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Journal
Dermatology Online Journal, 21(4)

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Publication Date
2015

DOI
10.5070/D3214026278

Volume 21 Number 4
April 2015

Photo vignette

Squamous cell carcinoma in the setting of chronic hidradenitis suppurativa; report of a patient and update of the literature.

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Dermatology Online Journal 21 (4): 12

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Abstract

Squamous cell carcinoma (SCC) developing in chronic hidradenitis suppurativa (HS) is rare, but failing to recognize the condition may have significant consequences. Dermatologists must be aware of the potential for malignant transformation and should have a low threshold for biopsy when clinical presentation is atypical. Herein we describe a 64-year-old woman with metastatic vulvar SCC that developed within an area of chronic HS. Like SCC associated with other chronic inflammatory disorders (Marjolin's ulcers), mortality is significant. Past reviews have reported death rates above 40% and our most recent update continues to support poor prognoses for these patients.

Keywords: Hidradenitis suppurativa; Squamous cell carcinoma

Introduction

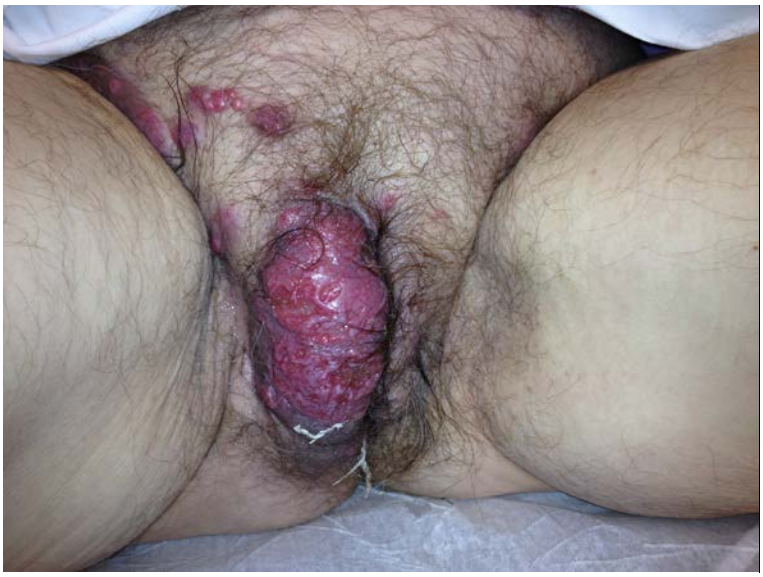
Hidradenitis suppurativa is a relatively common chronic inflammatory condition affecting the apocrine gland bearing skin of otherwise healthy individuals. Follicular occlusion, chronic relapsing inflammation, mucopurulent discharge, and progressive scarring characterize the disease. Rarely, malignant transformation may occur, with SCC being most commonly described. We add another report herein and update the literature on this topic to date.

