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Somatic and psychiatric comorbidities of hidradenitis suppurativa in children and adolescents.

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ABSTRACT

Background: Hidradenitis suppurativa (HS) is associated with various somatic and psychiatric comorbidities. Data regarding comorbidities in young HS patients are sparse.

Objective: We analyzed both somatic and psychiatric comorbidities in young patients in a nationwide HS cohort.

Methods: In this retrospective case-control study, data from cases of HS in young (aged ≥5 and <18 years) patients and age-matched controls with benign melanocytic nevi were collected from the Finnish Care Registry of Health Care. The prevalence of preselected comorbidities was compared between HS and control groups.

Results: A total of 153 HS cases were found in the specified age group. Of these, 34.0% had one or more somatic comorbidity compared with 4.9% of controls. At least one of the preselected psychiatric diagnoses was present before the age of 18 years in 15.7% of HS cases compared with 5.6% of controls. By the age of 23 years, at least one psychiatric comorbidity was identified in 23.5% of HS patients and 8.7% of controls.

Limitations: Despite being one of the largest HS cohorts ever studied, the number of young HS patients was relatively low. Since this was a registry-based study, it was not possible to verify the accuracy of International Classification of Diseases codes.

Conclusion: Physicians should monitor young patients with HS for both somatic and psychiatric comorbidities.

INTRODUCTION

Hidradenitis suppurativa (HS) typically begins in the second or third decade of life [1, 2]. The mean time from the onset of symptoms to a confirmed diagnosis has been variously reported as 7–14 years [3, 4]. Several comorbidities are associated with HS, including diabetes, metabolic syndrome, psychiatric disorders and inflammatory arthritis [5-8]. HS markedly impairs the patient's quality of life, especially in those whose symptoms have an early onset [9, 10].

HS is considered to be rare in children with prepubescent onset estimated to occur in 2% of patients [2]. However, in a Dutch study, 7.7% of HS patients reported having symptoms before their thirteenth birthday [11]. Patients with early-onset HS tend to have a family history and are likely to develop more widespread, but not necessarily more severe, disease than those with adult-onset HS [11, 12]. When early- and adult-onset HS were compared in adult patients, no differences were found in the prevalence of associated acne, rheumatoid arthritis or inflammatory bowel disease (IBD) [11]. A few case reports indicate a link between prepubertal HS and premature adrenarche, adrenal hyperplasia or metabolic syndrome. [13-15]

Few data are available on HS in pediatric populations [16], and the comorbidity profile of HS in childhood and adolescence has not been properly explored. The aim of this national registry-based case-control study was to elucidate the characteristics of comorbid diseases in HS patients under 18 years of age.

METHODS

Populations and databases

This was a retrospective matched case-control database study of all Finnish pediatric patients diagnosed with HS between 1987 and 2014. The statutory Finnish Care Register for Health Care was queried to identify patients who had received a diagnosis of HS (International Classification of Diseases (ICD)-9 codes 7058C and ICD-10 code L73.2) at least once during the study period. The study and the control groups were formed as described earlier [8]. Records of patients aged ≥ 5 and < 18 years old at the time of diagnosis were included in the study, since the youngest child with HS described in the literature was 5 years old [2] and infantile forms of HS resolve early in childhood [13, 17]. Four controls per HS case were randomly selected and matched by age and gender with melanocytic nevi cases. Diagnoses of comorbid diseases (Supplementary Table I) based on ICD-9 and 10 codes were gathered for cases and controls from the same registry first before the age of 18 years and again before the age of 23 years.

Statistical analyses

The characteristics of the study population are presented as proportions and means. A conditional logistic regression model was used to characterize proportional exposure between HS patients and controls for different diseases. Statistical analyses were performed using SAS software package (version 9.4, SAS Institute, Inc, Cary, NC, USA).

RESULTS

Characteristics of young patients with HS and melanocytic nevi

The original query yielded 4381 cases with HS [8]. Of these 153 cases were aged ≥5 and <18 years at diagnosis. For the present study, this subgroup was designated as youth-onset HS (yHS). The original query found 43248 cases of benign melanocytic nevi, 8475 of whom were aged ≥5 and < 18 years. After age and sex matching, 612 subjects formed the control group for the present study. The demographics of these subjects are summarized in Table I.

