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1. Lara M, Akinbami L, Flores G, et al. Heterogeneity of childhood asthma among Hispanic children: Puerto Rican children bear a disproportionate burden. *Pediatrics*. 2006;117:43–53.
2. Homa DM, Mannino DM, Lara M. Asthma mortality in US Hispanics of Mexican, Puerto Rican, and Cuban heritage, 1990–1995. *Am J Respir Crit Care Med*. 2000;161:504–509.
3. Rose D, Mannino DM, Leaderer BP. Asthma prevalence among US adults, 1998–2000: role of Puerto Rican ethnicity and behavioral and geographic factors. *Am J Public Health*. 2006;96:880–888.
4. Weiss KB, Shannon JJ, Sadowski LS, et al. The burden of asthma in the Chicago community fifteen years after the availability of national asthma guidelines: the design and initial results from the CHIRAH study. *Contemp Clin Trials*. 2009;30:246–255.
5. Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. *Eur Respir J*. 2005;26:319–338.
6. Asmusen L, Olson LM, Grant EN, et al. Reliability and validity of the Children's Health Survey for Asthma. *Pediatrics*. 1999;104:e71.
7. Josie KL, Greenley RN, Drotar D. Health-related quality-of-life measures for children with asthma: reliability and validity of the Children's Health Survey for Asthma and the Pediatric Quality of Life Inventory 3.0 Asthma Module. *Ann Allergy Asthma Immunol*. 2007;98:218–224.
8. Kumar R, Curtis LM, Khiani S, et al. A community-based study of tobacco smoke exposure among inner-city children with asthma in Chicago. *J Allergy Clin Immunol*. 2008;122:754–759.e1.

NONEPISODIC ANGIOEDEMA WITH EOSINOPHILIA

Episodic angioedema with eosinophilia, also known as Gleich syndrome, was first described in 1984.^{1–3} This syndrome was characterized by recurrent peripheral angioedema, fever, weight gain, elevated serum IgM level, and peripheral eosinophilia of unknown origin. It affected predominantly females and had a benign, relapsing course, lacking any internal organ involvement. A nonepisodic variant of angioedema has also been reported by Chikama et al and is observed frequently in Japan.^{3,4} The nonepisodic variant consisted of a single attack of persistent edema of the extremities associated with peripheral eosinophilia, lack of IgM level elevation, and, normally, a less severe course than the episodic type. To our knowledge, this is the first report of idiopathic, rapidly progressing, nonepisodic angioedema with

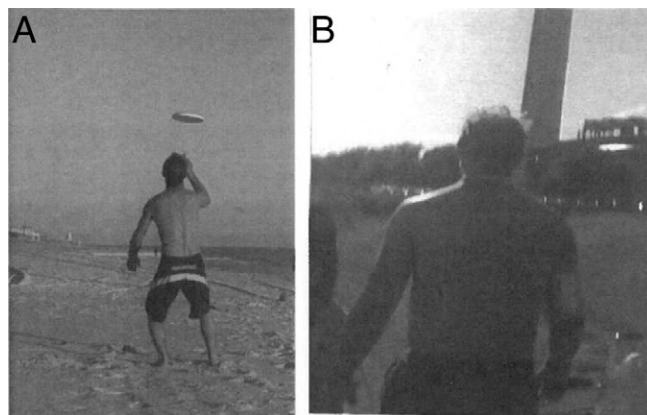


Figure 1. General appearance before (A) and during (B) the initial phase of the angioedema episode.

eosinophilia associated with mediastinal edema in a young man.

