Successful surgical treatment for squamous cell carcinoma arising from hidradenitis suppurativa
A case report and literature review
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Abstract
Rationale: Hidradenitis suppurativa (HS) is a disabling inflammatory disease mainly affecting apocrine glands. Marjolin ulcer (MU) is a term used to describe a rare type of squamous cell carcinoma (SCC) arising within sites of chronic wounds or preexisting scars. Chronic HS may result in a rare type of SCC, MU, which has a poor prognosis due to its high metastatic rate.

Concerns of the patient: Here we reported a 60-year-old male who developed SCC on the right buttock after suffering from HS for 15 years.

Interventions: Radical resection with clear margin was performed, after which topical negative pressure (TNP) was applied followed by split-thickness skin grafting.

Outcomes: In a 1-year follow-up, there was no recurrence of malignancy.

Lessons: Cases reported in English literature since 1991 were reviewed to get a general grasp of status quo. The authors conclude that chronic HS lesion especially in the gluteal region should be cautiously observed. Once tumor arisen from HS lesion, immediate radical excision should be performed. With assured clear margin, TNP could be chosen to offer a favorable environment for the survival of skin grafting.

Abbreviations: HS = hidradenitis suppurativa, SCC = squamous cell carcinoma, TNP = topical negative pressure, MU = Marjolin ulcer.

Keywords: hidradenitis suppurativa, squamous cell carcinoma, surgery

1. Introduction
Hidradenitis suppurativa (HS), also known as acne inversa and Verneuil disease, was first described by Velpeau in 1832. The prevalence of HS was estimated approximately 0.053% to 4.1% worldwide. Since the missed diagnosis rate of HS is high, the morbidity may be higher than that.[1,2] HS is a chronic, cicatricial disease mainly affecting apocrine-bearing areas in young and middle-aged adults. Histologic findings recognized it as a disorder of the follicular epithelium.[3] It often afflicts patients for many years with pain, malodor, and disfigurement. HS is brought to the attention of general or plastic surgeons only after the dissatisfac-

tion of multiple long-term trials of conservative therapy. Among those consequences, Marjolin ulcer (MU) has the poorest prognosis due to its high metastatic rate. MU is a term used to describe a rare type of squamous cell carcinoma (SCC) arising within sites of chronic wounds or preexisting scars.[4] Due to the low incidence, comprehensive review of the MU caused by HS is strongly needed. Here we presented the clinical and pathological characteristics as well as the treatment of MU. In addition, we also reviewed the recent reports on SCC arising from HS since 1991.

1.1. Consent
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

2. Case report
A 60-year-old male was suffering from repeated painful furuncles in the right buttock for 15 years. The lesion was mainly on the buttocks and perineal region accompanied by hypertrophy of the surrounding tissue. During this period, the patient had received incision and furuncle drainage for several times, however, the lesions were frequently recurrent. By May 2014, he developed an ulcerative tumor in the right buttock which forced him to consult further treatment. He was diagnosis of HS by dermatologist and underwent incision and furuncle drainage for several times, however, the lesions were frequently recurrent. By May 2014, he developed an ulcerative tumor in the right buttock which forced him to consult further treatment. He was diagnosis of HS by dermatologist and then administrated with oral antibiotics. His medical history was unremarkable except for a 40-year smoking habit. Physical examination revealed a 5 cm x 5 cm mass in the right buttock with crateriform ulcer and stinky purulence on the top (Fig. 1).
Besides, the surrounding tissue was hyperpigmented with tenderness. Pathological biopsy was performed twice right after diagnosis. The first examination revealed slight skin hyperkeratosis, irregular acanthosis, pseudoepitheliomatous hyperplasia (PEH) and infiltration of a few chronic inflammatory cell surrounding the perivasculatures in the superficial dermis. Second biopsy demonstrated verrucous carcinoma (a highly differentiated SCC) (Fig. 2), immunohistochemistry results showed negative human papillomavirus (HPV), p16 expression and high Ki67. Meanwhile, bacterial cultivation of the drained nodules revealed proteus mirabilis. Before admission, he was treated with chemotherapy for a week. Nevertheless, he terminated the therapy because of unbearable pain.

