

Letters

NASAL NITRIC OXIDE AS A MEASURE OF OSTEOMEATAL COMPLEX PATENCY IN NASAL POLYPS

Paranasal sinuses are the main source of nitric oxide in the human upper airway. The enzyme responsible for nitric oxide production comes from a calcium-independent inducible nitric oxide synthase in the epithelial cells lining the sinuses.¹⁻³ Inflammation leads to upregulation of inducible nitric oxide synthase with subsequent generation of large quantities of nitric oxide. Currently, there is no universally accepted method for measuring upper airway nitric oxide output, although several techniques have been described.⁴ Nasal polyps are a common condition in which low levels of nitric oxide are present,⁵ which is likely to reflect osteomeatal complex obstruction. The purpose of this case series was to examine the relationship between computed tomographic (CT) scores and nasal nitric oxide, the hypothesis being that the higher the CT score, the lower the production of nasal nitric oxide.

Consecutive nonsmoking patients with nasal polyp disease with or without asthma were selected from our rhinology clinic, a single-center specialty clinic in Tayside, Scotland, where patients were referred for assessment by their primary care physicians. Diagnosis of chronic rhinosinusitis with nasal polyps was made by otorhinolaryngologists according to the European Position Paper on Rhinosinusitis and Nasal Polyps 2007 criteria.⁶ Inclusion criteria were the presence of nasendoscopy of bilateral moderate-sized to large nasal polyps (grade >1) using the Lildholdt grading system (0 indicating no nasal polyps; 1, small polyps confined to middle meatus; 2, moderate polyps not crossing the lower edge of the inferior turbinate; and 3, large polyps crossing the lower edge of the inferior turbinate).⁷

All had at least 2 of the following symptoms for less than 12 weeks: anterior or posterior nasal discharge, nasal obstruction, or decreased sense of smell. Exclusion criteria included the following: treatment with an oral corticosteroid within 3 months, sinus surgery within 1 year, recent upper respiratory tract infection, mechanical nasal airway obstruction due to septal deviation greater than 50%, pregnancy, and lactation. From screening until the end of the study, no other rhinitis medications were permitted, including: antihistamines, leukotriene receptor antagonists, intranasal corticosteroids, and nasal decongestants. No antibiotics were permitted during the study. All had a sinus CT staging scan performed and underwent nasal nitric oxide measurements by an aspiration technique as previously described.⁴

Rhinosinusitis extent was staged by CT scans of the paranasal sinuses. The CT scans of the paranasal sinuses were scored using the modified Lund-MacKay system based on reconstructed axial sections^{8,9} (quantifying the percentage opacification of maxillary, frontal, anterior ethmoid, posterior ethmoid, and sphenoid sinuses as 0.0%, 1.1%-25%, 26%-50%, 51%-75%, 76%-99%, and 100% and summing the scores for each patient). All patients provided written consent, and the study was ethically approved.

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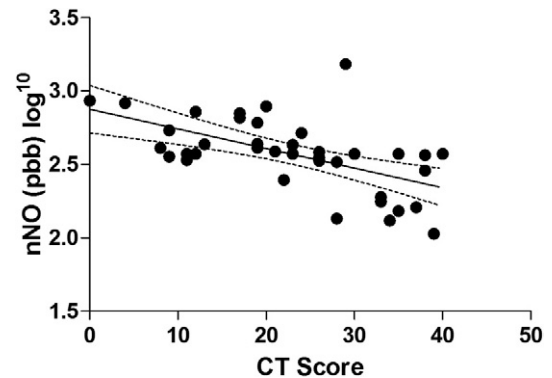


Figure 1. Nasal nitric oxide (nNO) levels according to computed tomographic (CT) scan results. Regression line and 95% confidence intervals are shown.

The case series included 38 patients (male:female ratio, 1.7:1; mean [SEM] age, 51.1 [2.43] years) with (n=11) or without (n=27) asthma. The mean (SEM) CT score (range, 0–40) was 22.8 (1.7), the median (interquartile range) anosmia visual analog scale score (range, 0–10) was 2 (3), and the mean (SD) total nasal score was 3.0 (3.25). The geometric means of nasal nitric oxide, total IgE, and peripheral blood eosinophils were 373.0 ppb, 89.1 IU/mL, and $0.34 \times 10^9/L$, respectively. A total of 50% of the patients tested positive for specific allergens or their total IgE levels were greater than 100 IU/mL.

Multiple linear regression analysis (Fig 1) showed that nasal nitric oxide was the strongest predictor of CT scan results, taking into account peripheral blood eosinophils, age, sex, IgE level, anosmia visual analog scale scores, and total nasal symptom score.

