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Pilonidal sinus disease: an intergluteal localization of hidradenitis suppurativa/acne inversa: a cross-sectional study among 2465 patients

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Summary

Background Hidradenitis suppurativa (HS), also referred to as acne inversa, is a debilitating skin disease characterized by inflammatory nodules, chronic abscesses and tunnels (fistulae and sinuses). The association with pilonidal sinus disease (PSD) is frequently reported but not well documented.
Objectives To determine the prevalence and characteristics of inflammatory skin lesions located in the intergluteal fold (IGF) of patients with HS.
Methods This was an international multicentre retrospective cross-sectional study based on data collection from a large cohort of patients with HS with and without histopathology.
Results From a total of 2465 patients with HS included in the study, 661 (27%) reported lesions in the IGF. These patients were significantly more often smokers and had more severe HS. Of the 238 patients with an available clinical diagnosis, intergluteal-HS (IG-HS) was diagnosed in 52 patients (22%) and PSD was diagnosed in 186 patients (78%). IG-HS was associated with the localization of HS in the proximity of the IGF, including the buttocks, genitals and the anus. There

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was a possibility of misclassification bias in this study as a clinical/image-based diagnosis or histopathology of the IGF lesions was not always available.

Conclusions The high prevalence of PSD suggests a strong link between both entities. Therefore, it may be useful to identify common pathophysiological mechanisms and develop common therapeutic strategies.

What's already known about this topic?

- The occurrence of pilonidal sinus disease has not been clearly reported among patients with hidradenitis suppurativa/acne inversa.

What does this study add?

- This is the first study that investigated the prevalence of pilonidal sinus disease among a large cohort of patients and identified the patient characteristics.
- Risk factors that might help to improve the management of patients were identified.

Pilonidal sinus disease (PSD) has been described under various names, such as pilonidal cyst, abscess or sinus. In 1880, Hodges first used the word 'pilonidal', combining the word 'pilus', which means hair in Latin, and 'nidus', which means nest.[1] The prevalence of PSD is not well documented. Histologically, PSD is most often defined by an epithelial track located in the skin of the gluteal cleft, generally containing hair, although alternative presentations have been described.[1] Originally considered a congenital disease, the acquired origin of PSD has also been discussed by several authors. These authors have also highlighted the role of predisposing factors such as smoking, male sex (the male to female ratio is 3 : 1), obesity and local friction.[2]

Hidradenitis suppurativa (HS), also known as acne inversa, is a chronic, inflammatory, recurrent, debilitating follicular skin disease that usually presents after puberty with painful, deep-seated, inflamed lesions in the apocrine gland-bearing areas of the body, most commonly the axillary, inguinal and anogenital regions.[3]

The pathophysiology of HS is not fully understood but likely includes an interaction between a complex genetic background and environment. As with HS, smoking, obesity and skin friction are risk factors for the development of PSD. However, unlike PSD, HS affects more women than men with a ratio of 1 : 3.[4,5] PSD histology combines features of chronic and acute inflammatory skin infiltrate, abscesses, follicular occlusion and sinus tract formation.[6–8]

A solitary intergluteal-HS (IG-HS) lesion may be clinically confused with PSD. Sonographic characteristics of PSD are also similar to key features observed in HS lesions, suggesting that PSD may be a variant or localized form of HS.[8] In the acute phase of PSD and IG-HS, patients typically present initially with pain, erythema and swelling in the midline gluteal cleft region. In the chronic phase, the formation of a cavity may cause chronically purulent discharge in both diseases. PSD lesions are histologically characterized by pseudocysts with granulation tissue surrounding hair shafts (not disrupted follicles) and a fistulous opening to the surface; epithelial coating can be seen in severe/relapsing cases. On the other hand, HS is primarily a folliculitis. Histology does not always help to distinguish between both entities.[7] Sharing the initial event of follicular occlusion, HS and PSD are part of the follicular tetrad, along with dissecting cellulitis of the scalp and acne conglobata.[6,9] In the phenotypical classification of Canoui-Poitrine *et al.*, patients with HS classified as LC2 had higher probabilities not only for breast and armpit involvement, but also for involvement of the ears, chest, back or legs and for follicular lesions including PSD.[10] Therefore, these factors raise the question of whether PSD and HS represent a spectrum of one disease or are separate entities.

