Glanzmann Thrombasthenia

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Synonyms of Glanzmann Thrombasthenia

- Glanzmann disease
- Glanzmann-Naegeli syndrome
- Glanzmann thrombasthenia
- Glanzmann thrombasthenia, type A
- glycoprotein complex IIb/IIIa, deficiency of
- GP IIb-IIIa complex, deficiency of
- GPIIb/IIIa receptor, deficiency of
- GTA
- platelet fibrinogen receptor deficiency
- thrombasthenia
- thrombasthenia of Glanzmann and Naegeli
- integrin αIIbβ3 receptor, deficiency of

Subdivisions of Glanzmann Thrombasthenia

- No subdivisions found

General Discussion

Glanzmann thrombasthenia (GT) is a rare inherited blood clotting (coagulation) disorder characterized by the impaired function of specialized cells (platelets) that are essential for proper blood clotting. Symptoms of this disorder usually include abnormal bleeding, which may be severe. Prolonged untreated or unsuccessfully treated hemorrhaging associated with Glanzmann thrombasthenia may be life threatening.

Signs & Symptoms

The symptoms of Glanzmann thrombasthenia usually begin at birth or shortly thereafter and include the tendency to bruise and bleed easily and sometimes profusely, especially after surgical procedures. Other symptoms may include susceptibility to easy bruising, nosebleeds (epistaxis), bleeding from the gums (gingival), intermittent gastrointestinal bleeding, and/or variably small or large red or purple-colored spots on the skin that are caused by bleeding in the skin (purpura). Women with GT often also have unusually heavy menstrual bleeding, irregular uterine bleeding, and excess bleeding in childbirth. Rarely, gastrointestinal bleeding and blood in the urine (hematuria) can occur. The

severity of the symptoms varies greatly. Some affected individuals have mild bruising and others have severe hemorrhages that can be life threatening.

Causes

Glanzmann thrombasthenia is inherited in an autosomal recessive pattern. An abnormality in either the gene for αIIb (glycoprotein IIb; GPIIb) or the gene for β3 (glycoprotein IIIa; GPIIIa) results in an abnormal platelet αIIbβ3 (GPIIb/IIIa) integrin family receptor and prevents platelets from forming a plug when bleeding occurs. Many different abnormalities in these genes have been identified. Recent evidence suggests that approximately 0.5% of healthy individuals in the general population are probably carrying one gene with an abnormal variant of αIIb or β3.

Genetic diseases are determined by the combination of genes for a particular trait that are on the chromosomes received from the father and the mother. Recessive genetic disorders occur when an individual inherits an abnormal variant of a gene from each parent. If an individual receives one normal gene and one abnormal variant gene for the disease, the person will be a carrier for the disease, but usually will not show symptoms. This is true for carriers of Glanzmann thrombasthenia. The risk for two carrier parents to both pass the defective gene and, therefore, have an affected child is 25% with each pregnancy. The risk to have a child who is a carrier, like the parents, is 50% with each pregnancy. The chance for a child to receive the normal genes from both parents and therefore be genetically normal for that particular trait is 25%. The risk is the same for males and females.

Affected Populations

Glanzmann thrombasthenia is a rare disorder that affects males and females in equal numbers. The symptoms of this disease are usually apparent at birth (neonates) or during infancy. Approximately 500 cases have been reported, but many cases have probably not been reported. This condition occurs with greater frequency in populations in which intermarriage within a group (consanguinity) is more prevalent such as in some regions of the Middle East, India, and France.

Related Disorders

Symptoms of other disorders listed below can be similar to those of Glanzmann thrombasthenia. Comparisons may be useful for a differential diagnosis:

Hemophilia is a rare inherited blood clotting (coagulation) disorder caused by an inactive or deficient blood protein, usually factor VIII or IX, both of which are needed for normal blood clotting. Factors VIII and IX are two of several proteins that enable the blood to clot. Hemophilia due to defects in either factor VIII or IX is found in males almost exclusively because these genes are on the X chromosome and these disorders can be classified as mild, moderate, or severe. The most common forms of bleeding are hemorrhage in joints and muscles and the most serious symptom of hemophilia is bleeding in the brain. Bleeding may begin spontaneously, that is, without any apparent

cause. Bleeding may cause permanent damage to the joints and muscles. People with hemophilia bleed for a longer period of time than people who have the normal amount of clotting factors in their blood. Bruises and trauma can trigger episodes of serious internal bleeding in people with this disorder. (For more information on this disorder, choose “hemophilia” as your search term in the Rare Disease Database.)

