Runny nose sign

Sequential rhinorrhea and syncope in dementia with Lewy bodies

Leonard L. Sokol, BSc; Alberto J. Espay, MD, MSc

Practical Implications

Consider administering a vasopressor prior to activities that generate syncope and substantial disability in Lewy body-related diseases.

Dementia with Lewy bodies (DLB) is characterized by a triad of core features: fluctuating cognition, visual hallucinations, and parkinsonism; other commonly associated features include REM sleep behavior disorder (RBD) and dysautonomia (e.g., orthostatic hypotension, urinary incontinence, constipation, and impotence).¹ Case-control studies have reported a higher prevalence of rhinorrhea in patients with Parkinson disease (PD) compared to healthy controls.^{2–6} Of interest, 76% of patients with PD reported rhinorrhea exacerbation while eating.² Further studies have corroborated a 5-fold increased prevalence of rhinorrhea in patients with PD compared to controls and also an association with lightheadedness among rhinorrhea-affected patients with PD.⁴

We report a patient with clinically probable DLB who presented with activity-dependent rhinorrhea consistently followed by hypotensive syncope, suggesting that the rhinorrhea–hypotension association may be temporally closer than previously suspected, and highlighting the value of nonpharmacologic therapeutic strategies in this clinical situation.

Case report

An 85-year-old Ashkenazi Jewish man, type 1 N370S Gaucher disease (GBA) carrier, with history of peripheral neuropathy, hyperlipidemia, and coronary artery bypass grafting, complicated by hypotension at age 74, and dream enactment behaviors suggestive of RBD, presented with a 5-year history of tremorless parkinsonism with visual hallucinations and fluctuating cognition at symptom onset, followed by orthostatic hypotension, meeting McKeith criteria for clinically probable DLB.¹ The patient denied a history of anosmia, diabetes, allergies, nasal, or sinus complaints. Eating, urinating, and defecating consistently induced rhinorrhea, followed by hypotensive syncope within minutes. Blood pressure (BP) during these events was documented to be as low as 60/40 mm Hg. However, his BP markedly fluctuated throughout the day, with readings as high as 180/100 in the sitting position.

Trials of nasal spray were futile. Carbidopa/levodopa exacerbated the hypotensive syncope and hallucinations and thus was discontinued. He refused separate trials of rivastigmine and quetiapine. To exclude CSF as the source of rhinorrhea, given that some triggering activities were associated with Valsalva-type actions, the patient's nasal discharge was examined for β -2 transferrin, which was negative. None of the patient's medications was known to have previously induced rhinorrhea and syncope.

The family referred to the sequential events of rhinorrhea and hypotensive syncope as the runny nose sign (video at Neurology.org/cp), and considered it his most disabling feature. Efforts at optimizing the dosage of fludrocortisone and midodrine did not reduce the frequency of these episodes. The patient would secrete copious clear, thick nasal discharge, invariably announcing hypotensive syncope within minutes. Rhinorrhea would continue

Video

Neurology.org/cp

James J. and Joan A. Gardner Center for Parkinson Disease and Movement Disorders, Department of Neurology, University of Cincinnati, OH.

Funding information and disclosures are provided at the end of the article. Full disclosure form information provided by the authors is available with the **full text of this article at Neurology.org/cp**.

Correspondence to: alberto.espay@uc.edu

unabated until the inciting activity was terminated. The behavioral phenomenology of his hypotensive syncope was as follows: first, diminished capacity to interact with his environment; second, coughing; and third, closure of eyelids and relaxation of neck extensors. Tactile or verbal stimuli elicited no response. His caregivers would place him supine on the floor and elevate his legs or position him in Trendelenburg using a recliner in order to help him restore consciousness. A dose of midodrine administered 30–45 minutes prior to the inducing activities (anticipating the onset of rhinorrhea) ameliorated the runny nose sign. Often this resulted in either a reduction in the sign’s incidence or an attenuation of its manifestation, such that syncope would not follow rhinorrhea (video, segment 2).

DISCUSSION

This case illustrates that activity-dependent rhinorrhea can be a unique and likely underrecognized manifestation of dysautonomia in patients with clinically probable DLB, due to unopposed parasympathetic drive.^{2,3} Patients with DLB have an increased risk of syncope/loss of consciousness,¹ which may be magnified among those with rhinorrhea.⁴ Several studies have also substantiated a greater prevalence of rhinorrhea in patients with PD than in healthy controls (table),^{2–6} with a range between 24% and 57%. Of interest, however, an association between rhinorrhea (a nondopaminergic feature⁴) and anosmia (a dopaminergic one), a well-established premotor deficit in PD, was confirmed by only 1⁶ of the 5 case-controlled studies examining such relationship. Further, rhinorrhea-affected patients with PD displayed no correlation with motor and nonmotor clinical variables in studies^{4–6} that explored these parameters.