The aim of our study was to evaluate the prevalence of inflammatory lesions in the intergluteal fold (IGF) in a large

cohort of patients with HS and analyse the patient characteristics.

Materials and methods

This study was explorative, cross-sectional and descriptive, and was conducted based on case note review/interviews and clinical assessment of patients referred to secondary/tertiary level care units (clinics or hospitals) that are specialized in HS management. Patients were recruited from different outpatient dermatology clinics cooperating with the Faster-and-Better research initiative of the European Hidradenitis Suppurativa Foundation e.V. (www.ehsf.eu). Centres were asked to include patients with HS whom they were currently managing or had previously managed, provided that (i) patients were consecutive within a determined period of time, and (ii) the answer to the question whether there was a past or a current inflammatory lesion in the IGF was available. In order to reduce the bias that can occur in retrospective cohort studies, we aimed to obtain the largest possible cohort and asked several centres to participate. Similarly, those centres were asked to include as many patients with HS as possible, provided that they met the above-mentioned eligibility criteria.

A specific questionnaire had to be completed, detailing sex, age, height, weight, smoking habits, family history of HS, disease activity (age at first boil, body regions involved, Hurley stage) and comorbid conditions, such as acne, dissecting cellulitis of the scalp, joint problems and gastrointestinal problems. We recorded whether there was a current or past inflammatory lesion in the IGF described in the patient case notes. In these cases, we recorded additional data including the age of onset, a family history of inflammatory lesion in the IGF and whether the lesion was recurrent. It is also important to note that the nature of the lesions in the IGF was classified as HS or PSD or undetermined, so only one possibility could be recorded. We defined 'patient diagnosis' as the diagnosis reported by the patient for a past lesion, 'clinical diagnosis' as the diagnosis reported by a physician (who examined the patient when completing the questionnaire or who cited the lesion in a medical document available in the patient's chart), and 'pathological diagnosis' as the diagnosis based on histopathological examination of a surgical specimen obtained through excision of the lesion (whether the surgery was performed at the time of the questionnaire or mentioned in the patient's chart). Owing to the retrospective nature of this study and the lack of agreed diagnostic criteria, we could not explore the clinical and pathological criteria used to establish the diagnosis of each entity. Overall, 12 centres from Europe, one centre from the Middle East and one centre from North America participated in the study by providing data from July 2016 to July 2017. The study was approved by the ethics committee of Erasme Hospital (EudraCT/CCB B406201627010).

Statistical analysis

All statistics were performed using Stata® 11.0 (College Station, TX, U.S.A.). Numerical data are presented with mean and SD after normality checking (combination of Skewness and Kurtosis tests). Differences between groups were examined accordingly using a t-test. Categorical data are presented with frequency and percentages, and comparisons between groups were performed using either a Fisher's exact test (to explore the links with all comorbidities except acne vulgaris) or a χ^2-test (for all other variables). As multiple statistical tests were performed, we considered a correction for multiple comparisons and used the false discovery rate Benjamini–Hochberg procedure (with a false discovery rate of 0.05). Differences were considered significant only if they were lower than the generated critical values.

To manage missing data in logistic regression analyses we performed multiple variable imputation using chained equations. Age at the time of the study, age at first boil, disease duration and age at IGF lesion occurrence were introduced as continuous variables in the model. All other variables were considered dichotomous (1 if present, 0 if not), except for Hurley stage, which was introduced as a categorical variable (stage I, stage II or stage III). To assess confounding variables in logistic regressions, a backward selection (with a P-value of 0.10) and a full multivariable model were used when distinguishing between patients with or without a lesion in the intergluteal region or patients with HS or PSD. We checked and met the assumptions recommended for logistic regression, including the binary nature of the dependent variables, the linearity of independent variables (using the Stata linktest) and the collinearity of the independent variables (because of collinearity, disease duration was consequently excluded from further regression analyses).