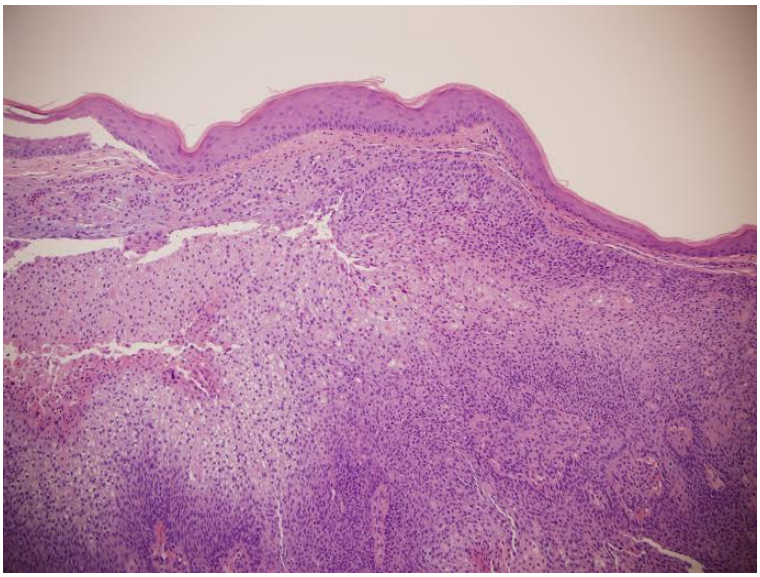
Case synopsis

A 64-year-old woman presented with large, swollen, red, painful nodules in the groin. She reported intermittent symptoms beginning in her twenties, but noted these always resolved without treatment. Over the past year she developed persistent nodules in the right groin, treated initially with antibiotic cream and testosterone, followed by 10 days of oral sulfamethoxazole-trimethoprim, which had no clinical effect. A fluctuant right labial mass developed, which was subsequently incised and the area cultured. Results from the bacterial culture identified normal skin flora. She subsequently completed 14 days of clindamycin

without improvement. Aside from intermittent constipation, review of systems was negative. She was then referred to the dermatology department.

Physical examination revealed a red-purple friable plaque of the right labia majora with satellite red-purple papules and nodules on the right mons pubis (Figure 1), accompanied by firm inguinal lymphadenopathy bilaterally. A punch biopsy was obtained from a satellite papule (Figure 2). A CT scan was performed of the pelvis (Figure 3).





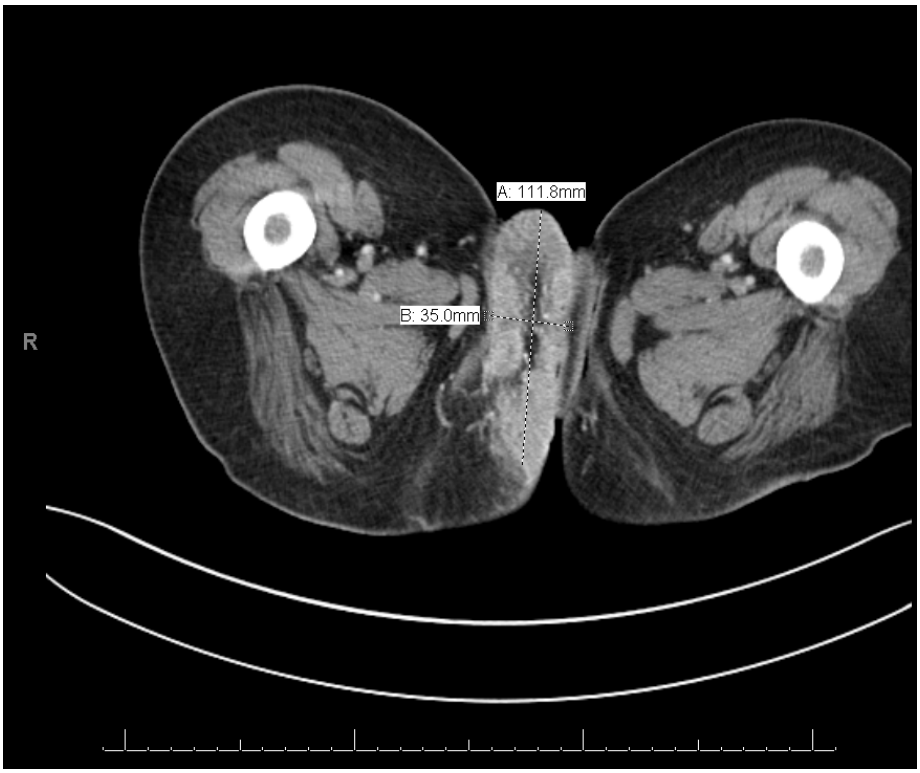


Figure 1. Examination of the vulvar area reveals a large erythematous friable plaque with surrounding satellite papule and nodules.

Figure 2. Histopathologic examination at 10x magnification of a satellite nodule. Atypical keratinocytes are seen within the dermis with no connection to the overlying epidermis, a finding consistent with metastatic squamous cell carcinoma.