In July 4, 2014, radical resection till deep fascia and 3cm free margin was performed under local anesthesia. During operation frozen pathologies of resection margin in the direction of 3, 6, 9, 12 o’clock showed tumor free (Fig. 3). Topical negative pressure (TNP) treatment was applied consecutively for a week and fresh granulation tissues was formation. Later, reconstruction with split-thickness skin grafting from lateral thigh was conducted, the skin grafting healed primarily under careful observation (Fig. 4). A year later, there is no evidence of tumor recurrence in this patient.

3. Discussion

3.1. Methodology of review

SCC arising from HS is also named as MU, which was characterized by aggressiveness and ulcerating. The incidence of MU arising from long-standing HS varies from 1% to 3.2%. Transformation from HS to SCC may be explained by chronic irritation and infection, which lead to proliferative epidermal changes and increased rate of spontaneous mutations. By far, HS complicating SCC was rarely reported despite a low occurrence rate of HS. To get a general grasp, we carried out a comprehensive search of “PubMed,” “Embase,” and “Web of science” using the following keywords: “hidradenitis suppurativa,” “acne inversa,” “Verneuil disease,” “follicular occlusion.
triad,” and “squamous cell carcinoma,” “Marjolin Ulcer” in English literature from January 1991 until now. Cases published before 1991 were excluded because they were out of date and had been reviewed by Williams et al.\(^6\) The flow chart of searching strategy is demonstrated in Fig. 5.

3.2. Epidemiologic characteristics

A total of 62 cases were reported from 41 separate articles. The overall information is demonstrated in Table 1. HS was diagnosed with an average age of 27.49 ± 10.16 years old ranging from 14 to 53 years old, which indicated that a younger HS onset may get a high malignant tendency as normally the onset age was in the second or third decade of life. The average diagnosis age of SCC was 54.12 ± 10.14 years old, while the average latency period of