Results

Prevalence and characteristics of an inflammatory lesion in the intergluteal fold of patients with hidradenitis suppurativa

We included 2465 patients with HS; 1567 women (64%) and 898 men (36%). Clinical data is presented in Table 1. A current or past lesion in the IGF was observed in 661 patients [26.8%, 95% confidence interval (CI) 25.1–28.6]. The mean age at IGF lesion occurrence was 23.1 years and it occurred as the first inflammatory skin lesion in 236 patients (10% of all patients with HS and 36% of patients with an IGF lesion) (Table 2). The prevalence by age is provided in Figure 1. These 661 patients were more frequently men and smokers (either past or current smokers), and were younger (35 years vs. 37 years) than patients without IGF lesion (Table 3). The mean age at first boil was significantly younger (20 years vs. 23 years). The classical axilla and groin regions were involved with the same frequency in the two groups. The breast was less frequently involved in patients with IGF lesions while the buttocks, genital, pubic and anal areas were more frequently involved (Table 3). HS was more severe in patients with IGF lesions, 22% of which had Hurley stage III disease, compared with 10% in the non-IGF group (Fig. 2). No differences were

Table 1 Description of the population (n = 2465)

	Number of patients with available data	Mean (SD) or n (%)	95% Confidence interval
Female sex	2465	1567 (64)	62–65
Mean age, years	2249	36.8 (12.6)	36.3–37.3
BMI (kg m^{-2})	2285	27.8 (6.3)	27.6–28.1
Current or past smokers	2416	1852 (77)	75–78
Family history of HS	2437	713 (29)	27–31
Mean age at first boil, years	2391	22.3 (10.0)	21.9–22.7
Mean HS duration, years	2364	14.4 (10.6)	14.0–14.9
Hurley stage			
I	2372	1044 (44)	42–46
II		1011 (43)	41–45
III		317 (13)	12–15
Regions involved			
Axilla	2384	1608 (67)	66–69
Breast	2324	522 (22)	21–24
Buttocks	2330	916 (39)	37–41
Groin	2394	1843 (77)	75–79
Pubis	1586	376 (24)	22–26
Genitals	2295	647 (28)	26–30
Anus	2300	398 (17)	16–19
Elsewhere	2343	539 (23)	21–25
Comorbidities			
Joints	2306	133 (6)	5–7
Gastrointestinal	2299	63 (3)	2–3
Acne vulgaris	2465	223 (9)	8–10
Acne conglobata	1633	98 (6)	5–7
Dissecting folliculitis	1650	34 (2)	1–3
Psoriasis	2465	44 (2)	1–2
Inflammatory lesion in the intergluteal fold	2465	662 (27)	25–29

BMI, body mass index; HS, hidradenitis suppurativa.

observed concerning associated inflammatory rheumatic and gastrointestinal diseases, but acne vulgaris and acne conglobata were more frequently associated with IGF lesions (Table 1). To assess which factors were independent predictors of the occurrence of an IGF lesion, we first managed missing data by multinomial implantation, then repeated univariate analyses with implemented data (Table 4), and then performed multivariate analysis. While age, acne conglobata, and genital and buttocks involvement did not remain significant, male sex, smoking habits, age at first boil, Hurley stage, acne vulgaris in addition to breast and anal involvement, were all confirmed as independent predictors of an IGF lesion. Body mass index (BMI) also proved to be a significant predictor (Table 4).

Patient, clinical and histopathological diagnosis for inflammatory lesions in the intergluteal fold of patients with hidradenitis suppurativa

Patient diagnosis was available for 554 of the 661 patients with IGF lesions (84%). Patients reported IG-HS in 11%, PSD in 83% and undetermined in 6%. A clinical diagnosis was available in 238 patients with IGF lesions (36%), according to clinical observation (n = 119) or surgical exploration (with or without clinical observation; n = 119).

In those patients, the clinical diagnosis was reported as IG-HS in 52 patients (22%, 95% CI 17–27), and PSD in 186 patients (77%, 95% CI 73–83). Patient and clinical diagnoses were consistent in 86% of the patients (208 of 241 patients for whom both the patient and the clinical diagnoses were available). While 6% of the patients who reported a PSD were clinically classified as HS, 6% of the patients who reported an IG-HS were clinically classified as PSD.

