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Diabetes mellitus and hypertension as risk factors for early diffuse idiopathic skeletal hyperostosis (DISH)

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Summary

Objectives: To describe and identify factors, in clinical practice, that might be useful increasing the index of suspicion for diffuse idiopathic skeletal hyperostosis (DISH), at a relatively young age.

Design: A group of 18 patients with DISH (12.8) who were diagnosed before the age of 50 years (group A) was compare with a group of 20 patients of similar age with osteoarthritis (group B), and 24 patients with DISH diagnosed after the age of 60 years (group C). Data collection included demographic characteristics, body region of main complaint evidence for enthesopathies or tendonitis, length of follow-up, body mass index (BMI), serum lipid profile, family history of diabetes mellitus (DM), and hypertension (HTS). The presence of concomitant diseases and use of medications was recorded at presentation and during the follow-up period.

Results: Patients in group A compared with group B, had statistically significant more pain in the lumbar and thoracic spine ($P = 0.001$ and 0.016, respectively), tendonitis/enthesopathies ($P = 0.004$), obesity (BMI ≥ 30, $P = 0.014$), and first degree relative with HTS and DM ($P = 0.015$ and 0.05, respectively). By the end of the follow-up, significantly more patients in group A were affected by DM compared with group B ($P = 0.007$).

Conclusions: Individuals in the fifth decade of life are likely to be affected by DISH if they are obese, have a first degree relative with either HTS or DM, complain of lumbar or thoracic spinal pain, and are affected by enthesopathies or tendonitis. The likelihood of relatively young patients with ≥ 3 clinical parameters to be affected with DISH, was six times higher than age and sex matched controls ($P = 0.004$).

Key words: DISH, Early onset, Spine, Inherited risks.

Introduction

Diffuse idiopathic skeletal hyperostosis (DISH) is a condition characterized by calcification and ossification of soft tissues, mainly ligaments and enthesis. Recognition that the condition is not limited to the spine, and also involves peripheral joints, led to the widely accepted term DISH[1,2]. Despite some similarities to osteoarthritis (OA), or its coexistence with OA, it has some features that allow it to be distinguished as a separate entity[3].

The reported prevalence of DISH varies according the age, ethnic origin, geographic location, and the clinical setting (i.e., hospital-based vs population based). The prevalence increases with age and has seldom been reported in individuals younger than 50 years of age.

The etiology of DISH is unknown. However, several metabolic, genetic, and constitutional factors were reported to be associated with this condition. These include: obesity, a high waist circumference ratio, hypertension (HTS), diabetes mellitus (DM), hyperinsulinemia, dyslipidemia, elevated growth hormone levels, elevated insulin like growth factor-1, hyperuricemia, use of retinoids and genetic factors[4–8]. A recent study showed that patients with DISH are more often affected by metabolic syndrome and have an increased risk for cardiovascular morbidity[9].

At present, the diagnosis of DISH is based on characteristic finding in radiographs of the thoracic spine, which are seldom requested. Due to the clinical and metabolic implications of such a diagnosis, and for research purposes, diagnosis at an earlier age may be beneficial. We tried therefore, to identify factors, in clinical practice, that may be useful in increasing the index of suspicion for this disorder, at a relatively young age. To the best of our knowledge, no previous studies have characterized this subgroup of patients with DISH.

Material and methods

From our cohort of 140 patients with DISH, we identified 18 patients (12.8%) who were diagnosed before the age of 50 (group A). The median age at diagnosis for the reminder of the cohort (122 patients) was 63.5 years (range 52–85). Group A was compared with 20 patients of similar age with OA (group B), and 24 patients with DISH diagnosed after the age of 60 years (group C). All the patients with DISH met the Resnick classification criteria[10], and all OA patients did not have radiological findings suggestive of DISH. Data collection included demographic characteristics, body region of main complaint (i.e., upper or lower limbs, cervical, thoracic, or lumbar spine, chest, hips and shoulders girdle), clinical or radiographic evidence for enthesopathies or tendonitis, length of follow-up, body mass index (BMI), serum lipid profile, family history of DM, HTS, and gout. The presence of ischemic heart disease (IHD), cerebral vascular events (CVE), DM, and HTS, were

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recorded at presentation and during the follow-up period. The uses of blood pressure lowering agents (BPLA), anti diabetic agents (ADA), lipid lowering agents (LLA), aspirin or other antiplatelet medications, allopurinol, and anti anginal medications (AAM) were also recorded at presentation and during the follow-up period. Data was collected from the patients' medical records. Whenever necessary, missing data were completed by telephone interview. The local Helsinki committee approved the study.

Data analysis was performed using the SPSS statistical package (SPSS, Chicago,IL). The relationships between two study groups (group A vs group B, group A vs group C) and other categorical clinical and laboratory parameters were examined using the Chi-square test or fisher's exact test for small groups.

t test or Mann-Whitney test were used to compare continuous variables between two independent study groups.

