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# Crystalline folliculitis revealed by non-aqueous staining technique

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## Abstract

Necrotizing infundibular crystalline folliculitis (NICF) is a rare superficial folliculitis characterized by expansive deposits of birefringent crystallized lipid. We report a case of NICF in a transplant patient presenting with folliculocentric acneiform papules across the lateral face and neck. Biopsy demonstrated intrafollicular crystalline deposits within an intact epidermis. Diagnostic crystals were identified using a non-aqueous histologic technique involving thick unstained sections. To our knowledge, this is the first report of NICF in a transplant patient. Our case suggests NICF is a follicular disorder and highlights a technique that may prevent loss of birefringent crystals and assist in facilitating accurate diagnosis.

*Keywords: necrotizing infundibular crystalline folliculitis, birefringent crystals, Pityrosporum, mucin, histologic techniques*

## Introduction

Necrotizing infundibular crystalline folliculitis (NICF) is a rare superficial acneiform deposition disease characterized by expansive deposits of crystallized lipid within a disrupted epidermis. Lucke et al. first described transepidermal elimination of urate-like crystals in 1991 [1]. They suggested it was a primary perforating disorder. Kossard and co-workers renamed it as NICF because they believed it was a form of crystalline follicular necrosis rather than a perforating disorder [2]. Sixteen cases have been previously described [1-7].

Necrotizing infundibular crystalline folliculitis has a

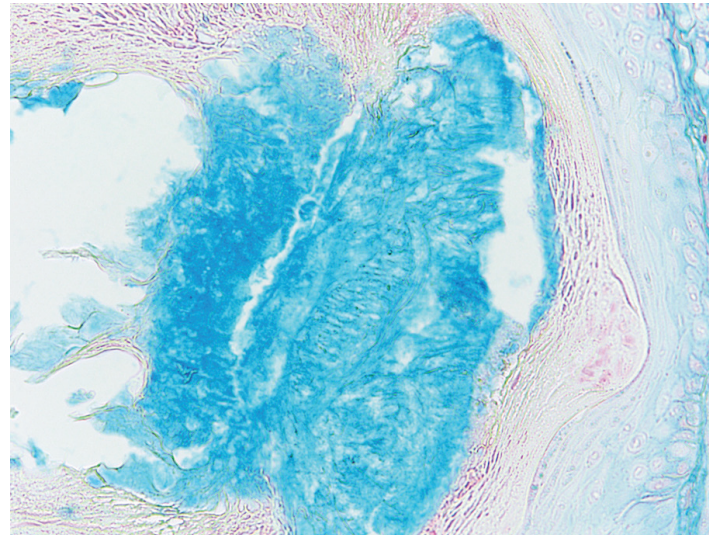
predilection for the back of elderly males and the face/neck of younger patients. Individual lesions consist of follicular waxy papules with erythematous borders. Histopathologic examination reveals disruption of the epidermis by urate-like crystalline deposits, often flanked by columns of parakeratin and embedded in a mucopolysaccharide matrix [4]. A link to the microbiome has been suggested because closed comedones contain identical appearing crystals, esterification of cholesterol by *Propionibacterium acnes* or *Malassezia* species may lead to urate-like crystals, and NICF has been successfully treated with antibiotics. Although follicular origin is strongly suspected because of predilection sites and clinical presentation, histopathologic images in previous studies have not demonstrated origin from an intact hair follicle. We describe a new case of NICF. This case is instructive because i) we used a nonaqueous histologic technique to demonstrate birefringent crystals in NICF; ii) we demonstrate crystal formation within the follicular canal by histology; iii) to our knowledge this is the first case of NICF reported in an immunocompromised patient.