Histopathological diagnosis was available in 116 of the 661 patients with IGF lesions (18%). When available, it was reported as IG-HS in 37 patients (33%) and PSD in 76 patients (67%). Clinical and pathological diagnoses were consistent in 88% of the patients (102 of 116 patients for whom both the clinical and the pathological diagnoses were available). While 11% of the IGF lesions clinically classified as PSD were eventually classified as IG-HS, none of those clinically classified as IG-HS were eventually diagnosed as PSD. The two lesions reported as IG-HS by the patients and clinically reported as PSD were eventually reclassified as HS by the pathological examination.

Factors associated with a clinical hidradenitis suppurativa lesion in the intergluteal fold

Additionally, we investigated the characteristics of patients clinically classified as IG-HS vs. PSD (Table 5). Patients with clinical IG-HS were significantly older (40 years vs. 32 years, $P < 0.001$) and less frequently women (29% vs. 47%, $P = 0.019$). The mean BMI was significantly lower (26 kg m^{-2} vs. 29 kg m^{-2}, $P = 0.025$). The prevalence of tobacco smoking and a family history of HS were not different between the two groups. Only one of the patients with clinically classified IG-HS had a family history of PSD (2%), whereas a family history of PSD was observed in 15% of the patients with clinically classified PSD ($P = 0.003$). Both HS and IG-HS occurred later if the IGF lesion was clinically classified as HS [25 years vs. 21 years ($P = 0.015$) and 29 years vs. 24 years ($P = 0.001$), respectively]. Patients with clinically classified IG-HS more frequently had HS lesions in the gluteal, genital and anal area (Table 5). HS severity was significantly worse in patients with IG-HS, as 69% were reported as Hurley stage III, compared with 25% in the PSD group. No association was found between the clinical diagnosis and the comorbidities (Table 5). Similar results were obtained when patients were classified into two groups (PSD vs. IG-HS) according to pathological diagnosis (Table S1; see Supporting Information).

Using multivariable regression for exploratory analyses, we found that axillary involvement (negatively), in addition to Hurley stage and anal, genital or gluteal involvement (positively) proved to be independent predictors of the clinical diagnosis of IG-HS (Table 6).

Table 2 Characteristics of the patients with hidradenitis suppurativa (HS) and an inflammatory lesion in the intergluteal fold (IGF)

	No inflammatory lesion in the IGF, n = 1804 (73%)		Description of an inflammatory lesion in the IGF, n = 661 (27%)		
	Mean (SD) or n (%)	95% CI of the mean or the proportion	Mean (SD) or n (%)	95% CI of the mean or the proportion	Statistical analysis[a] P-values
Female sex	1264 (70)	68–72	303 (46)	42–50	**< 0.001**
Mean age, years	37.3 (13.0)	37–38	35.4 (11.3)	35–36	**< 0.001**
BMI, kg m^{-2}	27.8 (6.5)	27–28	28.0 (6.3)	28–28	0.470
Current or past smokers	1320 (77)	75–79	532 (84)	81–87	**< 0.001**
Family history of HS	528 (30)	27–32	185 (28)	25–32	0.523
Mean age at first boil, years	23.1 (10.7)	23–24	20.1 (7.8)	20–21	**< 0.001**
Mean HS duration, years	14.2 (10.8)	14–15	15.2 (10.1)	14–16	0.032
Regions involved					
Axilla	1164 (67)	65–69	444 (69)	65–73	0.309
Breast	410 (24)	22–26	112 (18)	15–21	**0.002**
Buttocks	629 (37)	35–39	287 (46)	42–50	**< 0.001**
Groin	1347 (77)	75–79	496 (77)	74–81	0.847
Pubis	234 (22)	19–24	142 (27)	24–31	**0.015**
Genitals	441 (26)	24–28	206 (34)	30–37	**< 0.001**
Anus	240 (14)	13–16	158 (26)	22–29	**< 0.001**
Elsewhere	373 (22)	20–24	166 (26)	22–29	**0.029**
Comorbidities					
Joints	97 (6)	5–7	36 (6)	4–8	0.924
Gastrointestinal	52 (3)	2–4	11 (2)	1–3	0.077
Acne vulgaris	138 (8)	6–9	85 (13)	10–15	**< 0.001**
Acne conglobata	50 (5)	3–6	48 (9)	7–12	**< 0.001**
Dissecting folliculitis	22 (2)	1–3	12 (2)	1–4	0.686
Psoriasis	32 (2)	1–2	12 (2)	1–3	0.945

[a]P-values are presented in bold when considered as significant after Benjamini–Hochberg correction (false discovery rate at 0.05).