In general, 34.0% of patients with yHS had at least one of the pre-specified somatic comorbidities and 15.7% at least one of the psychiatric comorbidities. 9.2% of subjects with yHS had at least one of each type of comorbidity. (Fig. 1)

Somatic and psychiatric comorbidities in young HS patients

Comparisons between the cases and controls demonstrate that the yHS group had substantially higher somatic and psychiatric morbidity (Table II, III) at the age of 18 years. To clarify the possibility of comorbidities accumulating with increasing age, the prevalence of comorbidities was analyzed again at 23 years of age. No significant differences in patterns of somatic comorbidity were found between the ages of 18 and 23 (data not shown). However, when the prevalence of each psychiatric disorder was evaluated again at the age of 23 years, 23.5% of patients in the yHS group and 8.7% of nevi controls had received at least one psychiatric diagnosis (Table III, Fig. 2)

DISCUSSION

This study demonstrates that children and adolescents with HS are vulnerable to the accumulation of comorbidities. As well as various somatic comorbidities, occurring in as many as 34.0%, psychiatric comorbidities are common in HS patients from adolescence. Psychiatric disorders were the most common single group of comorbidities, present in 15.7% of the yHS population at the age of 18 years. Notably, the proportion had increased to 23.5% by the age of 23 years. This result may be an underestimate, because approximately half the HS patients studied had not reached the age of 23 by the end of the follow-up period. The prevalence of major depression increased from 8.5% to 15.7% in the HS group with a five-year advance in age. In contrast, the proportion of patients in the control group with a diagnosis of depression showed only a slight increase from 3.4% to 4.9% with the same age advance. The prevalence of anxiety in the HS group did not increase so substantially (5.9% to 9.2%), but because anxiety often develops into depression in younger people [18], it is possible that some earlier cases of anxiety were later recognized as depression.

Previously, utilizing the same registry, we found that up to 24.1% of all HS patients were diagnosed with at least one psychiatric disorder. Thus, mentaldisorders are even more common in HS than in patients with psoriasis [8]. At 23.5%, the rate of psychiatric disorders in the yHS group at the age of 23 years almost reached the level in the overall HS population. The frequency of depression at the age of 23 in this cohort of yHS patients was 15.7%, which is comparable with the 15.3% we found in the overall HS population. [8]

In the present study, IBDs were significantly more common in the yHS group than in the control group, indicating that IBDs are associated with HS from an early age. A recent Danish study found an association between HS and IBDs in an adult population although the frequency of IBDs in the HS population was fairly low, at 2.1% [19]. Finland has one of the highest frequencies in the world of IBDs (approximately 0.8% of the general population) [20]. In our study population IBDs were particularly common in the yHS group, affecting 3.3% of patients. The peak incidence of IBDs typically occurs between the ages of 20 and 40 years, although the incidence has been increasing in the pediatric

population [21]. Studies suggest a female predominance in Crohn's disease [21], which could partially explain the finding that most of the patients in the yHS group were girls. The onset of IBD early in life may be associated with a more severe and complicated disease course and possibly even with an elevated risk for intestinal cancer [22]. It is therefore important for clinicians to consider that children with HS may also have IBD and to suggest appropriate screening measures.

We found that inflammatory joint diseases including spondyloarthopathies were significantly more frequent in the yHS group than in controls. Spondyloarthropathies are known to be associated with HS, particularly in male patients [23]. Since this association is already strong in young HS patients, it is important for physicians to look for musculoskeletal symptoms and possible signs of inflammatory joint disease.

A diagnosis code of acne was recorded in 13.7% of yHS patients, compared with 0.7% of the control group. This points to a likelihood of more severe acne in HS, although some HS patients may have been misdiagnosed with acne, which could lead to an overestimation of acne in the yHS group.

In our study, 5.9% of the patients in the yHS group had a diagnosis of obesity, a significantly greater proportion than in the control group. In adult HS populations, rates of obesity have varied from 12% to 88% [24]. It is probable that 5.9% is an underestimation since physicians might hesitate to record the diagnosis code for obesity if the weight problem was not striking for fear of stigmatizing the young patient. Type 1 diabetes and hypertension were more common in the yHS group than in the control group but the difference was not significant.

During the study period, Down syndrome occurred in approximately 0.13% of live births in Finland [25]. In our study, 4.6% (7/153) of patients with yHS had Down syndrome, suggesting a clear association between these two conditions. The odds ratio (OR) for this outcome could not be calculated, because no patient in the control group had Down syndrome. Since the onset of HS symptoms happens at an earlier

age in individuals with Down syndrome [26], it may have been overrepresented in our young HS population, and thus the prevalence of 4.6% may not reflect the true rate in the entire population of HS patients. Thyroid disorders were more common in patients with HS than in controls, as found also in an adult population [7]. This result was not considered significant because 2/7 (28.6%) of our patients with yHS and Down syndrome were diagnosed with a thyroid disorder, and thyroid diseases is more frequent in individuals with Down syndrome [27]. On the other hand, although obesity is more common in Down syndrome [27], no patient with both yHS and Down syndrome was diagnosed as obese. Consequently, the association between HS and obesity seems to be apparent in childhood. No individual with Down syndrome in the yHS group was diagnosed with a psychiatric disorder by the age of 23.Thus our findings regarding the prevalence of mental disorders could not be confounded by Down syndrome, which has been associated with psychiatric vulnerability in adulthood [28].

