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 ketaconazole 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 possible 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.

REFERENCES

1. Knight A, Kolin A. Long-term efficacy and safety of beclomethasone dipropionate aerosol in perennial rhinitis. Ann Allergy 1983;50:81-8.
2. Tarlo S, Cockcroft D, Dolovich J, Hargreave F. Beclomethasone dipropionate aerosol in perennial rhinitis. J ALLERGY CLIN IMMUNOL 1977;59:232-6.
3. Holopainen E, Malmberg H, Binder E. Long-term follow-up of intranasal beclomethasone treatment: a clinical and histologic study. Acta Otolaryngol 1982;386(suppl):270-3.
4. Physicians Desk Reference (Medical Economics Data, Publisher), 1992;574-5, 1844-5, 2126-8, 2299-2300.
5. Kirkpatrick C. Host factors in defense against fungal infections. Am J Med 1984;77:1-12.

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 coincidently 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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posures such as animals, dust, mildew, or irritants did not appear to exacerbate her problem. She had never smoked, used recreational drugs, or been treated with over-the-counter nasal sprays. The nasal discharge was so copious that the patient had difficulty eating. The patient's care provider noted that 8 years ago she was placed on 2.5 mg fluphenazine hydrochloride twice a day and 2 mg benztropine mesylate three times a day for behavior control, and that 4 years ago the dosing of these medications was incrementally decreased and discontinued over a period of 3 months. The provider recalled that a few days after these medications were stopped, rhinorrhea developed in the patient. She also had tardive dyskinesia while on the antipsychotic drug regimen, which never resolved. Prior therapy for the rhinorrhea included treatment with standard and nonsedating antihistamines and topical corticosteroids, with no apparent effect. Examination of the patient's nares revealed excessive clear secretions with a somewhat pale mucosa, but otherwise the examination was normal. The patient was sniffing approximately once every 10 seconds. Skin testing for immediate hypersensitivity to a panel of 31 seasonal and perennial aeroallergens revealed no significant wheal and flare reactions. Sinus radiographs were within normal limits. The patient was placed on a regimen of nasal ipratropium bromide three puffs three times per day to be taken with a perforated baby bottle nipple fitted on an oral inhaler. One month later the patient and her care provider returned to the clinic and both reported total cessation of the patient's rhinorrhea. On physical examination, both the sniffing and the copious secretions were found to have disappeared. The patient has been maintained for the past 3 months on this therapy with no recurrence of rhinorrhea and no apparent side effects.

DISCUSSION

The onset of marked rhinorrhea in this patient was coincident with the cessation of fluphenazine hydrochloride and benztropine mesylate therapy. Rhinorrhea without precipitating irritant exposure is consistent with a variant of vasomotor rhinitis, which in this case may be drug induced. The enhanced nasal secretory response in vasomotor rhinitis may be due to hypersensitivity of muscarinic receptors in the nasal mucosa or may be due to an abnormally increased efferent cholinergic mechanism.[1] Although a hypersecretory response to topical cholinergic agents has been seen with vasomotor rhinitis,[2] recent work shows no difference between patients with vasomotor rhinitis and healthy patients in the saturability or affinity of ligand binding to nasal muscarinic receptors.[3]

Phenothiazines have complex influences on neurotransmitter-receptor activity in the central nervous system. Phenothiazines cause a relative increase in cholinergic versus dopaminergic neurotransmitter activity.[4] Phenothiazines are known to affect hypothalamic and brainstem mediation of vasomotor reflexes and accelerate the turnover of acetylcholine in subcortical brain.[4] The tardive dyskinesia present in our patient 4 years after the cessation of antipsychotic therapy demonstrates a permanent drug-induced alteration in extrapyramidal neural pathways. Might these drugs also cause a persistent upregulation of parasympathetic efferent activity leading to nasal hypersecretion?

Combined fluphenazine hydrochloride and benztropine mesylate therapy has peripheral antimuscarinic activity. This prolonged muscarinic antagonist action might induce a hypersensitivity of muscarinic receptors in the nasal mucosa or simply mask an increased efferent cholinergic activity. In either case, rhinorrhea would manifest on drug withdrawal.

The efficacy of topical ipratropium bromide for treating the hypersecretion of vasomotor rhinitis is reported.[2, 5] Ipratropium bromide blocks muscarinic receptors in nasal mucosa and would be effective in the setting of increased muscarinic receptor sensitivity or increased parasympathetic efferent activity. Whatever the precise alteration in neural control of nasal secretions, this case appears to demonstrate a previously unrecognized side effect of antipsychotic drug therapy with significant morbidity and an excellent response to treatment.

REFERENCES

1. Arne P, Lundblad L, Lundberg JM. Capsaicin and nicotine-sensitive afferent neurons and nasal secretions in healthy human volunteers and in patients with vasomotor rhinitis. Br J Pharmacol 1989;96:693-701.
2. Sjogren I, Jonsson L, Koling A, et al. The effect of ipratropium bromide on nasal hypersecretion induced by methacholine in patients with vasomotor rhinitis. Acta Otolaryngol (Stokh) 1988;106:453-9.
3. Van Megan VJ, Klaasen AB, Rodriguez de Miranda JF, et al. Alterations of muscarinic acetylcholine receptors in the nasal mucosa of allergic patients in comparison with nonallergic individuals. J ALLERGY CLIN IMMUNOL 1991;87:521-9.
4. Baldessarini RJ. Drugs and the treatment of psychiatric disorders. In: Goodman GA, ed. The pharmacologic basis of therapeutics. New York: Pergamon Press, 1990:386-400.
5. Jessen M, Bylander A. Treatment of non-allergic nasal hypersecretion with ipratropium and beclamethasone. Rhinology 1990;28:77-81.