A 34-year-old, otherwise healthy construction worker presented to the emergency department in summer 2008 with generalized fatigue, muscle aches, slight fever, and significant upper extremities swelling with no evidence of rashes (Fig 1). He had been vacationing at his trailer in Southeastern Ontario but denied any prior respiratory tract infection, trauma, bug bites, or use of new medications. Initial investigations showed a marginally elevated peripheral white blood cell count (WBC) and eosinophil count. An upper-extremity blood clot was ruled out, and he was discharged home on comfort measures with a presumed diagnosis of a viral myositis. Two days later, he returned to the hospital with rapidly progressing generalized edema involving his face, neck, arms, upper chest, and abdomen. His weight had increased by 34.5%, his vital signs were stable, and he was afebrile. Physical examination revealed no rashes; he had no enlarged lymph nodes or organomegaly. Subsequently, he developed worsening shortness of breath requiring oxygen and pleuritic chest pain. His blood work showed a markedly elevated WBC and eosinophils count, peaking at $62.6 \times 10^9/L$ and $45 \times 10^9/L$, respectively; his initial hemoglobin level was 126 g/L, and his platelet count was $152 \times 10^3/\mu L$. He maintained normal levels of urea, creatinine, serum electrolytes, and liver enzymes. Computed tomography of the chest ruled out pulmonary embolus but revealed bilateral pleural effusions; cardiac magnetic resonance imaging demonstrated a small pericardial effusion, but no obvious infiltration of cardiac muscle was noted. The deltoid muscle biopsy performed at the initial emergency department visit revealed eosinophil infiltration with intact muscle fibers. Quantitative measurement of immunoglobulins, complement (C3, C4, C1 esterase inhibitor, and C1q binding), and vitamin B₁₂ levels were within normal limits. A bone marrow aspiration and biopsy confirmed marked hypereosinophilia with no leukemic features. Thorough workup failed to identify any infectious, parasitic, autoimmune, or neoplastic cause for this condition, including a lack of the *FIP1L-PDGFR* mutant gene. His symptoms responded well to oral steroids administered at 1 mg/kg. He was taken off oxygen within 4 to 5 days and his edema subsided; he had deconditioned significantly within 10 days and required intensive physiotherapy. He was discharged home on a 3-month, slow-tapering regimen of oral steroids and achieved his preex-

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isting weight in 6 weeks. His WBC and eosinophil count returned to normal values within 3 months, and close monitoring has shown no recurrence of angioedema or hypereosinophilia for more than 24 months without steroid therapy.

Our patient was a 34-year-old man who developed 1 episode of angioedema that affected the face, trunk, and upper extremities with significant weight gain, fevers, and marked eosinophilia. Unlike Gleich syndrome, this case is consistent with nonepisodic central angioedema with eosinophilia, in a young man and exhibiting a rapidly progressive course with mediastinal involvement. Despite eosinophilic infiltration noted in the deltoid muscle biopsy specimen, no obvious cardiac muscle infiltration was found, and his IgM level remained normal.³⁻⁵ The absence of an increased serum IgM level was also reported in the reviewed cases of nonepisodic angioedema observed in Japan. However, the authors of these reviews noted a predominance of young women (mean age of 26 years) and localization of the angioedema peripherally, affecting mainly the distal extremities. Moreover, unlike previous reports, our patient did not experience any associated urticarial lesions or pruritic papules.⁶⁻⁸ Although Gleich syndrome is believed to have a benign course, this case demonstrates a rapidly progressive presentation that may have led to significant decompensation in the patient's status, if left untreated. Similar to previous reports, our patient's symptoms responded remarkably well to oral steroids tapered during 3 months and his condition remained idiopathic.

This case presentation is, to our knowledge, the first reported observation of an idiopathic, rapidly progressing, nonepisodic central angioedema and significant hypereosinophilia, with asso-

ciated fever, weight gain, and mediastinal involvement in a young man.

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1. Gleich GJ, Schroeter AL, Marcoux JP, Sachs MI, O'Connell EJ, Kohler PF. Episodic angioedema associated with eosinophilia. *Trans Assoc Am Physicians*. 1984;97:25-32.
2. Gleich GJ, Schroeter AL, Marcoux JP, Sachs MI, O'Connell EJ, Kohler PF. Episodic angioedema associated with eosinophilia. *N Engl J Med*. 1984;310:1621-1626.
3. Banerji A, Weller PF, Sheikh J. Cytokine-associated angioedema syndromes including episodic angioedema with eosinophilia (Gleich's syndrome). *Immunol Allergy Clin North Am*. 2006;26:769-781.
4. Chikama R, Hosokawa M, Miyazawa T, Miura R, Suzuki T, Tagami H. Nonepisodic angioedema associated with eosinophilia: report of 4 cases and review of 33 young female patients reported in Japan. *Dermatology*. 1998;197:321-323.
5. Matsuda M, Fushimi T, Nakamura A, Ikeda S. Nonepisodic angioedema with eosinophilia: a report of two cases and a review of the literature. *Clin Rheumatol*. 2006;25:422-425.
6. Bochner BS, Friedman B, Krishnaswami G, Schleimer RP, Lichtenstein LM, Krogel C. Episodic eosinophilia-myalgia-like syndrome in a patient without L-tryptophan use: association with eosinophil activation and increased serum levels of granulocyte-macrophage colony-stimulating factor. *J Allergy Clin Immunol*. 1992;89:1064.
7. Mizukawa Y, Shiohara T. The cytokine profile in a transient variant of angioedema with eosinophilia. *Br J Dermatol*. 2001;144:169-174.
8. Wolf C, Pehamberger H, Breyer S, Leiferman KM, Wolff K. Episodic angioedema with eosinophilia. *J Am Acad Dermatol*. 1989;20:21-27.