient movement) were excluded.

Imaging

All CT studies were performed on the following CT scanners: Mx8000 Quad 4 slices, Mx8000 IDT 16 slices, Brilliance 40, 64 and 128 (Philips Medical Systems, Eindhoven, The Netherlands) and 64-slice VCT LightSpeed (GE Medical Systems, Milwaukee, WI, USA). Slice thickness ranged between 0.6 and 2.5 mm. Images were reconstructed in bone algorithm, reformatted in multiplanar planes and evaluated in the sagittal orientation.

Developing and validating a semi-quantitative scoring system for DISH

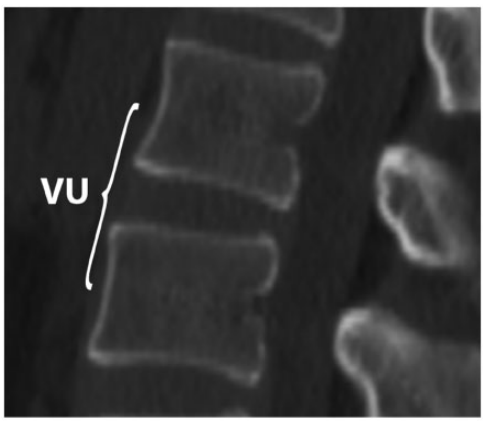
A new semi-quantitative scoring system was developed for the evaluation of osteophyte progression in DISH based on the suggested X-ray scoring system for DISH by Mata *et al.* [8], on the radiographic scoring method for AS [the modified Stokes AS Spinal Score (mSASSS)] [12, 13] and on the observations of Baraliakos *et al.* [7, 14] in the evaluation process of spinal X-rays of DISH patients. The semi-quantitative scoring system refers to individual vertebral units (VUs) included in their entirety on the sagittal CT reconstruction view of the spine. A VU is defined as the area between the lower border of the upper vertebral body and the upper border of the lower vertebral body (Fig. 1) [15]. The scoring system is comprised of six grades ranging between no osteophytes and fully confluent bridging osteophytes as follows: 0 = no osteophytes, 1 = $\geqslant$1 small osteophytes ($\leqslant$50% of the intervertebral disc space), 2 = $\geqslant$1 large osteophytes (>50% of the intervertebral disc space), 3 = anterior longitudinal ligament (ALL) calcification, 4 = ALL calcification and $\geqslant$1 osteophytes, 5 = bridging between calcified ALL and one osteophyte, 6a = bridging between calcified ALL and both osteophytes and 6b = bridging between both osteophytes without ALL calcification (Table 1 and Fig. 2).

Five randomly chosen CT scans with a minimum of 10 (range 10–19) VUs per patient were scored separately by two readers (a musculoskeletal radiologist and a senior resident) at two different time points with a minimum interval of 1 month between scorings. The new scoring system was evaluated for reader reproducibility and interreader reliability.

CT evaluation and scoring

The two readers evaluated all patients' CT images in consensus and scored each VU that was included in its entirety in the sagittal scan. The readers were not aware

Fig. 1 VU for the evaluation of CT images in the spine of patients with DISH



of the indication for performing the CT scan, but they were aware of the patient's age and the chronology of the CT scans. Each patient's CT scans for all available time points were evaluated at the same session, starting with scoring of the earliest CT scan and continuing in chronological order until the last scan.

Table 1 The new scoring system for evaluation of spinal lesions in patients with DISH as assessed by sagittal CT reformates

Score	Definition[a]
0	No changes
1	⩾1 small osteophytes[b]
2	⩾1 large osteophytes[c]
3	ALL calcification
4	ALL calcification and ⩾1 osteophytes
5	Bridging between calcified ALL and one osteophyte
6a	Bridging between calcified ALL and both osteophytes
6b	Bridging between both osteophytes without ALL calcification

[a]Scoring refers to individual VUs included in their entirety on the sagittal CT reconstruction view of the spine. [b]A small osteophyte ⩽50% of the intervertebral disc space. [c]A large osteophyte >50% of the intervertebral disc space.

Statistical analysis

Data were analysed with the SPSS 16 package (SPSS, Chicago, IL, USA). Intraclass correlation coefficients (ICCs) were calculated by two-way random analysis of variance for absolute agreement. An ICC is presented for each VU level. The 95% CI for the ICC is presented, as is the *P*-value for the ICC. *P*-values <0.05 were considered to be statistically significant. ICC values were interpreted as follows: 0–0.2 = poor agreement, 0.3–0.4 = fair agreement, 0.5–0.6 = moderate agreement, 0.7–0.8 = strong agreement and >0.8 = almost perfect agreement. The percentage of both intra- and interobserver agreement is also reported.

