

Essential or Primary Thrombocythemia

No. 12 in a series providing the latest information on blood cancers

Highlights

- Essential thrombocythemia (ET) is one of a group of disorders known as myeloproliferative diseases.
- ET begins with one or more acquired changes (mutations) to the DNA of a single blood-forming cell. This results in the overproduction of blood cells, especially platelets, in the bone marrow.
- About half of individuals with ET have a mutation of the JAK2 gene. The role that this mutation plays in the development of the disorder, and the potential implications for new treatments, is being investigated.
- Individuals with ET may not have symptoms. However, symptoms may include: burning, or throbbing, pain in the feet, headaches, dizziness, blood clots or abnormal bleeding episodes.
- ET does not generally shorten life expectancy. Still, medical supervision of individuals with ET is important to prevent or treat complications.

Introduction

Essential or primary thrombocythemia (ET) is one of several “myeloproliferative diseases,” a term used to describe a group of disorders that share several features, notably the “clonal” overproduction of one or more blood cell lines. All clonal disorders begin with one or more changes (mutations) to the DNA in a single cell: the cells that are in marrow and the blood are the offspring of that one mutant cell. Other myeloproliferative diseases include polycythemia vera and idiopathic myelofibrosis.

The effects of ET result from uncontrolled blood cell production, notably of platelets. Because the disease arises from a change to an early blood-forming cell that has the capacity to form red cells, white cells and platelets, any combination of these three cell lines may be affected – usually each is affected to some degree.

In ET, there is mainly an overproduction of platelet-forming cells, called “megakaryocytes,” in the marrow. This results in the release of too many platelets into the blood. A platelet is a small blood cell. Its function is to start the process of forming a plug (clot) in response to blood vessel injury in order to prevent or minimize bleeding. When platelets are present in very high numbers they may not function normally and may cause a blockage in blood vessels, known as a “thrombus.” Less often, a high number of platelets can also cause bleeding problems.

Another word for platelet is “thrombocyte.” The term “thrombocytopenia” means an excess of platelets in the blood. ET is also called “primary thrombocytopenia.” The term “primary” or “essential” indicates that the increase in platelets is not the result of an underlying condition. “Secondary thrombocytopenia” is the term for a condition that results in very high platelet counts in reaction to another problem, such as inflammatory disease, removal of the spleen, or iron deficiency in adults. These conditions are not myeloproliferative diseases. A patient with secondary thrombocytopenia should have a return to normal platelet counts once the primary disorder is treated successfully.

The cause of ET is not fully understood. About half of patients with ET have a mutation of the JAK2 (Janus kinase 2) gene in their blood cells. Whether or not a patient has the mutation does not appear to affect the nature or course of the disease. Research is under way to determine the precise role of JAK2 mutations and to identify other mutations in ET patients.

There are an estimated number of 0.1 to 2.4 new cases per 100,000 people each year. ET occasionally occurs in older children, but is mostly diagnosed in adult men and women.

ET does not generally shorten life expectancy. However, medical supervision is important to prevent or treat thrombosis, a serious complication that can affect vital organs such as the brain or the heart. Also, for untreated pregnant patients with ET, there is a risk to the survival of the fetus.

This fact sheet discusses the diagnosis, treatments and additional resources for information and support for ET.

How is essential thrombocythemia diagnosed?

Signs, symptoms and complications

Many patients with essential thrombocythemia do not have any symptoms. Patients with signs or symptoms may have:

- Burning or throbbing pain in the feet, sometimes worsened by heat, exercise, or when the legs are hanging down for long periods. The skin of the legs and feet may have a patchy reddish color. “Erythromelalgia,” the medical term for this condition, is caused by diminished blood flow (microcirculation) to the feet and toes.
- Headache, dizziness, weakness or numbness on one side of the body, slurred speech and other signs of inadequate flow of blood to the brain called transient ischemic attacks.
- Thrombosis (abnormal clotting), which usually occurs in an artery, but sometimes occurs in a vein.
- Unexpected or exaggerated bleeding. Abnormal bleeding is infrequent and usually occurs only in the presence of a very high platelet count.
- An enlarged spleen (detected by physical examination or ultrasound imaging). This occurs in about 50 percent of patients.

