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Report

# Suppurative keloids: a complication of severe keloid disease

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## Abstract

**Background** Some keloids show cystic cavities that give rise to acute inflammatory flares and oozing. These suppurative keloids (SK) have rarely been systematically studied. We conducted a retrospective cohort study to evaluate SK frequency and its risk factors. We also reviewed microbiological analyses as well as the histological features of removed SKs.

**Methods** Between July 1, 2015, and September 30, 2016, all adult patients attending a specialized keloid clinic were asked to participate. Clinical information and microbiological results were extracted from each patient's file. Histological features were observed and interpreted.

**Results** In this study, we observed an SK rate of 26% for a mean keloid history of 17.2 years. Male gender, African ancestry, and a family history of keloids were significantly associated with suppuration. Microbiological examination revealed commensal skin flora 7/9 (77.8%), *Staphylococcus aureus* 1/9 (11.1%), and *Enterococcus faecalis* 1/9 (11.1%).

**Conclusion** Suppuration is a common complication of keloids occurring in patients with severe keloid disease and may arise from pilosebaceous occlusion and aseptic inflammation.

## Introduction

Keloids result from an intradermal fibroproliferative process that occurs in response to dermal injury or spontaneously.[1,2] Keloids have a chronic, long-lasting course and tend to recur after excision. They can occur in all skin types but are more frequent and severe in people of African or Asian descent.[3] Keloids may cause functional impairment and cosmetic disfigurement and are often associated with low patient-reported quality of life.[4] In addition to cosmetic disfigurement, keloids frequently cause pruritus, tenderness, and pain. Moreover, some keloids show cystic cavities that give rise to acute inflammatory flares with pain, redness, tenderness, and ultimately pus discharge (Fig. 1).[5,6] Suppurative keloids (SK) are commonly referred to as "superinfections" but have rarely been systematically studied. In the medical literature, there are few studies regarding its frequency, risk factors, management, pathophysiology, or the hypothetical role of infectious agents. Here, we conducted a retrospective cohort study to evaluate the frequency and risk factors of SK. We also reviewed the microbiological results of all bacteriological samples taken from SK in our study population as well as the histological features of surgically removed keloids. Finally, we discuss the management of SK.

## Methods

Between July 1, 2015, and September 30, 2016, all adult patients attending a specialized keloid clinic were asked to participate in a prospective study on genetic susceptibility to keloid formation. Patients gave their informed consent, and the clinical characteristics of their keloid disease were collected in a database for use in our study.

The diagnosis of keloid disease was made on clinical grounds; acne keloidalis nuchae (AKN) was not considered as a manifestation of keloid disease.

