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Squamous cell carcinoma in perineal, perianal, and gluteal hidradenitis suppurativa: Experience in 12 Patients

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Abstract

Background: Few reports describe squamous cell carcinoma (SCC) arising in hidradenitis suppurativa (HS).

Objective: The two objectives were 1) to describe the clinical characteristics, pathologic findings, and postoperative outcomes of SCC in HS; and 2) to assess whether human papillomavirus (HPV) is involved in the pathogenesis.

Materials and Methods: Cases of SCC in HS were identified through institutional medical records (1976–2013) and the Rochester Epidemiology Project. Tumor specimens were assessed for HPV DNA/RNA with in situ hybridization.

Results: Twelve patients were identified (11 caucasian, 9 men). All SCCs involved gluteal, perianal, or perineal skin; one patient had, in addition, involvement of the vagina. Surgical excision was done on all 12 patients, 4 of whom had a colostomy. Mean duration of HS before SCC development was 28.5 years (range, 15–53 years). Mean follow-up was 4.3 years after surgical excision. Seven of 12 patients followed had postoperative SCC recurrence. SCC caused death despite wide surgical excision in these 7 patients. Of the remaining 5 patients, 4 are unknown and 1 that did not recur had an in-situ SCC (Bowen's disease carcinoma). SCC was not associated with high-risk or low-risk HPV.

Conclusions: Invasive SCC arising in HS carries a high risk of death.

Keywords

hidradenitis; squamous cell carcinoma; human papillomavirus; surgery; outcome; radiation; chemotherapy; recurrence

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Introduction

Hidradenitis suppurativa (HS) is a progressive inflammatory disorder of the axilla, groin, and perineum. HS is uncommon but not rare; a population-based study utilizing the Rochester Epidemiology Project revealed age- and sex-adjusted incidence of 6.0 per 100,000 person-years and a prevalence of 129.1 per 100,000 person-years. Primary lesions are often complicated by scarring and bacterial infection. Occurrence of squamous cell carcinoma (SCC) in long-standing HS lesions has been reported (Table 1)^{1–11}. However, there are limited clinical, pathologic, and operative data on patients with SCC arising in HS. Fewer than 100 cases have been published, and clinical series are limited.

In the published reports of SCC in HS, almost all patients are men and the most common location of SCC development is within perianal or buttock HS.^{1,4} SCC typically develops several decades after the initial HS diagnosis,^{5,12} and in many patients, SCC leads to death.⁵ The lone epidemiologic data on SCC in HS are from a population-based study across Sweden that identified 5 cases of SCC arising in 2,119 HS patients from 1965 to 1997.²

In the present study, our aims were 1) to describe the clinical characteristics, pathologic findings, and postoperative outcomes of SCC arising in HS patients seen at our institution; and 2) to assess whether human papillomavirus (HPV) may be involved in the pathogenesis of SCC arising in HS.

Materials and Methods

The Mayo Clinic Institutional Review Board approved this study.

Mayo Clinic Rochester Case Series

Our institution's database was queried for all consecutive patients who received a diagnosis of HS and SCC from January 1, 1976, through December 31, 2013. Cases of HS were confirmed according to the diagnostic criteria described by Alikhan et al.¹⁶ SCC was confirmed with biopsy.

The following data were abstracted from a retrospective chart review of confirmed cases of SCC in HS: gender, race, date of birth, smoker status (current, former, or never), duration of HS before SCC diagnosis, anatomic area of HS and SCC involvement, presence of SCC within lymph nodes, measured tumor size, predominant grade of SCC differentiation, clinically measured depth of tumor invasion, previous treatment modality used, presence or absence of SCC at peripheral and deep cut surgical margins, local recurrence, distal metastasis and disease-specific death. Tumor size was calculated using clinical tumor length, width and depth measurements at surgical excision.