There are case reports of early-onset HS associated with certain hormonal imbalances and metabolic syndrome [13-15], but we did not find any patient with premature adrenarche or adrenal hyperplasia. Metabolic syndrome was diagnosed in three individuals in the HS group compared with one in the control group. The prevalence of metabolic syndrome might be an underestimation, because the diagnosis code is relatively new and has been utilized in Finland only since the late 1990s.

Although our study utilizes one of the largest nationwide yHS cohorts ever studied, it contains no more than 153 young cases with a diagnosis of HS, which may cause low statistical power. Another weakness is that in a register-based nationwide study it is not possible to verify the accuracy of the HS diagnosis or the ICD-9/10 diagnoses of comorbidities. The data in the Finnish Care Register for Health Care have been shown to be accurate and can be considered reliable [29]. In addition, previous studies from the United States have shown that HS diagnosis in hospital registers has a reasonably high positive predictive value [7, 30].

Based on our nationwide registry study, young patients with HS carry a considerable risk for many somatic and psychiatric comorbidities and the prevalence of mental disorders increases rapidly during young adulthood. Therefore, young patients need substantial care not only for their HS lesions but also for the comorbidities of HS, which may accumulate over time.

Abbreviations used:

HS	Hidradenitis suppurativa
yHS	youth-onset HS
BMI	Body mass index
IBD	Inflammatory bowel disease
ICD	International Classification of Diseases
OD	Odds ratio
CI	Confidence interval

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Table I. Characteristics of patients in the youth-onset hidradenitis suppurativa and control groups.

	HS	**Melanocytic nevi**
Patients		
N	153	8475
Age in years*	15.6 (±2.1)	11.1 (±3.9)
Girls	72.6%	57.1%
Matched patients		
N#	153	612
Age in years*	15.6 (±2.1)	15.4 (±2.2)
Girls	72.6%	72.6%

yHS, youth-onset hidradenitis suppurativa

*Data given as mean ± standard deviation

#Age and gender matched in a 1:4 ratio.

Table II. Somatic comorbidities in the yHS and control groups in patients under 18 years.

Comorbidity*	**Group**	**N (%)**	**OR (95% CI)**
Acne	yHS	21 (13.7)	27.2 (8.11 – 91.3)
	Nevi	4 (0.7)	Reference
Diabetes, type 1	yHS	4 (2.6)	2.41 (0.67 – 8.66)
	Nevi	7 (1.1)	Reference
Down syndrome	yHS	7 (4.6)	Reference
	Nevi	0 (0.0)	Reference
Hypertension	yHS	3 (2.0)	Reference
	Nevi	0 (0.0)	Reference
Inflammatory bowel diseases	yHS	5 (3.3)	10.0 (1.94 – 51.5)
	Nevi	2 (0.3)	Reference
Inflammatory joint diseases#	yHS	8 (5.2)	4.57 (1.66 – 12.6)
	Nevi	7 (1.1)	Reference
Metabolic syndrome	yHS	3 (2.0)	12.0 (1.25 – 115)
	Nevi	1 (0.2)	Reference
Obesity	yHS	9 (5.9)	12.0 (3.25 – 44.3)
	Nevi	3 (0.5)	Reference
Pilonidal sinus	yHS	2 (1.3)	8.00 (0.73 – 88.2)
	Nevi	1 (0.2)	Reference
Thyroid disorders	yHS	4 (2.6)	6.97 (1.25 – 38.8)
	Nevi	3 (0.5)	Reference

* There were no cases with diagnosed type 2 diabetes, polycystic ovarian disease, premature adrenarche, adrenal hyperplasia, lupus, dermatomyositis, scleroderma or Sjögren's syndrome in the yHS group.

#including reactive, rheumatoid and psoriatic arthritis, ankylosing spondylitis and undifferentiated spondyloarthropathies

yHS, youth-onset hidradenitis suppurativa; Nevi, melanocytic nevi; OR, odds ratio; CI, confidence interval

Table III. Psychiatric comorbidities in the yHS and control groups analyzed at the ages of 18 and 23 years of age.