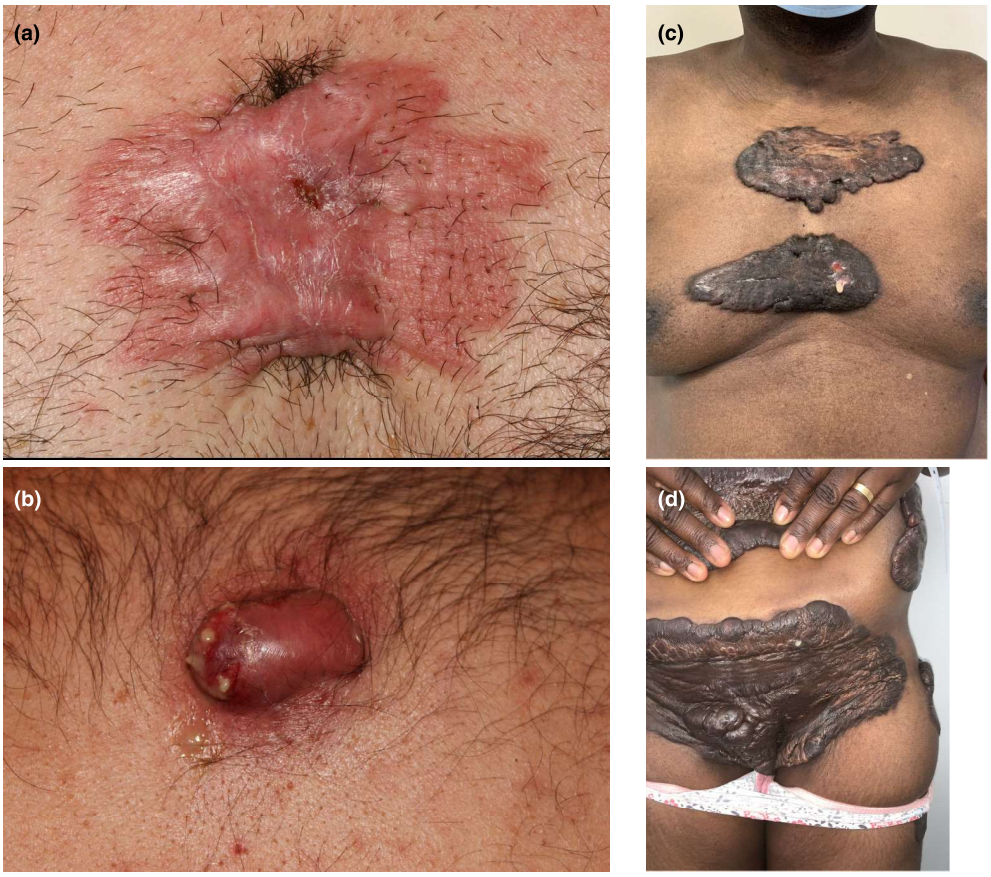


**Figure 1** Clinical presentation of suppurative keloids. (a) Chest keloid with lateral extension and fibrotic occlusion of hairs; (b) keloid with redness, tenderness and visible purulent drainage, (c) keloid of the chest in a man with visible purulent drainage; (d) suppuration in a woman with severe keloid disease

The following information was extracted from each patient's file: age, gender, ancestry, number of keloids, keloid symptoms, presence of SK, topography, keloid triggering factors, family history of keloids, and age at first keloid occurrence, as well as the microbiological results of all bacteriological samples taken from SK. Histological features of surgically removed keloids were collected and read by an experienced dermatopathologist (LD).

This study was conducted in compliance with good clinical practices and with the Declaration of Helsinki principles. According to the French public health code, there was no need to inquire for ethical clearance to use these data.

The manuscript was prepared following STROBE guidelines. Categorical variables were reported as percentages, and continuous variables were expressed as their mean along with their maximum and minimum values. For univariate analyses, we used the Wilcoxon test on continuous variables and Fisher's test on categorical variables. For multivariate analyses, we used logistic regression on patient-level variables only (not keloid-related variables). The level of significance was defined at 0.05. All analyses were carried out using R software (version 3.6.1).

Multivariate analyses were conducted with the following variables: gender, mean age, African ancestry, family history of keloids, and mean age at first keloid. Keloid number, symptoms, topography, and triggering factors were excluded from multivariate analyses because most patients had several keloids both with and without suppuration, at different locations, with variable symptoms and triggering factors.

## Results

### Comparison of demographic and clinical characteristics of patients with and without SK

In total, 114 patients were eligible for the study (Table 1). Five were excluded from analysis because of missing data. The mean duration of keloid history was 17.2 years (range 0–59 years). Over this period, 30 patients (26%) had experienced bouts of suppuration from at least one of their keloids.

#### *Univariate analysis*

The sex-ratio (male:female) was significantly higher in patients with SK compared with patients without SK (1.30:1 vs. 0.52:1;

**Table 1** Demographic by group of keloids with or without suppuration

| | Keloids with suppuration | Keloids without suppuration | Univariate analyses (*P*) | Multivariate analyses (*P*) | Odds ratio (CI 95%) |
|---|---|---|---|---|---|
| Number of patients | 30 | 79 | | | |
| Gender | | | 0.048* | 0.018* | 3.3 (1.2, 9) |
| Female | 13 (43%) | 52 (66%) | | | |
| Male | 17 (57%) | 27 (34%) | | | |
| Sex-ratio (M:F) | 1.30:1 | 0.52:1 | | | |
| Mean age (years) | 38.8 years | 39.6 years | 0.997 | 0.483 | NS |
| Geographic origin | | | 0.044* | | |
| Sub-Saharan Africa | 20 (67%) | 33 (43%) | | | |
| Caribbean | 7 (23%) | 19 (24%) | | | |
| Asia | 1 (3%) | 8 (10%) | | | |
| Other | 2 (7%) | 19 (24%) | | | |
| African ancestry (Sub-Saharan Africa & the Caribbean) | 27 (90%) | 52 (67%) | 0.009* | 0.035* | 4.8 (1.1, 20.1) |
| Number of keloids | | | 0.013 | NA | NA |
| 1 | 1 (3%) | 17 (22%) | | | |
| 2–5 | 16 (53%) | 41 (52%) | | | |
| 6–10 | 3 (10%) | 12 (15%) | | | |
| >10 | 10 (33%) | 9 (11%) | | | |
| Clinical symptoms | | | | | |
| Pruritus | 30 (100%) | 68 (86%) | 0.033* | NA | NA |
| Pain | 22 (73%) | 49 (62%) | 0.369 | – | |
| Topography | | | | | |
| Thorax | 21 (70%) | 48 (61%) | 0.505 | NA | NA |
| Abdomen | 6 (20%) | 13 (16%) | 0.778 | – | |
| Back | 8 (27%) | 15 (19%) | 0.434 | – | |
| Head & neck | 14 (47%) | 16 (20%) | 0.008* | – | |
| Arms & legs | 13 (43%) | 10 (13%) | 0.001* | – | |
| Perineum | 9 (30%) | 15 (19%) | 0.3 | – | |
| Ears | 8 (27%) | 20 (25%) | 1 | – | |
| Trigger | | | | | |
| Surgery | 14 (47%) | 41 (52%) | 0.672 | NA | NA |
| Trauma | 10 (33%) | 17 (22%) | 0.221 | – | |
| Piercing | 1 (17%) | 15 (19%) | 1 | – | |
| Acne | 14 (47%) | 22 (28%) | 0.072 | – | |
| Folliculitis | 12 (40%) | 12 (15%) | 0.009* | – | |
| Spontaneous | 16 (53%) | 31 (39%) | 0.201 | – | |
| Shaving | 2 (7%) | 2 (3%) | 0.303 | – | |
| Family history of keloids | 20 (67%) | 26 (33%) | 0.002* | 0.041* | 2.9 (1.1, 8.0) |
| Mean age at first keloid | 18.4 years | 23 years | 0.065 | 0.716 | NS |