## Case Synopsis

A 46-year-old woman presented with a 1-month history of flesh-colored 1-2 mm papules across the lateral face and neck (**Figure 1**). The patient reported intermittent acne throughout her life and was being treated with 50 mg oral doxycycline/day. Past medical history was significant for chronic immunosuppression with mycophenolate mofetil and tacrolimus following renal transplantation. The patient denied drug allergies, recent travel history, and exposure to new medications, chemicals, pets, or changes in living arrangements. Family medical

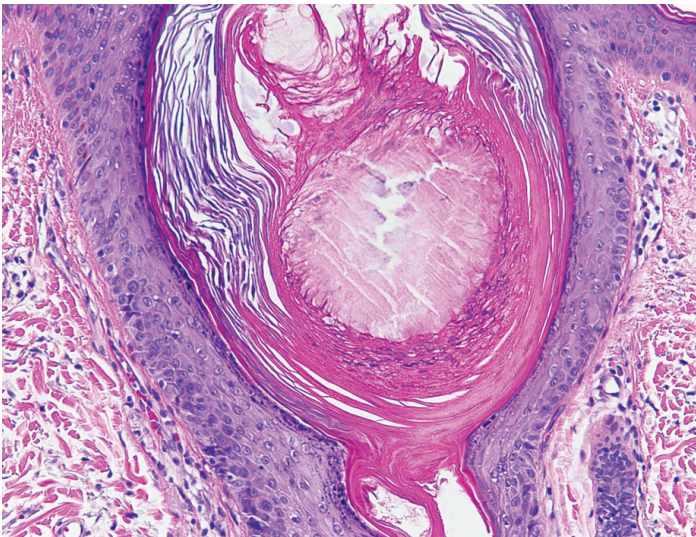


**Figure 1.** Flesh-colored 1-2 mm flesh-colored papules across the lateral neck.

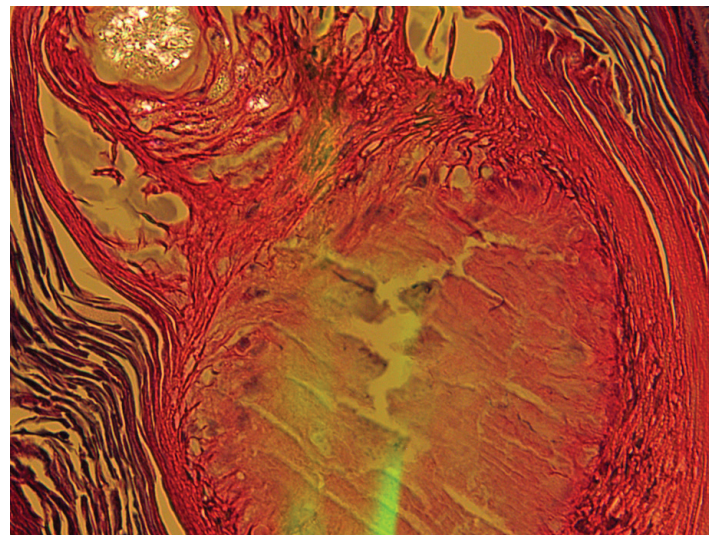


**Figure 3.** The deposit is mucopolysaccharide-rich. (colloidal iron, 40x).

history was unremarkable. The clinical differential diagnosis was viral trichodysplasia, syringomas, and Pityrosporum folliculitis. A punch biopsy from a papule on the neck was obtained for histopathologic examination.



