CONDITION

Aase syndrome

Learn about Aase syndrome, a very rare condition involving anemia and congenital differences of the thumbs or other bones, including diagnosis, treatment, and follow-up.

WHAT IT IS
Very rare congenital anemia with skeletal differences

BODY SYSTEM
Blood and bones

MAIN SYMPTOMS
Pale skin, fatigue, shortness of breath, thumb differences

WHAT CAUSES IT
Unknown, sometimes inherited

HOW IT IS DIAGNOSED
Blood tests, physical findings, genetic testing, sometimes bone marrow biopsy

MAIN TREATMENT
Anemia treatment and specialist supportive care

CAN IT BE CURED?
Sometimes - transplant corrects marrow, not bones

IS IT AN EMERGENCY?
Sometimes - with severe breathing difficulty

LONG-TERM OUTLOOK
Variable, with some needing repeated anemia treatment

Overview

Aase syndrome is a very rare condition involving anemia and differences in how certain bones develop before birth. The most characteristic skeletal finding is a thumb with three bones instead of the usual two. This is called a triphalangeal thumb. Other hand, arm, shoulder, facial, or heart differences may also occur.

The anemia usually results from reduced production of red blood cells in the bone marrow. Bone marrow is the soft tissue inside bones that makes blood cells. Red blood cells carry oxygen throughout the body. When too few are produced, a person may look pale, tire easily, or become short of breath.

Aase syndrome has been described in only a small number of families and medical reports. Its definition has also changed over time. Some experts consider it part of the spectrum of

Diamond-Blackfan anemia syndrome, another rare disorder in which the bone marrow does not make enough red blood cells. Others use Aase syndrome as a descriptive diagnosis for the combination of anemia and particular skeletal differences. Because of this uncertainty, a person's medical team may use Diamond-Blackfan anemia guidance when planning testing, treatment, and monitoring.

The condition can vary considerably. Some people need repeated treatment for anemia, while others have milder blood problems. Skeletal differences may affect appearance only or may interfere with hand movement. Care usually involves a hematologist, who specializes in blood disorders, along with other specialists based on the person's needs.

Symptoms

Signs may be present at birth or become noticeable during infancy. Symptoms depend on the severity of the anemia and the congenital differences.

Possible effects of anemia include:

A thumb may have three bones, giving it a long or finger-like appearance. One or both thumbs can be affected. The thumb may have limited movement, and the muscles at its base may be small. Some people have reduced or absent knuckles, narrow or sloping shoulders, or differences involving the forearms.

Other findings reported in people diagnosed with Aase syndrome include a cleft palate, small or unusually shaped ears, drooping upper eyelids, and congenital heart defects. These features are not present in everyone. Their presence alone does not establish the diagnosis.

Severe shortness of breath, fainting, chest pain, blue or gray lips, extreme weakness, or difficulty waking requires emergency medical attention. These can be signs that the body is not receiving enough oxygen, although they may also have other causes.

- Pale skin, lips, or nail beds
- Low energy, unusual sleepiness, or weakness
- Poor feeding or reduced activity in an infant
- Shortness of breath
- A fast heartbeat
- Slow growth or difficulty gaining weight

Causes and risk factors

The exact cause of Aase syndrome has not been established. Older reports suggested that it may sometimes follow an autosomal dominant inheritance pattern. This means that one altered copy of a gene could be enough to cause the condition. However, a single gene responsible for all cases has not been confirmed.

Diamond-Blackfan anemia syndrome can be caused by changes in genes involved in making ribosomes. Ribosomes are structures inside cells that help build proteins. Developing red blood cells are especially sensitive when ribosomes do not work normally. This can reduce red blood cell production and may also affect development of the thumbs, face, heart, or other parts of the body.

Because Aase syndrome may overlap with Diamond-Blackfan anemia, clinicians may test genes linked to that disorder. A negative genetic test does not necessarily rule out the condition. Current testing cannot identify the cause in every person with a compatible pattern of anemia and congenital differences.

A person may be the first in a family to have the condition. This can happen because of a new genetic change or because the cause is not inherited in a simple way. When a disease-causing genetic change is found, a genetic counselor can explain what it may mean for parents, siblings, and future children. The chance of inheritance depends on the specific result rather than the diagnostic name alone.

Aase syndrome is present from birth. It is not caused by diet, parenting, an infection during everyday contact, or something a person did.

Diagnosis

Diagnosis can be challenging because Aase syndrome is exceptionally rare and does not have one universally accepted diagnostic test. Evaluation usually combines the person's blood results, physical findings, medical history, and genetic testing.

A complete blood count measures red blood cells, white blood cells, platelets, and hemoglobin, the oxygen-carrying protein in red blood cells. Anemia is shown by low hemoglobin or a low red blood cell level. The red cells may be larger than usual, a finding called macrocytosis.

A reticulocyte count measures young red blood cells. A low count suggests that the bone marrow is not producing enough new cells. White blood cell and platelet levels are often less affected, although results can vary.