### Table 1

**Overall information of patients with squamous cell carcinoma arising from hidradenitis suppurativa since 1991.**

| Author       | Year | Gender | Age of SCC diagnosis, y | Duration before SCC, y | Location of carcinoma | Histology | Surgery performed for SCC | Other interventions | Outcome                        |
|--------------|------|--------|-------------------------|------------------------|-----------------------|-----------|---------------------------|-------------------|--------------------------------|
| Mendonca     | 1991 | M      | 57                      | 35                     | Right buttock         | WD        | WLE with grafts and temporary colostomy | NR                | No recurrence at 1 y          |
| Williams     | 1991 | M      | 27                      | 11                     | Gluteal               | WD        | WLE                       | NR                | No recurrence at 1 y          |
| Welsh        | 1993 | M      | 50                      | 20                     | Left buttock          | PD        | Excision                  | NR                | Died 2 mo later               |
| Pérez-Diaz   | 1995 | M      | 60                      | 25                     | Posterior perineum    | MD        | WLE                       | NR                | No recurrence at 1 y          |
| Shukla       | 1995 | F      | 71 (2)                  | ≥50                    | Sacrum                | NR        | 2 times radical excision with skin graft due to unclear margin | Palliative radiotherapy | No recurrence at 4 y          |
| Duffesne     | 1996 | F      | 52                      | 36                     | Right buttock, perianal | MD        | Excision by the fresh-tissue Mohs micrographic technique | chemotherapy | Died of metastasis 7 mo after diagnosis of SCC |
| Malaguarnera | 1996 | M      | 66                      | 20                     | Perineal area         | PD        | Radical excision          | NR                | Died 7 mo after diagnosis     |
| Gur          | 1997 | M      | 63                      | 10                     | Buttocks, perineal, inguinal | WD        | 2 times radical excision and split-thickness skin graft due to unclear margin | NR                | No recurrence at 2 y          |
| Li           | 1997 | M      | 68                      | 50                     | Perianal              | MD        | 2 times resection due to SCC recurrence at 5 mo | NR                | NR                            |
| Ritz         | 1998 | M      | 61                      | 45                     | Gluteal               | PD        | WLE                       | Radiotherapy      | Died 4 mo after diagnosis due to rapid tumor progression Without improvement or deterioration 1 mo after dismissal |
| Nijhawan     | 1998 | M      | 59                      | 30                     | Right buttock         | WD        | Debridement               | NR                | Died of metastasis 19 wk after SCC diagnosis |
| Lin          | 1999 | M      | 55                      | 30                     | Left posterior thighs and buttocks | PD        | 2 times WLE with split-thickness skin grafts, LN dissection due to lymphadenopathy | NR                | Died of metastasis 19 wk after SCC diagnosis |
| Manolitsas   | 1999 | F      | 52                      | 30                     | Right vulval          | WD        | WLE with primary closure  | lyMPHadenopathy   | Uncomplicated recovery        |
| Cosman       | 2000 | M      | 47                      | 10–20                  | Left buttocks         | WD        | Radical excision          | WLE with flap and skin graft. | NR                | Alive at 3 mo Died of cachexia and pneumonia 1 y after the operation |
| Ishizawa     | 2000 | M      | 49                      | 21                     | Buttock               | WD        | WLE with flap and skin graft | Radiotherapy | Died 3 mo later Died 18 mo later |
| Altunay      | 2002 | M      | 54                      | 30                     | Right buttock         | MD        | None                      | Multiple surgical interventions | NR                | Radiotherapy and chemotherapy |
| Bocchini     | 2003 | M      | NR                      | NR                     | Gluteal               | NR        | None                      | Radiotherapy and chemotherapy | NR                | Radiotherapy and chemotherapy |
| Crain        | 2005 | M      | 51                      | 35                     | Left scapular         | NR        | WLE with flap graft       |                  | Died 2 wk later               |
| Author          | Y     | Sex | Age of SCC diagnosis, y | Duration before SCC, y | Location of carcinoma | Histology | Surgery performed for SCC | Other interventions | Outcome                    |
|-----------------|-------|-----|------------------------|------------------------|-----------------------|-----------|---------------------------|---------------------|---------------------------|
| Rosenzweig      | 2005  | M   | 50                     | 20                     | Perineal              | WD        | 3 times WLE due to unclear margin | NR                  | No recurrence at 18 mo     |
| Short           | 2005  | F   | 57                     | 15                     | Vulva                 | NR        | WLE                        | NR                  | Died 26 mo after diagnosis |
| Maclean         | 2007  | M   | 50                     | 32                     | Buttocks              | NR        | Three times radical excision with flap and split skin grafts, including APR of the rectum and groin due to recurrence | NR                  | Died of metastasis half year later |
|                 |       | F   | 61                     | 40                     | Pelvis, right vulva, groin | NR        | None                       | Palliative radiotherapy and chemotherapy | Died of metastasis 2 mo after surgery |
|                 |       | M   | 47                     | 9                      | Perianal              | NR        | None                       | Palliative radiotherapy and chemotherapy | Died 9 mo after diagnosis |
| Kurokawa        | 2007  | M   | 72                     | 30                     | Buttock               | WD        | Excision                   | NR                  | Died of metastasis 2 mo after surgery |
|                 |       | M   | 50                     | 30                     | Right buttock         | PD        | None                       | Chemotherapy        | Died of metastasis half year later |
| Achour          | 2008  | M   | 60                     | 30                     | Perianal              | WD        | Excision and left lateral colectomy | NR                  | No recurrence at 18 mo     |
| Constantinou    | 2008  | M   | 46                     | 20                     | Perianal              | PD        | Exploratory laparotomy with end sigmoid colectomy | NR                  | Died on the second postoperative day |
|                 |       | M   | 63                     | NR                     | Perineal and thigh    | WD        | Radical excision           | Radiotherapy and chemotherapy | Died 2 mo after discharge |
| Balk            | 2009  | M   | NR                     | 30                     | Perianal, gluteal     | NR        | Excision with rotation flap; APR due to recurrence | NR                  | Died of metastasis 2 mo after surgery |
| Chandramohan    | 2009  | M   | 40                     | 22                     | Perianal              | WD        | Excision with bilateral gluteal rotation flaps and split-thickness skin grafting, protective colectomy | NR                  | No recurrence at 1 y      |
| Ito             | 2009  | M   | 59                     | 43                     | Left scapular         | PD        | WLE with left LN dissected | Radiotherapy and chemotherapy | Died of metastasis 18 mo after initiated therapy |
| Katz            | 2009  | M   | 61                     | >20                    | Left buttock          | WD        | Excision, gluteal rotation flap, and V-Y flap adipocutaneous advancement flap; partial flap loss covered by split-thickness skin graft | NR                  | NR                        |
| Lavogiez        | 2010  | M   | 57                     | 20                     | Buttock               | WD        | Two times WLE due to recurrence | NR                  | Died of metastasis 2 y after surgery |
|                 |       | M   | 38                     | 20                     | Buttock               | VC        | WLE                        | NR                  | No recurrence at 11 y      |
|                 |       | M   | 57                     | 37                     | Buttock               | VC        | WLE                        | NR                  | Died 3 mo after surgery, Died of lung metastasis 2 mo after relapse |
|                 |       | M   | 68                     | 40                     | Left buttock          | WD        | APR and ilioinguinal bilateral lymphadenectomy | NR                  | Alive at 36 mo            |
|                 |       | M   | 67                     | 40                     | Right buttock         | WD        | WLE                        | NR                  | Alive at 36 mo            |
|                 |       | M   | 51                     | 20                     | Perianal, gluteal     | VC        | WLE                        | NR                  | Alive at 36 mo            |
|                 |       | M   | 56                     | 20                     | Perineal, buttocks    | VC        | WLE                        | NR                  | Alive at 36 mo            |
|                 |       | M   | 62                     | 35                     | Inguinoscrotal         | WD        | WLE and bilateral inguinal lymphadenectomy | Radiotherapy | Alive at 24 mo            |
|                 |       | M   | 49                     | 20                     | Perianal              | VC        | APR                        | Radiotherapy        | Alive at 24 mo            |
|                 |       | M   | 44                     | 20                     | Perianal              | VC        | WLE                        | NR                  | Alive at 24 mo            |
|                 |       | M   | 41                     | 20                     | Buttocks              | WD        | WLE                        | NR                  | Alive at 24 mo            |
SCC developed from HS was 27.13±9.93 years. Nevertheless, Chang et al[2] reported an acute malignancy transformation from HS lesion despite a more than 30 years latency period. Yu et al[7] divided the latency period into preulceration and postulceration periods, pointing out that duration of ulceration played an important role in malignant transformation. Therefore cautious surveillance and more aggressive treatment should be executed in ulcerated patients. Even though female had a high prevalence of HS, those who suffered from MU are practically male with a ratio of 6.75:1. The most predisposing site of Marjolin ulcer (MJ) included buttocks and perianal region, existing in most cases and sometimes affecting sacrum, groin, thighs, and vulva region. Regional factor may also play a role in SCC formation as it seldom affected the axillary area. One possible explanation may be that