CI, confidence interval; M, male; F, female.
*indicates statistically significant values.

$P = 0.048$). The mean age and the mean age at first keloid were similar in both groups. With regard to origin, African ancestry was significantly more frequent in patients with SK than in patients without SK (90% vs. 67%; $P = 0.009$). The number of keloids in SK patients tended to be higher than in non-SK patients, but this difference was not statistically significant. The rate of pruritus in SK patients was significantly higher than that in non-SK patients (100% vs. 86%; $P = 0.033$). Patients were more prone to have keloids located on the head and neck or the arms and legs than patients without suppuration (respectively 47% vs. 20%; $P = 0.008$ and 43% vs. 13%; $P = 0.001$); however, SK-specific topography was not recorded. The triggers of keloid formation were similar in the two groups, except for the frequency of folliculitis in SK patients, which was significantly higher than in non-SK patients (40% vs. 15%; $P = 0.009$). Furthermore, a family history of keloids was significantly more frequent in SK patients than those without suppuration (67% vs. 33%; $P = 0.002$).

### *Multivariate analysis*

In multivariate analysis, male gender, African ancestry, and a family history of keloids were significantly associated with suppuration,

 

with respectively OR = 3.3 (1.2, 9; $P = 0.018$), OR = 4.8 (1.1, 20.1; $P = 0.035$) and OR = 2.9 (1.1,8; $P = 0.041$) (Table 1).

### Microbiological findings on keloids with suppuration

Nine of the 30 SK patients had bacteriological swabs of pus taken from their lesions. None of the patients had been treated with antibiotics. Direct microbiological examination and culture revealed commensal skin flora for seven patients (7/9; 77.8%), *Staphylococcus aureus* for one patient (1/9; 11.1%), and *Enterococcus faecalis* for one patient (1/9; 11.1%).

### Histological findings on keloids with suppuration

Among the 30 SK patients, 12 underwent keloid excision and subsequent histological examination (Fig. 2). All samples showed keloidal tissue that contained a chronic inflammatory infiltrate with lymphocytes and plasma cells. Suppurative areas were seen upon histological examination in 6 of 12 keloids (50%), corresponding to inflammation around hair follicles in all cases. These keloids were commonly located in the head/neck region (7/12; 58.3%). Epidermoid cysts were found in five patients (5/12; 42%). Foreign material was present within the tissue in one lesion, observed as finely granular or amorphous eosinophilic deposits surrounded by a variable infiltration of histiocytes.

## Discussion

In this study, we observed an SK rate of 26% for a mean keloid history of 17.2 years; suppuration thus seems to be a common complication of keloids consistent with a previous study that showed an SK rate of 25%.[7]

Our study's main limitations are the retrospective analysis, recruitment of in patients with severe keloid disease, which may overestimate the suppuration rate, the type of microbiological collection based on swab cultures, which are less accurate than tissue culture. Nevertheless, several hypotheses and conclusions can be formulated. To our knowledge, this is the first paper that is aiming to systematically study the occurrence and assess risk factors of SK in a cohort of keloid patients.