Bernard-Soulier syndrome is a rare inherited blood clotting (coagulation) disorder characterized by abnormalities of platelets, including very large (giant) platelets that do not adhere normally to damaged blood vessels because of an abnormal Glycoprotein Ib/IX/V complex. Symptoms include a tendency to bleed excessively and bruise easily. People with Bernard-Soulier syndrome tend to bleed profusely from cuts and other injuries. Nosebleeds and unusually heavy menstrual flow are also common. Bleeding into the skin may cause small pinpoint hemorrhage (petechiae) or large purple-colored spots (purpura) in different areas of the body. (For more information on this disorder, choose “Bernard-Soulier” as your search term in the Rare Disease Database.)

May-Hegglin anomaly is a rare inherited disorder of blood platelets and certain white blood cells characterized by reduced numbers of very large (giant) platelets. Patients usually do not bleed excessively unless they have very low platelet counts. (For more information on this disorder, choose “May Hegglin” as your search term in the Rare Disease Database.)

Storage pool disease (SPD) is a rare inherited disorder of blood platelets characterized by clotting dysfunction due to the platelets’ inability to store and release certain clotting factors. Symptoms may include mild bleeding, nosebleeds, and heavier than normal menstrual periods. People with some forms of storage pool disease may also have abnormally low levels of blood platelets (thrombocytopenia).

Some platelet disorders may be associated with congenital conditions such as Wiskott-Aldrich syndrome and thrombocytopenia with absent radius syndrome. (For more information on these disorders choose “Wiskott Aldrich,” and “thrombocytopenia absent radius,” as your search terms in the Rare Disease Database.)

Diagnosis

Most individuals affected with Glanzmann thrombasthenia have a normal number of platelets but have a prolonged bleeding time, which means it takes longer than usual for a standardized cut to stop bleeding. Platelet aggregation studies are abnormal and show that platelets are not able to clump together when stimulated as they should to form platelet aggregates. Glanzmann thrombasthenia is definitively diagnosed by tests that determine if there is a deficiency of the αIIbβ3 (GPIIb/IIIa) receptor. These tests usually involve monoclonal antibodies and flow cytometry. Genetic tests can identify the DNA mutations responsible for the disorder in the genes ITGA2B and ITGB3.

Carrier and prenatal testing by DNA analysis is possible if the specific gene abnormality has been identified in an affected family member. Otherwise prenatal testing can be performed based on analyzing the fetus’s platelet αIIbβ3.

Standard Therapies

Treatment
Some individuals with GT may require blood platelet transfusions. Since transfusions may continue to be necessary throughout life, affected individuals may benefit from transfusions from HLA-matched donors. Some patients develop antibodies to transfused platelets and these antibodies may diminish the benefit from subsequent platelet transfusions.

In 2014, NovoSeven RT, a recombinant factor VIIa product, was approved to treat Glanzmann thrombasthenia. This medication is indicated to treat bleeding episodes and perioperative management when platelet transfusions are not effective. Treatment is usually given prior to most surgical procedures or should be available if needed. Platelet transfusions are usually necessary prior to delivery.

Nosebleeds can usually be treated with nasal packing or application of foam soaked in thrombin. Regular dental care is important to prevent bleeding from the gums.

Hormonal therapy can be used to suppress menstrual periods.

Other treatment of GT is included use of antifibrinolytic agents alone or in combination with other therapies.

Genetic counseling is recommended for people with GT and their families.

Investigational Therapies

Bone marrow or peripheral blood hematopoietic stem cell transplantation has successfully cured a number of patients with severe disease.

Information on current clinical trials is posted on the Internet at www.clinicaltrials.gov. All studies receiving U.S. government funding, and some supported by private industry, are posted on this government web site.

For information about clinical trials being conducted at the NIH Clinical Center in Bethesda, MD, contact the NIH Patient Recruitment Office:
Tollfree: (800) 411-1222
TTY: (866) 411-1010
Email: prpl@cc.nih.gov

Some current clinical trials also are posted on the following page on the NORD website: https://rarediseases.org/for-patients-and-families/information-resources/news-patient-recruitment/

For information about clinical trials sponsored by private sources, contact: www.centerwatch.com.

For information about clinical trials conducted in Europe, contact: https://www.clinicaltrialsregister.eu/

Supporting Organizations

- Genetic and Rare Diseases (GARD) Information Center
  - PO Box 8126
  - Gaithersburg, MD 20898-8126
  - Phone: (301) 251-4925
  - Toll-free: (888) 205-2311
  - Website: http://rarediseases.info.nih.gov/GARD/
- NIH/National Heart, Lung and Blood Institute
  - P.O. Box 30105
  - Bethesda, MD 20892-0105
  - Phone: (301) 592-8573
  - Email: nhlbiinfo@rover.nhlbi.nih.gov
  - Website: http://www.nhlbi.nih.gov/

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