Nasal nitric oxide accounted for 32.9% of the variation (as R^2) in CT scores and was inversely correlated with sinus CT scores ($P < .001$). The Pearson correlation coefficient (Fig 1) indicated a high level of correlation at $R = -0.574$.

When segregating the asthmatic patients from the nonasthmatic patients, there are fewer patients with asthma in our cohort; however, the correlation in these patients between CT scores and nasal nitric oxide is not significant. In the larger population of nonasthmatic patients, the correlation of raw nasal nitric oxide values is less than .01 with a high Pearson correlation coefficient of 0.60.

In a population of consecutive nonsmoking adults with nasal polyposis, with or without asthma, our results confirm that the measurement of nasal nitric oxide is inversely correlated with CT scan scores, as described previously.⁶ Although asthmatic patients can have increased lower airway nitric oxide, in our measurements, the velum was closed, so theoretically, lower airway nitric oxide should not have influenced upper airway nitric oxide. Nasal nitric oxide may be an inexpensive and valuable surrogate marker of osteomeatal complex patency in the absence of a CT scan, which can provide rapid information in a clinic setting to guide treatment. We did not include a control group who had nasal airway obstruction without nasal polyps (ie, patients with persistent allergic rhinitis without osteomeatal complex occlusion). As such, we are unable to

validate the specificity of nasal nitric oxide as a polyposis screening test.

In this prospective case series, we demonstrated that nasal nitric oxide is inversely correlated with CT sinus scores. This would imply that nasal nitric oxide could be used as a rapid marker of osteomeatal complex patency in a clinic setting and thus may be of potential benefit in monitoring response to therapy.

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HENOCH-SCHÖNLEIN PURPURA AFTER HEPATITIS A VACCINATION

Henoch-Schönlein purpura (HSP) is the most common of the childhood vasculitides. HSP is a mostly benign, self-limiting clinical entity. Classic findings include nonthrombocytopenic purpura mostly confined to the legs and buttocks, arthralgias, abdominal pain, and renal disease. HSP is mediated by IgA immune complex deposition in various tissues and small-sized blood vessels. The immune complex deposition may be triggered by infections with distinct bacteria and viruses.¹ HSP has also been reported after the administration of several vaccines.^{2–4} To our knowledge, there is no report in the literature of HSP related to the hepatitis A vaccine. We describe an unusual case of HSP in a 22-month-old boy after the administration of the hepatitis A vaccine.

A previously healthy, 22-month-old, Hispanic boy with an unremarkable medical history presented to our hospital with bilateral lower extremity swelling associated with an erythematous violaceous rash of the dorsal and plantar areas. Onset of swelling was 2 days before admission and was first noted in the left foot and then in the right foot 1 day later. The patient received his first dose of the hepatitis A (Havrix) vaccine 2 weeks before admission. No other vaccines were adminis-

tered that day or in the preceding weeks. Three to 4 hours after receiving the hepatitis A vaccine, the patient developed a maculopapular rash on his face and legs that persisted for 3 days. The patient also started to have loose stools daily until the day of admission. Four days before admission, the patient had decreased oral intake, had decreased activity, and developed a productive cough and rhinorrhea.

On physical examination, the patient was afebrile and vital signs were unremarkable. The patient had 1+, bilateral, nonpitting pedal edema, left greater than right. The infant had palpable confluent purpura and mild erythema on the dorsal and plantar aspects of both feet (Fig 1). No vesicles or pustules were noted, and the results of the remainder of the examination were unremarkable. Laboratory testing was significant for elevated inflammatory markers, including a C-reactive protein level of 1.2 mg/L (reference range, <0.9 mg/L) and an erythrocyte sedimentation rate of 13 mm/h (reference range, <11 mm/h). Other laboratory results included unremarkable serum chemical analysis results, urinalysis results, liver function test results, antinuclear antibody, serum complement levels, and stool study findings. Skin biopsy was not performed because of the strong clinical suspicion for a diagnosis of HSP and in light of the patient's improvement with supportive care, including oral rehydration. The patient did not require steroids, and there was a marked improvement of symptoms by hospital day 3 at which time the patient was discharged from the hospital. Since being discharged, the patient has had no recurrence of symptoms.

HSP is an autoimmune acute leukocytoclastic vasculitis presenting predominantly in childhood and is initiated by IgA immune complex deposition.⁵ Approximately 75% of cases occur between 4 and 11 years of age, with a peak incidence at 5 years, and males are affected twice as commonly as females.⁵ HSP usually involves the skin, gastrointestinal system, joints, and/or kidneys.⁶ Current diagnostic criteria for HSP



Figure 1. Palpable confluent purpura and mild erythema on the dorsal and plantar aspects on infant's left foot.

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