

## Dermatopathology

# Cytokeratin expression in pilonidal sinus

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### Summary

**Background** Pilonidal sinus (PS) is considered to belong in the category of follicular occlusion diseases (acne triad).

**Objectives** The aim of our study was to elucidate the pathogenesis of PS by evaluating its cytokeratin (CK) expression.

**Methods** CK expression in nine cases of PS was studied immunohistochemically using six antikeratin antibodies.

**Results** Infundibular-like epithelium contained CK1, 10 and 14 similar to normal infundibulum, but it did not contain CK17. In non-infundibular-like epithelium, CK14, 16 and 17 were detected similar to that in normal outer root sheath. CK expression in PS was similar to that in hidradenitis suppurativa, suggesting that sinus epithelium may be fragile, hyperproliferative and undifferentiated.

**Conclusions** PS can be classified in the same entity as follicular occlusion diseases based on CK expression.

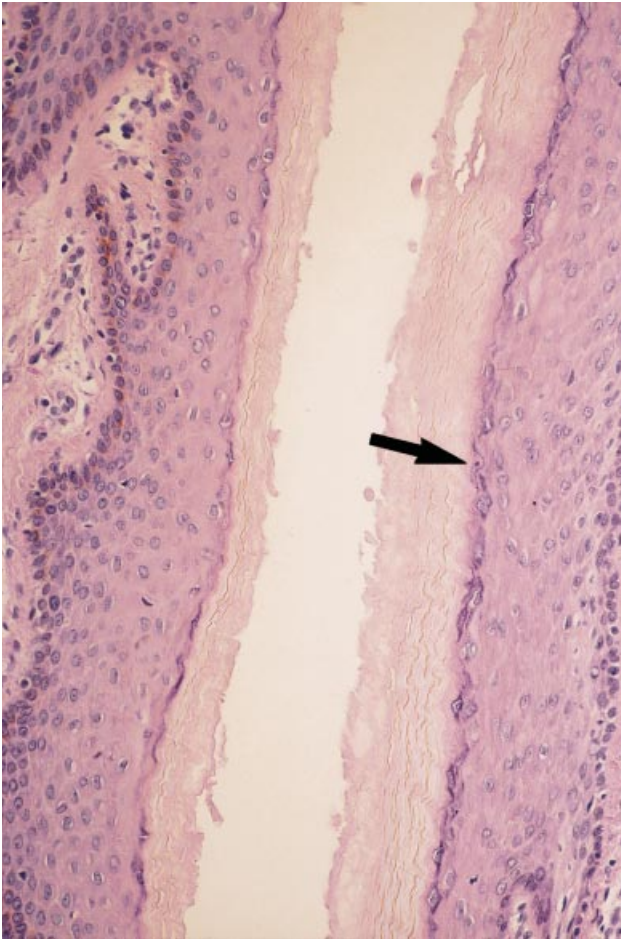
**Key words:** cytokeratin, pilonidal sinus

Pilonidal sinus (PS), also called pilonidal cyst with epithelial lining as draining sinus, occurs most frequently in the middle line of the gluteal fold. It sometimes becomes inflamed, resulting in a subcutaneous abscess with recurrent infection. Histopathological findings in PS show follicular hyperkeratosis of the infundibulum with plugging and dilatation of the follicle. The early inflammatory event is perifolliculitis with neutrophils, lymphocytes and histiocytes, leading to rupture of follicular epithelium. Once the follicular epithelium had been ruptured, foreign-body materials such as corneocytes, bacteria, sebum and hairs were spilled into dermis and subcutaneous tissue, giving rise to the forming of granulomatous lesions and fibrosis. In 1956, Pillsbury *et al.*<sup>1</sup> advocated the concept of the follicular occlusion triad (acne triad), which includes acne conglobata, hidradenitis suppurativa (HS) and dissecting cellulitis. Recently, Plewig and Steger<sup>2</sup>

