

Nasal candidiasis in a patient on long-term topical intranasal corticosteroid therapy

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Evidence regarding the efficacy and safety profile of long-term topical intranasal corticosteroids for the treatment of chronic rhinitis has been accumulating over the nearly 20 years that they have been available.¹⁻³ Because inhaled oral corticosteroids have been associated with the development of oropharyngeal candidiasis in some patients, it has been assumed that prolonged use of topical intranasal corticosteroids might cause nasal mucosal candidiasis in some patients as well. Possibly because of this theoretic concern, *Physicians' Desk Reference* product information for all topical intranasal corticosteroids caution that their use, based on clinical studies, may rarely result in localized infections of the nose and pharynx with *Candida albicans*.⁴ In reality, no macroscopic or clinically apparent evidence of nasal candidiasis as a result of long-term use of topical intranasal corticosteroids has ever been reported in the literature. The following is a case report describing what initially appeared to be one such patient.

CASE REPORT

A 62-year-old white woman monitored in our allergy clinic for 2 years for perennial nonallergic rhinitis and recurrent acute sinusitis had routine follow-up. She reported a 2-week history of increasing nasal irritation and congestion, hoarseness, and mild fatigue, but previously she had been in her usual state of good health. She denied having any other respiratory or constitutional symptoms. Her medications included topical intranasal beclomethasone dipropionate (BDP) (Vancenase AQ-Schering Corp., Kenilworth, N.J.): two sprays each nostril twice a day $\times$ 1.5 years (which had proved very efficacious in controlling her rhinitis), guaifenesin 600 mg by mouth twice a day as needed, as well as salsalate 750 mg by mouth three times a day for osteoarthritis and premarin/provera. She had recently completed a 10-day course of an unknown antibiotic for clinical

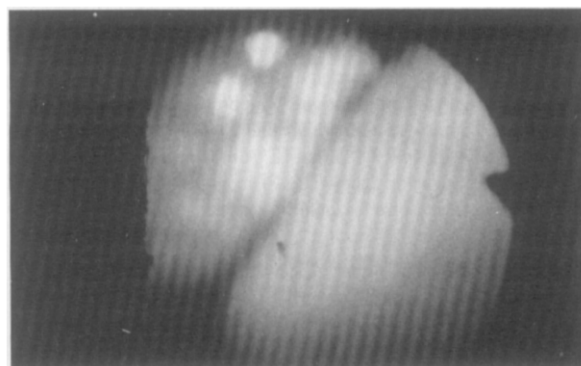


FIG. 1. Rhinoscopic view of the right middle turbinate demonstrates multiple patchy white exudates with surrounding erythema.

sinusitis prescribed by a primary care physician in her hometown.

Physical examination revealed mild tenderness to maxillary sinus percussion bilaterally. On nasal speculum examination white patchy exudates with surrounding erythema were seen on slightly edematous middle turbinates bilaterally. The oropharynx was normal without evidence of thrush. No lymphadenopathy was noted. Nail beds and scalp were normal. The remainder of the physical examination was unremarkable as shown in Fig. 1. Fiberoptic rhinolaryngoscopy revealed diffuse patchy white exudates with surrounding erythema intranasally, located predominantly on the middle turbinates bilaterally. No ulcerative or mass lesions were noted. Potassium hydroxide preparation of one of the exudative lesions revealed pseudomycelia and clusters of grapelike yeast cells consistent with *Candida albicans*.

The patient was instructed to discontinue the intranasal BDP and begin regular saline nasal irrigations. Coronal CT scan of the sinuses revealed a right concha bullosa and a left maxillary sinus mucous retention cyst, but otherwise no evidence of acute or chronic sinusitis. Persistent nasal candidiasis was noted at 1-month follow-up, and the patient was begun on ketoconazole 400 mg by mouth twice a day. At that time, a workup for underlying immunodeficiency was initiated.

Laboratory values obtained

IgG was 791 mg/dl (nl 667-1702) with normal IgG subclasses. IgM was 36 mg/dl (nl 56-264), IgA was 54 mg/dl (nl 74-362), and IgE was 2.7 IU/ml (nl 10-150). Isohemagglutinins (ABO group B): anti A of 1:1, C3 and C4 were normal. Anergy panel: Two of five antigens were

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positive (tetanus toxoid and mumps)-Negative candida at 1:500 and 1:100. Normal serum protein electrophoresis, liver and thyroid function tests, lactic dehydrogenase, electrolytes, calcium, creatinine, and erythrocyte sedimentation rate. Negative ANA, RF, and HIV-1 ELISA. Hematocrit 41.5%, white blood cell count 17,100 with 42% neutrophils, 35% lymphocytes, 7% atypical lymphocytes, 8% monocytes, 8% eosinophils, and a normal platelet count (WBC count was 11,000, with a normal differential 15 months earlier). Repeat WBC count 1 month later was 18,500, with 57% lymphocytes (small and mature appearing on the peripheral smear with associated smudge cells).

A diagnosis of chronic lymphocytic leukemia (CLL)-stage A was confirmed by hematology/oncology evaluation. The patient remained clinically stable, and after 8 weeks on oral ketoconazole therapy, her nasal candidiasis and sinus symptoms had improved, but not fully resolved. She had, however, developed a symptomatic candidal infection in her right external auditory canal, which was responding to topical antifungal therapy.

DISCUSSION

This patient's nasal candidiasis, initially thought to be a rare complication of long-term topical intranasal BDP, did not resolve after discontinuing the drug and instituting oral antifungal therapy. The patient's nasal candidiasis appears to have been the initial clinical manifestation of a CLL-induced partial cellular immunodeficiency with selective anergy to candida (as well as depressed levels of IgM and IgA). It is debatable whether prolonged use of topical intranasal corticosteroids (and possibly the recent course of oral

antibiotics) may have altered this patient's nasal mucosal immunity sufficiently to render it more susceptible to candidiasis than the oropharynx, which is far more commonly involved in those with cellular immunodeficiency.⁵ The persistence of nasal candidiasis months after discontinuing topical intranasal BDP and the subsequent development of candidal otitis externa while on oral ketoconazole therapy argues more that the use of topical intranasal BDP was coincidental rather than a cofactor in the development of nasal candidiasis in this patient.

Debate (and product labeling) aside, clinically apparent nasal candidiasis developing in conjunction with long-term topical intranasal corticosteroid therapy appears to be *so very unusual* as to warrant an evaluation for underlying cellular immune dysfunction.

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Rhinorrhea related to antipsychotic drug therapy

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Patients with vasomotor rhinitis are thought to have nasal congestion and rhinorrhea caused, at least in part, by abnormal neural reflexes involving parasympathetic innervation of the nose. We present a case of severe, debilitating rhinorrhea that began coinci-

dently with the cessation of long-term therapy with fluphenazine HCL (Prolixin) and benztropine mesylate (Cogentin) and appears to be a drug withdrawal phenomenon.

CASE REPORT

Ms. L.G. was a 74-year-old mentally retarded woman who had lived in a private home with a care provider for 22 years. Over the previous 4 years her provider had noticed a constant runny nose with nasal sniffing. Her rhinorrhea consisted of copious amounts of clear secretions. Nasal itching, sneezing, or eye problems were not present. She had no history of nasal surgery, nasal polyps, or epistaxis. No seasonal pattern existed to her rhinorrhea, and specific ex-

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