Figure 3. CT revealing a large perineal mass. A measures the anterior posterior length of the tumor and B the horizontal dimension of the mass.

Histopathalogical examination of the skin biopsy specimen revealed a nodular proliferation of atypical keratinocytes within the dermis displaying abnormal cornification towards the center, suggesting a diagnosis of squamous cell carcinoma (SCC). Tissue sections showed lack of continuity of the malignant cells with the overlying epidermis, findings consistent with a metastatic lesion. Immunostaining was positive for CK-7 and negative for CK-20, GCDFP-15, and CEA. CT exam of the abdomen and pelvis demonstrated extensive retroperitoneal lymphadenopathy, bilateral inguinal masses, a large mass in the right perineal region, and bilateral lung base pulmonary nodules.

Given the extent of tumor involvement, an attempt to control or shrink the metastases with combination cisplatin and 5-FU was begun. Radiation therapy to the pelvis was eventually added with good response there. Nineteen months after original diagnosis the patient was still alive, but with signs of progressive disease in the neck and abdominal aortic area.

Discussion

Vulvar cancer accounts for 4% of all genital malignancies among women, making it relatively rare in gynecologic disease. Unfortunately, the incidence of vulvar cancer continues to rise in the U.S., with the number of newly diagnosed cancers predicted

to increase [1]. Ninety percent of vulvar cancer is SCC [1] with the remainder being melanoma, basal cell carcinoma, adenocarcinoma or sarcoma.

Predominately a disease of elderly women, vulvar cancer's incidence peaks during the 8th decade of life, with the majority of lesions arising on the vulva (80%); the clitoris (10%) and lower commissure (10%) may also be involved [2]. Lesions usually present unilaterally and may manifest as discoloration, ulceration, and endophytic or exophytic growths [2]. Itch is the most common symptom, although it can present as pain, bleeding, or an asymptomatic lump [3].

SCC in the setting of chronic hidradenitis suppurativa (HS) has been thought to be a rare complication. However, many more patients are now being reported. Lavogiez et al., demonstrated an incidence of SCC of 4.6% in their cohort of 217 patients with HS [4]. Since they last reviewed the literature in 2010 and found 65 reported cases [5-12], another 21, including ours, have been published (Table 1) [5-13]. Thus, there are now a total of 86 patients reported with this association [4-12,14,15]. The average age of this most recent collection of patients is 51 years, similar to the mean of 49 previously estimated by Lavogiez et al [4]. Also, the most recent publications continue to demonstrate a high preference for males (20/21 patients), in agreement with previous estimations. This finding is especially striking, given the much higher estimated prevalence of HS in females.

Table 1. Update of published patients with hidradenitis suppurativa and squamous cell carcinoma reported since last review by Lavogiez et al., in 2010.

Author(s), Year	**Tumor location**	**Age (years)**	**Gender**	**Race**	**Metastases**	**Outcome**
Scheinfeld,[5] 2014	Perineal and anal area	47	Male	Not reported	Not reported	Death 11 months following diagnosis
Poh et al.,[6]2014	Right thigh	56	Male	Not reported	Not reported	Not reported
Matoso et al.,[7] 2014	Scrotum	48	Male	Not reported	None	Alive 67 months following diagnosis
Herschel et al.,[8] 2014	Sacrum	52	Male	Not reported	Inguinal lymph nodes	Not reported
Belli, S, [9] 2012	Gluteal	40	Male	Not reported	Not reported	Disease free for 5 years
	Gluteal	54	Male	Not reported	Not reported	Disease free for 2 years

Pagliarello et al.,[10] 2011	Buttock	45	Male	Not reported	Inguinal lymph nodes and lungs	Death 9 months later
Losanoff et al.,[11] 2011	Perineal area	69	Male	Not reported	None	Disease free 12 months following diagnosis
	Left perineum	66	Male	Not reported	Pelvis	Death, time from diagnosis not reported
Vogelaar et al,[12] 2010	Left inguinal area	42	Male	Not reported	None	Disease free for 6 months following diagnosis
Grewal et al.,[13] 2010	Right buttock	34	Male	Hispanic	Pelvic bone and muscles	Death, time not specified
	Perineum and right buttocks	35	Male	White	None	Death from pneumonia, time not specified
	Buttocks and perianal	65	Male	White	Not reported	Death, time not specified
Obredor et al.,	Buttocks	47	Male	Not reported	Not reported	Not