Thrombosis is a more common complication of ET than is bleeding. This complication can be very serious if the clot blocks blood flow to an organ, such as the brain (causing a stroke) or heart (causing a heart attack). Older patients with underlying vascular disease and very high platelet counts (1,000,000 per microliter and above) may be at highest risk for thrombosis, but there is no definitive way to gauge risk. Clotting complications can occur in patients with a slightly elevated platelet count.

Uncontrolled ET can cause pregnancy complications, including:

- Spontaneous abortion (miscarriage)
- Fetal growth retardation
- Premature delivery
- Placental abruption (premature separation of the placenta and uterus).

Occasionally, ET can transform into another myeloproliferative disorder. The disease can transform into acute leukemia or myelodysplasia, but this is an uncommon occurrence.

Diagnosis

Essential thrombocythemia may be identified in symptom-free patients when a blood test (done as part of a periodic health examination) shows a higher than normal platelet count. Or, a physician may order blood tests for a patient who has a blood clot, unexpected bleeding, or a mildly enlarged spleen and, as a result, note a markedly elevated platelet count.

A platelet count is measured as part of a blood test called a “complete blood count” (CBC). Normal platelet values range from about 175,000 to 350,000 platelets per microliter of blood in most laboratories. ET is a consideration if:

- The platelet count is above 600,000/ml of blood and remains high over a period of observation. Most ET patients have counts above 600,000 platelets per microliter of blood. Occasionally, ET is diagnosed in patients with platelet counts that are high normal (between 350,000 and 600,000 platelets per microliter of blood).
- There is no other evident cause for the elevated platelet count.

The diagnosis of ET cannot be confirmed by laboratory tests alone. Further examination and testing are needed to rule out other conditions that could be the cause of the patient’s high platelet count. In most cases, the diagnosis of ET is made based on:

- A high platelet count that persists over time
- JAK2 mutation in the patient’s blood cells
- A slightly lower than normal blood hemoglobin concentration (mild anemia) and a slightly higher than normal white cell count (especially neutrophils, a type of white blood cell)
- The absence of evidence for other clonal blood diseases that can be accompanied by increased platelets
- An examination of the marrow.

Although a bone marrow examination is not strictly necessary to make the diagnosis, it is often done as it can be helpful to confirm the diagnosis. The marrow of a patient with ET shows a significant increase in platelet-forming cells (megakaryocytes) and masses of platelets.

Generally, a physician will consider other conditions first to determine if any of them are the cause of the increase in platelets. Several conditions can cause an increase in platelets, including:

- Inflammatory disorders, such as active arthritis or gastrointestinal inflammatory disease
- Iron deficiency anemia
- An undetected (occult) cancer
- History of splenectomy (removal of the spleen).

What is the treatment for a patient with essential thrombocythemia?

A hematologist (a physician who specializes in blood disorders) can recommend specific treatment and management for a patient with essential thrombocythemia.

Treatment decisions are based on the patient's risk for clotting or bleeding complications. For some patients with no signs of the disease other than an increased platelet count, the risk of complications may be low. Patients with low risk, especially younger individuals with no other cardiovascular risk factors, may only need periodic medical checkups.

Physicians may use chemotherapy to reduce high platelet counts in patients with previous bleeding or clotting episodes, or in patients who are at high risk for such complications. Risks for clotting complications include:

- A history of a clot
- Cardiovascular risk factors, such as high cholesterol, diabetes, smoking, obesity or hypertension
- Advanced age (although studies are not definitive about this factor)

Risk factors for bleeding include:

- A very elevated platelet count (over 2 million platelets per microliter of blood)
- Standard-dose aspirin or other nonsteroidal anti-inflammatory drug (NSAID) use.

Drug therapy

The drugs used most commonly to treat ET are hydroxyurea (Hydrea®), anagrelide (Agrylin®) and interferon alfa (Intron® A, Roferan-A®).

Hydroxyurea is a myelosuppressive drug (an agent that suppresses the marrow's production of blood cells) that can be used as initial therapy for ET. Hydroxyurea often is successful in decreasing platelet count within several weeks, with few short-term side effects.

