CONDITION

Chediak-higashi syndrome

Learn how Chediak-Higashi syndrome affects immunity, skin and eye pigment, bleeding, and the nervous system, including diagnosis, treatment, and warning signs.

WHAT IT IS
Rare inherited disorder affecting immunity, pigmentation, blood clotting and nerves

BODY SYSTEM
Immune, skin and eyes, blood and nervous systems

MAIN SYMPTOMS
Recurrent infections, partial albinism, easy bleeding, movement and balance problems

WHAT CAUSES IT
Inherited LYST gene variants

HOW IT IS DIAGNOSED
Blood smear and LYST genetic testing

MAIN TREATMENT
Stem cell transplantation

CAN IT BE CURED?
No, neurologic problems may still progress

IS IT AN EMERGENCY?
Sometimes, persistent fever with marked tiredness

LONG-TERM OUTLOOK
Variable, with severe early disease or progressive neurologic problems

Overview

Chediak-Higashi syndrome is a rare inherited disorder that affects the immune system, skin and eye coloring, blood clotting, and nervous system. Signs often begin in infancy or childhood, although milder forms may not be recognized until later.

The condition is caused by harmful changes in the LYST gene. This gene helps cells move and release materials stored in small internal sacs called lysosomes and related structures. When this process does not work normally, several types of cells are affected.

White blood cells may have trouble killing bacteria and other germs. This can lead to repeated or severe infections. Pigment-producing cells may not distribute melanin normally, causing partial albinism. Melanin is the substance that gives color to the skin, hair, and eyes. Platelets, which help stop bleeding, may also work less effectively.

Many people with the classic form develop an intense immune reaction called the accelerated phase . This is a form of hemophagocytic lymphohistiocytosis, or HLH. During HLH, immune cells become overactive and may damage the blood cells, liver, spleen, brain, and other organs. It requires prompt specialist treatment.

Chediak-Higashi syndrome varies considerably. Some people have severe infections and HLH early in life. Others have a milder or "atypical" form with fewer childhood infections but increasing problems with movement, balance, sensation, or thinking later in life.

Early recognition matters because a stem cell transplant can correct many of the immune and blood-related problems. However, it may not prevent all long-term nervous system complications.

Symptoms

Symptoms differ according to the form of the condition and the person's age. Not everyone has every feature.

Partial albinism may be noticeable at birth or in early childhood. Possible features include:

Immune system problems can cause repeated infections, especially bacterial infections involving the skin, mouth, throat, lungs, or other respiratory passages. Infections may be unusually severe, slow to clear, or likely to return. Fever, cough, skin redness, swelling, drainage, or mouth sores should be discussed promptly with the care team.

Platelet abnormalities can cause mild to moderate bleeding symptoms. These may include easy bruising, frequent nosebleeds, bleeding from the gums, or heavier-than-expected bleeding after an injury or procedure. Menstrual bleeding may also be heavy.

Nervous system symptoms can occur in childhood or develop gradually during adolescence or adulthood. They may include:

The accelerated phase may cause persistent fever, marked tiredness, swollen lymph nodes, an enlarged liver or spleen, jaundice, unusual bleeding, or a rapid decline in health. Blood tests may show falling levels of red blood cells, white blood cells, and platelets. These symptoms need urgent medical assessment because they may reflect HLH, a serious but treatable immune complication.

- Light-colored or silvery hair, sometimes with a metallic appearance
- Skin that is lighter than that of other family members
- Light sensitivity, also called photophobia

- Rapid, involuntary eye movements called nystagmus
- Reduced sharpness of vision
- Eyes that appear lighter in color
- Muscle weakness
- Tremor or poor coordination
- Difficulty walking or keeping balance
- Numbness, tingling, or reduced sensation
- Slower thinking or changes in school or work performance
- Seizures in some people

Causes and risk factors

Chediak-Higashi syndrome results from disease-causing variants in both copies of the LYST gene. LYST helps control the size, movement, and release of lysosomes and related cell structures.

In immune cells, abnormal lysosomes can interfere with the destruction of germs. In pigment cells, melanin forms large clumps instead of being distributed evenly. Platelets may lack or have abnormal dense granules, which contain substances needed for normal clot formation. Similar problems within nerve cells may contribute to progressive neurologic symptoms.

The condition follows an autosomal recessive inheritance pattern. This means an affected person usually inherited one altered LYST gene copy from each parent. Parents who carry one altered copy generally do not have the syndrome.

When both parents are carriers, each pregnancy has:

These probabilities apply separately to each pregnancy. Genetic counseling can help families understand test results, inheritance, testing for relatives, and reproductive options.

Having a family history or parents who are related by blood can increase the chance that both parents carry the same rare gene variant. However, the condition may also appear in a family with no previously recognized history.

- A 1 in 4 chance of producing a child with the condition
- A 1 in 2 chance of producing a child who is a carrier
- A 1 in 4 chance of producing a child who inherited neither altered copy

Diagnosis

Diagnosis is based on the person's features, laboratory findings, and genetic testing. Because Chediak-Higashi syndrome is rare, evaluation often involves specialists in immunology, hematology, genetics, neurology, and ophthalmology.