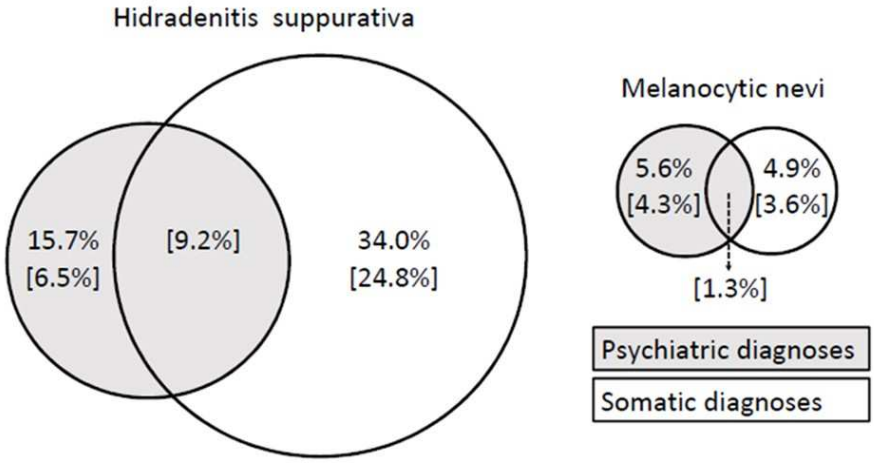
Comorbidity	Group	< 18 years old		< 23 years old	
		N (%)	OR (95% CI)	N (%)	OR (95% CI)
All psychiatric disorders	yHS	24 (15.7)	3.31 (1.86 – 5.90)	36 (23.5)	3.31 (2.05 – 5.36)
	Nevi	34 (5.6)	Reference	53 (8.7)	Reference
Major depression	yHS	13 (8.5)	2.68 (1.29 – 5.58)	24 (15.7)	3.64 (2.04 – 6.49)
	Nevi	21 (3.4)	Reference	30 (4.9)	Reference
Anxiety, dissociative, stress-related, somatoform, and other nonpsychotic mental disorders	yHS	14 (9.2)	2.61 (1.30 – 5.26)	21 (13.7)	3.00 (1.64 – 5.48)
	Nevi	23 (3.8)	Reference	32 (5.2)	Reference
Anxiety disorders	yHS	9 (5.9)	3.43 (1.39 – 8.47)	14 (9.2)	3.87 (1.84 – 8.14)
	Nevi	11 (1.8)	Reference	15 (2.5)	Reference
All psychotic disorders	yHS	3 (2.0)	6.00 (1.00 - 35.9)	3 (2.0)	2.40 (0.57 – 10.0)
	Nevi	2 (0.3)	Reference	5 (0.8)	Reference

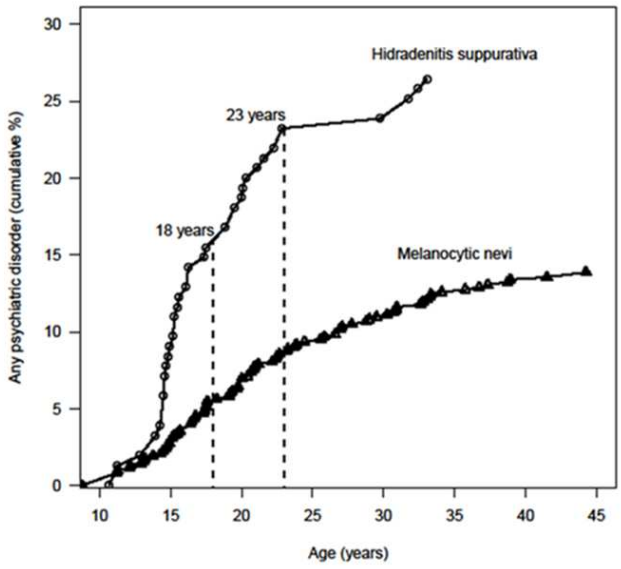
yHS, youth-onset hidradenitis suppurativa; Nevi, melanocytic nevi; OR, odds ratio; CI, confidence interval

FIGURE LEGENDS

Fig. 1. Prevalence of psychiatric and somatic morbidity in young patients with HS and melanocytic nevi. In parenthesis: pure or comorbid prevalence of psychiatric or somatic disorders.

Fig. 2. The cumulative prevalence of 'any psychiatric disorder' in the youth-onset hidradenitis suppurativa and melanocytic nevi groups.





Capsule summary:

- Epidemiologic data on hidradenitis suppurativa in childhood and adolescence are sparse
- This study demonstrates the psychiatric and somatic comorbidities of hidradenitis suppurativa in young patients.
- Young patients with hidradenitis suppurativa need care for the comorbidities of HS, which may accumulate over time.