

Pediatric Dermatology

P2000

Newly diagnosed neonatal-onset multisystem inflammatory disease (NOMID/CINCA) in a 6-year-old boy

Michelle Jeffries, DO, Phoenix Children's Hospital, Phoenix, Arizona, United States; Kaleo Ede, MD, Phoenix Children's Hospital, Phoenix, Arizona, United States; Michael Shishov, MD, MPH, Phoenix Children's Hospital, Phoenix, Arizona, United States; Ronald Hansen, MD, Phoenix Children's Hospital, Phoenix, Arizona, United States; Yebabe Mengesha, MD, Phoenix Children's Hospital, Phoenix, Arizona, United States

The inpatient pediatric dermatology service was consulted on a 6-year-old boy for evaluation of a rash that had been present since birth. He had a complex medical history of communicating hydrocephalus status post ventriculoperitoneal shunt, chronic meningitis, bilateral sensorineural hearing loss & papilledema (diagnosed on admission), headaches, developmental delay, conjunctivitis, reactive airway disease, gastroesophageal reflux, iron deficiency anemia, osteomyelitis, arthropathy, intermittent fevers and rash. On examination he had dysmorphic facial features and several 3 mm to 4 cm pink urticarial papules and plaques on his trunk. A 3 mm skin biopsy specimen was obtained from a lesion on his back which demonstrated a mild perivascular and periadnexal inflammatory infiltrate of neutrophils, lymphocytes and rare eosinophils consistent with urticaria. Laboratory studies demonstrated leukocytosis, anemia, thrombocytosis, and elevated ESR and CRP. Lumbar puncture had a high opening pressure and cerebrospinal fluid analysis revealed pleiocytosis. Genetic testing revealed a heterozygous mutation in the Cold-Induced Autoinflammatory Syndrome 1 (CIAS1) gene. The constellation of clinical features, laboratory studies and genetic analysis were consistent with a diagnosis of Neonatal-Onset Multisystem Inflammatory Disease/Chronic Infantile Neurological Cutaneous and Articular syndrome (NOMID/CINCA). His rash, fevers, headaches and arthritis improved with Anakinra and oral Prednisolone. NOMID/CINCA is one of the cryopyrin-associated periodic syndromes that presents in the neonatal period with inflammation in the skin, joints and central nervous system. The differential diagnosis, characteristic features and treatment of NOMID/CINCA will be reviewed.

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Pediatric Dermatology

P2001

An eight-year-old boy with cutaneous metastases of systemic anaplastic large cell lymphoma presenting as arthropod bite on histologic examination: When clinical history and dermatopathology do not match

Jennifer Alston DeSimone, MD, Georgetown University Hospital, Department of Dermatology, Washington, District of Columbia, United States; C. Lisa Kauffman, MD, Georgetown University Hospital (former affiliation), Washington, District of Columbia, United States; Paula Bourelly, MD, Georgetown University Hospital (formerly affiliated), Washington, District of Columbia, United States

We present a case of an eight-year-old boy who initially presented with a single erythematous papule and axillary lymphadenopathy. Skin biopsy and histopathologic exam revealed findings consistent with arthropod bite. Systemic symptoms of fever and fatigue developed and progressed without response to antimicrobial therapy. Consistent communication between the primary clinician and the dermatopathologist led to six sequential evaluations of deeper tissue sections, all of which were consistent with arthropod assault. In an effort to correlate the clinical history with the histopathology, a seventh tissue block sample was evaluated, which revealed anaplastic large cell lymphoma. This case is illustrative of the critical importance of clinician to dermatopathologist communication and cooperation in the diagnostic process of challenging clinical dilemmas.

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P2002

Neonatal lupus erythematosus with central nervous system involvement

José Suárez, MD, Service of Dermatology, Hospital Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain; Carmen Marrero, MD, Service of Pediatric, Santa Cruz de Tenerife, Spain; Ricardo Fernández de Misa, MD, PhD, Service of Dermatology, Hospital Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain; Vicente García, MD, Service of Radiology, Hospital Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain

A male newborn was admitted because an enlargement of both cerebral ventricles was diagnosed by ultrasonography at 8^o month of gestational age; during the first pregnancy of a 28-yr-old mother with Graves-Basedow disease and cryoglobulinemia.