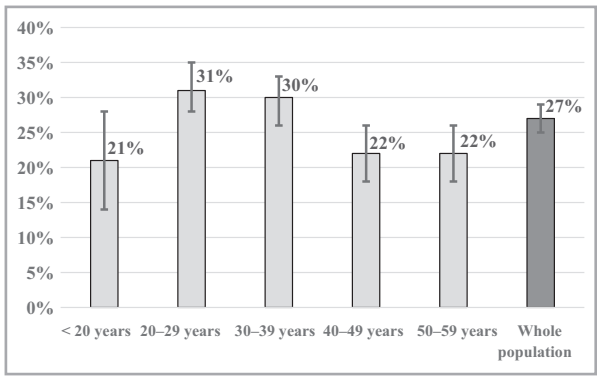

Fig 1. Prevalence of an inflammatory lesion in the intergluteal fold of patients with hidradenitis suppurativa depending on age. The 95% confidence intervals for each age group and the whole population are presented as error bars.

Table 3 Characteristics of the inflammatory lesion in the intergluteal fold (IGF) when present (n = 661)

	Number of patients with available data	Mean (SD) or n (%)	95% Confidence interval
Mean age at IGF lesion occurrence, years	447	23.1 (8.4)	22–24
IGF lesion as the first occurring lesion	661	236 (36)	32–39
Family history of IGF lesion	508	70 (14)	11–17
Recurrent IGF lesion (after surgery)	597	163 (25)	24–31
Patient diagnosis	554		
Hidradenitis suppurativa		61 (11)	8–14
Pilonidal sinus disease		493 (89)	84–94

Discussion

To the best of our knowledge, the possible association of HS and PSD has not been studied in detail. In the present cohort of 2465 patients with HS, using data from 14 centres from different countries, we observed a prevalence of 27% for IGF skin lesions. The exact prevalence remains elusive, but studies using diverse cohorts provide estimates of 4.6–30% for PSD in patients with HS.[11–17] Therefore, a direct and statistically significant comparison with the general population is still warranted, but the proportion of PSD within this HS cohort seems to be higher than the 1–9% prevalence observed in the general population.[18–21] The evaluation of the prevalence of PSD among a large cohort of patients with HS represents a complex challenge. Interestingly, we observed that the IG-HS

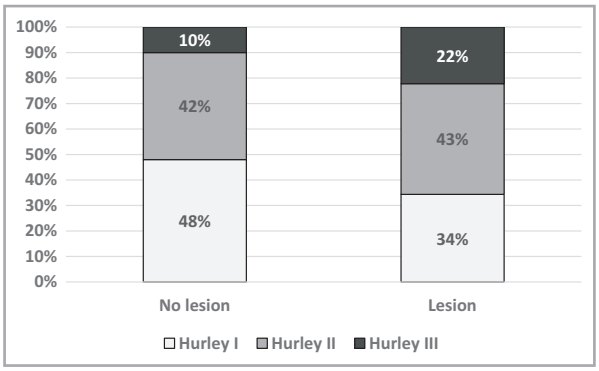

Fig 2. Classification of patients with hidradenitis suppurativa according the Hurley stage in the presence or absence of an inflammatory lesion in the intergluteal fold.
The P-value < 0.001 was considered significant after Benjamini–Hochberg correction (false discovery rate at 0.05). The 95% confidence intervals for each Hurley stage are as follows: 'No lesion' group – Hurley stage I, 45.2–50%; Hurley stage II, 40.1–44.8%; Hurley stage III, 8.6–11.5%; 'Lesion' group – Hurley stage I, 30.8–38.2%; Hurley stage II, 39.2–47.0%; Hurley stage III, 19.3–25.9%.

lesion was associated with localization of HS in the proximity of the IGF lesion, including buttocks, genitals and anus.