A complete blood count may identify low levels of certain blood cells. A laboratory professional can examine a blood smear under a microscope. Very large granules within several types of white blood cells are a characteristic finding and may provide an important early clue.

Other testing may include:

If the accelerated phase is suspected, doctors may order blood counts, liver tests, clotting tests, triglycerides, fibrinogen, ferritin, and tests for inflammation or immune activation. Bone marrow testing may sometimes be used. No single HLH result should be interpreted alone; doctors consider the overall pattern.

Other inherited conditions can also cause light pigmentation, immune problems, or bleeding. These include Griscelli syndrome, Hermansky-Pudlak syndrome, and some inherited forms of HLH. Genetic testing helps distinguish among them.

When a familial LYST variant is known, relatives may be offered targeted testing. Testing before or during pregnancy may also be possible after counseling with a genetics professional.

- Genetic testing for harmful variants in the LYST gene
- Immune function tests, including tests of natural killer cell activity
- Platelet function or bleeding evaluations
- Microscopic examination of hair, which may show large, uneven pigment clumps
- Eye and vision examinations
- Neurologic assessment and, when needed, nerve or brain testing

Treatment and management

Care is individualized and usually coordinated through a center experienced in inherited immune disorders and HLH. Treatment addresses infections, bleeding, vision and skin concerns, neurologic symptoms, and the risk of accelerated-phase disease.

Allogeneic hematopoietic stem cell transplantation , often called a bone marrow or stem cell transplant, is the main treatment for the immune and blood-related features. Donor stem cells replace the person's blood-forming cells with cells that have normal LYST function.

Transplantation may reduce the risk of severe infections and future accelerated-phase episodes. It is generally considered before major organ damage develops, but the timing depends on the person's health, disease pattern, donor options, and transplant-center assessment.

A transplant has important risks, including serious infection, organ effects, rejection, and graft-versus-host disease, in which donor immune cells attack the recipient's tissues. Families should discuss expected benefits and risks with an experienced transplant team. A successful transplant does not reliably prevent progressive neurologic problems because it does not replace nerve cells throughout the body.

Bacterial infections require prompt evaluation and treatment. Depending on the person's infection history and immune function, specialists may consider preventive antimicrobial treatment. Vaccination plans should be reviewed with the immunology or transplant team because recommendations may change before and after transplantation.

The accelerated phase requires urgent specialist care. Treatment aims to control the overactive immune response, support affected organs, and prepare eligible patients for stem cell transplantation. HLH-directed therapy may include corticosteroids like prednisone or hydrocortisone , chemotherapy or immune-suppressing medicines, and other targeted treatments selected by the specialist team.

Bleeding risk should be discussed before surgery, dental work, or invasive tests. The hematology team may recommend specific laboratory evaluation or supportive treatment. People should not start aspirin, ibuprofen, supplements, or other products that may affect platelets without checking with their clinician.

Additional management may include:

- Sunglasses, corrective lenses, and low-vision support
- Sun-protective clothing and broad-spectrum sunscreen
- Physical or occupational therapy for weakness and coordination problems
- Neurologic monitoring and treatment of specific symptoms
- Educational or workplace support when vision or neurologic changes affect daily activities
- Genetic counseling and psychosocial support for the individual and family

Complications

The main early complications are severe or recurrent infections, bleeding, and accelerated-phase HLH. Serious infections can spread to the bloodstream or damage the

lungs and other organs.

HLH may cause low blood cell counts, liver inflammation, clotting problems, neurologic injury, and failure of multiple organs. Early recognition and treatment are important.

Long-term nervous system complications may include peripheral neuropathy, which is damage to nerves outside the brain and spinal cord; difficulty with balance and coordination; muscle weakness; tremor; and changes in thinking. These problems may progress even after successful transplantation.

Vision impairment and light sensitivity may affect school, work, driving, and daily activities. Sun exposure can damage lightly pigmented skin, so ongoing protection is important.

Complications may also result from intensive immune treatment or transplantation. The care team monitors for infection, medicine effects, graft-versus-host disease, organ problems, and changes in blood counts.

Follow up

Routine follow-up should be planned with the immunology, hematology, transplant, genetics, eye, and neurology teams as appropriate. Visits may include blood counts, liver tests, infection review, bleeding assessment, vision checks, and evaluation of movement, strength, sensation, learning, or memory.

Families should have a written plan explaining whom to call for fever, infection symptoms, bleeding, or possible HLH. Instructions may be different during immune-suppressing treatment or after transplantation.

Contact the care team promptly for a new fever, worsening cough, painful skin redness, pus or drainage, unusual bruising, repeated nosebleeds, increasing weakness, new balance problems, or a major change in energy. Fever thresholds and response plans should follow the person's specialist instructions.

Seek urgent medical assessment for persistent fever with marked tiredness, abdominal swelling, jaundice, rapidly increasing bruising, or a sudden decline in health. These symptoms can occur during the accelerated phase but may have other causes.

Call emergency services for trouble breathing, a seizure lasting several minutes or repeated seizures, fainting, severe confusion, uncontrolled bleeding, blue or gray lips, or difficulty waking the person.

Sources

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