CONDITION

Systemic mastocytosis

Systemic mastocytosis is a condition in which abnormal mast cells build up in internal organs and release symptom-causing chemicals.

WHAT IT IS
Clonal mast cell buildup in organs outside the skin

BODY SYSTEM
Immune system, bone marrow, skin, gut, and bones

MAIN SYMPTOMS
Flushing, itching, abdominal symptoms, severe allergic reactions

WHAT CAUSES IT
Usually an acquired KIT gene change

HOW IT IS DIAGNOSED
Bone marrow biopsy with mast cell markers and KIT testing

MAIN TREATMENT
Symptom medicines and targeted therapy for advanced forms

CAN IT BE CURED?
Sometimes - stem cell transplant may cure selected advanced cases

IS IT AN EMERGENCY?
Sometimes - breathing trouble, fainting, or throat swelling

LONG-TERM OUTLOOK
Often stable for years; advanced forms can shorten life

Overview

Systemic mastocytosis is a condition in which abnormal mast cells collect in internal organs. "Systemic" means that areas beyond the skin are involved, most often the bone marrow. The gut, liver, spleen, lymph nodes, and bones may also be affected.

Mast cells are part of the immune system. They release histamine and other chemicals during allergic and inflammatory reactions. In systemic mastocytosis, there are too many abnormal mast cells, and they may release these chemicals too easily.

This can cause flushing, itching, digestive problems, light-headedness, or anaphylaxis. Anaphylaxis is a severe allergic reaction that can affect breathing or blood pressure. In more advanced forms, the buildup of mast cells can interfere with how organs work.

Systemic mastocytosis is divided into several forms. Nonadvanced forms include bone marrow mastocytosis, indolent systemic mastocytosis, and smoldering systemic mastocytosis. Advanced forms include aggressive systemic mastocytosis, systemic mastocytosis with another blood or bone marrow cancer, and mast cell leukemia.

These forms can behave very differently. Many people have a nonadvanced condition that remains stable for years. Advanced systemic mastocytosis needs closer monitoring and treatment aimed at reducing the abnormal mast cells.

Symptoms

Symptoms may come from the chemicals released by mast cells, the buildup of mast cells in organs, or both. They may be constant, come in episodes, or change over time.

Common symptoms include:

Some people have bone thinning, called osteoporosis, which can lead to fractures. Others have enlarged lymph nodes, liver, or spleen.

Symptoms caused by organ damage are more concerning. These may include unintentional weight loss, poor absorption of food, fluid collecting in the abdomen, low blood cell counts, or reduced liver function. These findings are more typical of advanced forms and are not present in everyone.

Episodes can have triggers. Possible triggers include insect stings, alcohol, sudden temperature changes, skin friction, emotional stress, infections, and certain medicines. Triggers are individual. A substance that causes symptoms in one person may be well tolerated by another.

- Flushing, itching, hives, or reddish-brown skin spots
- Abdominal pain, diarrhea, nausea, heartburn, or bloating
- Light-headedness, fainting, a racing heartbeat, or low blood pressure
- Headaches, fatigue, difficulty concentrating, or bone and muscle pain
- Severe allergic reactions, sometimes without hives or other skin symptoms

Causes and risk factors

Systemic mastocytosis usually begins with an acquired change in a gene called KIT . KIT helps control mast cell growth and survival. The most common change is known as KIT D816V.

"Acquired" means the change develops in certain cells during a person's lifetime. It is usually not inherited from a parent and is not something you caused through food, stress, or lifestyle.

There are no well-established lifestyle risk factors. The condition can occur in adults of any background. Systemic mastocytosis in adults is different from skin-limited mastocytosis, which is more often seen in children and may improve as a child grows.

Some people also have hereditary alpha-tryptasemia, an inherited trait that can raise the usual blood tryptase level and may affect mast-cell symptoms. This trait does not itself cause systemic mastocytosis, but it can complicate the interpretation of test results.

Diagnosis

Diagnosis usually begins with a review of symptoms, previous allergic reactions, medicines, skin findings, and possible triggers. Blood tests may include a baseline serum tryptase level. Tryptase is a protein mainly released by mast cells.