This atypical case highlights the potential association of rhinorrhea and autonomic dysfunction in patients with neurodegenerative parkinsonism. While the pathophysiologic basis of rhinorrhea in PD remains undetermined,⁶ Lewy pathology in autonomic structures (submandibular gland, cervical superior ganglion, cervical sympathetic trunk, and vagal nerve) may lay anatomical–physiologic substratum for a range of dysautonomic features (e.g., sialorrhea, sialopenia, and dysphagia).⁷ It is unclear whether the GBA mutation carrier state of our patient may have heightened vulnerability to this particular complication; however, we conjecture that rhinorrhea may serve as an early dysautonomic feature, eventuating in syncope. Further clinical and pathologic correlative studies are warranted to explore the pathophysiology of rhinorrhea in synucleinopathies. Although rhinorrhea in patients with PD was initially described as a minor nuisance,³ our report suggests otherwise

Table Case-control studies evaluating the relationship between rhinorrhea and PD

Reference	SR prevalence of patients with PD with rhinorrhea, %	Rhinorrhea-olfactory relationship in patients with PD (measurement)	Rhinorrhea-PD group clinical outcomes
2	48	NC (SR)	76% exhibit rhinorrhea exacerbation during eating; 86% recall that rhinorrhea followed onset of motor symptoms
3	47–57	NC (SR)	25%–38% exhibit rhinorrhea exacerbation during eating; 57% report rhinorrhea onset within 6 months of PD diagnosis
4	35	NC (UPSIT)	NC with imaging (DTBZ PET) or nonmotor variables; 52% exhibit lightheadedness
5	24	NC (UPSIT)	NC with motor (UPDRS II and III; PDQ-39 scores) or nonmotor variables
6	33.3	C (SR)	Greater prevalence of rhinorrhea in males (62.3%) than in females (38.7%); NC with motor or nonmotor variables

Abbreviations: C = correlation; NC = no correlation; PD = Parkinson disease; PDQ = Parkinson’s Disease Questionnaire; SR = self-reported; UPDRS = Unified Parkinson’s Disease Rating Scale; UPSIT = University of Pennsylvania Smell Identification Test.

and emphasizes the disability generated by the related and often undertreated orthostatic hypotension.

REFERENCES

1. McKeith IG, Dickson DW, Lowe J, et al. Diagnosis and management of dementia with Lewy bodies: third report of the DLB consortium. *Neurology* 2005;65:1863–1872.
2. Friedman JH, Amick MM, Chou KL. Rhinorrhea and olfaction in Parkinson disease. *Neurology* 2008;70:487–489.
3. Friedman JH, Amick MM. Rhinorrhea is increased in Parkinson's disease. *Mov Disord* 2008;23:452–454.
4. Chou KL, Koeppe RA, Bohnen NI. Rhinorrhea: a common nondopaminergic feature of Parkinson's disease. *Mov Disord* 2011;26:320–323.
5. Sedig L, Leibner J, Ramjit AL, et al. Is rhinorrhea an under-recognized intrinsic symptom of Parkinson disease? A prospective pilot study. *Int J Neurosci* 2010;120:258–260.
6. Kano O, Yoshioka M, Nagayama H, et al. Rhinorrhea in Parkinson's disease: a consecutive multicenter study in Japan. *J Neurol Sci* 2014;343:88–90.
7. Del Tredici K, Hawkes CH, Ghebremedhin E, Braak H. Lewy pathology in the submandibular gland of individuals with incidental Lewy body disease and sporadic Parkinson's disease. *Acta Neuropathol* 2010;119:703–713.

Received August 15, 2015. Accepted in final form September 22, 2015.

AUTHOR CONTRIBUTIONS

L.L. Sokol: research project conception, organization, execution; writing of the first draft of manuscript.
A.J. Espay: research project conception, organization, execution; review and critique of manuscript.

STUDY FUNDING

No targeted funding reported.

DISCLOSURES

L.L. Sokol reports no disclosures. A.J. Espay serves on scientific advisory boards for Solvay (now Abbvie), Chelsea Therapeutics, TEVA, Impax, Merz, Pfizer, Solstice Neurosciences, Eli Lilly, Acadia, and USWorldMeds; serves as an Associate Editor of the *Journal of Clinical Movement Disorders* and on the editorial boards of *Parkinsonism and Related Disorders* and *The European Neurological Journal*; receives publishing royalties from Lippincott Williams & Wilkins and Cambridge University Press; serves as a consultant for Chelsea Therapeutics, Cynapsus, Lundbeck, Abbvie, and Acadia; serves on speakers' bureaus for UCB, TEVA, American Academy of Neurology, and the Movement Disorders Society; has received honoraria from UCB, TEVA, Acadia, the American Academy of Neurology, and the Movement Disorders Society; and receives research support from the NIH, CleveMed/Great Lakes Neurotechnologies, and the Michael J. Fox Foundation. Full disclosure form information provided by the authors is available with the **full text of this article at Neurology.org/cp**.

Get Clinical Practice Content Sooner

What you **do** know: *Neurology® Clinical Practice* publishes 6 times per year.

What you **might not** know: *Neurology® Clinical Practice* now publishes content **online ahead of print!**

- Get your message to our readers sooner
- Receive the latest clinical and health policy updates more often
- Sign up to receive **Publish Ahead of Print alerts**