The reader is encouraged to write possible diagnoses for each case before turning to the discussion. We invite readers to contribute case presentations and discussions. Please inquire first by contacting Dr. Nazarian at LFredN@aol.com.

Author Disclosure
Drs Alsheikh-Ali Absi, Kin, Hanna, Matthews, Brands, Kortuem, Davis, and Pane did not disclose any financial relationships relevant to these cases.

Frequently Used Abbreviations
ALT: alanine aminotransferase
AST: aspartate aminotransferase
BUN: blood urea nitrogen
CBC: complete blood count
CNS: central nervous system
CSF: cerebrospinal fluid
CT: computed tomography
ECG: electrocardiography
ED: emergency department
EEG: electroencephalography
ESR: erythrocyte sedimentation rate
GI: gastrointestinal
GU: genitourinary
Hct: hematocrit
Hgb: hemoglobin
MRI: magnetic resonance imaging
WBC: white blood cell

Case 1 Presentation
A 16-year-old boy is seen in the ED with a history of headache, blurred vision, and proptosis of his right eye. One week ago, he described his right eye as feeling “a little bigger than the left.” His primary care physician prescribed antibiotic eye drops. Two days ago, the boy developed frontal headache, blurred vision, and visible prominence of his right eye. He denies any history of trauma or fever.

Physical examination shows a temperature of 99.1°F (37.3°C), a respiratory rate of 18 breaths/min, a heart rate of 86 beats/min, and a blood pressure of 110/80 mmHg. His right eye demonstrates significant proptosis and partial ptosis. Extraocular movements are limited, especially on right lateral gaze. Both conjunctivae and sclerae appear normal. The right side of his face and cheek are slightly swollen. The right pupil is approximately 5 mm and the left approximately 3 mm in diameter. No red reflex is noted in the right eye, and the afferent pupillary reflex is absent in the right eye but intact in the left eye. His visual acuity is 20/200 in the right eye (OD) and 20/25 in the left eye (OS); they were 20/40 OD and 20/25 OS 6 months ago. All other cranial nerves appear intact.

Initial laboratory results are a WBC count of 13.6 × 10^9/L (13.6 × 10^6/μL), with 77% neutrophils and 17.3% lymphocytes, and Hgb of 14.7 g/dL (147 g/L). Urinalysis results and serum electrolyte concentrations are normal. An imaging study reveals the diagnosis.

Case 2 Presentation
A 15-year-old girl comes to the ED because of erythematous and tender nodules on the soles of both feet. Stating that the pain has an intensity of 10 on a scale of 10, she is unable to walk or bear weight on either foot. Her temperature today has been 102°F (38.9°C). Yesterday, she awoke with sharp, shooting pains in her soles but had been afebrile. Two days ago, she had played a double-header basketball game. She did not change her socks in between the games and described her feet as being sweaty during that time. After the game, she had spent approximately 1 hour in a new hot tub.

On physical examination, the girl appears apprehensive and uncomfortable but is afebrile. Multiple erythematous macules and plaques are present on both soles, including the lateral edges and the tips of the toes. The plaques are indurated and exquisitely tender to touch. She has limited mobility of the toes but good capillary refill and normal pulses. No lymph nodes are palpable.

Radiographs of her feet are read as normal. A WBC count is 25.2 × 10^9/L (25.2 × 10^6/μL), with 88% neutrophils. A C-reactive protein (CRP) value is elevated at 19.8 mg/dL (188.6 nmol/L) (normal, <0.8 mg/dL [7.6 nmol/L]). She is admitted to the hospital, and additional evaluation reveals the diagnosis.

Case 3 Presentation
A 16-month-old boy presents with a 3-week history of diarrhea and an 2-lb weight loss. He passes five large, foul-smelling stools each day, but has no vomiting or fever. There is no history of recent travel, camping, or ill contacts. The family has city water and no pets. He started child care 5 weeks ago.

On physical examination, the patient is afebrile and has stable vital signs. His weight is 11.9 kg (57th percentile) and height is 82 cm (57th percentile). He is fussy but consolable. His mucous membranes are dry, and his abdomen is soft and non-
tender, with moderate distention and normoactive bowel sounds.

Abdominal radiographs show mild distention of both small and large bowel, with air-fluid levels in the right colon. His WBC is 26×10^9/mL (26×10^9/L), with 1% neutrophils (absolute neutrophil count of 0.260×10^9/mL [0.260×10^9/L]), 52% lymphocytes, 2% monocytes, and 45% eosinophils. Electrolytes, liver function tests, ESR, and C-reactive protein values are normal. Stool guaiac test result is negative.