We examined the clinical characteristics of keloid patients and identified that male gender, African ancestry, presence of pruritus, a folliculitis trigger, localization on the head/neck (exclusive of AKN) or arms/legs, and a family history of keloids are potentially associated with suppuration. Besides, patients with suppuration seemed to have more severe keloid disease, with more pruritus and a higher number of keloids. The overrepresentation of the arms/legs localization may be associated with the severe form of keloid disease. To reduce the risk of bias, we also performed multivariate analysis, and we showed that male gender, African ancestry, and a family history of keloids are risk factors of suppuration.

In most cases, microbiological analyses of suppuration detected commensal skin flora, suggesting that suppuration is rarely an infection process. Additionally, pathological analyses demonstrated that the suppurative areas correspond to cyst formation and inflammation of the pilosebaceous ostia. From our findings, it appears that SKs may result from fibrotic occlusion of pilosebaceous ostia followed by cyst formation, inflammation, and liquefaction of the pilosebaceous content and their eventual discharge through solitary or multiple sinuses. This process of pilosebaceous ostia occlusion may explain the overrepresentation of the head/neck (especially in the beard area) localization already described in the literature, which may explain the overrepresentation of male sex in patients with SK.[5,6] Finally, the pilosebaceous unit's sebum, when it ruptures, can cause a foreign body reaction, thus the development of keloid scarring.[8] Here, we described the pathological findings of SK for the first time and hypothesized some pathogenesis outcomes that may be allowed to further investigations.

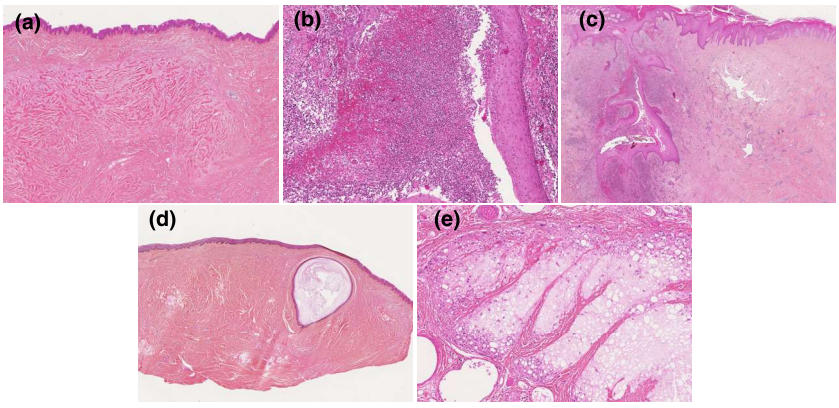


**Figure 2** Pathological presentation of suppurative keloids. (a) Cross-section of a keloid lesion, the thick hyaline bundles of collagen contrast with the more typical bundles below (Hematoxylin and eosin, ×2.5); (b) suppurative keloid (Hematoxylin and eosin, ×10); (c) superficial and deep folliculitis, rupture has occurred into the dermis (Hematoxylin and eosin, ×1.25); (d) cystic cavity filled with laminated keratin lined by a stratified squamous epithelium that includes a granular layer (Hematoxylin and eosin, ×1.25); (e) corticosteroid injection site; pale, foamy material surrounded by a palisade of macrophages. (Hematoxylin and eosin, ×20)

 

Two previous studies had already suspected similar pathogenesis, but they presumed that inflammation was likely because of bacteriological superinfection.[5,6] Our microbiological and pathological data suggest that true pyogenic infection is less frequent than an aseptic process similar to the one involved in hidradenitis suppurativa (HS). This inflammatory process resulting in suppuration may occur because of proinflammatory factors, such as interleukin (IL)-1$\alpha$, IL-1$\beta$, IL-6, and the tumor necrosis factor (TNF)-$\alpha$, which are upregulated in keloid tissues.[9] Interestingly, one study on 10 patients with suppuration associated with HS and keloids reported that three patients, who had received the TNF-$\alpha$ blocker adalimumab, showed a subsequent reduction in keloid size, pruritus, and suppuration.[10]

In our clinical practice, formerly, most of our patients were told to stop corticosteroid injections and take oral antibiotics during suppurative flares of their keloids since such flares were usually diagnosed as true infections (without bacteriological confirmation).

In our cohort, patient with SK and commensal skin flora on swab, were treated by corticosteroid injection only, with good result on suppuration.[11–13] Further studies to assess corticosteroid injection only versus corticosteroid injection and antibiotic regimen are required.

## Conclusion

SK is a common complication of keloids. Male gender, African ancestry, and a family history of keloids are potentially associated with SK. Pathogenesis may arise from the fibrotic occlusion of pilosebaceous ostia, followed by aseptic inflammation and finally discharge through sinuses.

## Acknowledgments

The patients in this manuscript have given written informed consent to the publication of their case details.

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