Results

Sixty-four patients out of the 157 evaluated had spinal CT studies in the institution's PACS. Twenty-eight patients had one CT only and were thus excluded from the study. Also excluded were two patients whose CTs did not conform to Resnick's criteria and eight patients with low-quality CT scans. Twenty-six patients (a total of 93 CT examinations) fulfilled the inclusion criteria [male:female ratio 21:5, mean age 57 years (range 41–71) at first CT examination, mean age 62 years (range 44–79) at final CT examination]. A total of 398 VUs were evaluated at 93 time points. The medical indications for CT examinations of the 26 study patients were malignancy follow-up ($n = 17$), chronic lung disease follow-up ($n = 4$),

Fig. 2 The DISH scoring system in detail presented (**a**) schematically and (**b**) on sagittal CT reformates of the spine

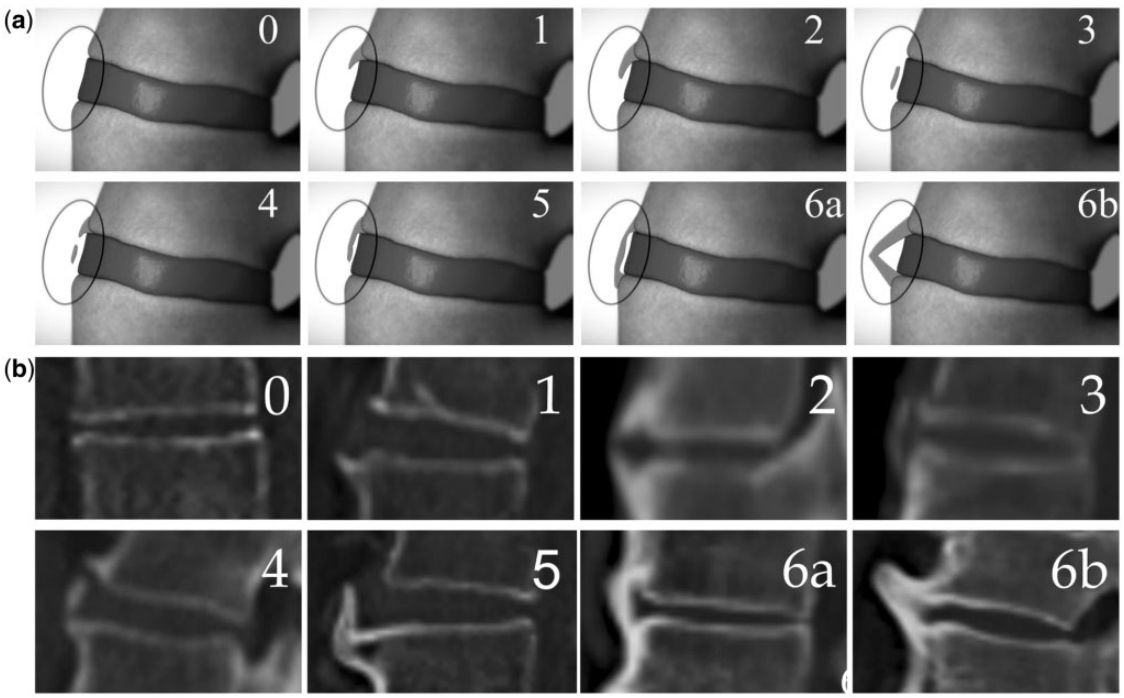


Table 2 Intra- and interobserver agreement by VU spinal level

VU level	Intraobserver agreement		Interobserver agreement	
	ICC (95% CI)	*P*-value	ICC (95% CI)	*P*-value
D2–3	0.569 (0, 0.914)	0.153	0.320 (0, 0.960)	0.393
D3–4	0.403 (0, 0.869)	0.231	0.240 (0, 0.665)	0.922
D4–5	0.995 (0.977, 0.999)	<0.0001	0.672 (0, 0.979)	0.211
D5–6	1	<0.0001	0.989 (0.894, 0.999)	0.002
D6–7	1	<0.0001	0.989 (0.894, 0.999)	0.002
D7–8	1	<0.0001	0.727 (0, 0.982)	0.157
D8–9	1	<0.0001	0.375 (0, 0.856)	0.684
D9–10	1	<0.0001	0.528 (0, 0.947)	0.224
D10–11	1	<0.0001	0.990 (0.923, 0.999)	<0.0001
D11–D12	1	<0.0001	0.994 (0.958, 0.999)	<0.0001
D12–L1	1	<0.0001	0.970 (0.754, 0.997)	0.002
Overall thoracic	0.953 (0.93, 0.969)	<0.0001	0.851 (0.735, 0.916)	<0.0001
L1–L2	1	<0.0001	0.983 (0.833, 0.999)	0.004
L2–L3	1	<0.0001	0.727 (0, 0.982)	0.157
L3–L4	0.984 (0.926, 0.997)	<0.0001	0.640 (0, 0.976)	0.212
L4–L5	0.992 (0.964, 0.998)	<0.0001	0.727 (0, 0.982)	0.157
L5–S1	0.996 (0.980, 0.999)	<0.0001	0.911 (0, 0.994)	0.048
Overall lumber	0.987 (0.975, 0.993)	<0.0001	0.842 (0.613, 0.937)	<0.0001

ICC value interpretation: 0–0.2: poor agreement; 0.3–0.4: fair agreement; 0.5–0.6: moderate agreement; 0.7–0.8: strong agreement; >0.8: almost perfect agreement.

nephrolithiasis follow-up ($n = 2$), and one patient each with vascular disease, back pain and trauma.

Validation of the semi-quantitative scoring system