A raised baseline tryptase can support the diagnosis, but it does not confirm systemic mastocytosis by itself. Some people with the condition have a tryptase level below the usual diagnostic threshold. Other conditions and inherited traits can also raise tryptase.

A bone marrow biopsy is usually the key test. A small sample of marrow is removed, commonly from the back of the hip bone, and examined for clusters of abnormal mast cells. Laboratory tests check the appearance of the cells and look for unusual surface markers, such as CD25, CD2, or CD30.

Testing for an activating KIT gene change is also important. Highly sensitive testing may find KIT D816V in blood or bone marrow even when the amount of abnormal genetic material is low.

Diagnosis is based on an accepted combination of findings. These include clusters of mast cells in bone marrow or another internal organ, abnormal mast-cell shape or markers, a KIT mutation, and a persistently raised baseline tryptase. A skin biopsy can identify mast cells in a skin lesion, but it cannot by itself confirm systemic involvement.

If systemic mastocytosis is found, further tests help identify its form and check organ health. These may include:

- A complete blood count and liver chemistry tests
- Bone-density scanning and, when needed, bone imaging
- Ultrasound or other imaging of the liver, spleen, or lymph nodes

- Tests for another blood or bone marrow condition
- Measurement of KIT mutation levels in selected cases

Treatment and management

Treatment is matched to the form of systemic mastocytosis, the symptoms it causes, and whether organs are being damaged. Care often involves a hematologist, who specialises in blood and bone marrow conditions, together with an allergist or immunologist.

For nonadvanced systemic mastocytosis, treatment often focuses on controlling the effects of mast-cell chemicals. Options may include antihistamines like cetirizine or loratadine for itching and flushing, acid-reducing medicines like omeprazole or lansoprazole for stomach symptoms, and other medicines that block or limit mast-cell mediators.

Many people at risk of anaphylaxis are advised to carry prescribed adrenaline, also called epinephrine, auto-injectors. You should receive clear instructions about when and how to use them. People with an allergy to bee or wasp venom may be offered venom immunotherapy, which gradually reduces sensitivity under specialist supervision.

Treatment may also address specific complications. This can include medicines for osteoporosis, nutritional support for poor absorption, or treatment for anemia and other low blood counts.

Avoiding known personal triggers can help, but broad restrictions are not usually helpful. Do not stop a necessary medicine or remove large groups of foods without medical advice. If you need surgery, anesthesia, contrast dye, or a dental procedure, tell the care team about systemic mastocytosis in advance so an individual plan can be made.

Targeted medicines can reduce the number and activity of abnormal mast cells. Avapritinib may be used for eligible adults with indolent systemic mastocytosis whose symptoms remain inadequately controlled, and for certain advanced forms. Midostaurin is another targeted treatment used for advanced systemic mastocytosis. Availability and eligibility differ by country and individual circumstances.

Other treatments that reduce abnormal blood cells, such as cladribine or interferon, are used in selected cases. If there is an associated blood cancer, that condition may also need its own treatment.

An allogeneic stem cell transplant replaces the blood-forming system with donor cells. It may offer a chance of cure for a small, carefully selected group with advanced disease. It also has substantial risks and is not a routine treatment for indolent systemic mastocytosis.

Complications

Anaphylaxis is an important possible complication. It may be triggered by an insect sting, food, medicine, or another exposure, but sometimes no trigger is found.

Long-term effects can include osteoporosis and fractures. Digestive symptoms may interfere with eating or nutrient absorption. Repeated episodes of low blood pressure can cause fainting and injuries.

Advanced systemic mastocytosis can damage the bone marrow, liver, spleen, or gut. Possible results include anemia, easy bruising, frequent infections, liver dysfunction, fluid in the abdomen, weight loss, and an enlarged spleen.

Some people have systemic mastocytosis together with another blood or bone marrow cancer. This is a specific advanced category and strongly affects treatment and outlook. It does not mean that everyone with indolent systemic mastocytosis will develop leukemia.