| Author         | Year | Sex | Age of SCC diagnosis, y | Duration before SCC, y | Location of carcinoma                                      | Histology | Surgery performed for SCC                                                                 | Other interventions                    | Outcome                        |
|----------------|------|-----|------------------------|------------------------|------------------------------------------------------------|-----------|--------------------------------------------------------------------------------------------|----------------------------------------|--------------------------------|
| Grewal 2010    | M    | 48  | 7                      | 20                     | Buttocks                                                  | WD        | WLE with amputation of the coccyx and the inferior part of the sacrum                     | Radiation                             | Alive 6 mo after surgery       |
| M             | 35   | NR  | Perineum, hips, scrotal area, coccyx | WD                    | Excision with right groinian procedure and rotational myocutaneous flaps | MD        | Died of pneumonia                                                                         |                                        |                                |
| Büyükasık 2011 | M    | NR  | 30                     | 30                     | Buttocks                                                  | WD        | WLE                                                                                       | None                                   | Died of metastatic squamous cell cancer |
| Losanoff 2011  | M    | 69  | 30                     | Perineal               | WD                                                          | MD        | Sigmoid colostomy for local division                                                      | None                                   | Died of pneumonia              |
| Pagliarello 2011 | M    | 45  | 30                     | Right buttock          | WD                                                          | MD        | WLE                                                                                       | None                                   | Died of metastatic SCC*        |
| Belli 2012     | M    | 54  | 30                     | Gluteal                | WD                                                          | MD        | WLE with local advancement flap following VAC and Y-V flap (right side), subcutaneous transposition flap (left side) and a subsequent mesh-graft transplantation of the remaining defect; 6 mo later surgical removal of metastatic LNs | None                                   |                                |
| Herschel 2014  | M    | 52  | 34                     | Sacral, gluteal         | MD                                                          | MD        | En bloc resection following VAC and Y-V flap (right side), subcutaneous transposition flap (left side) and a subsequent mesh-graft transplantation of the remaining defect; 6 mo later surgical removal of metastatic LNs | None                                   |                                |
| Matos 2014     | F    | 48  | NR                     | Scrotum                | NR                                                          | NR        | Excision with dermal graft and debridement                                                | Radiation                             | Alive at 9 mo with signs of progressive disease |
| Chang* 2014    | M    | 50  | During hospital Stay 9 | Buttck, perineal        | NR                                                          | NR        | No recurrence at 47 mo                                                                   | Radiation                             |                                |
| Poh 2014       | M    | 56  | 30                     | Right thigh            | WD                                                          | NR        | Palliative radiotherapy and chemotherapy                                                  | None                                   | Died of metastasis 1 y later   |
| Scheinfeld 2014 | M    | 47  | Since early adulthood  | Perineal and anal areas | NR                                                          | NR        | Died of metastasis 1 y later                                                               |                                        |                                |
| Peña 2015      | F    | 64  | 44                     | Right labia majora     | NR                                                          | NR        | Radiotherapy                                                                              | None                                   |                                |
| Verdeli 2016   | M    | 78  | 25                     | Right gluteal          | MD                                                          | MD        | Died of sepsis                                                                             |                                        |                                |