A total of 68 VUs in five patients were evaluated twice by each of the two observers. The overall intraobserver exact agreement was 90.7% with an ICC of 0.971 (95% CI 0.960, 0.980, $P = 0.0001$). The first and second readers had almost perfect intraobserver agreement rates of 90.0% and 94.3% with ICC values of 0.942 (95% CI 0.905, 0.964) and 0.998 (95% CI 0.997, 0.999), respectively. This difference was not statistically significant ($P = 0.346$). The overall exact interobserver agreement was 59.4%, with a strong interclass correlation of 0.893 (95% CI 0.827, 0.934, $P = 0.0001$). The intra- and interobserver agreements (ICCs) by specific spinal level are presented in Table 2.

CT scoring of DISH

There was an average of six (range two to seven) CT scans evaluated per patient, and the average time between the first and last scans was 5.6 years (range 3–10 years). The distribution of the evaluated VUs was as follows: 7 were VUs of the lower cervical spine (included in thoracic CT scans) in two patients, 319 were VUs of the thoracic spine in 26 patients and 72 were VUs of the lumbar spine in 22 patients. At baseline, 214 VUs in 24 patients (54% of the total number of VUs evaluated) had already established bridging osteophytes. The average DISH score of the first and last CT scans increased from 4.3 (S.D. 1.6) to 4.4 (S.D. 1.6) in the entire cohort with an average progression rate of 0.68 (S.D. 0.3) units/year. The average time for a DISH score to increase by 1 scoring unit was 1.6 years/unit (S.D. 0.4). In 6/26 (23%) patients there was no change in scores for any of the VUs evaluated along an average of 5.2 (S.D. 1.94) years. The DISH score of 48 VUs (12% of the total 398 VUs) in the remaining 20/26 (77%) patients increased from an average of 2.3 to 5.3 (18 VUs in the thoracic spine and 30 VUs in the lumbar spine) over an average period of 5.6 (S.D. 3.1) years. The average DISH scores for the different spinal regions are presented in Table 3.

A total of 234 VUs with bridging osteophytes were scored as 6: 216 in the thoracic spine, 15 in the lumbar spine and 3 in the cervical spine. Two patterns of bridging osteophyte formation were graded by the new scoring system. One was osteophyte growth occurring parallel to ALL calcification and eventually fusing to form a flowing osteophyte, which was scored as 6a and observed in 66% of the VUs (156/234). The other was osteophyte fusion without apparent ALL calcification, which was scored as 6b and observed in 33% of the VUs (78/234). Both patterns were observed concomitantly in 15 (56%) patients, with no predilection for a spine location (Figs. 3 and 4). This tendency of a greater percentage of bridging osteophytes with ALL ossification (score 6a) was apparent both in the thoracic and lumbar spine with no statistically significant difference [thoracic spine (6b/6a: 65/151) and lumbar spine (6b/6a: 6/9)].