Assessment for HPV in Tumor Specimens

All patients were assessed for evidence of HPV infection with concurrent DNA and RNA in situ hybridization (ISH) on paraffin-embedded tumor specimens. Each specimen requires the following quality indicators: DNA/RNA integrity score (1+ nuclear staining), negative control, and control tissue positivity (2+). DNA ISH was performed with the low- and

high-risk Patho-Gene kit (Enzo Life Sciences, Inc, Farmingdale, New York) with probes evaluating for low-risk genotypes (6 and 11) and high-risk genotypes (16, 18, 31, 33, and 51). RNA ISH was performed with the RNAscope VS Target Probe kit (Advanced Cell Diagnostics, Inc, Newark, California), which evaluates high-risk genotypes (16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, and 82).

Results

Mayo Clinic Rochester Case Series

From January 1, 1976, through December 31, 2013, the records of 12 patients with SCC arising in HS were identified using our study criteria.

Demographic, operative, and follow-up data are presented in Tables 2 through 4. Almost all patients were caucasian (11 of 12; the race of 1 was unknown) and men (9 of 12). Two of the 12 patients tested positive for human immunodeficiency virus; the other 10 were not tested. In most patients, medical management with topical antibiotics, oral antibiotics, and biologic therapies, such as adalimumab, had been utilized prior to surgical management and SCC diagnosis. By location, gluteal SCC was most common (8 of 12), followed by perianal (6 of 12), perineal (4 of 12) and vulvar (1 of 12) SCC. Mean age at HS diagnosis was 27.7 years (range, 12–57 years); mean age at SCC diagnosis was 56.7 years (range, 37–73 years); and mean duration of HS before SCC development was 28.5 years (range, 15–53 years) (Table 2).

Figure 1 shows representative photographs of SCC arising in HS. At diagnosis, 2 patients had SCC in the lymph nodes and no patients had distant metastases at initial SCC diagnosis. Two patients had Bowen's disease type SCC in situ. Among the other 9 patients, 4 had well-differentiated and 5 had moderately differentiated usual-type SCC (Figure 2). The median clinical depth of tumor invasion was 2.1 cm (range, 1–4 cm). Perineural invasion was observed in 50% of patients. When reported, the surgical margin for SCC excision ranged from 1 to 2 cm with a variable excision depth. Median tumor size at resection was 36.7 cm³ (range, 1–1,008 cm³). In one case, clinically evident HS was not completely excised.

For all patients in the cohort, treatment included wide surgical excision of the tumor (Table 3). Four of the 12 patients underwent colostomy. Abdominal exploration was performed in 3 operations. Eight of the 12 patients had complete macroscopic resection with negative microscopic margins (R0 resection). Two of the 12 had complete macroscopic resection of disease but with positive peripheral microscopic margins (R1 resection); both patients had subsequent excision with negative margins, and 1 of the 2 patients received radiotherapy. In 2 patients, SCC was diagnosed intraoperatively and the procedure was halted with incomplete macroscopic resection and residual gross disease (R2 resection). Radiotherapy was used in 1 of these 2 patients and was planned for the other, but the second patient had a rapidly declining disease course and was too frail to proceed with the planned therapy.

Radiotherapy was used in half the patients (6 of 12) (Table 4). Chemotherapy was used in 1 patient. Mean postsurgical follow-up was 4.3 years (range, 0.2–25.3 years). Disease recurred postoperatively in 7 of 12 patients. Six patients had local recurrence of SCC, 1 had SCC in

the lymph nodes, and 1 had local recurrence of SCC in addition to metastases to the lung and lymph nodes. One patient had no SCC recurrence at all, and for the other 4 patients, SCC recurrence status was unknown. SCC was the cause of death in the majority of the cohort (7 of 12); for 3 patients, the cause of death was unknown.

Assessment for HPV in Tumor Specimens

HPV evaluation of all tumors by DNA and RNA ISH showed absence of involvement by high-risk and low-risk genotypes (Figure 2). In addition, morphologic evidence of koilocytic atypia was absent.