Prevention

Systemic mastocytosis cannot currently be prevented. The KIT change that usually causes it develops within affected cells and is not known to result from lifestyle choices.

You may be able to prevent some symptom episodes by learning your personal triggers and following an anaphylaxis plan. Keeping a record of symptoms and exposures can help identify patterns. Avoiding everything reported as a possible mast-cell trigger is unnecessary and may make daily life harder.

Regular monitoring can help find bone loss, blood-count changes, or organ problems before they cause major symptoms. This does not prevent the underlying condition, but it can reduce the impact of complications.

Living with it and what to expect

The course depends mainly on whether the condition is nonadvanced or advanced. Most adults diagnosed with indolent systemic mastocytosis have a long-lasting condition that may remain stable for many years. Symptoms can still fluctuate, even when the number of mast cells has not clearly changed.

Skin symptoms may persist. Digestive problems and allergic-type episodes may improve with treatment but can return after infections, stress, or exposure to a personal trigger. A tryptase

result can help with monitoring, but the number does not always match how severe you feel.

Routine follow-up may include a review of symptoms and reactions, blood counts, liver tests, tryptase, and bone health. A sudden change in symptoms, blood results, weight, or organ size may lead to additional testing.

Advanced forms are more likely to progress and may shorten life. Their course is influenced by organ damage, genetic findings, response to treatment, and whether another blood cancer is present. New targeted treatments have expanded the options available, but they do not remove the need for ongoing monitoring.

Many people with nonadvanced disease continue working, exercising, travelling, and having families. Planning can make these activities safer. This may include carrying emergency medicine, wearing medical identification, and discussing pregnancy, travel, or planned procedures with the relevant care team.

When to get medical help

Call emergency services for possible anaphylaxis, especially if you have:

If you have been prescribed an epinephrine auto-injector, use it as instructed without waiting to see whether the reaction settles. Emergency assessment is still needed after its use because symptoms can return.

Contact your usual care team promptly for new or worsening symptoms such as unexplained weight loss, persistent diarrhea, increasing abdominal swelling, jaundice, unusual bruising, repeated infections, or new severe bone pain.

Routine follow-up is appropriate for stable flushing, itching, digestive symptoms, or fatigue that are already part of your care plan. Mention any change in their pattern, frequency, or effect on daily life at your next review.

- Trouble breathing, wheezing, or throat or tongue swelling
- Fainting, collapse, confusion, or severe weakness
- A sudden widespread reaction involving more than one body system
- Rapidly worsening symptoms after an insect sting, food, or medicine

Common questions

Is systemic mastocytosis cancer?

It is classified as a clonal blood and bone marrow condition, meaning abnormal cells have grown from one changed cell. Some forms behave slowly and may remain stable for decades. Advanced forms behave more like other blood cancers and require treatment to reduce the abnormal cells.

What is the life expectancy with systemic mastocytosis?

People with nonadvanced forms often have a life expectancy close to that of the general population, although symptoms can affect quality of life. Advanced forms can shorten life. Outlook is influenced by organ damage, genetic changes, associated blood conditions, and response to treatment.

Can a normal tryptase result rule it out?

No. A baseline tryptase level is useful, but it cannot confirm or exclude systemic mastocytosis on its own. Diagnosis relies on bone marrow or other tissue findings together with mast-cell markers and genetic testing.

Can systemic mastocytosis turn into leukemia?

Mast cell leukemia is a rare advanced form of mastocytosis. Progression from an indolent form is possible but is not the usual course. Changes in blood counts, organ function, or symptoms are assessed during follow-up.

Do I need to avoid all common mast-cell triggers?

No. Trigger lists are not universal. Avoid exposures that have clearly caused your symptoms, while continuing foods, activities, and medicines you tolerate. Discuss suspected medicine reactions before stopping treatment.

Is systemic mastocytosis inherited?

Usually not. The common KIT mutation is generally acquired and is found only in affected cells. Rare inherited conditions can alter tryptase levels or mast-cell reactions, but they are separate from systemic mastocytosis.

Sources

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