Mammillary Fistula as a Manifestation of Acne Inversa (Hidradenitis Suppurativa): Report of Two Cases

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Mammillary fistula (MF), or Zuska’s disease, is a recognized and well-documented clinical entity. Among the many articles on MF, none makes a comment on, much less a survey of, extramammary physical findings, although authors from Zuska onward have noted the similarity of MF to anal fistula in presentation and treatment.1,2

In the cases presented here, we noted hidradenitis suppurativa (HS) lesions on physical examination in two consecutive patients with bilateral MF at a veterans’ surgical clinic. These cases raise the question of whether such lesions might be found if looked for in other patients with MF, and whether MF might be associated with HS.

CASE REPORTS
Patient 1: A 46-year-old, nonlactating female veteran who smoked had periodic evaluation for inverted nipples and chronic, bilateral areolar margin drainage from fistulous openings (Figs. 1A, 1B). She also had a left groin lesion that had been intermittently inflamed and abscessed. It showed the cicatrization and violaceous discoloration characteristic of HS. The other characteristic HS sites (axillae, perineum, and so forth) were uninvolved. We recommended excision of all three lesions (bilateral areolar and left groin). She elected to have just the breast lesions removed.

We performed bilateral mammillary fistulectomies, using a probe to delineate the tracts, which in both cases went from the external opening at the areolar margin to the duct orifice at the nipple. The tracts were excised to just under the nipple (Fig. 2), which was preserved, and both wounds were left open. Pathology from both sides revealed normal overlying epidermis and extensive chronic inflammation surrounding ducts extending deep into the connective tissue and adipose tissue, where there was abscess formation. There was no neoplasia. The pathologist’s diagnosis was chronic inflammation and abscess formation, compatible with HS. The

Figure 1. (A) Right mammillary fistula (patient 1). (B) Left mammillary fistula (patient 1).
wounds healed uneventfully, the cosmetic result was acceptable, and the lesions have not recurred at 43 months. The groin lesion remains quiescent.

Patient 2: A 42-year-old, nonlactating female veteran who smoked had a left areolar margin external opening of a MF, with periodic drainage and abscess formation. She had a quiescent lesion, apparently of the same type, on the right breast, which had last abscessed several months earlier and was not inflamed on presentation. She also had a left axillary hidradenitis lesion with ongoing inflammation and chronic infection. Other characteristic HS sites were uninvolved. We recommended excision of all three lesions (bilateral areolar and left axilla). This was performed as described in patient 1, along with standard excision of the left axillary lesion, including all tracts and inflamed skin. She had a simultaneous epigastric herniorrhaphy.

Histologic examination of the left breast specimen revealed foci of epidermal hyperplasia with basal cell hyperpigmentation, focally becoming continuous with a fibroinflammatory lesion containing granulation tissue-type blood vessels and abundant, mainly chronic inflammatory cells. Mammary ducts were hyperplastic, and there was one focus of nuclear stratification and some atypia. The few mammary lobules present were not proliferative. Some of the mammary ducts/lobules were surrounded by chronic inflammatory cells. The pathologist's diagnosis was “consistent with HS.” The right breast specimen showed unremarkable epidermis, with dermis and subcutis replaced by scar, with focal keloid-type collagen.

In the left axillary specimen, the deep dermis/subcutis showed extensive acute and chronic inflammatory infiltrate under unremarkable epidermis. The sweat glands were of apocrine/eccrine morphology. The pathologist’s diagnosis was “consistent with HS.”

The patient’s wounds healed uneventfully, and the lesions have not recurred in 44 months. The patient was diagnosed with HIV infection 34 months after the previously mentioned excision, and she has had a groin abscess (presumably another HS lesion) incised and drained at another facility.