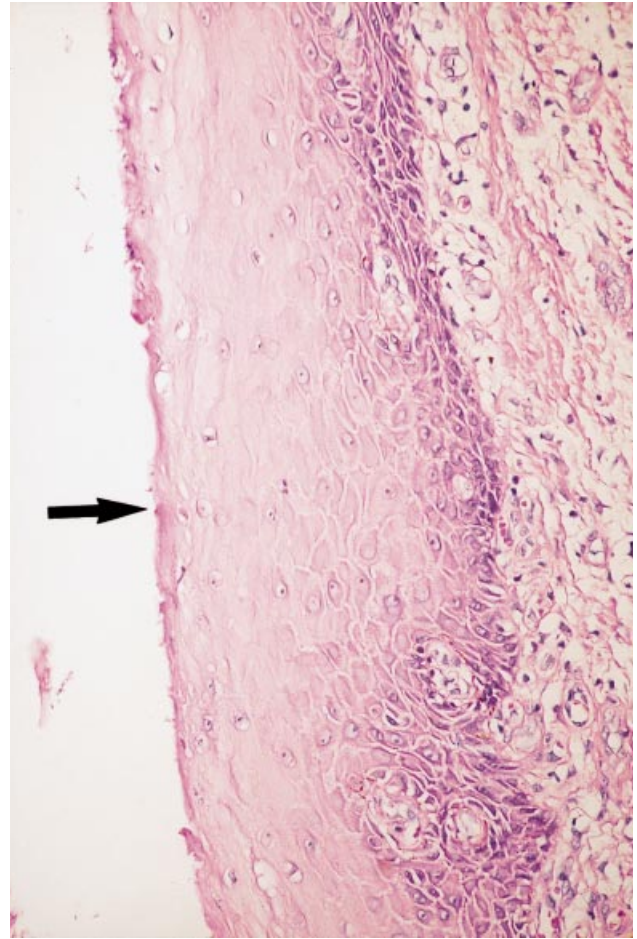
proposed a new concept of acne tetrad that includes PS with acne triad. In addition, Plewig *et al.*<sup>2,3</sup> advocated a new term: acne inversa. Although the aetiology in PS remains ambiguous, gender, onset at puberty, familial disposition, hypertrichosis and obesity have been regarded as contributory factors.<sup>4</sup> The pathogenesis of PS is concerned with an HS-related disorder demonstrating follicular retention hyperkeratosis in the infundibulum.

Among the intermediate filaments, cytokeratin (CK) is the most diversified cytoskeleton tonofilament in epithelial cells, divided into 20 subclasses according to molecular weight and isometric pH.<sup>5</sup> CK is a useful marker for the differentiation of epithelial cells and facilitates evaluation of the origin of epithelial tumours to elucidate the pathogenesis of PS. Recently, keratin expression of the sinus tract in HS has been investigated.<sup>6,7</sup> However, CK expression in PS has not been studied. The aim of our study was to clarify immunohistochemically CK expression in PS, and to compare that with the previous study in HS.<sup>7</sup>

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**Figure 1.** Type A epithelium, an infundibular-like epithelium, has granular layers with keratohyalin granules (arrow) in pilonidal sinus (haematoxylin and eosin, original magnification  $\times 100$ ).



**Figure 2.** Type B epithelium, non-infundibular-like epithelium, has no granular layers with keratohyalin granules (arrow) (haematoxylin and eosin, original magnification  $\times 100$ ).

## Materials and methods

Samples of PS were surgically excised from nine male patients. The age of the patients ranged from 22 to 46 years. All specimens were obtained from the buttock. These specimens were cut into 5–7  $\mu\text{m}$  thickness, then fixed in formalin, and embedded in paraffin. The sections were stained with haematoxylin and eosin for histopathological examination. For the immunohistochemical study, a deparaffinized sample of each respective section was incubated with six different antikeratin antibodies for 30 min. The antikeratin antibodies used in this study were 34 $\beta$ B4 (CK1),<sup>8</sup> LHP1 (CK10),<sup>9</sup> LL001 (CK14),<sup>10</sup> LL025 (CK16),<sup>11</sup> E3(CK17)<sup>12</sup> and b190 (CK19)<sup>13</sup> (all purchased from Novo Castra Laboratories Ltd, Newcastle upon Tyne, U.K.). Immunohistochemical procedures were performed according to the labelled streptavidin–biotin

method (LSAB, Dako, Carpinteria, CA, U.S.A.), as previously reported.<sup>7</sup>