Extensive skin lesions, macrocephaly, hepatosplenomegaly and axial hypotonia were noted at birth. Laboratory studies revealed thrombopenia (24.000 platelets/mm³) and antinuclear (speckled pattern: titer > 1/1280), anti-ENAs, anti-Ro/SSA, Anti-La/SSB and p-ANCA antibodies. A transfontanelar ultrasonography performed a day after delivery showed enlargement of both lateral cerebral ventricles that was more evident in the left ventricle, the third ventricle was also dilated. No calcifications were seen. A computerized tomography of the brain demonstrated an ischemic softening in the posterior temporal area with enlargement and asymmetry of lateral cerebral ventricles. Three muscular intraventricular cardiac communications were seen in a cardiac ultrasound study.

Skin biopsy showed subtle changes with sporadic necrotic keratinocytes, occasional keratotic plugging and wavy hyperkeratosis, with no hydropic degeneration neither broadening of the basal membrane. No inflammatory infiltrate was seen perivascularly or interstitially. Vasculitis was absent. Direct immunofluorescence was useless due to technical problems.

The infant was treated with systemic steroids and intravenous immunoglobulins with a good response. CNS involvement is not a frequent manifestation of neonatal lupus erythematosus. Recognition of abnormal neuroimaging as a manifestation of neonatal lupus erythematosus is important when evaluating a newborn with multisystemic disease.

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Verruciform xanthoma in a healthy 9-year-old male

Christine M. Cole, MD, Mayo Clinic Scottsdale, Scottsdale, Arizona, United States; Alison K. Adams, MD, Mayo Clinic Scottsdale, Scottsdale, Arizona, United States; Michelle L. Jeffries, DO, Phoenix Children's Hospital, Phoenix, Arizona, United States; Richard A. Bernert, MD, Sonora Quest Laboratories, Tempe, Arizona, United States; Ron C. Hansen, MD, Phoenix Children's Medical Group, Phoenix, Arizona, United States

A 9-year-old, healthy Caucasian male was seen in the pediatric dermatologic clinic for non-pruritic, non-tender scrotal lesions that had been present for approximately one year. There were eight, skin colored, soft, pedunculated, discrete papules clustered on the right side of the scrotum. There was one papule centrally that was pink and larger than the others with a hemorrhagic crust at the distal tip.

A biopsy was performed and histopathologic examination revealed hyperkeratosis, papillated epidermal hyperplasia, elongation of the rete ridges, and dermal papillae filled with numerous large foam cells that were negative for S100, but positive for CD68. The findings were consistent with a diagnosis of verruciform xanthoma.

Verruciform xanthoma is a rare entity commonly presenting as asymptomatic verrucous, papillary, or planar plaques. They usually occur in the oral cavity, but the second most common site of involvement is the genitalia. The cause of this condition is unknown, however, it may occur as a result of epithelial degeneration leading to the uptake of keratinocyte lipid by dermal dendrocytes, and thus may represent a reactive pattern. Trauma and HPV have also been reported as possible etiologies.

While verruciform xanthoma is more commonly found in middle-aged males, there are a number of reports of cases in the pediatric population. All previous reports in children however have been associated with co-existing medical conditions, such as CHILD syndrome, lipid storage disease, dystrophic epidermolysis bullosa, Milroy disease, Leaky capillary syndrome, and in a 12-year-old male with graft-versus-host disease and squamous carcinoma. This case is remarkable for the occurrence of verruciform xanthoma in a child without other associated medical conditions.

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P2004

Subgroup analyses (age, gender and therapy history) of etanercept in pediatric patients with psoriasis

Amy Paller, MD, Dept of Dermatology – Northwestern University Medical School, Chicago, Illinois, United States; Amy Paller, MD, Children's Memorial Hospital and Northwestern University Medical School, Chicago, Illinois, United States; Gregory Kricorian, MD, Amgen Inc., Thousand Oaks, California, United States; Richard Langley, MD, Dalhousie University Division of Dermatology, Halifax, Nova Scotia, Canada