DISCUSSION

Although several previous texts have mentioned nontuberculous breast fistula,3 the first focused case series on breast duct fistula was written by Zuska and colleagues1 in 1951. The term “Zuska’s disease” is more appropriate than most medical eponyms, because both the author and the index patient of the original series (husband and wife, respectively) were named Zuska.1,4 The term “mammillary fistula” was coined by Atkins2 in 1955. He and others showed that, analogous to the cryptoglandular origin of anal fistula, MF followed the rupture of an abscess connected with a major lactiferous duct.5 Many series have been published over the last 50 years, the largest of which included 96 cases.6

Several breast conditions have been implicated in the etiology of MF, but none convincingly. Nipple inversion, with consequent duct orifice obstruction and inflammation, was put forward as a possible cause in a few early series in which most patients had nipple inversion.2,7 This has not been borne out in subsequent series, in which the rate of nipple inversion is roughly 50%.8 Lacking a standard definition or classification of nipple inversion, it is hard to compare studies. Nipple inversion can be produced by fibrosis after any inflammation, suggesting that inflammation might be a cause rather than a consequence of nipple inversion.9

Duct ectasia, also known as comedomastitis and associated with periductal mastitis, is a common concomitant diagnosis.10 Like fibrocystic change, duct ectasia has such a broad spectrum of presentation that it is virtually meaningless as a diagnostic category. It is a near-universal, involutional change of the aging breast, almost always asymptomatic, appearing in the majority of
postmortem specimens: Sandison\textsuperscript{11} found microscopic duct ectasia along with cysts in 72\% of 800 breasts, but macroscopic duct ectasia in only 11\%. Although some authors distinguish between symptomatic and incidental duct ectasia, there is no convincing evidence that the association between duct ectasia and MF is anything but coincidental.\textsuperscript{12,13}

Squamous metaplasia is almost always associated with MF and has been suggested to be pathogenic,\textsuperscript{14} but squamous metaplasia is common in irritative and inflammatory lesions of many organs, including the breast, and so might be a secondary change. Illustrating the widespread tendency to attribute pathogenesis to features that might be results rather than causes, Abramson\textsuperscript{19} catalogues theories of duct obstruction by squamous metaplasia, by ectopic sebaceous glands, or even by free hair shafts, as in a common but false theory about pilonidal sinus.

Keratin plugging with subcutaneous duct rupture, whether or not associated with squamous metaplasia, is an intuitively attractive etiologic mechanism supported by histologic findings in many cases.\textsuperscript{13,15} This is very similar to the mechanism posited in recent years for HS, now often (and appropriately) termed “acne inversa,” a disease initiated by follicular rupture.

The strong relationship between smoking and MF was first documented by Schäfer and colleagues\textsuperscript{17} and further supported by Bundred and colleagues.\textsuperscript{18} Women with nonlactational breast abscesses were more likely to be smokers than women with lactational abscesses, and there was a notable association between smoking and recurrence. Continuing the parallels between MF and HS, recent literature points out a strong association between smoking and the onset of HS. In a 1999 article, König and colleagues\textsuperscript{19} point out that HS can “remarkably ... be categorized as a smoking sequel that is neither of vascular nor neoplastic nature.” The same had been said a decade earlier about pilonidal sinus.

Bacterial cultures of MF effluent have yielded disparate organisms, as would be expected from a fistula that is secondarily colonized or infected.\textsuperscript{20} In one study, most initial cultures grew staphylococci, but recurrent lesions grew mixed organisms.\textsuperscript{4} This mirrors the more extensive literature on the bacteriology of HS, pilonidal sinus, and anal fistula, which like MF are anatomic lesions that are always colonized and can be infected, but in which the infection is a secondary rather than causative feature. Colonization occurs with skin organisms first and then with a variety of others when antibiotics, surgical intervention, or both alter the initial equilibrium.

Medical treatments other than antibiotics for fistulizing inflammation of the breast are reported in two studies, neither of which has been repeated or carried forward. In 1952 Harán\textsuperscript{21} reported “follicular hormone” treatment of nontuberculous breast fistula, and in 1982 Peters and colleagues\textsuperscript{22} described treatment of nonpuerperal mastitis with bromocriptine. Aside from these reports, there is near-universal agreement that MF is a disease requiring surgical intervention.