## Results

Based on the histological findings, the epithelial lining in PS was composed of two distinct types of cornifying epithelium. The former, similar to infundibular-like keratinization, was classified as type A epithelium, which had a granular layer with keratohyaline granules (Fig. 1). The latter, non-infundibular-like keratinization without keratohyaline granules was classified as type B epithelium (Fig. 2). Of the nine cases, type A epithelium was found in seven, and type B in two.

CK expression in normal pilosebaceous units, PS and HS is summarized in Table 1. Immunohistochemical expression of CK in normal pilosebaceous units was

**Table 1.** CK expression in normal pilosebaceous unit, PS and HS

Type of CK	Normal pilosebaceous unit					PS		HS		
	Epidermis	IF	ORS	SD	SC	Type A	Type B	Type A	Type B	Type C
CK1	+	+	-	-	-	+	-	+	- ~ (+)	-
	(sb)	(sb)				(sb)		(sb)		
CK10	+	+	-	-	-	+	-	+	- ~ (+)	-
	(sb)	(sb)				(sb)		(sb)		
CK14	+	+	+	+	+	+	+	+	+	+ ~ ++
	(b)					(b)		(b)		
CK16	-	-	+	-	-	-	+	-	+	+
			(sb)				(sb)		(sb)	(sb)
CK17	-	+	+	+	-	-	+	-	+	+
		(sb)	(sb)	(sb)			(sb)		(sb)	(sb)
CK19	-	-	- ~ (+)	-	-	-	-	-	-	-
			(b)							

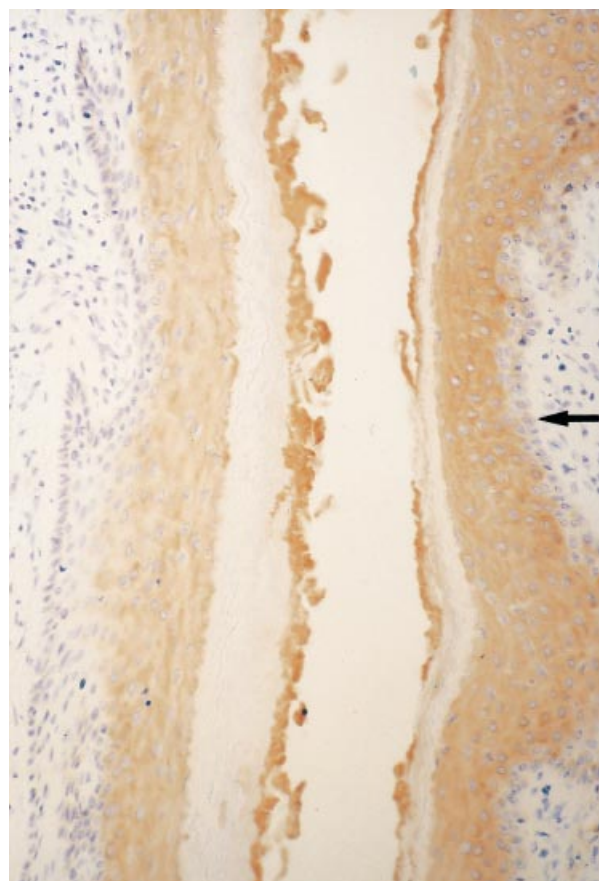
CK, cytokeratin; PS, pilonidal sinus; HS, hidradenitis suppurativa; IF, infundibulum; ORS, outer root sheath; SD, sebaceous duct; SC, sebaceous cells; sb, suprabasal; b, basal.

referred to in a previous report.<sup>7</sup> In brief, CK1 and 10 were present in suprabasal layers of the infundibulum

