

CORRESPONDENCE AND REPLY

Role of fern test in rhinosinuitis

To the Editor

We read with great interest the study by Nnabue and Pletcher concerning the aberrant morphology of the septal submucosal glands and the reduced production of mucin in chronic rhinosinuitis (CRS).¹ In fact, there is growing interest regarding the alterations of nasal secretions in patients with rhinitis as defective mucociliary clearance (MCC) seems to play a crucial role in the pathogenesis of CRS. As highlighted by the authors, the protective mucous layer, the airway surface liquid layer, and the cilia of the respiratory epithelium are the three functional components of the MCC apparatus, which represents the primary innate defense mechanism of the upper respiratory system. When one or more of these components is altered, the MCC is compromised. In this context, the authors performed biopsies from the posterior septum of 12 patients with CRS and 14 non-CRS controls, demonstrating that the submucosal nasal glands (SMGs) of the posterior septum had altered morphology and reduced density in patients with CRS who were undergoing remodeling or atrophy. Also notable is the reduction of Mucin 5B in patients with CRS, as shown by immunofluorescence analysis. These alterations could contribute to the impairment of MCC in CRS, and therefore represent a potential target for future diagnostic approaches.

In a previous study we highlighted the importance of introducing into clinical practice assessment of mucus alterations in patients with rhinopathies, as these alterations could represent a biomarker of damage to epithelial cells.² In particular, we performed the fern test on 182 patients with rhinitis and 30 healthy subjects as controls. Among the patients with rhinitis, 59 suffered from allergic rhinitis, 32 from infectious rhinitis, 31 from CRS with nasal polyps, 30 from nonallergic rhinitis with eosinophilia syndrome, and 30 from nonallergic rhinitis with neutrophils. Therefore, we evaluated the nasal samples according to Rolando's score, attributing a score for the fern pattern of each sample.³ All healthy patients had a type I (uniform fern pattern with closely branching arborization) or type II (well-distinguished but less branching arborization) fern pattern. On the other hand, as we had hypothesized, patients with rhinitis frequently presented with "pathologic" type III (scarce or single ferns) or type IV (absence of ferns) fern patterns (Figure 1).

The finding of altered fern patterns in subjects with rhinitis supports the hypothesis that the altered rheology of the mucus could compromise its functions, including lubrication, barrier, and defense against infectious agents and noxious substances. In fact, mucus is composed of mucins, DNA fragments, lipids, ions, proteins, cells, cellular debris, and water. The inflammation underlying rhinitis alters the balance between these components and therefore the fernlike reaction. Furthermore, the altered mucus itself represents a factor that induces a vicious circle that exacerbates the inflammatory disease. Considering that mucins, especially Mucin 5B, represent the most important component of mucus, we believe that there is a close relationship between the reduction of SMGs with Mucin 5B and the altered ferning reaction. Mucins, through a macromolecular reorganization that occurs rapidly after secretion, create a functional mucous barrier transforming from a condensed form to an expanded and linear conformation. A process of counter-ion replacement drives this mucin expansion. Thus, the change in osmotic pressure of the mucus system is believed to trigger the phase transition from condensed to expanded states. Evidently, alterations of the extracellular calcium concentration or of the pH can dramatically hinder mucin expansion and mucus swelling.^{4,5} This highlights the importance of maintaining a regulated ionic balance and tight control of pH during different stages of mucin biosynthesis and secretion within the mucus barrier and explains how the inflammation can alter the expansion of the mucins and the ferning reaction, which could be an expression of the mucins remodeling process. In this sense, the normal pattern of ferns and the correct expression of Mucin 5B can both be considered nothing more than the expression of the same balance between mucins and electrolytes.

Further studies would help to better understand the mechanisms that determine the dysmorphic phenotypes of the SMGs and therefore the decreased expression of Mucin 5B in patients with rhinopathies.

Finally, the role of mucins in altering the fern reaction and compromising MCC should be better clarified. However, we further emphasize the importance of introducing an evaluation of the characteristics of nasal secretions in the diagnostic process of patients with nasal pathologies. In this context, the fern test, unlike the other sophisticated

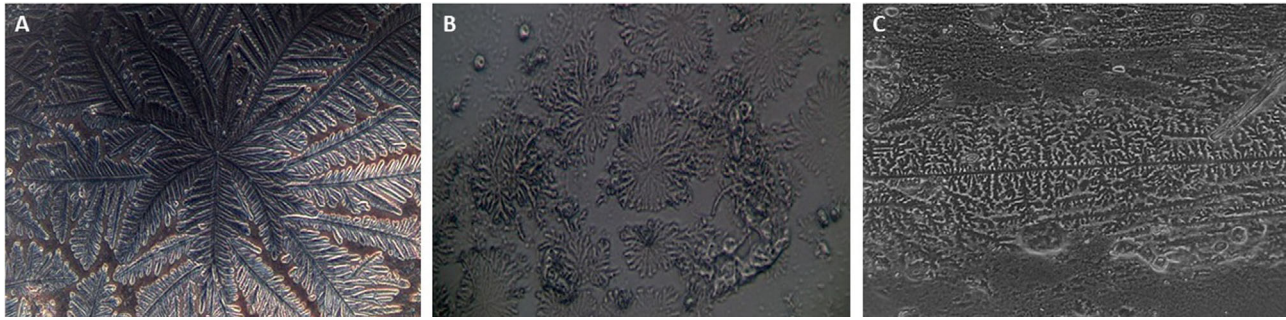


FIGURE 1 Phase-contrast microscopy at 1000× magnification. Examples of different grades of nasal ferning, classified according to the Rolando scoring. (A) Type I (normal) fern pattern in a nasal specimen of a healthy patient. (B) Type III fern pattern with scattered ferns and rare branching in a nasal specimen of a patient with CRSsNP. (C) Type IV fern pattern in a nasal specimen of a patient with CRSwNP showing a strongly impaired fern reaction. CRSwNP = chronic rhinosinusitis with nasal polyps.

tools available today, represents a simple, inexpensive, and noninvasive method to investigate mucus alterations.

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