HS is a multifaceted disease and one of the main challenges is to determine a clinical classification that mirrors pathophysiological mechanisms and theranostic significance. Whether patients with HS who have PSD constitute a particular subgroup has been suggested when integrating PSD in the so-called HS follicular phenotype or in the follicular tetrad.[6] The main limitation of our study is its retrospective nature; clinical diagnosis was based on the diagnostic conclusion reported in the medical charts but the criteria used to obtain this diagnosis were never mentioned. In fact, a precise definition of PSD and an agreed list of criteria to ascertain the diagnosis are still lacking. The presence of a midline dimple and the presence of hair within a cyst or an abscess are usually reported as diagnostic criteria but both are not necessarily present. Even clear pathological criteria are still warranted. Similar ultrasonographic features have been reported for both HS and PSD,[9] suggesting that distinguishing between IG-HS and PSD can be difficult. The major limitation of our work is the retrospective design of the study, which could be associated with a lack of accuracy in the recorded data. Imaging and/or histopathological analysis were not always found in the medical charts, depending on variable management of the included centres, and represent another limiting factor of our work. We found that 77% and 67% of the IGF lesions observed in patients with HS were considered as PSD upon clinical and pathological examinations, respectively. This suggests that the prevalence of PSD is around 20% in patients with HS.

In contrast to its relatively high prevalence, the factors associated with the primary occurrence of PSD have been only scarcely explored. The suggested factors include overweight, excess

Table 4 Clinical factors influencing the occurrence of an inflammatory lesion in the intergluteal fold of 2465 patients with hidradenitis suppurativa (HS) (univariate and multivariate regression analyses after multinomial imputation of missing data)

	Univariate analyses			Multivariate analysis		
	Odds ratio	95% Confidence interval	P-values[a]	Odds ratio	95% Confidence interval	P-values[b]
Female sex	0.36	0.30–0.43	**< 0.001**	0.40	0.32–0.49	**< 0.001**
Age	0.99	0.98–0.99	**0.001**	0.99	0.98–0.99	0.040
BMI	1.00	0.99–1.02	0.542	1.02	1.00–1.04	**0.028**
Smokers	1.50	1.19–1.88	**< 0.001**	1.61	1.25–2.06	**< 0.001**
Family history of HS	0.93	0.76–1.14	0.496	0.80	0.64–1.00	0.052
Age at first boil	0.97	0.96–0.98	**< 0.001**	0.96	0.95–0.97	**< 0.001**
Hurley stage	1.69	1.49–1.93	**< 0.001**	1.56	1.35–1.81	**< 0.001**
Axilla	1.10	0.91–1.33	0.331	0.87	0.70–1.09	0.230
Breast	0.72	0.57–0.90	**0.005**	0.66	0.51–0.87	**0.003**
Buttocks	1.42	1.18–1.70	**< 0.001**	1.12	0.91–1.38	0.289
Groin	1.01	0.81–1.26	0.903	1.08	0.84–1.39	0.759
Pubis	1.23	0.97–1.56	0.091	1.11	0.83–1.47	0.476
Genitals	1.39	1.14–1.68	**< 0.001**	1.24	0.99–1.55	0.058
Anus	2.05	1.64–2.57	**< 0.001**	1.68	1.29–2.17	**< 0.001**
Elsewhere	1.26	1.02–1.56	0.034	0.89	0.70–1.14	0.369
Joints	0.99	0.68–1.47	0.998	1.24	0.80–1.91	0.331
Gastrointestinal	0.56	0.28–1.12	0.102	0.57	0.27–1.22	0.149
Acne vulgaris	1.78	1.34–2.37	**< 0.001**	1.65	1.21–2.26	**0.002**
Acne conglobata	2.02	1.40–2.91	**< 0.001**	1.26	0.82–1.95	0.288
Dissecting folliculitis	1.12	0.52–1.42	0.759	0.69	0.28–1.37	0.415
Psoriasis	1.02	0.52–2.00	0.945	0.78	0.37–1.62	0.506

BMI, body mass index. [a]P-values are presented in bold when considered significant after Benjamini–Hochberg correction (false discovery rate at 0.05). [b]P-values are presented in bold (indicating significance) when $P < 0.05$.