Additional blood tests may look for nutritional deficiencies, inflammation, infection, bleeding, kidney or liver disease, and other explanations for anemia. In a suspected Diamond-Blackfan

anemia-related disorder, clinicians may check fetal hemoglobin or red-cell adenosine deaminase activity. These results can support the diagnosis but are not conclusive by themselves.

A bone marrow aspiration or biopsy may be considered. During this procedure, a small sample of liquid marrow or marrow tissue is removed, usually from the hip bone. The sample may show a marked reduction in developing red blood cells while other blood cell lines remain relatively preserved.

X-rays can define the structure of the thumbs, hands, arms, or shoulders. An echocardiogram, which uses ultrasound to examine the heart, may be appropriate when a congenital heart difference is suspected. Other imaging depends on the physical examination.

Genetic testing may use a panel that includes genes associated with Diamond-Blackfan anemia and other inherited bone marrow failure disorders. Testing should be interpreted with a genetics professional because some findings are uncertain and do not prove that a genetic change caused the symptoms.

Treatment and management

Treatment is based on the severity of anemia, the person's age, test results, and the effects of any congenital differences. Because evidence specific to Aase syndrome is limited, a hematologist may use established approaches for Diamond-Blackfan anemia or other disorders of reduced red blood cell production.

Red blood cell transfusions can raise hemoglobin and improve oxygen delivery. They may be needed when anemia is severe, causes symptoms, or affects growth and development. Some people need transfusions only during certain periods, while others need them regularly.

Repeated transfusions can cause excess iron to build up in the liver, heart, and hormone-producing organs. The body has no efficient way to remove this additional iron. Clinicians therefore monitor iron levels and may use imaging to measure iron in organs. Iron chelation medicines help the body remove excess iron when treatment is needed.

Corticosteroids like prednisone or hydrocortisone can increase red blood cell production in some people with Diamond-Blackfan anemia. These medicines do not work for everyone and can cause important effects on growth, bones, blood pressure, blood sugar, infection risk, and the eyes. The decision to try or continue a corticosteroid requires specialist supervision. It should not be started, stopped, or changed without medical guidance.

A hematopoietic stem cell transplant replaces the blood-forming system with stem cells from a donor. It can correct the bone marrow disorder but does not reverse congenital skeletal

differences. Transplantation carries serious short- and long-term risks, so it is generally considered only in selected situations after detailed evaluation at an experienced center.

Hand therapy may help with strength and function. An orthopedic or hand surgeon can assess whether surgery could improve movement or stability. Heart defects, cleft palate, or other structural findings are managed by the relevant specialists. Nutritional and developmental support may be useful when anemia or feeding problems have affected growth.

People should not take iron supplements unless testing shows that they need them and a clinician recommends treatment. Anemia caused by poor red blood cell production is not the same as iron-deficiency anemia, and unnecessary iron may add to iron overload.

Complications

Untreated or severe anemia can reduce oxygen delivery to the body's tissues. It may affect energy, feeding, growth, exercise tolerance, and heart function. Prompt treatment can reduce these effects.

Potential complications also come from long-term treatment. Repeated transfusions may lead to iron overload or, less commonly, immune reactions against donated blood cells. Corticosteroids can affect growth, bone strength, metabolism, and infection risk. Stem cell transplantation can cause infection, organ injury, infertility, or graft-versus-host disease, in which donor immune cells attack the recipient's tissues.

Thumb and upper-limb differences may make grasping, writing, dressing, or other daily tasks harder. Early occupational therapy and an individualized surgical assessment can help preserve function.

People with Diamond-Blackfan anemia syndrome have increased risks of certain cancers and other long-term health problems. It is not clear whether every person given the historical diagnosis of Aase syndrome has the same risks. The medical team should decide whether Diamond-Blackfan anemia surveillance is appropriate based on the person's clinical and genetic findings.

Follow up

Regular follow-up is important even when anemia is stable. The schedule depends on age, treatment, and the certainty of the diagnosis.

Routine visits may include:

Contact the treating team promptly for a clear increase in paleness, fatigue, shortness of breath, fast heartbeat, poor feeding, reduced activity, or unexpected bruising. These symptoms need assessment but are not always an emergency.

Seek urgent medical advice for a fever in someone who has had a stem cell transplant, is taking immune-suppressing medicine, or has been told that their immune system is impaired. Emergency care is appropriate for severe breathing difficulty, chest pain, fainting, blue or gray lips, confusion, or signs of a serious transfusion reaction such as breathing trouble, swelling, or rapidly worsening illness during or soon after a transfusion.

- A blood count and review of anemia symptoms
- Monitoring of growth, development, and nutrition
- Assessment of hand function and other congenital differences
- Checks for transfusion-related iron overload
- Review of corticosteroid or transplant-related effects
- Heart, bone, hormone, and cancer surveillance when appropriate
- Updates to genetic counseling as testing improves

Sources

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