There is some evidence that hydroxyurea is associated with an increased risk for patients to develop acute leukemia after long-term therapy. However, it is thought to have much less potential for causing leukemia than other myelosuppressive agents, such as radiophosphorus and alkylating agents, such as melphalan (Alkeran®) and chlorambucil (Leukeran®). Hydroxyurea is generally not used for treating younger patients or patients without symptoms.

Anagrelide is a non-cytotoxic drug (an agent that does not kill cells) that effectively decreases platelet formation in most patients. It has not been associated with increased risk for leukemia and is a therapy alternative to other treatments, such as hydroxyurea.

Side effects of anagrelide can occur, including fluid retention, heart and blood pressure problems, headaches, dizziness, nausea, and diarrhea. Older patients and patients with heart disease are generally not treated with anagrelide.

Interferon alfa is another treatment for lowering platelet counts in patients with ET. However, it is not used in most patients because, in comparison to other treatments for ET, it is less convenient to administer (it is given by injection), can be more costly than some of the other treatment options, and may cause troublesome side effects. Some patients develop moderately severe flu-like symptoms, confusion, depression or other complications.

Low-dose aspirin may be effective for patients with recurring clotting complications. It may also increase bleeding risk. For these reasons, the use of aspirin in treating ET is controversial at present. However, pregnant patients may be treated with low-dose aspirin to reduce the risk of miscarriage, fetal growth retardation, premature delivery or other complications. Aspirin should be avoided for at least one week prior to delivery to reduce any risk of bleeding complications in the mother or the newborn.

Plateletpheresis is a process that uses a device to skim platelets from a patient's blood and then return the plasma (the liquid portion of blood) and red cells to the patient. It is only used in emergency situations, such as acute clotting complications, when the platelet count is very high and needs to be reduced quickly. The platelet-reducing effect of this therapy is temporary.

Research and Clinical Trials

The Leukemia & Lymphoma Society is funding research for myeloproliferative diseases, including research to investigate:

- The potential for developing new treatments to inhibit the activity of an enzyme linked to the JAK2 mutation. Researchers believe this enzyme causes an overproduction of blood cells.
- The identification of other oncogenes (cancer genes) for ET and other myeloproliferative diseases that may be suitable targets for new drug therapies.
- New therapies to prevent or treat thrombosis (clots) associated with ET and other myeloproliferative diseases.

Researchers continue to look for more effective ways to treat ET by conducting clinical trials (research studies) of new therapies or new combinations of therapies.

Current information about specific clinical trials for ET can be obtained by calling the Information Resource Center of The Leukemia & Lymphoma Society at (800) 955-4572 or the National Cancer Institute at (800) 4-CANCER or (800) 422-6237.

The Leukemia & Lymphoma Society

The Leukemia & Lymphoma Society is a national voluntary health agency with chapters throughout the United States and Canada. The Society provides education and support services for the public and for cancer treatment professionals.

Callers may speak directly with an Information Specialist, Monday-Friday, 9 - 6 p.m., ET (800) 955-4572. To contact an Information Specialist, click on Live Help (10 a.m. - 5 p.m.) on the Society's Web site or email us at infocenter@LLS.org.

To find the Society chapter nearest you contact:

The Leukemia & Lymphoma Society

1311 Mamaroneck Avenue
White Plains, NY 10605
(800) 955-4572 or www.LLS.org

The Society provides free fact sheets and booklets that can be ordered via the 800 number or through Free Materials on the Web site, www.LLS.org.

Resources

The Association of Cancer Online Resources (ACOR)

An Internet-based public charity dedicated to improving the quality of care for cancer patients and the quality of life of patients, survivors and caregivers. ACOR provides support and information through its unique online community, which includes mailing lists, information on specific forms of cancer and links to additional resources.

The MPD Foundation

The MPD (Myeloproliferative Diseases) Foundation is a nonprofit organization dedicated to funding research into new treatments for myeloproliferative diseases and ultimately finding a cure. The organization also provides information and support to people who have myeloproliferative diseases.

The National Cancer Institute (NCI)

Part of the National Institutes of Health, NCI functions as a national resources center for information and education about all forms of cancer including myeloproliferative diseases.

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