APR = abdominoperineal resection, LN = lymph node, MD = moderate-differentiated squamous cell carcinoma, NR = not reported, PD = poorly differentiated squamous cell carcinoma, SCC = squamous cell carcinoma, VAC = vacuum assisted closure therapy, VC = verrucous carcinoma, WD = well-differentiated squamous cell carcinoma, WLE = wide local excision.

* Presumed acute Marjolin ulcer.
male tends to have a high morbidity in anogenital or perineal region while female in axillary. Concomitant diseases accompanied with these cases included hypercalcemia, follicular occlusion triad, Crohn disease, osteomyelitis, spina bifida, polynoopathy, etc.

3.3. Pathology and prognosis
Pathology was recorded according to Broder classification. Even though well and moderately differentiated SCC accounted for the vast majority of MU (85%), nearly half patients died within 2 years. Possible reasons were listed as follow: Identification of malignant transformation on the background of chronic skin inflammation is relatively difficult; presence of sinus tract allows easy spread of cancer; lesion biopsy sometimes presents false negative results just like the case we presented. Thus, it tends to have a long journey from the onset of MU to final treatment. Besides, HPV infection was assumed to play a carcinogenic role in SCC arising in HS. It was concluded that positive p16/HPV expression with high Ki67 was associated with basaloid/warty morphology of SCC, while negative p16/HPV expression with low Ki67 was associated with usual morphology. However, our case (verrucous carcinoma) was inconsistent with the former conclusion since negative HPV/p16 expression with high Ki67 was demonstrated.

3.4. Treatment recommendation
Based on American Joint Committee on Cancer Guidelines, primary surgical excision was recommended for invasive cutaneous SCC. Radiation therapy was typically reserved for patients who are unable to undergo surgical excision while chemotherapy has not been proved to be effective. According to our review, 53 out of 62 cases received surgical intervention. To avoid the existence of small focus of tumor, meticulous excision with clear margins of tumor biopsy are recommended. Lavogiez et al.

3. Conclusion
HS may get malignant transformation under chronic inflammatory irritation. Cautious surveillance and active intervention should be taken especially in the gluteal involvement subtype of ulcerating patients. Once SCC was found in HS lesion, radical excision with extended region and clear margins should be performed timely to avoid tumor metastasis. By virtue of TNP, split-thickness skin grafting could be survived even under chronic inflammatory environment. Regular follow-up should be taken in case of tumor recurrence.

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