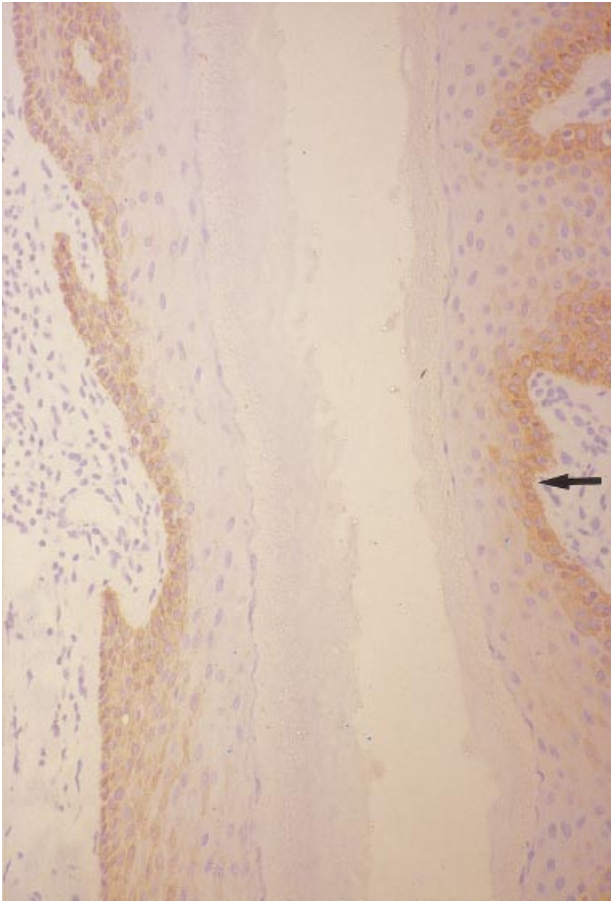


**Figure 3.** In normal pilosebaceous unit, CK17 was present in suprabasal layers of the infundibulum (arrow) (original magnification  $\times 100$ ).

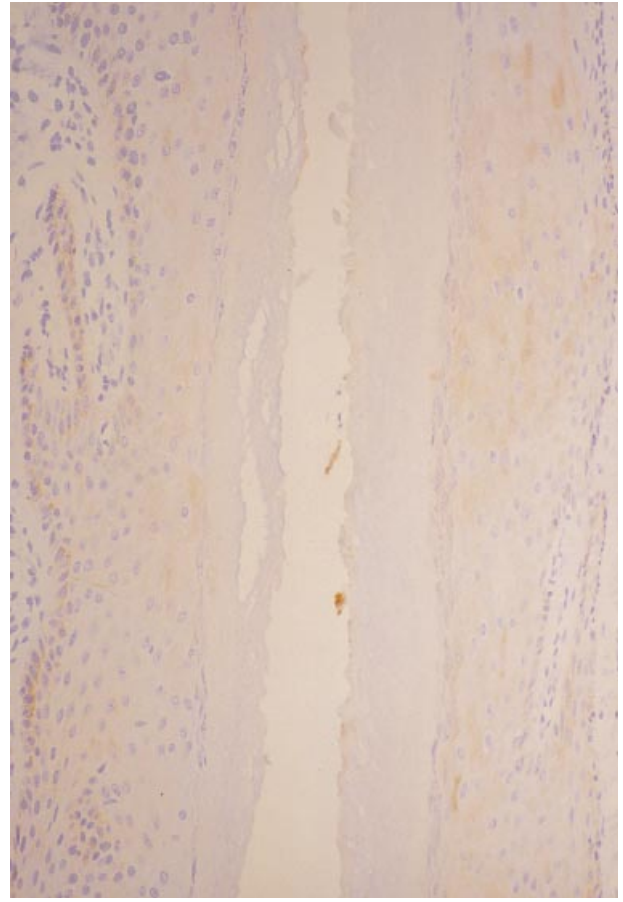
above the orifice of the sebaceous duct. CK14 was found in basal layers of the infundibulum, and in all layers of the outer root sheath, and sebaceous apparatus. CK16 was detected in suprabasal layers of the outer root



**Figure 4.** In pilonidal sinus, CK10 was present in the suprabasal layers of type A epithelium (arrow) (original magnification  $\times 100$ ).