Discussion

In spite of it being a relatively common and well-recognized condition, little is known about the pathophysiology

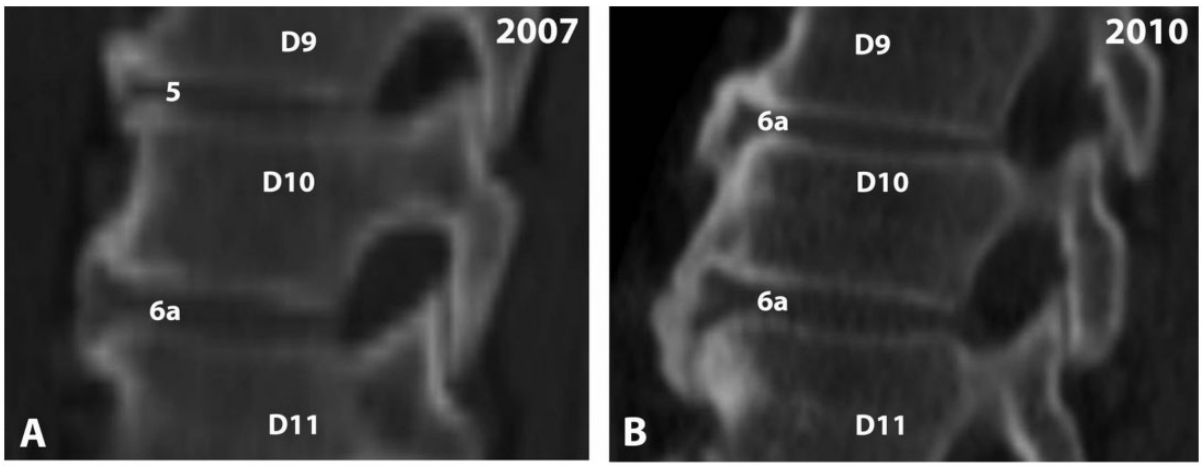
Table 3 Average CT DISH scores of different spinal locations at the first and last time points

	Score at first scan	Score at last scan	Time between scans (years)
Cervical spine[a]	4.5 (2.2)	4.5 (2.2)	5.1 (2)
Thoracic spine	4.9 (1.9)	5.3 (1.5)	4.6 (2)
Lumbar spine	1.9 (1.7)	2.6 (1.8)	4.7 (2.3)
Total DISH score[b]	11.3 (1.9)	12.4 (1.8)	4.8 (2.1)

Values are mean (S.D.). [a]Limited to C3–C7 vertebrae. [b]Calculated for the entire cohort.

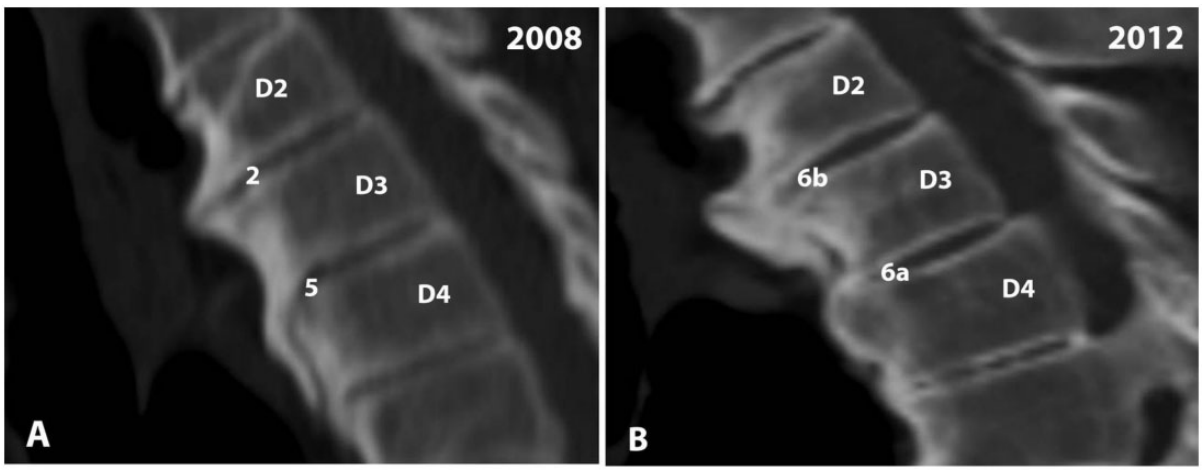
and course of DISH. In the current study we evaluated the radiographic course and natural progression of bridging osteophyte formation in DISH on CT scans. We utilized a new semi-quantitative scoring system that was found to be highly reproducible and to have very high to almost perfect intra- and inter-ICC rates. There was a very slow rate of bridging osteophyte formation with both DISH patterns, one of osteophyte growth integrating into a calcified ALL and the other with fusion of two opposing osteophytes but without ALL calcification. These two patterns were shown to also appear concomitantly in the same patient with no predilection to spinal location.