In a 48-week study, 211 children (4 to 17 yrs) with psoriasis (PsO) involving $\geq 10\%$ body surface area and PASI score ≥ 12 were randomly assigned 1:1 in a 12-week double-blind (DB), placebo (Pbo)-controlled treatment period to once-weekly subcutaneous Pbo or etanercept (ETN) 0.8 mg/kg (≤ 50 mg), followed by 24 weeks of open-label (OL) ETN, then a 12-week randomized DB withdrawal-retreatment period (patients received Pbo or ETN as long as they maintained response; otherwise, were retreated with OL ETN). In subgroup analyses, efficacy results were examined by gender, age (children, 4–11 years; adolescents, 12–17 years), and prior systemic therapy (yes/no). Safety results were examined by gender and age. In the study's primary analysis at week 12, PASI 75 was achieved by 57% of ETN patients compared with 11% of Pbo patients ($P < 0.001$). Regardless of subgroup classification, consistently more ETN patients achieved PASI 75 at week 12 compared with Pbo patients, as shown in the following table:

PASI 75 Response at Week 12

	Placebo n/N (%)	Etanercept n/N (%)
Primary endpoint results:	12/105 (11%)	60/106 (57%)
Gender:		
Boys	6/53 (11%)	30/55 (55%)
Girls	6/52 (12%)	30/51 (59%)
Age:		
Children (4–11 years)	4/38 (11%)	22/38 (58%)
Adolescents (12–17 years)	8/67 (12%)	38/68 (56%)
Prior Systemic Therapy:		
Yes	7/62 (11%)	31/58 (53%)
No	5/43 (12%)	29/48 (60%)

n = number with response; N = number in group or subgroup

Although total exposure to study drug during the 48-week study varied widely (ETN, 164.8 pt-yrs; Pbo, 18.8 pt-yrs), adverse events (AEs) occurred at similar or lower rates in ETN patients (554.5/100 pt-yrs) than Pbo patients (765.4/100 pt-yrs). In subgroup analyses by age and gender, most AE rates also were similar. Upper respiratory infections and nasopharyngitis were the most common events. ETN was well tolerated and demonstrated consistently higher responses than placebo in pediatric patients with moderate to severe plaque psoriasis across these subgroups.

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Stopping and restarting etanercept therapy in pediatric patients with psoriasis

Lawrence Eichenfield, MD, Rady Children's Hospital and Health Center, San Diego, California, United States; Amy Paller, MD, Children's Memorial Hospital, Chicago, Illinois, United States; Elaine Siegfried, MD, Saint Louis University, St. Louis, Missouri, United States; Gregory Kricorian, MD, Amgen Inc., Thousand Oaks, California, United States

Psoriasis (PsO) is a chronic inflammatory disease that affects both adults and children. Some therapeutic agents are used to treat psoriasis in an intermittent or rotational manner. Data indicate that etanercept (ETN) is safe when stopped and restarted in adult patients, but little information has been reported with ETN used intermittently in the pediatric population.

In a 48-week study, 211 children (4 to 17 yrs) with PsO involving $\geq 10\%$ body surface area and PASI score ≥ 12 were randomly assigned 1:1 in a 12 week double-blind (DB), placebo (Pbo)-controlled period to once-weekly (QW) subcutaneous Pbo or ETN 0.8 mg/kg (≤ 50 mg), followed by a 24 week period of open-label (OL) ETN (0.8 mg/kg QW), then a 12 week randomized DB withdrawal-retreatment period (eligible patients received Pbo or ETN as long as they maintained response [withdrawal period]; otherwise, were retreated with OL ETN [retreatment period]). Of the 138 patients who entered the 12 week withdrawal-retreatment period, 94% of patients began this phase with a PASI 75 response. Sixty-nine patients each were re-randomized to Pbo or ETN (0.8 mg/kg QW), 1 patient from the ETN group was lost to follow-up, and 137 patients completed the period. Of these, 95 (69%) patients (55 [81%] ETN, 40 [58%] Pbo) remained on blinded study drug during the 12 week period, and 42 patients (13 [19%] ETN; 29 [42%] Pbo) were retreated with OL ETN. Of the retreated patients, 7 (58%) ETN and 10 (36%) Pbo patients had regained a PASI 75 response by the last visit in retreatment.

During the withdrawal-retreatment period, no patient had a serious adverse event (AE) or infection, or withdrew from study. During withdrawal, 36 (52.9%) ETN and 32 (46.4%) Pbo patients had ≥ 1 AE; incidence of nasopharyngitis and headache was higher in ETN patients (10.3% and 8.8%) than Pbo patients (2.9% and 2.9%). During retreatment, the incidence of at least one AE (18 [42.9%]) must be interpreted with caution because of small sample size. In this study, ETN 0.8 mg/kg QW was effective and well tolerated in pediatric patients with moderate to severe plaque psoriasis.

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