**Figure 5.** In pilonidal sinus, CK 14 was present in basal layer of type A epithelium (arrow) (original magnification  $\times 100$ ).



**Figure 6.** In pilonidal sinus, CK17 was absent in type A epithelium (original magnification  $\times 100$ ).

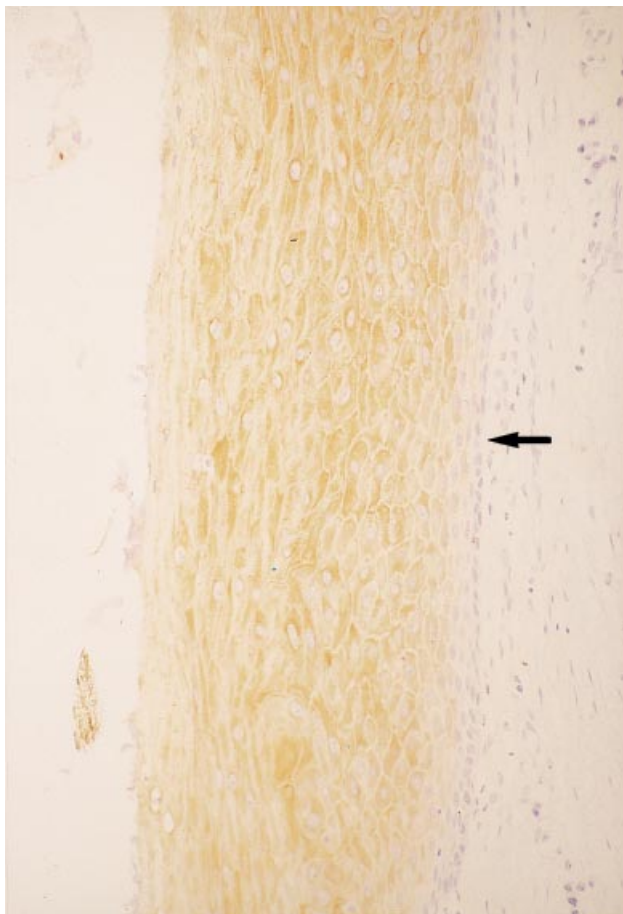
sheath below the opening of sebaceous duct. CK17 was present in suprabasal layers of the infundibulum (Fig. 3) and sebaceous duct, and in all layers of the outer root sheath. CK19 was found in the outermost layer of the outer root sheath in the hair bulge.

Concerning CK expression in PS, CK10 was found in suprabasal layers of type A epithelium (Fig. 4) as well as CK1. CK14 was observed in the basal layer of type A epithelium (Fig. 5). Compared with the presence of CK17 in normal infundibulum (Fig. 3), CK17 was absent in type A epithelium in PS (Fig. 6). CK16 and 19 were not present in type A epithelium. In type B epithelium, CK1 and 10 were not found. CK14 was seen at all layers of type B epithelium. A strong positive reaction for CK16 was found in the suprabasal layers of type B epithelium (Fig. 7) as well as CK17. CK19 was not found in type B epithelium. CK expression of overlying epidermis in PS was consistent with that in normal epidermis.

## Discussion

PS belongs in the follicular occlusion tetrad. The histopathology of PS has been reported.<sup>4</sup> Søndena and Polland<sup>4</sup> showed that the epithelial lining in PS has keratohyaline granules, and is derived from the epidermis. However, in our study, type B epithelium, which had no keratohyaline granules, was clearly observed.

As a whole, CK expression in PS was comparable with that in HS as previously reported.<sup>7</sup> Type A epithelium resembles infundibular epithelium because of the presence of CK1 and 10 in the suprabasal layers and CK14 in the basal layer, and the absence of CK16 and 19. However, CK17 was not found in type A epithelium. In the infundibulum, CK17 was found in the suprabasal layers of normal skin. CK17, spatial keratin, has a function related to the three-dimensional cytoskeleton structure.<sup>12</sup> The absence of CK17 in type



**Figure 7.** In pilonidal sinus, CK16 was found in the suprabasal layers of type B epithelium (arrow) (original magnification  $\times 100$ ).