Discussion

This study showed that SCC in HS is most common in men with gluteal, perianal, and perineal disease many years after the initial onset of HS. Although seldom encountered, invasive SCC in the context of HS is aggressive and carries a high risk of death. In all patients with invasive SCC and known cause of death, SCC was the cause of their death.

Before this study, the only epidemiologic data on SCC in HS were from a 2001 review of the Swedish National Cancer registry of hospitalized patients over a 32-year period; that review identified 5 patients with SCC arising in HS out of 2,119 total HS patients.²

Most of the patients were Caucasian (11 of 12) which probably reflects the rural, midwestern location of the patient population. The predominance of men in the present cohort is consistent with other series.^{1,4,6–11} Only 1 published series on SCC in HS has had a predominance of women,² but, interestingly, most studies have shown HS to be more common in women than men. However, men have been shown to have a higher burden in the perianal/perineal region than that in women, the most common site of SCC development in HS.¹⁷

Gluteal, perianal, and perineal disease predominated in our study and in all other reported series.^{1,3,4,6–11} No report has described SCC arising in axillary HS.^{1,3,4,6–11}

At HS diagnosis, patients in our cohort had a mean age of 27.7 years (range, 12–57 years); mean age at SCC diagnosis was 56.7 years (range, 37–73 years). These mean ages are consistent with those in previous reports (Table 1). Mean duration of HS before SCC development was 28.5 years (range, 15–53 years) as shown in prior series.^{1,3,7,8,11} These findings suggest that early HS onset and long-standing HS disease and chronic inflammation may predispose to SCC development in the perineal/buttock perirectal areas.

In our cohort, 2 of 12 patients (16.7%) had nodal metastases at SCC diagnosis. Similarly, nodal metastases have been documented in a minority of published cases.^{1,4,8} Lavogiez et al¹ similarly found lymph node metastases in 2 of 13 patients. Distant metastases at initial SCC diagnosis were reported for individual patients in prior series,^{3,4,9,10} but distant metastases did not occur at initial SCC diagnosis in the present cohort.

Our entire cohort underwent wide surgical excision, as was the practice in other series.^{1–4,6–11} Four of the 12 patients underwent colostomy to preserve anal/rectal function. Given

the high mortality rate observed in this study, consideration of Mohs micrographic surgery could be considered. Radiotherapy was used in half the patients (6 of 12); its use has been reported in the literature, typically for palliative care.^{1,4} Disease recurred postoperatively in 7 of 12 patients (58.3%). Similarly, a prior review of all published reports to date showed a 63% rate of local recurrence after SCC resection.⁹

In our cohort, SCC was the cause of death for over half the cohort (58.3%; 7 of 12); cause of death was unknown for 3 patients. Of the seven patients with invasive SCC and known cause of death, all seven died of their disease despite aggressive medical and surgical management. SCC was also a common cause of death in published reports. In large-scale reviews, approximately half the patients with SCC arising in HS died of metastatic disease.⁵

Lavogiez et al¹ found an association of HPV coinfection with SCC that was detected with polymerase chain reaction methodology. In that series, all 8 tested patients had HPV infection, and all had at least 1 high-risk genotype (HPV 16, 18, and 68). Two patients concomitantly harboured a low-risk genotype, HPV 6. In the present cohort, none of our 12 patients had any association with high- or low-risk HPV coinfection on ISH. One biologic hypothesis for the absence of HPV infection is the physical distance from common sites of infection to the site of SCC. This, however, cannot entirely explain HPV negativity in the lesions arising from the perianal region (6 of 12 patients). Another hypothesis is based in the methodology; ISH allows for discriminant localization of the infected cells within the tumor. Another hypothesis includes epidemiologic variation in population cohorts from previously published studies.

Limitations of this study include its retrospective nature.

In conclusion, we found that the occurrence of SCC in HS is most common in men with chronic gluteal, perianal, and perineal HS. All patients were treated with surgical excision and despite aggressive surgical and radiotherapeutic intervention, all our patients with adequate follow up (7/7) with invasive SCC died from SCC related causes. We did not find an association with HPV infection, as was reported in a previous series.