Table 5 Exploration of the factors related to hidradenitis suppurativa (HS) or pilonidal sinus disease (as assessed by clinical observation) in patients with an inflammatory lesion in the intergluteal fold (IGF)

	Pilonidal sinus disease, n = 186 (78%)		HS in the IGF, n = 52 (22%)		Statistical analysis
	Mean (SD) or n (%)	95% CI	Mean (SD) or n (%)	95% CI	P-values[a]
Female sex	87 (47)	40–54	15 (29)	16–42	**0.019**
Mean age, years	32.2 (9.8)	31–34	40.2 (12.6)	37–44	**< 0.001**
BMI, kg m^{-2}	28.8 (7.1)	28–30	26.4 (5.1)	25–28	**0.025**
Current or past smokers	142 (77)	71–83	44 (88)	79–97	0.078
Family history of HS	38 (21)	15–27	10 (19)	8–30	0.794
Mean age at first boil, years	21.1 (8.7)	20–22	24.9 (10.4)	22–28	**0.015**
Mean HS duration, years	11.3 (7.9)	10–13	15.4 (11.8)	12–19	**0.007**
Hurley stage					**< 0.001**
I	69 (38)	31–45	4 (8)	0–15	
II	68 (37)	30–44	12 (23)	11–35	
III	46 (25)	19–31	36 (69)	56–82	
Regions involved					
Axilla	130 (77)	71–83	32 (62)	48–75	0.032
Breast	37 (25)	18–32	6 (12)	3–21	0.033
Buttocks	54 (35)	27–43	37 (71)	59–84	**< 0.001**
Groin	131 (78)	72–84	39 (75)	63–87	0.657
Pubis	48 (32)	24–40	18 (35)	21–48	0.730
Genitals	38 (26)	19–34	31 (60)	46–73	**< 0.001**
Anus	25 (17)	11–24	23 (44)	30–58	**< 0.001**
Elsewhere	60 (37)	30–45	17 (33)	20–47	0.630
Comorbidities					
Joints	5 (3)	0–7	3 (6)	0–12	0.488
Gastrointestinal	1 (1)	0–2	1 (2)	0–6	0.478
Acne vulgaris	28 (15)	10–20	6 (12)	3–21	0.513
Acne conglobata	11 (8)	3–12	8 (15)	5–26	0.121
Dissecting folliculitis	3 (2)	0–4	3 (6)	0–12	0.214
Psoriasis	4 (2)	0–4	3 (6)	0–12	0.207
Mean age at IGF lesion occurrence, years	23.7 (7.8)	22–25	28.9 (10.9)	26–32	**0.001**
IGF lesion as the first occurring lesion	55 (30)	23–36	25 (48)	34–62	**0.014**
Family history of IGF lesion	22 (15)	9–21	1 (2)	0–6	**0.003**
Recurrent IGF lesion (after surgery)	52 (36)	28–44	28 (58)	44–73	**0.008**

[a]P-values are presented in bold when considered significant after Benjamini–Hochberg correction (false discovery rate at 0.05).

hair in the IGF, stiff hair, male sex, prolonged sitting time, family history of PSD and poor hygiene.[22–25] In our series we found that, when compared with patients without a lesion in the IGF, patients with HS who had such lesions were more frequently men. A male predisposition was observed when comparing PSD and HS lesions within the group of patients who had an IGF lesion. While clearly associated with HS,[3] smoking has been reported as a prognostic factor for recurrence and delayed healing after surgery but not as a predisposing factor to PSD.[26] Patients with IG-HS were more frequently smokers, but we could not associate smoking habits with a clinical diagnosis of IG-HS or PSD. Patients with HS who had an IGF lesion were significantly younger at the onset of HS. These patients had the disease for a longer duration and the risk of an IGF lesion in HS increases over time. However, although we cannot exclude a bias owing to the retrospective nature of the evaluation, our results suggest that IGF lesions occur early (Fig. 1). Among patients with HS who had an IGF lesion, the lesion occurred earlier and more frequently in a family context of PSD, if it was classified as a PSD lesion. In contrast, true IG-HS lesions recurred more frequently after surgery than PSD lesions. We identified a new phenotype of patients with HS who have an IGF lesion as the first manifestation of the disease. We also identified risk factors such as male sex, smoking, late onset, no family history of PSD and recurrence after surgery, which could be indicative of the possibility of future HS occurrence. Further studies are needed to compare HS-associated PSD with HS-free PSD and confirm the contribution of a genetic background component involved in the aetiopathogenesis.