The patient is admitted and placed on bowel rest with intravenous fluids. His diarrhea improves, but immediately returns when the diet is advanced. Results of stool culture, rotavirus antigen, Clostridium difficile toxin testing, and examination for polymorphonuclear cells are negative. Three specimens are negative for ova and parasites. Eosinophils are found in the stool, and the stool alpha-1-antitrypsin concentration and fecal fat are elevated.

Esophagogastroduodenoscopy (EGD) and sigmoidoscopy yield normal findings on inspection. The pathology report reveals the diagnosis.

Case 1 Discussion
The presence of proptosis and partial ptosis (Fig. 1) warranted imaging. CT scan of the brain and orbit showed a mass on the right side, with extension into the orbit, ethmoid sinus, sphenoid sinus, right pterygoid process, and right middle cranial fossa (Fig. 2). These features were highly suggestive of an angiofibroma involving the right orbit, leading to the diagnosis of a juvenile nasopharyngeal angiofibroma (JNA). A biopsy performed at a pediatric oncology center confirmed the diagnosis of angiofibroma. The patient was started on radiation therapy and evaluated for possible surgical intervention.

Differential Diagnosis
Any acute visual loss constitutes an emergency. Sudden, unilateral, painless significant loss of vision can be caused by a number of disorders, including central retinal artery or vein occlusion, embolus, ischemic optic neuropathy, vitreous hemorrhage, retinal detachment, and optic neuritis. Painful loss can be due to acute closed-angle glaucoma, uveitis, and corneal hydrops.

When evaluating a patient whose visual loss is accompanied by proptosis, specific conditions should be kept in mind, including orbital cellulitis. Infection of the orbit may occur as an extension of periorbital cellulitis, bacterial ethmoid sinusitis, or adjacent facial infection. Orbital infection causes pain, primarily retroorbital, which is aggravated by ocular movement. Other features of orbital cellulitis, in addition to loss of vision, are: edema and erythema of the lid, which were not present in this patient; proptosis; conjunctival inflammation; and chemosis. Generally, affected patients tend to be very ill, toxic, and lethargic. CT scan of the orbit shows involvement of subperiosteal bone or abscess formation, in which case urgent referral to ophthalmology is warranted.

Orbital tumors can cause visual loss with proptosis. Neuroblastoma is the most common lesion to metastasize to the orbit in children. Affected patients usually present with the acute onset of proptosis (unilateral or bilateral) and ecchymosis of the eyelids. Retinoblastoma is the most common intraocular malignancy, albeit a relatively uncommon tumor, of childhood, usually occurring in younger children, with 95% of cases diagnosed before the age of 5 years. Presenting signs in older children are leukokoria, decreased visual acuity, pain, floaters, and strabismus. Most of these tumors are unilateral. Proptosis has been described but is unusual. The occurrence of this tumor is a good reason for assessing the red reflex in both eyes, starting at the time of birth.

Orbital cavernous hemangiomas are benign sinoorbital tumors found in adults. These slow-growing vascular tumors can present with painless and progressive proptosis of the eye. Most are unilateral. Decreased visual acuity, diplopia, decreased extraocular muscle movement, and papillary dysfunction can occur.

Idiopathic orbital inflammatory syndrome, which used to be referred to as orbital pseudotumor, is a nonspecific inflammation of the orbit, the cause of which is unknown. The
condition can be either unilateral or bilateral and usually presents with headache, orbital pain, proptosis, eyelid edema or erythema, decreased or restricted eyeball movement, and diplopia. Initially, this disorder can mimic an orbital neoplasm. Extension into a paranasal sinus occurs rarely. It is much more common in adults but does occur in children.

Cranio-orbital fibrous dysplasia is a benign, slow-growing bone lesion in which normal cancellous bone is replaced by immature woven bone and fibrous tissue. Manifestations occur in the first 2 to 3 decades of life and include exophthalmos, abnormal extraocular movement, visual impairment, and cosmetic deformity.

### The Condition

JNA, which was the cause of this patient’s findings, is a benign tumor occurring exclusively in adolescent males, with an age range of 7 to 19 years. Females in whom JNA is diagnosed should undergo genetic testing. (1) The tumor is rare in patients older than 25 years. The lesions usually are encapsulated masses composed of vascular tissue and fibrous stroma, with coarse or fine collagen fibers. The lesion originates in close proximity to the posterior attachment of the middle nasal turbinates, near the superior border of the sphenopalatine foramen.