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Abbreviations

HPV	human papillomavirus
HS	hidradenitis suppurativa
ISH	in situ hybridization
REP	Rochester Epidemiology Project

SCC squamous cell carcinoma

References

1. Lavogiez C, Delaporte E, Darras-Vercambre S, Martin De Lassalle E, et al. Clinicopathological study of 13 cases of squamous cell carcinoma complicating hidradenitis suppurativa. *Dermatology*. 2010;220(2):147–53. [PubMed: 20029163]
2. Lapins J, Ye W, Nyren O, Emtestam L. Incidence of cancer among patients with hidradenitis suppurativa. *Arch Dermatol*. 2001;137(6):730–4. [PubMed: 11405761]
3. Jackman RJ. Hidradenitis suppurativa: diagnosis and surgical management of perianal manifestations. *Proc R Soc Med*. 1959;52(Suppl):110–2.
4. Maclean GM, Coleman DJ. Three fatal cases of squamous cell carcinoma arising in chronic perineal hidradenitis suppurativa. *Ann R Coll Surg Engl*. 2007;89(7):709–12. [PubMed: 17959012]
5. Losanoff JE, Sochaki P, Khoury N, Levi E, et al. Squamous cell carcinoma complicating chronic suppurative hidradenitis. *Am Surg*. 2011;77(11):1449–53. [PubMed: 22196655]
6. Mora RG, Perniciaro C. Cancer of the skin in blacks. I. A review of 163 black patients with cutaneous squamous cell carcinoma. *J Am Acad Dermatol*. 1981;5(5):535–43. [PubMed: 7298919]
7. Talmant JC, Bruant-Rodier C, Nunziata AC, Rodier JF, et al. [Squamous cell carcinoma arising in Verneuil's disease: two cases and literature review]. *Ann Chir Plast Esthet*. 2006;51(1):82–6. [PubMed: 16488526]
8. Kurokawa I, Nishimura K, Yamanaka K, Mizutani H, et al. Cytokeratin expression in squamous cell carcinoma arising from hidradenitis suppurativa (acne inversa). *J Cutan Pathol*. 2007;34(9):675–8. [PubMed: 17696913]
9. Constantinou C, Widom K, Desantis J, Obmann M. Hidradenitis suppurativa complicated by squamous cell carcinoma. *Am Surg*. 2008;74(12):1177–81. [PubMed: 19097532]
10. Grewal NS, Wan DC, Roostaeian J, Rubayi SR. Marjolin ulcer in hidradenitis suppurativa: case reports. *Ann Plast Surg*. 2010;64(3):315–7. [PubMed: 20179481]
11. Anderson MJ, Jr., Dockerty MB. Perianal hidradenitis suppurativa; a clinical and pathologic study. *Dis Colon Rectum*. 1958;1(1):23–31. [PubMed: 13512158]
12. Huang C, Lai Z, He M, Zhai B, et al. Successful surgical treatment for squamous cell carcinoma arising from hidradenitis suppurativa: A case report and literature review. *Medicine (Baltimore)*. 2017;96(3):e5857. [PubMed: 28099342]
13. St Sauver JL, Grossardt BR, Leibson CL, Yawn BP, et al. Generalizability of epidemiological findings and public health decisions: an illustration from the Rochester Epidemiology Project. *Mayo Clin Proc*. 2012;87(2):151–60. [PubMed: 22305027]
14. Rocca WA, Yawn BP, St Sauver JL, Grossardt BR, et al. History of the Rochester Epidemiology Project: half a century of medical records linkage in a US population. *Mayo Clin Proc*. 2012;87(12):1202–13. [PubMed: 23199802]
15. St Sauver JL, Grossardt BR, Yawn BP, Melton LJ, et al. Data resource profile: the Rochester Epidemiology Project (REP) medical records-linkage system. *Int J Epidemiol*. 2012;41(6):1614–24. [PubMed: 23159830]
16. Alikhan A, Lynch PJ, Eisen DB. Hidradenitis suppurativa: a comprehensive review. *J Am Acad Dermatol*. 2009;60(4):539–61; quiz 62–3. [PubMed: 19293006]
17. Kohorst JJ, Baum CL, Otley CC, Roenigk RK, et al. Surgical Management of Hidradenitis Suppurativa: Outcomes of 590 Consecutive Patients. *Dermatol Surg*. 2016;42(9):1030–40. [PubMed: 27340739]

Figure 1.