Results

Gender distribution was similar in all groups. The median age at diagnosis for groups A, B, and C was 46, 51 and 70 years, respectively, and the median follow-up was 6, 6, and 3.5 years, respectively. Patients in group A compared to group B, had more statistically significant pain in the lumbar and thoracic spine ($P = 0.001$ and 0.016, respectively), they were significantly more often affected by tendonitis and/or enthesopathies ($P = 0.004$), and were significantly more likely to be obese (BMI ≥ 30, $P = 0.014$). They were also more likely to have a first degree relative with HTS and DM ($P = 0.015$ and 0.05, respectively) (Table I). The difference in family history of HTS and DM was maintained even when compared to group C ($P = 0.031$ and 0.009, respectively). No other significant differences, in favor of group C, were noted. The prevalence of IHD, CVE, DM and HTS did not differ between the groups at the time of diagnosis. These findings did not change at the end of the follow-up except for the prevalence of patients affected with DM which was significantly higher in group A compared to group B ($P = 0.007$). No significant differences were observed in the serum levels of total cholesterol, high density lipoproteins (HDL), low density lipoproteins (LDL), triglycerides (TG), and in the pattern of medications use at the time of the diagnosis, except for more use of aspirin and BPLA in group C vs group A. By the end of the follow-up a borderline significance was observed for use of ADA in group A vs group B (Table II). Sixty seven percent of patients in group A had at least three of the significant parameters (thoracic spine pain, lumbar spine pain, obesity, and family history of HTS or DM), compared to only 10% in group B. Patients in group A with ≥ 3 of these parameters were six times more likely to be affected by DISH when compared to patients in group B (85% vs 14% $P = 0.004$).

Admissions to hospital were similar between the groups. A higher rate of admissions for cardiovascular diseases (myocardial infarction, unstable angina pectoris, stroke or transient ischemic attack) was observed for group C.

Discussion

This study demonstrated that patients with DISH, diagnosed at a relatively young age, were significantly more often affected by pain in the thoracic spine, lumbar spine tendonitis and/or enthesopathies compared to patients with similar age and gender distribution not affected by DISH. These patients also had a significantly higher prevalence of obesity, first degree relatives with DM or HTS, and were more likely to develop DM during follow-up. These patients did not differ significantly in most aspects from patients with DISH diagnosed at an older age, except in the case of a family history of DM and HTS.

The prevalence of DISH increases with age, but is extremely variable according to the population studied, and can be as high as 26% in females and 35% in males of a hospital population[11]. An autopsy study reported that in a series of 75 spines studied at autopsy 28% had DISH[12]. Only a few studies reported the prevalence in patients before 50 years of age, and some recent studies did not look into this group at all[13]. However, the reported prevalence in the fifth decade of life was extremely low ranging from 0.3% to 0.2% in males and females, respectively in the Finish population to none in the female Italian population[14,15]. It was estimated that a period of at least 10 years is needed for the pathologic process to evolve completely suggesting, that the pathologic process starts in the fourth decade of life[16]. Therefore, identifying DISH at a relatively early age poses a diagnostic challenge. The relatively high prevalence of patients with DISH in the present study can be ascribed to the population of patients referred to a rheumatology clinic, and probably to the

Table I

Group A – patients with DISH diagnosed at, or before the fifth decade of life; group B – patients without DISH; group C – elderly patients with DISH. BMI – body mass index; DM – diabetes mellitus; HTS – hypertension

	Demographic and clinical characteristics of the study groups				
	Group A, $N = 18$ (%)	Group B, $N = 20$ (%)	*P*, A vs B	Group C, $N = 24$ (%)	*P*, A vs C
Female	7 (38.9)	4 (20)	NS	12 (50)	NS
Age at diagnosis (median)	46 (38–50)	51 (44–55)	NS	70 (60–85)	<0.0001
Years follow-up (median)	6 (1–14)	6 (1–23)	NS	3.5 (2–9)	NS
Main area of complain:					
Shoulder girdle	6 (33)	4 (20)	NS	10 (42)	NS
Upper limbs	9 (50)	9 (45)	NS	10 (42)	NS
Hip girdle	2 (11)	1 (5)	NS	1 (4)	NS
Lower limbs	6 (33)	9 (45)	NS	13 (54)	0.17
Cervical spine	6 (33)	3 (15)	NS	7 (29)	NS
Thoracic spine	7 (39)	1 (5)	0.016	7 (29)	NS
Lumbar spine	8 (44)	0	0.001	5 (21)	0.1
Chest	1 (6)	0	NS	2 (8)	NS
General pain	2 (11)	4 (20)	NS	2 (8)	NS
Tendonitis/enthesopathy	8 (44)	1 (5)	0.004	6 (25)	NS
BMI Kg/m^2 (mean)	34.2	30.6	0.083	32.8	NS
BMI ≥ 30 kg/m^2	15 (83)	9 (45)	0.014	15 (63)	0.14
First degree relatives with DM	12 (67)	7 (35)	0.05	6 (26)	0.009
First degree relatives with HTS	11 (61.1)	5 (25)	0.015	7 (30)	0.031