

Gastrointestinal Stromal Tumors

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What is GIST?

Gastrointestinal stromal tumors, or GISTs, are a relatively uncommon type of cancer that occurs in the gastrointestinal (GI) tract. GISTs are believed to start in special cells found in the wall of the GI tract, called the *interstitial cells of Cajal* (ICCs), or in very early cells that can develop into ICCs. ICCs are part of the autonomic nervous system, which sends signals to the GI tract. Some have called these cells the "pacemakers" of the GI tract. The nerve signals they send cause muscles of the digestive organs to contract, which helps to move food and liquid through the GI tract.

Although these tumors can start anywhere in the GI tract, they occur most often in the stomach (50% to 70%) or the small intestine (20% to 30%). The rest are found in the esophagus, large intestine (colon and rectum), and anus.

How many people develop GIST?

Until recently, GISTs were thought to be extremely rare. However, recent advances in diagnosis and classification methods have shown that GISTs may be more common than previously believed. Based on data from a Swedish epidemiology study, experts believe that in the U.S., as many as 4,500 to 6,000 new cases of GIST occur each year. Of these, about 1,500 have already spread to distant sites when they are initially found.

Risk Factors

There are no known factors that have specifically been identified as increasing a patient's risk for GIST. The disease is thought to be predominantly caused by a mutation or change in an enzyme called Kit (CD117), which is found on the surface of normal cells. In healthy individuals, the role of Kit is to signal cells to grow and divide. However, in patients with GIST, a malfunctioning Kit signals the cells to constantly grow and divide out of control, and they become cancerous.

In rare cases, GISTs have been found in several members within the same family. These family members inherited a gene mutation (usually the c-Kit that leads to GIST. But most GISTs are sporadic (they are not passed down from generation to generation), and their cause is unknown.

Why GIST Develops (Pathophysiology)

The exact cause of GIST is unknown. However, we do know that there is a change in an oncogene called *c-kit* of almost all patients with GIST. The *c-kit* gene is found in all cells of the body. It leads to the formation of a protein called KIT. This protein causes the cell to grow and divide. Usually the *c-kit* gene is inactive. It is only activated if there is a need for more interstitial cells of Cajal (ICCs). In most GISTs the *c-kit* gene is mutated and is always active. This may explain why the cancer forms. The cells are always growing and dividing. In families that have many members with GISTs, doctors have found inherited mutations of the *c-kit* gene.

In some GISTs, a different gene mutation causes the cell to make too much of a protein called PDGFRA. This has the same effect on the cell as does KIT.

These proteins (KIT and PDGFRA) act as enzymes called tyrosine kinases. These are important in the diagnosis and treatment of GIST.

GIST Symptoms

GISTs are difficult to diagnose because in the early stages of the disease, they often do not cause any physical symptoms. In later stages, the most common symptoms of GIST are:

- Vague abdominal pain
- Early feeling of fullness (satiety)
- Vomiting
- Abdominal bleeding (blood in stool or vomit)
- Fatigue due to anemia (low blood counts)

However, these symptoms may also be an indicator of a wide range of other, less serious, conditions. People who experience any of these symptoms should speak with their doctor.

GIST Diagnosis

GIST is often diagnosed during routine tests for other, more common, conditions. To obtain more knowledge about the cause of a patient's symptoms, a doctor might conduct the following tests:

- Upper endoscopy (inspection of organs or cavities using a device called endoscope)
- Laparoscopy (abdominal exploration using a device called a laparoscope)
- Colonoscopy (examination of the lining of the entire rectum and colon)
- Barium X-rays (helps find abnormalities of the lining of the esophagus, stomach, and intestines)
- Ultrasound (using sound waves to take images of internal organs)
- Computed tomography (CT or CAT) scan (a radiographic technique that produces a film that represents a detailed cross section of tissue structure)
- Magnetic resonance imaging (MRI) (another medical imaging technique)
- Positron emission tomography (PET) (another medical imaging technique)

These tests help determine whether patients have a tumor or tumors, where the tumor or tumors are located, how big they are, and whether or not the cancer has spread outside of the GI system (metastasized).

If a tumor is present, a tissue sample, or biopsy, is needed for the doctor to determine whether it is malignant (cancerous) or benign (non-cancerous), and to determine what type of cancer it is. If the tumor is a sarcoma, further testing of the tissue will determine the type of sarcoma and how rapidly the disease is likely to spread.

After the biopsy, the tumor sample is sent to a specialist called a pathologist who examines the cells and tissues. The pathologist will also test the tumor sample for the presence of Kit/CD117 - the enzyme thought to be responsible for most GISTs.

Prognostic Factors

Important factors include the size of the tumor, its grade, and whether it has already shown signs of spread in the abdomen.

Doctors often use these factors to separate patients into very low-, low-, intermediate-, and high-risk groups. These groupings describe the risk of the cancer spreading to distant areas in the body.

Whether or not a tumor has already spread to other areas at the time it is found is an important factor in determining outlook. It may have an effect on whether certain treatment options, such as surgery, are available.

When these tumors are cancerous and spread away from the initial (primary) site, they most often spread within the abdomen, and, in particular, to the liver. Less often, they may also spread to the lungs and bone. Spread to the lymph nodes, brain, and elsewhere is not common. About half the time, the tumor is still localized when it is found; one fourth of the time it has spread to nearby tissues and one fourth of the time it has spread to distant sites.

Treatment

Surgery is the standard treatment for primary resectable gastrointestinal stromal tumor (GIST). However, surgical resection is seldom curative, and by 5 years after complete removal of their tumor, half of patients so treated have relapsed.

Imatinib is the first-line treatment in patients with metastatic or unresectable GIST. It has resulted in durable objective response or stable disease in approximately 85% of patients with advanced GIST and is well tolerated.

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