JNA usually presents as nasal obstruction, epistaxis (mostly unilateral and recurrent), headache, and facial swelling. The lesion also can present with anosmia, hyposmia, otalgia, serous otitis media due to eustachian tube blockage, and hearing impairment. The combination of orbital mass and proptosis can occur in 10% to 15% of cases. Radiologic findings characteristic of JNA are tumor location in the nasopharynx, widening of the pterygopalatine fossa, and erosion of the pterygoid process.

CT scan provides good imaging of bone changes. MRI is better than CT scan at demonstrating the difference between tumor and fluid retention in the paranasal sinuses, extension of the intracranial mass, tumor vascularity, and soft-tissue margins. Typical radiologic findings combined with a characteristic clinical manifestation allow initial diagnosis.

The tumor can be staged, with stage I representing tumors limited to the nasal cavity and nasopharynx with no bony destruction and stage IV encompassing tumors that invade the cavernous sinus, region of the optic chiasma, or pituitary fossa.

### Therapy and Prognosis

Medical therapy includes use of a testosterone receptor blocker such as flutamide, which is reported to bring about 44% tumor reduction in stage I and II tumors. Another modality is radiotherapy, which has brought about 80% cure rates in some centers. Stereotaxic radiotherapy (gamma knife) delivers a lower dose of radiation to surrounding tissues. Three-dimensional conformal radiotherapy has been used to treat extensive JNA or intracranial extension. Surgical therapy also is employed but carries a risk of excessive bleeding.

### Lessons for the Clinician

Acute visual loss with or without proptosis should prompt clinicians to consider the possibility of an orbital tumor. Imaging and urgent referral to ophthalmology or oncology is the appropriate management when the diagnosis is suspected. (Mohammed Alsheikh-Ali Abi, MD, Lin Lin Kin, MD, Antoin Hanna, MD, Lincoln Medical and Mental Health Center, Bronx, NY)

### Reference


### Case 2 Discussion

A dermatology consultation resulted in a clinical diagnosis of neutrophilic eccrine hidradenitis (NEH). Histologic examination and culture of a skin biopsy confirmed the diagnosis. Pain control was achieved with 5% lidocaine patches. After 2 days, the patient’s pain was well controlled, and she was able to walk without assistance. Biopsy revealed a neutrophilic infiltrate surrounding the eccrine glands, which was consistent with NEH. The biopsy culture subsequently grew *Pseudomonas* from the broth after 5 days, and the patient was treated with topical gentamicin.

### Differential Diagnosis

The presence of painful lesions on both soles of the feet is an uncommon complaint. The differential diagnosis includes erythema multiforme, erythema nodosum (EN), chilblains, Sweet syndrome, and NEH. This patient’s history, along with the laboratory study results, narrowed the differential diagnosis. Erythema multiforme major (Stevens Johnson syndrome) most often is associated with a drug reaction, but this patient had not taken medications. Erythema multiforme minor occurs most often after a recent herpes simplex virus infection, and the lesions usually are not limited to the soles of the feet. EN may present similarly but frequently is associated with a drug reaction or infection. Localization to the soles of the feet also is highly atypical for EN.

Chilblains typically occurs after exposure to cold temperatures and
presents initially with lesions that itch and burn, subsequently progressing to tender nodules. Chilblains typically is not associated with elevated inflammatory markers. Sweet syndrome is rare in children, but when it does occur, it usually is preceded by an infection. In adults, Sweet syndrome is associated with malignancy. The lesions are well demarcated and have a predilection for the upper extremities, neck, and face; they also appear more superficially located in the skin. NEH presents with painful nodules and plaques, which in the pediatric population often are located on the soles and, less often, the palms (Fig. 3). NEH is associated with elevated inflammatory markers.

The Condition

NEH once was believed to be a rare neutrophilic dermatosis associated with malignancy and chemotherapy. Most adult cases are linked with the use of chemotherapy in acute myelogenous leukemia, Hodgkin disease, non-Hodgkin lymphoma, and chronic lymphocytic leukemia. Previous reports also have linked NEH with bacterial infections. However, over the past decade, there have been numerous case reports and series of healthy children presenting with NEH. In the pediatric population, the lesions of NEH typically affect the palmarplantar surfaces, leading to different names given to conditions that have a similar histologic picture, including idiopathic palmarplantar hidradenitis and idiopathic recurrent palmarplantar hidradenitis (IRPH).