Squamous Cell Carcinoma (SCC) Arising in Hidradenitis Suppurativa (HS). A, Patient 7 at SCC diagnosis with 2 draining ulcers and a background of inflammatory HS. B, Patient 6, 1 month after SCC diagnosis from a 3×5-cm nodule involving the right side of the vulva, posterior vaginal wall, perineum, and perianal skin. C, Patient 8 after wide surgical excision, 6 months after initial SCC diagnosis. D, Patient 11 at SCC diagnosis with 2 ulcers and a background of inflammatory HS.

Figure 2. Squamous Cell Carcinoma (SCC) Arising in Hidradenitis Suppurativa (HS). Patient 6 with invasive, well-differentiated SCC arising in an adjacent fistula tract of HS (hematoxylin-eosin, original magnification $\times 100$).

Table 1.

Published Series of SCC Arising in HS^a

Reference	No. of Patients	Gender	Mean Age of HS Diagnosis, y	Mean Age of SCC Diagnosis, y	Location	Duration of HS Before SCC, y	Treatment	Follow-up	SCC-Related Mortality, No.
Kohorst et al (present study)	12	M (9), F (3)	27.7	56.7	Gluteal, perianal, perineal	Mean, 28.8	Excision (12), radiotherapy (5), chemotherapy (2)	Mean, 4.3 y (including death)	8
Lavogiez et al ¹	13	M (13)	26.5	53.3	Gluteal, perianal, perineal	Mean, 25.3	Excision (13), radiotherapy (1)	Mean, 2.5 y (including death)	3
Lapins et al ²	5	M (1), F (4)	36.3	52.6	Unk (5)	Unk (5)	Unk (5)	Unk (5)	Unk (5)
Jackman ³	4	Unk	Unk	Unk	Perineal, gluteal	Range, 19–32	Excision (4)	Unk (4)	1
Maclean and Coleman ⁴	3	M (2), F (1)	25.6	52.7	Perianal, gluteal, perineal	9, 10, 18	Excision (1), radiotherapy (3), chemotherapy (2)	2.2 y (death), 2 mo (death), 9 mo (death)	3
Losanoff et al ⁵	2	M (2)	32.5	67.5	Gluteal, perineal	40, Unk	Excision (2)	1 y, 1 y (death)	1
Mora and Pemiciaro ⁶	2	M (2)	Unk	50.5	Perineal, perianal	5, Unk	Excision (1), unk	2 y, 5 mo (death)	1
Talmant et al ⁷	2	M (2)	27.5	67.5	Perianal	40, 40	Excision (2)	1.5 y (death), 2 mo	1
Kurakowa et al ⁸	2	M (2)	31	61	Gluteal	30, 30	Excision (2)	7 mo (death), 7 mo (death unrelated)	1
Constantinou et al ⁹	2	M (2)	Unk	54.5	Perianal, gluteal	20, Unk	Excision (2)	2 d (death), unk	2
Grewal et al ¹⁰	3	M (3)	Unk	44.5	Perianal, gluteal, thigh	20, Unk (2)	Excision (3), radiotherapy (1)	None (death [3])	3
Anderson and Dockerty ¹¹	2	M (2)	Unk	Unk	Perianal, gluteal	25, 32	Excision (2)	2 y (death), unk	1

Abbreviations: HS, hidradenitis suppurativa; SCC, squamous cell carcinoma; Unk, unknown.

^a Parenthetical values are number of patients.

Table 2.

