Systemic mastocytosis

Description

Systemic mastocytosis is a blood disorder that can affect many different body systems. Individuals with the condition can develop signs and symptoms at any age, but it usually appears after adolescence.

Signs and symptoms of systemic mastocytosis often include extreme tiredness (fatigue), skin redness and warmth (flushing), nausea, abdominal pain, bloating, diarrhea, the backflow of stomach acids into the esophagus (gastroesophageal reflux), nasal congestion, shortness of breath, low blood pressure (hypotension), lightheadedness, and headache. Some affected individuals have attention or memory problems, anxiety, or depression. Many individuals with systemic mastocytosis develop a skin condition called urticaria pigmentosa, which is characterized by raised patches of brownish skin that sting or itch with contact or changes in temperature. Nearly half of individuals with systemic mastocytosis will experience severe allergic reactions (anaphylaxis).

There are five subtypes of systemic mastocytosis, which are differentiated by their severity and the signs and symptoms. The mildest forms of systemic mastocytosis are the indolent and smoldering types. Individuals with these types tend to have only the general signs and symptoms of systemic mastocytosis described above. Individuals with smoldering mastocytosis may have more organs affected and more severe features than those with indolent mastocytosis. The indolent type is the most common type of systemic mastocytosis.

The severe types include aggressive systemic mastocytosis, systemic mastocytosis with an associated hematologic neoplasm, and mast cell leukemia. These types are associated with a reduced life span, which varies among the types and affected individuals. In addition to the general signs and symptoms of systemic mastocytosis, these types typically involve impaired function of an organ, such as the liver, spleen, or lymph nodes. The organ dysfunction can result in an abnormal buildup of fluid in the abdominal cavity (ascites). Aggressive systemic mastocytosis is associated with a loss of bone tissue (osteoporosis and osteopenia) and multiple bone fractures. Systemic mastocytosis with an associated hematologic neoplasm and mast cell leukemia both involve blood cell disorders or blood cell cancer (leukemia). Mast cell leukemia is the rarest and most severe type of systemic mastocytosis.

Individuals with the milder forms of the condition generally have a normal or near normal life expectancy, while those with the more severe forms typically survive months

or a few years after diagnosis.

Frequency

Systemic mastocytosis is estimated to occur in 1 per 10,000 to 20,000 individuals worldwide.

Causes

Systemic mastocytosis occurs when white blood cells called mast cells, which are produced in bone marrow, abnormally accumulate in one or more tissues. In most cases of systemic mastocytosis, the accumulated mast cells have a mutation in a gene called *KIT*. The *KIT* gene provides instructions for making a protein that plays an important role in development and activity of mast cells. The KIT protein stimulates chemical signaling pathways that are involved in the growth and division (proliferation) of many types of cells, including mast cells. In systemic mastocytosis, *KIT* gene mutations are somatic, which means they are acquired during a person's lifetime. These mutations result in a KIT protein that is always turned on (activated). As a result, signaling pathways are overactive, leading to increased production and accumulation of mast cells.

In systemic mastocytosis, mast cells most often accumulate in the bone marrow, which is where new blood cells are made. Mast cells can also gather in other tissues such as the gastrointestinal tract, lymph nodes, spleen, or liver. In severe cases, excessive accumulation of mast cells can interfere with normal organ functioning. Mast cells normally trigger inflammation during an allergic reaction. When mast cells are activated by an environmental trigger, they release proteins (called mediators) that signal an immune response. In systemic mastocytosis, excess mast cells mean more mediator proteins are being released in the tissues where the cells accumulate, leading to an increased immune response. In affected individuals, triggers that can activate mast cells include changes in temperature, friction and minor trauma, surgery, insect stings, vaccines, anxiety, and stress. Certain medications can also be triggers, including aspirin, opioids, or non-steroidal anti-inflammatory drugs (NSAIDs).

Mutations in additional genes seem to modify the severity of systemic mastocytosis, often resulting in a more aggressive disease and shorter survival. These genes primarily play roles in controlling the proliferation of cells or regulating the activity of other genes that are important in development.

Learn more about the genes associated with Systemic mastocytosis

- ASXL1
- DNMT3A
- KIT
- RUNX1
- TET2

Additional Information from NCBI Gene:

- SRSF2

Inheritance

This condition is generally not inherited but arises from a somatic mutation in the body's cells that occurs after conception.

Other Names for This Condition

- Mast cell disease, systemic
- Mastocytosis, systemic
- Systemic mast cell disease
- Systemic mast-cell disease
- Systemic mastocytoses
- Systemic tissue mast cell disease

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Systemic mast cell disease (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0221013/)

Genetic and Rare Diseases Information Center

- Systemic mastocytosis (https://rarediseases.info.nih.gov/diseases/8616/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Systemic mastocytosis%22)

Catalog of Genes and Diseases from OMIM

- MASTOCYTOSIS, CUTANEOUS; MASTC (https://omim.org/entry/154800)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Mastocytosis,+Systemic%5BMAJR%5D%29+AND+%28systemic+mastocytosis%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

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