The cause of this disease remains unclear. A few pediatric case reports have documented a positive biopsy culture for *Pseudomonas aeruginosa*. Another patient in a single case report developed IRPH at the same time she had hot tub folliculitis. In 2001, Fiorillo and associates (1) suggested a diagnosis of “*Pseudomonas* hot-foot syndrome” after 40 patients developed erythematous nodules on their soles after exposure to a community pool and one patient had a culture from a lesion that grew *P. aeruginosa*. Associations also have been reported with wet footwear and excessive physical activity.

Diagnosis

With increasing recognition of NEH, a diagnosis can be established based solely on the clinical picture. Patients frequently present with the sudden onset of painful, erythematous nodules and plaques. Often, there is a history of increased physical activity prior to presentation. The lesions may be isolated to the palmarplantar surfaces, as is most common in the pediatric population, or can be scattered on the trunk and limbs. FEVERS may start prior to the onset of the lesions. Patients may have an elevated WBC count and CRP value. If the diagnosis is in doubt, a skin biopsy can be obtained for confirmation. Histologic examination reveals a neutrophilic infiltrate around the eccrine glands, particularly the ductal segments. Neutrophilic abscesses often are present next to the eccrine coils.

Treatment

In general, the literature suggests supportive care as the primary treatment for NEH, which is a self-limiting illness. Most patients improve with a few days of rest. Nonsteroidal anti-inflammatory agents may be useful to treat the intense pain. This patient achieved excellent pain control with a 5% lidocaine patch to each sole, a therapy that has not been reported previously in the literature as being useful in this circumstance. The role of antibiotics has been questioned, but such treatment may benefit patients who have a positive culture from biopsy.

Lessons for the Clinician

NEH appears to be a much more common condition than once thought. The entity is well documented in the dermatology literature, but is mentioned infrequently in pediatric journals. NEH generally is self-limited, has a benign course, and can be treated with symptomatic and supportive care. The diagnosis may be made on clinical grounds; a biopsy may be performed to confirm the diagnosis. A lidocaine patch may be useful in controlling the localized pain.

Clinicians should suspect this condition in patients who report a sudden, painful skin eruption involving the palms and soles. The history also can help distinguish this diagnosis from others in the differential diagnosis. *Pseudomonas* infection and extreme physical activity played an important role in this patient’s presentation. Clinicians should seek

![Figure 3. Clinical presentation of a patient who has developed neutrophilic eccrine hidradenitis of her feet following a hot tub exposure and extreme physical activity.](Image)
such details in the history from patients presenting with other painful dermal eruptions. (Gretchen Matthews, MD, Chad K. Brands, MD, Kimberly Kortuem, MD, Mark Davis, MD, Mayo Clinic College of Medicine, Rochester, Minn.)

Reference

Case 3 Discussion

Biopsy of the stomach and duodenum revealed expansion of the lamina propria by an abundance of eosinophils and plasma cells. These findings were consistent with a diagnosis of eosinophilic gastroenteritis (EG).

The patient’s diet was limited to a hypoallergenic formula for 4 weeks, after which he was reintroduced to a regular toddler diet one food at a time. Radioallergosorbent testing (RAST) revealed a high reaction to egg white and wheat, which he now avoids. Three months later, he is gaining weight, has only 8% peripheral eosinophils, and has no further diarrhea.

The Condition

EG should be considered in any patient who has GI symptoms and peripheral eosinophilia. Eosinophils can infiltrate any mucosal layer of the GI tract, from the esophagus to the rectum.

Isolated mucosal involvement may result in abdominal pain, nausea, vomiting, dysphagia, food impaction, chest pain, diarrhea, weight loss, protein-losing enteropathy, anemia, and intestinal perforation. Patients who have involvement of the muscular layer may experience pyloric or intestinal obstruction and early satiety. Infiltration of the subserosa may lead to eosinophilic ascites.

Although frequently idiopathic in adults, an allergic origin has been proposed for most pediatric patients. Approximately 50% of patients describe a history of allergy or food intolerance. Most have increased total and food-specific immunoglobulin E (IgE) concentrations. In sensitized individuals, specific food antigens may react with IgE bound to mast cells, causing degranulation and release of eosinophil chemotactic factors. Activated eosinophils are attracted to the area and release degranulation products that both damage the gut wall and elicit additional mast cell degranulation, creating a vicious cycle.