2009						reported
Miquel et al., 2009	Left Buttock	65	Male	Not reported	Inguinal lymphnodes, abdomen, pelvis and Iliac bone	Death, one month after diagnosis
Katz et al., 2009	Left buttock	61	Male	Not reported	None	Not reported
Chandramohan et al., 2009	Perianal	40	Male	Not reported	None	Disease free 12 months after diagnosis
Balik, 2009	Gluteal and perianal area	Not reported	Male	Note reported	Not reported	Death within 8 months of diagnosis
Constantinou, 2008	Perianal area	46	Male	White	Colon, small bowel and mesentery	Death, 2 days after diagnosis
	Perianal and thigh areas	63	Male		Sacrum and lumbar spine	Death, time from diagnosis not reported

The prognosis for patients with HS who develop SCC within the diseased area appears poor. Maclean et al in their 2007 review determined that 48% of patients died within two years of diagnosis [14]. Nine of the 21 (42.9%) patients reviewed here have also died of their disease, further supporting the gravity of the diagnosis.

Including our patient, only 4 have been reported to develop SCC in the vulvar area in the setting of chronic HS (Table 2) [14-16]. Outcomes of patients with vulvar associated SCC appear similar to those located in other locations. Of the four reported, one death occurred and in our patient death looks likely given the findings of other metastatic lesions despite treatment.

Table 2. Reports of vulvar squamous cell carcinoma occurring in patients with hidradenitis suppurativa

Author(s), Year	**Tumor location**	**Age (years)**	**Gender**	**Race**	**Metastases**	**Outcome/Follow up**
Peña et al, 2015	Right labia	64	Female	White	Lymph nodes, and lungs	Alive after 19 months, but with signs of progressive disease
Crain et al,[18] 2005	Right labial fold	44	Female	Black	Lymph nodes and right pubic bone	Death 6 months after diagnosis
Short et al.,[15] 2005	Right labia minora	57	Female	Not reported	None	Not reported
Manolitsas et al.,[16] 1999	Vulva	52	Female	Maltese	None	Not reported

Interestingly, SCC has not been found in the context of axillary hidradenitis [14]. This has led some authors to suggest more vigilance and lower threshold for surgical intervention in patients with extra-axillary involvement [14,15], as these individuals may be at higher risk for SCC development.

Features that may distinguish vulvar carcinoma from HS are the lack of scarring, sinus tracts, and fistulae [17]. Additionally, HS is noted to have intermittently symptomatic lesions, whereas vulvar carcinomas will be persistent and relentless. Rock hard lymph nodes fixed to underlying fascia are more consistent with tumor infiltration than intermittent infections that accompany HS. Also, large friable plaques do not typify HS. However, in HS patients with chronic draining wounds the diagnosis of malignancy maybe less straight forward, because chronic draining fistulas can appear similar to a malignant ulceration. Although biopsies for hidradenitis are typically nonspecific and not required to establish the diagnosis, they will rule out malignant processes and should be considered in the setting of an uncertain clinical picture.

Conclusion

Squamous cell carcinoma in the setting of chronic hidradenitis suppurativa is an increasingly reported finding, and one with potentially significant clinical import. Most affected patients are male and involve the perianal and perineal areas. Death rates appear to be high, similar to other SCC-associated chronic inflammatory disorders (Marjolin's ulcers). Early recognition of this entity should be the goal of both patients and physicians. Although more data is necessary to estimate the incidence and prevalence of SCC in HS patients, current evidence suggests surveillance for this disease may be warranted in patients, especially males with longstanding HS outside the axillary area.

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