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55 Kenosia Avenue
PO Box 1968
Danbury, CT 06813-1968
Phone: 203.744.0100
Toll Free: 1-800-999-6673
Fax: 203.798.2291

Neonatal-onset Multisystem Inflammatory Disease

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Synonyms of Neonatal-onset Multisystem Inflammatory Disease

- Chr infantile neurologic cutaneous articular syndrome
- CINCA
- NOMID

Disorder Subdivisions

- Chronic infantile neurologic cutaneous articular syndrome
- NOMID
- NOMID

General Discussion

Neonatal-onset multisystem inflammatory disease (NOMID), also known as chronic infantile neurologic cutaneous articular (CINCA) syndrome, is a rare, congenital, systemic, inflammatory condition distinguished by fever, rash, joint disease, and central nervous system (CNS) disease. The hallmark of NOMID is onset during infancy or early childhood.

NOMID is the most severe form of the cryopyrin associated periodic syndromes (CAPS) caused by mutations in the CIAS1/NLRP3 gene. These syndromes are characterized by fever, rash, and joint pain.

Symptoms

In addition to fever, symptoms of NOMID involve the skin, CNS and joints. Skin rashes occur in all patients within the first six weeks of life and persist throughout their lives. CNS symptoms include chronic meningitis, mental retardation, seizures and sensory organ dysfunction, which results in vision and hearing loss. Joint inflammation and joint and bone deformities range in severity. Enlargement of the knee-cap is also characteristic of NOMID.

Other symptoms include stunted growth, enlargement of the liver and spleen, an abnormal increase in the number of white blood cells, an elevation in levels of the protein amyloid A and C-reactive protein in the blood and an increase in the erythrocyte sedimentation rate (blood tests used to measure elevations of these markers can detect or grade inflammation). In addition, abnormal facial features can sometimes be seen.

NOMID shares symptoms, and should not be confused, with juvenile idiopathic arthritis (JIA). High recurrent fevers, joint pain, deforming joint disease and rash are symptoms of both NOMID and JIA. However, NOMID is differentiated by the onset of skin disease at birth and a persistent rash. In addition, many patients with NOMID have nonspecific joint pain and enlargement of the knee-cap, while patients with JIA present with inflamed synovial joints, such as the shoulder or knee, increased production of fluid in the synovial joints and warm, swollen, stiff joints.

NOMID patients suffer from frequent, almost daily flare-up episodes which cause great discomfort, can be very debilitating, and may require medical assistance during the episodes. Some patients are unable to walk or bear weight on their legs due to joint damage and/or pain. The majority of children with NOMID have cognitive and mental deficits and/or learning disabilities as well as vision and hearing loss. There is a 20 percent mortality rate before adulthood associated with NOMID.

Causes

About 50-60 percent of those who are diagnosed with NOMID have heterozygous mutations in a gene identified as the CIAS1/NLRP3 gene that codes for the protein cryopyrin (NALP3). Mutations in this gene are hypothesized to cause increased activity of a protein complex containing cryopyrin. This protein complex is known as the inflammasome and regulates inflammation in the body. Increased inflammasome activity results in increased release of a protein known as interleukin (IL) 1ß, which leads to

symptoms of inflammation such as fever and joint pain.

Affected Populations
Since NOMID is a newly discovered condition, the actual incidence and prevalence of the disease is difficult to determine.

Related Disorders
Symptoms of the following disorders can be similar to those of NOMID, and there is significant phenotypic overlap. Comparisons may be useful for a differential diagnosis.

Familial cold autoinflammatory syndrome (FCAS), also known as familial cold urticaria, is a rare, inherited inflammatory disorder characterized by intermittent episodes of rash, fever, joint pain and other signs/symptoms of systemic inflammation triggered by exposure to cold. Onset of FCAS presents during infancy and early childhood and persists throughout the patient's life. FCAS is one of the cryopyrin associated periodic syndromes (CAPS) caused by mutations in the CIAS1/NLRP3 gene.

Muckle-Wells syndrome (MWS) is one of the cryopyrin associated periodic syndromes (CAPS). Individuals with MWS often have episodic fever, chills, and painful joints. Sometimes these symptoms are exacerbated by cold similar to the related condition FCAS, but can also be triggered by other stimuli or unprecipitated. In most cases, MWS patients develop progressive hearing loss. In some MWS cases amyloidosis develops later in life, a disease in which an abnormal accumulation of the protein amyloid occurs in a patient's tissues and organs. Accumulation of amyloid in the kidneys results in damage and often kidney failure if untreated.

Standard Therapies
Diagnosis
Diagnosis of NOMID is determined through an evaluation of a patient's symptoms and medical history. Confirmation of the diagnosis is achieved through genetic testing although almost half of all NOMID patients do not possess a mutation in the CIAS1/NLRP3 gene.
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Treatment
While there are currently no medications indicated for the treatment of NOMID, therapies that suppress the inflammation, including high-dose corticosteroids, disease-modifying antirheumatic drugs, and biologic agents, are often used to treat the condition. These treatments tend to be only moderately effective, however, with inflammation persisting in most children. In recent clinical studies, investigational interleukin-1 inhibitors had encouraging preliminary results in addressing the inflammatory features of the conditions in study patients, but these product candidates have not been approved by the Food and Drug Administration for the treatment of NOMID

Investigational Therapies
Regeneron Pharmaceuticals submitted to the US Food and Drug Administration a biologics license application (BLA) for its IL-1 Trap (rilonacept) for consideration as a

long-term treatment for CAPS. The IL-1 Trap is a long-acting inhibitor of interleukin (IL) 1 and if approved, would be the first medication indicated for the treatment of CAPS.

Anakinra, an IL-1 receptor antagonist, has shown promise in improving symptoms in several small series and reports of patients with MWS; however, it is not approved by the FDA for the treatment of MWS or any of the CAPS diseases at this time.

Novartis Pharmaceuticals is currently developing an IL-1 antibody, which has been reported to be effective in CAPS.

Information on current clinical trials is posted on the Internet at www.clinicaltrials.gov. All studies receiving U.S. government funding, and some supported by private industry, are posted on this government web site.

For information about clinical trials being conducted at the NIH Clinical Center in Bethesda, MD, contact the NIH Patient Recruitment Office:

Tollfree: (800) 411-1222
TTY: (866) 411-1010
Email: prpl@cc.nih.gov

For information about clinical trials sponsored by private sources, contact: www.centerwatch.com

Organizations related to Neonatal-onset Multisystem Inflammatory Disease

- Genetic and Rare Diseases (GARD) Information Center

  PO Box 8126
  Gaithersburg MD 20898-8126
  Phone #: 3015193194
  800 #: 8882052311
  e-mail: gardinfo@nih.gov
  Home page: http://www.genome.gov/10000409

- Madisons Foundation

  PO Box 241956
  Los Angeles CA 90024
  Phone #: 3102640826
  800 #: N/A
  e-mail: getinfo@madisonsfoundation.org
  Home page: http://www.madisonsfoundation.org

- NIH/Office of Rare Diseases

Steve Groft, Pharm.D.
Bethesda MD 20892-
Phone #: 3014024336
800 #:
e-mail: hh70f@nih.gov
Home page: http://www.rarediseases.info.nih.gov/ord/

- NOMID Alliance, Inc.

  P.O. Box 590354
  San Francisco CA 94159
  Phone #: 4158318782
  800 #: N/A
  e-mail: site_manager@nomidalliance.net
  Home page: http://www.nomidalliance.net

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