Diagnosis

EG is diagnosed by endoscopic biopsy of the mucosa, which demonstrates 20 or more eosinophils per high-power field, although some gastroenterologists are proposing that the diagnostic number be reduced to 15. The mucosa may appear grossly normal but can reveal prominent mucosal folds, hyperemia, nodularity, or ulceration. Specimens should be taken from both abnormal and normal tissue because microscopic evaluation may demonstrate the characteristic changes in tissue that looks normal. Numerous biopsy samples should be obtained due to the patchy nature of the disease.

Peripheral eosinophil counts in patients who have EG typically range from 5% to 35% but are normal in 20% of cases. Anemia may result from blood loss with mucosal disease. The serum albumin concentration is low in up to 30% of cases, and protein loss can be detected by a stool alpha-1-antitrypsin measurement. Severe protein loss may result in low immunoglobulin values. Thirty-three percent of patients develop steatorrhea. The ESR usually is normal.

Radiographic changes are nonspecific, and abnormalities are absent in nearly 50% of patients. Prominent, thickened mucosal folds may be present in the stomach, small intestine, or colon. The small intestine may be dilated.

Differential Diagnosis

Many diseases couple GI symptoms with peripheral eosinophilia. Most can be differentiated from EG with the use of routine laboratory tests and endoscopic evaluation.

Intestinal parasites such as *Ancylostoma*, *Strongyloides*, *Toxocara*, *Trichuris*, *Trichinella*, and *Ascaris* cause eosinophilia and may be excluded by examination of three stool specimens for ova and parasites. In some cases, the organisms are found only in intestinal aspirates obtained during colonoscopy. Serologic testing for children who have geophagic pica should be considered to exclude visceral larva migrans. Infestation with the dog hookworm *Ancylostoma caninum* may mimic EG, with eosinophilic infiltration of the gut mucosa and development of ascites.

Crohn disease and ulcerative colitis rarely may be associated with peripheral eosinophilia. These disorders can be excluded on mucosal biopsy by their lack of rampant eosinophilic infiltration.

Malignancies are a rare but important cause of obstructive symptoms and eosinophilia in children and include lymphoma, gastric cancer, and colon cancer. For patients who have extremely high eosinophil counts, acute eosinophilic leukemia is a significant consideration. The key to this patient’s diagnosis was the variation in symptoms with dietary intake, although if endoscopic biopsy results had been negative, bone marrow biopsy would have been appropriate.

Pediatrics in Review Vol.29 No.2 February 2008 65
Treatment and Prognosis
If left untreated, patients afflicted with EG can undergo spontaneous remission or progress to severe malabsorption and malnutrition.

No randomized, controlled clinical studies have evaluated treatments in EG. For patients who have isolated mucosal involvement, it is reasonable to attempt dietary changes, especially for those who have a history of food intolerance or allergy. Eliminating foods identified by skin prick testing or RAST has shown mixed results but may be appropriate initial treatment for patients whose disease is mild. Patients whose disease is significant may require amino acid-based elemental formulas to obtain complete resolution. Once remission is achieved, food groups are reintroduced gradually, and screening endoscopy is performed every 3 months.

Glucocorticoids are the cornerstone of treatment for patients who fail dietary measures and in those who have obstructive symptoms or ascites. Improvement generally occurs within 2 weeks regardless of the bowel layer affected, and the dose then may be tapered gradually. Up to 50% of adult patients relapse repeatedly and require low-dose maintenance prednisone. Outcome studies have not been performed in children, but evidence suggests that younger patients respond better to dietary manipulations and have fewer relapses. When the disease presents in infancy and can be linked to specific food sensitization, the probability of remission by late childhood is high.

Lessons for the Clinician
Patients who have chronic diarrhea present a diagnostic challenge to the clinician, with a wide differential diagnosis. When early tests reveal a peripheral eosinophilia, the diagnosis narrows. Pediatricians, who are familiar with parasitic disease, may not identify EG as a potential cause. Early endoscopic biopsy and initiation of elemental formula may prevent substantial malabsorption, malnutrition, and weight loss in these patients.

(Laurie A. Pane, MD, Children’s National Medical Center, Washington, DC)

To view Suggested Reading lists for these cases, visit www.pedsinreview.org and click on Index of Suspicion.