Surgical strategies for MF have included drainage alone, fistulotomy, fistulectomy, excision of all major lactiferous ducts (“Hadfield’s procedure”\textsuperscript{23}), and simple mastectomy. Drainage alone is clearly inadequate.\textsuperscript{24} The success of fistulotomy and fistulectomy makes excision of all major ducts seem excessive, and mastectomy is clearly unnecessary.\textsuperscript{25} Fistulotomy necessitates dividing a portion of the nipple, but fistulectomy can be done by raising the nipple and excising the fistula from underneath it, thereby perhaps achieving a better cosmetic result. After the fistula is opened or excised, the wound should be left open, because closure carries a major risk of infection and recurrence.\textsuperscript{26} Closure with antibiotic coverage might have acceptable results.\textsuperscript{27}

With the supposition that nipple inversion begins or perpetuates the MF process, some surgeons have emphasized everting the nipple, although others note that a properly excised fistula does not recur, regardless of whether the nipple is left inverted.\textsuperscript{28} Sclerotherapy, with injection of a caustic astringent and antiseptic, has been reported as effective in one series.\textsuperscript{29} In both nipple eversion and caustic injection, one imagines that the procedure causes enough inflammation to disrupt the fistula, creating a de facto fistulectomy. HS lesions can also be overwhelmed by local iatrogenic inflammation, as in the case of liposuction treatment for HS.

HS is the predominant manifestation of the broader syndrome of acne inversa. The four elements of the “acne tetrad”—HS, pilonidal sinus, acne conglobata of the trunk, and dissecting scalp perifolliculitis—are covered under the rubric of acne inversa. Of the common manifestations of acne inversa/HS, one—pilonidal sinus—has been viewed as a distinct condition, but it may be just another in the list of areas that can be affected either in isolation or in conjunction with others. MF, rarer than pilonidal sinus and previously always treated as an isolated lesion of the breast, might be an-
other such example. As the molecular characteristics of the cells lining sinus tracts in acne inversa are worked out, it might be of interest to apply the same methods to MF.

Our cases illustrate the association in two patients between bilateral MF and extramammary foci of HS. The groin lesion in patient 1 had the characteristic clinical findings of HS, and the axillary lesion in patient 2 had these features and characteristic histopathology. It is interesting, though by no means conclusive, that the MF lesions should be histopathologically consistent with HS in our cases. Both MF and HS are clinical diagnoses with confirmatory (rather than pathognomonic) histologic findings of acute and chronic inflammation with sinus and abscess formation. Although these features are non-specific, it is striking that the two lesions are grossly and histologically nearly identical, except that HS is viewed as a disease that can appear variably in several locations, and MF is seen as involving the nipple-areolar complex. They share epidemiologic features, including the association with smoking, and their treatment is identical, namely excision or destruction of chronically inflamed tracts. One might reasonably suggest that the two lesions could be manifestations of the same dermatologic process.

HS involving the breast is frequently reported, but it is usually described in the inframammary folds. One previously reported case of “severe mammary HS” appears to have been similar to our cases, in that a nonlactating woman had bilateral periareolar draining sinuses, and chronic HS lesions in the “axillae, groin, and perineum.” Another report on “areolar hidradenitis” includes one patient who had bilateral areolar and inguinal HS lesions. Although these case reports do not use the term MF, like our cases they form a bridge between the two otherwise separate bodies of literature on acne inversa/HS and MF.

In the predominantly male population of our veterans’ health care system, we see HS frequently but MF very rarely, and it was striking to find HS lesions in two consecutive patients with MF. We will likely not be able to explore this relationship further, because patients with breast diseases remain scarce in our practice. Surgeons who see patients with MF more frequently might wish to examine their patients for HS/acute inversa lesions in the typical sites (axillae, inframammary folds, umbilicus, groins, inner thighs, labia or scrotum, perineum, anal margin, the postscatral “pilonidal” area, the retroauricular areas, and the occipital scalp). A critical look at all the skin surface of MF patients will determine whether what we have observed is a statistical fluke or a previously unrecognized, genuine association.

CONCLUSIONS

We present two patients with MF and concurrent acne inversa/HS lesions. These cases raise the question of whether MF might be a manifestation of acne inversa. Despite the ample literature on MF and the very extensive literature on HS, this is a previously unrecognized association, suggesting either that these cases are unusual or that they demonstrate something that has not been seen because it has not been looked for. In its lack of description of associated conditions, the literature contains the implicit assumption that MF is an isolated lesion of the breast. Our cases challenge that assumption, and it remains for surgeons who see MF frequently to confirm or deny the suggested association with acne inversa/HS.

REFERENCES