Demographic Characteristics of Patients With HS Complicated by SCC

Patient	Sex	Race	HIV	SCC Location	Age at HS Dx, y	Age at SCC Dx, y	Duration of HS Before SCC, y	SCC in Lymph Nodes at Dx	SCC Grade ^a	Depth of Clinical SCC Invasion, cm
1	M	Caucasian	Unk	Gluteal, perianal	12	37	24	No	1	2.4
2	M	Caucasian	Unk	Gluteal, perianal	24	52	28	No	1	2.0
3	F	Caucasian	Unk	Perianal, perineal	42	57	15	No	IS	IS
4	F	Caucasian	Unk	Perianal, perineal	15	39	24	No	IS	IS
5	M	Caucasian	Unk	Perianal, perineal	17	70	53	No	1	2.0
6	F	Caucasian	Unk	Perianal, perineal, vulva/vaginal	47	63	16	Yes	2	2.2
7	M	Caucasian	Unk	Gluteal	38	63	25	Yes	2	3.1
8	M	Caucasian	Yes	Gluteal	17	57	39	No	2	1.4
9	M	Caucasian	Yes	Gluteal	Unk	53	Unk	No	2	2.3
10	M	Caucasian	Unk	Gluteal	20	51	30	No	1 (V)	1.0
11	M	Unknown	Unk	Gluteal	57	73	15	No	2	4.0
12	M	Caucasian	Unk	Gluteal	16	60	44	No	1	3.0

Abbreviations: Dx, diagnosis; HIV, human immunodeficiency virus; HS, hidradenitis suppurativa; IS, in situ; SCC, squamous cell carcinoma; Unk, unknown; V, verrucous.

^aSCC Grade according to the Broder classification

Table 3.

Operative Characteristics of Patients with HS Complicated by SCC

Patient	Tumor Size, cm ³	Perineural Invasion	Operative Details	Completeness of Resection
1	126	No	Wide excision with colostomy and abdominal exploration	R1; negative microscopic margins on subsequent operation
2	37	No	Wide excision with colostomy and abdominal exploration	R0
3	1	No	Wide excision only	R0
4	2	No	Wide excision only	R0
5	136	Yes	Wide excision with proctectomy	R0
6	91	Yes	Wide excision with vulvectomy and abdominal exploration	R0
7	1,008	Yes	Wide excision only	R0
8	15	Yes	Wide excision only	R1; negative microscopic margins on subsequent excision
9	180	Yes	Wide excision with Hartmann procedure (rectosigmoid colon resection with end colostomy and anorectal stump closure)	R2; excision halted after SCC diagnosis
10	22	No	Wide excision with colostomy	R0
11	36	No	Wide excision only	R0
12	10	Yes	Wide excision only	R2; excision halted after SCC diagnosis

Abbreviations: HS, hidradenitis suppurativa; R0, complete macroscopic resection with negative microscopic margins; R1, complete macroscopic resection with positive microscopic margins; R2, incomplete macroscopic resection with residual gross disease; SCC, squamous cell carcinoma.

Table 4.

Follow-up Characteristics of Patients with HS Complicated By SCC

Patient	Radiotherapy, cGy	Chemotherapy	Follow-up, y	Recurrence	SCC-Related Death
1	No	Yes	1.2	Yes (nodal)	Yes
2	No	No	3.2	Yes (local)	Unk
3	No	No	13.0	Unk	No
4	No	No	25.3	No	No
5	1,750	No	None	Unk	Unk
6	No	No	0.2	Unk	Unk
7	7,000	No	0.3	Yes (local, nodal, and distant)	Yes
8	5,940	No	5.9	Unk	Yes
9	5,040	No	6.0	Yes (local)	Yes
10	4,500	No	0.7	Yes (local)	Yes
11	No	No	0.6	Yes (local)	Yes
12	4,500	No	0.6	Yes (local)	Yes

Abbreviations: cGy, centigray; HS, hidradenitis suppurativa; SCC, squamous cell carcinoma; Unk, unknown; y, years.