A epithelium may reflect a fragile follicular structure, resulting in the rupture of the follicle, which subsequently forms a subcutaneous abscess. The cyst formation may be related to the mutation of CK17.<sup>14</sup>

The immunohistochemical expression of type B epithelium was comparable with that of the outer root sheath. Like the outer root sheath in normal skin, CK14 was found in all layers, and CK16 and 17 were present in the suprabasal layers of type B epithelium. CK1 and 10 were absent in type B epithelium as well as in the outer root sheath. The results of our study suggested that type B epithelium is more undifferentiated and hyperproliferative.

From the perspective of CK expression, CK expression in PS was comparable with that in HS, which supports the concept of Plewig *et al.*<sup>2,3</sup> who have advocated that PS belongs in the follicular occlusion tetrad (acne tetrad) category.

## References

- 1 Pillsbury DM, Shelley WB, Kligman AM. Bacterial infections of the skin. In: *Dermatology* (Pillsbury DM, Shelley WB, Kligman AM, eds), 1st edn. Philadelphia: WB Saunders, 1956: 482–9.
- 2 Plewig G, Steger M. Acne inversa (alias acne triad, acne tetrad or hidradenitis suppurativa). In: *Acne and Related Disorders* (Marks R, Plewig G, eds). London: Martin Dunitz, 1988: 345–57.
- 3 Plewig G, Kligman AM. Acne inversa. In: *Acne and Rosacea* (Plewig G, Kligman AM, eds), 3rd edn. Berlin: Springer-Verlag, 2000: 309–13.
- 4 Søndena K, Polland ML. Histology of chronic pilonidal sinus. *APMIS* 1995; **103**: 267–72.
- 5 Moll R, Schiller DL, Franke WW. Identification of protein IT of the intestinal cytoskeleton as a novel type I cytokeratin with unusual properties and expression patterns. *J Cell Biol* 1990; **111**: 567–80.
- 6 Kurzen H, Jung EG, Hartschuh W *et al.* Forms of epithelial differentiation of draining sinus in acne inversa (hidradenitis suppurativa). *Br J Dermatol* 1999; **41**: 231–9.
- 7 Kurokawa I, Nishijima S, Kusumoto K *et al.* An immunohistochemical study of cytokeratins in hidradenitis suppurativa (acne inversa). *J Int Med Res* (in press).
- 8 Gown AM, Vogel AM. Monoclonal antibodies to intermediate filament proteins of human cells: unique and cross-reactivity antibodies. *J Cell Biol* 1982; **95**: 414–24.
- 9 Leigh IM, Purkis PE, Whitehead P *et al.* Monospecific monoclonal antibodies to keratin 1 carboxyterminal (synthetic peptide) and to keratin 10 as markers of epithelial differentiation. *Br J Dermatol* 1993; **29**: 110–19.
- 10 Purkis PE, Steel JB, MacKenzie IC *et al.* Antibody markers of basal cells in complex epithelia. *J Cell Sci* 1990; **97**: 39–50.
- 11 Wetzels RHW, Kuijpers HJH, Lane EB *et al.* Basal cell-specific and hyperproliferation-related keratins in human breast cancer. *Am J Pathol* 1991; **138**: 751–63.
- 12 Troyanovsky SM, Guelstein VI, Tchipsheva TA *et al.* Patterns of expression of keratin 17 in human epithelia: dependency on cell position. *J Cell Sci* 1989; **93**: 419–26.
- 13 Lindberg K, Rheinwald JG. Suprabasal 40 kd keratin (K19) expression as an immunohistologic marker of premalignancy in oral epithelium. *Am J Pathol* 1989; **134**: 89–98.
- 14 Covello SP, Smith FJD, Smitt JHS *et al.* Keratin 17 mutations cause either steatocystoma multiplex or pachyonychia congenita type 2. *Br J Dermatol* 1998; **139**: 475–80.