Whether a precise distinction between PSD and HS is clinically relevant when managing a lesion of the IGF in patients with HS remains a matter of discussion. The occurrence of an inflammatory IGF lesion has to be reconsidered by surgeons. Patients with recurrent flares of IGF lesions (with or without a confirmed diagnosis of PSD) with no other skin involvement have to be followed up in dermatology to track the diagnosis of HS disease. Interestingly, surgery would be preferred for PSD, whereas systemic therapies could be offered for HS. The high prevalence of PSD in patients with HS is, in fact, not inconsistent with the acquired origin theory of PSD.

Table 6 Clinical factors influencing the hidradenitis suppurativa (HS) nature (rather than a pilonidal sinus disease) of an inflammatory lesion in the intergluteal fold (IGF) of 238 patients with HS (univariate and multivariate regression analyses after multinomial imputation of missing data – exploratory study)

	Univariate analyses			Multivariate analysis		
	Odds ratio	95% Confidence interval	P-values[a]	Odds ratio	95% Confidence interval	P-values[b]
Female	0.46	0.24–0.90	0.023	2.01	0.71–5.70	0.186
Age	1.06	1.03–1.09	**< 0.001**	1.05	0.99–1.10	0.052
BMI	0.94	0.89–0.99	0.042	0.98	0.90–1.07	0.611
Smokers	2.41	0.93–6.25	0.070	2.32	0.63–8.51	0.204
Family history of HS	0.90	0.42–1.97	0.799	0.83	0.26–2.69	0.760
Age at first boil	1.04	1.01–1.07	0.017	0.97	0.92–1.04	0.411
Hurley stage	3.90	2.36–6.45	**< 0.001**	3.79	1.99–7.19	**< 0.001**
Axilla	0.48	0.25–0.92	0.028	0.43	0.15–1.30	0.136
Breast	0.38	0.15–0.97	0.043	0.17	0.04–0.69	**0.013**
Anal, genital and/or buttocks	7.58	2.63–21.9	**< 0.001**	6.50	1.85–22.9	**0.004**
Elsewhere	0.47	0.21–1.05	0.066	0.60	0.16–2.28	0.450
Acne vulgaris	0.74	0.29–1.89	0.523	1.08	0.29–4.06	0.904
Acne conglobata	2.43	0.94–6.27	0.067	2.52	0.47–13.5	0.278
Dissecting folliculitis	3.53	0.76–16.3	0.107	8.80	0.99–77.5	0.050
Family history of IGF lesion	0.19	0.04–0.91	0.038	0.19	0.02–1.49	0.113
Recurrent IGF lesion (after surgery)	2.32	1.12–4.85	0.025	1.79	0.65–4.95	0.255

BMI, body mass index. [a]P-values are presented in bold when considered significant after Benjamini–Hochberg correction (false discovery rate at 0.05). [b]P-values are presented in bold (indicating significance) when $P < 0.05$.

Karydakis's concept of *HxFxV* formula in PSD pathophysiology is now widely accepted and suggests that PSD occurs owing to the association of free hair (H – hair), the vacuum effect that drives hair embedding in the IGF during movement of the gluteal region (F – force), and the vulnerability of the skin (*V* – vulnerability).[27,28] HS may predispose to PSD by weakening the skin (folliculitis, for example) and thereby increasing the *V* parameter of Karydakis's formula.

We conclude from our work that IGF lesions occur in about one-fourth of patients with HS. These lesions are not always PSD; about one-third correspond clinically to real HS lesions. We identified a new clinical phenotype of patients with HS who have IGF lesions (male predominance, younger age, smoking, family history of PSD, higher recurrence rate, more severe disease), which probably deserves to be considered when attempting to elucidate this complex and multifaceted disease.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Table S1 Exploration of the factors related to hidradenitis suppurativa or pilonidal sinus disease (as assessed by pathological exploration) in patients with an inflammatory lesion in the intergluteal fold.

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