**Figure 2.** Acellular amorphous spherical deposit within the upper follicular canal. (H&E, 40x).

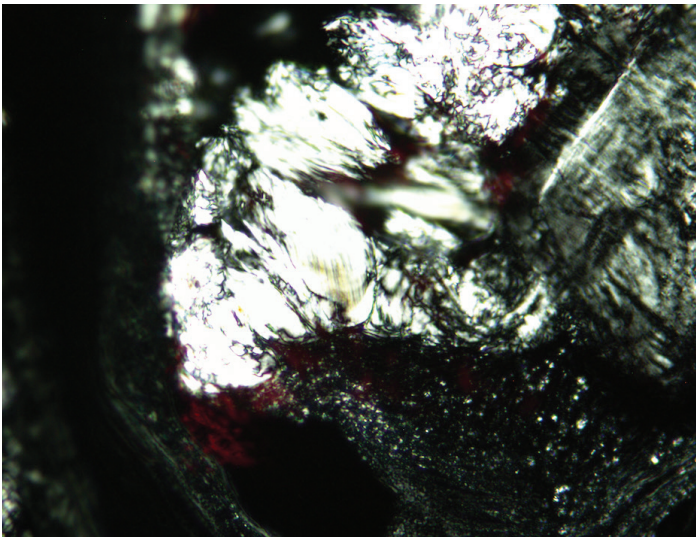


**Figure 4.** Trace birefringence with polarized light microscopy performed on a routine section. (H&E, 40x).

Biopsy demonstrated a well-circumscribed amorphous nodule within a dilated superficial follicular canal (**Figure 2**). The material was circumscribed by parakeratin and highlighted with colloidal iron (**Figure 3**). Polarized light microscopy of the hematoxylin-eosin section revealed focal trace birefringent crystals (**Figure 4**). Water-soluble crystals such as urate acid crystals are dissolved

during aqueous staining procedures such as hematoxylin-eosin. Thick, unstained sections can be used to identify gout in almost half of skin biopsies in which crystals were unapparent on routine hematoxylin-eosin sections [8]. We hypothesized this technique might be useful in NICF. We obtained an unstained section at 10 micrometers, precluding water exposure from the histology floatation bath and the aqueous stations in our automated hematoxylin-eosin stainer. The unstained section contained copious birefringent crystals (**Figure 5**). PAS stain demonstrated Pityrosporum yeast at the edge of the crystalline follicular plug. Gram stain was negative for significant bacteria. These findings were consistent with a diagnosis of early or evolving NICF. The patient was treated with a 7-day course of 200





**Figure 5.** Copious birefringent crystals are revealed with a 10-micrometer water-free histologic preparation. (unstained section, 40x.)

mg oral itraconazole with improvement, although an increase in tacrolimus levels accompanied the improvement. The patient was then advised to discontinue the itraconazole and to start applying selenium sulfide shampoo to the affected areas 3 times weekly.

## Case Discussion

Histopathologic images from previous reports of NICF have depicted interruption of the epidermis by a deposit of urate-like crystals. Hypotheses on their follicular origin rest upon their clinically folliculocentric distribution, predilection for sebaceous sites in some cases and presence of similar material in closed comedones. However, previous histopathologic images have not shown clear origin within an intact hair follicle. The absence of follicular epithelium has been attributed to necrosis, but none of the previous reports contain photomicrographs demonstrating necrotic follicular epithelium. This has led to speculation that some cases may represent a primary acquired perforating dermatosis. The findings in our patient suggest NICF is a follicular disorder rather than a perforating disease. It is noteworthy that our patient had a prior history of acne vulgaris. NICF might represent a secondary complication of other follicular diseases. The clinical presentation was not typical of acne, but her history of acne vulgaris may have predisposed her to NICF. Alternatively, crystal formation in our case may have been a secondary complication of *Pityrosporum* folliculitis. The

clinical presentation was similar to *Pityrosporum* folliculitis and *Pityrosporum* yeast were identified on histology. Additionally, the response to itraconazole and selenium sulfide suggests *Pityrosporum* was involved.

This is the first case of NICF in a transplant patient. Previous investigators have speculated that the crystalline aggregates are induced by bacteria or fungi. Some cases have been successfully treated with antibiotic therapy. If NICF is mediated by the follicular microbiome, it would seem immunosuppressed patients might be at higher risk. Further studies are needed to assess the incidence and manifestations of NICF among immunosuppressed patients.

## Conclusion

In sum, we describe a case of early evolving NICF in an immunosuppressed patient. The crystalline deposits lay within a dilated superficial follicular canal, indicating NICF is a follicular disease. The findings could be described as secondary NICF because the epidermis was not disrupted and the patient had a prior history of a folliculo-sebaceous disorder (acne vulgaris) and the afflicted follicle contained *Pityrosporum* yeast. NICF may represent a secondary complication of pre-existent follicular pathology rather than a disease sui generis. Birefringent crystals were revealed by examining an unstained thick section with polarized light microscopy. We posit that NICF is more common than widely recognized and use of a non-aqueous histologic technique may improve recognition of NICF.

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