Fig. 3 CT DISH scoring of the VUs of D9–10 and D10–11 of a 46-year-old female over a 3-year period



The fusion process of ALL calcification with osteophytes in D9–10 vertebra and the thickening of a flowing osteophyte in D10–11 are demonstrated.

Fig. 4 CT DISH scoring of the VUs of D2–3 and D3–4 of a 63-year-old male over a 4-year period



The fusion process of osteophytes without ALL calcification between D2 and D3 and the fusion of ALL with osteophytes between D3 and D4 is demonstrated.

To the best of our knowledge, the progression of DISH as demonstrated on CT has not been described before. We found a mean progression of one DISH grade per 1.6 years, indicating roughly 10 years of progression until reaching one of the two common end-stage pathways of DISH. This rate of progression had been previously suggested by clinical observation [16]. Baraliakos *et al.* [7] recently conducted a study on lateral radiographs of the cervical and lumbar spine. Authors used the mSASSS score to analyse the spatial progression of both DISH and AS and found comparable rates of 1.3 units/year. The use of different scoring methods between their study and ours precludes comparisons of these rates, but the general notion of slowly progressive disease adds construct validity to our suggested scoring system.

In agreement with previous work, Baraliakos *et al.* [7, 14] described two types of osteophytes in DISH: one type includes osteophytes that are more vertically oriented and much more prevalent in AS patients, and the other type includes osteophytes that are more horizontally oriented. The latter have a degenerative appearance and appear more commonly in DISH patients than in AS patients. Due to limitations in assessment of the thoracic spine on lateral radiographs, Baraliakos *et al.* [7] evaluated only cervical and lumbar spine radiographs. We found both patterns to occur in the thoracic and lumbar vertebrae in the current study: the more vertical osteophytes (score 6a) were found in 66% of the VUs, while the more horizontal osteophytes (score 6b) were found in 33% of the VUs. Baraliakos *et al.* [7] reported a higher number of VUs per patient for osteophytes with $<45^{\circ}$ (correlating to our score of 6a) compared with osteophytes with $>45^{\circ}$ (correlating to our score of 6b) in both the DISH and AS groups. The pathogenesis of new bone formation in DISH is traditionally attributed to a degenerative process [17, 18], although an inflammatory mechanism has also been suggested [7]. The tendency for more vertically oriented osteophytes may indicate an underlying inflammatory rather than a degenerative pathogenesis of DISH.

In addition to flowing osteophytes classically described as originating from the ALL entheses, vigorous calcified peripheral enthesopathy is a hallmark presentation of DISH, and both are related to excessive bone formation in entheseal locations. These changes in DISH were also attributed to a degenerative process. Indeed, many conditions, including degenerative processes, have been described as the cause of enthesopathy, however, whether this is indeed the process underlying entheseal excessive bone formation in DISH patients needs to be critically questioned. Classic degenerative changes of the spine are related to disc degeneration and protrusion resulting in reduced intervertebral height and the sequella of abutting vertebral plates, e.g. subchondral bone sclerosis and osteophyte formation. This is probably not the process occurring in DISH since preserved disc space is one of its hallmarks. Moreover, although DISH often coexists with OA, they differ in their prevalence in the general population, gender distribution and anatomic site of primary involvement, as well as in their presence and distribution in the spine and peripheral joints. DISH has therefore been considered by Mader [19] as being a distinct clinical entity. An inflammatory pathogenesis is also suggested by the fact that >80% of DISH patients complain of morning stiffness [5]. Further investigations are clearly warranted to provide a better understanding of the pathogenesis, which in combination with early diagnosis, may allow preventive measures to be instituted early in order to halt progression of the disease.

There are a several limitations to our study: they are its retrospective consensus-based nature, its small cohort (especially of the lumbar and cervical spine cases) and the lack of any correlation with clinical data, which is needed for further validation of the suggested scoring system.

In conclusion, our new scoring system may assist in predicting the progression of DISH into its end-stage confluent osteophyte form. The two patterns of bridging osteophytes described suggest a possible inflammatory pathogenesis in addition to or instead of a degenerative one. Investigation of a larger cohort of DISH patients with more extensive radiological, clinical and biochemical data is warranted to understand the etiopathogensis of the disease in greater depth.

Rheumatology key messages

- Vertically oriented osteophytes in DISH are frequent and may indicate an inflammatory pathogenesis.
- In DISH patients, a full-flowing osteophyte forms slowly over a period of approximately 10 years.

Disclosure statement: The authors have declared no conflicts of interest.

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