CLINICAL VIGNETTE

Idiopathic Thrombocytopenic Purpura

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Case Report

The patient is an 87-year old male with a history of CLL, hyperlipidemia, CAD s/p CABG, GERD, hypertension, and DJD who presented to the ER with a 24-hour history of spontaneous epistaxis. He had tried applying direct nasal pressure at home without success and went to the ER as the bleeding continued. He had no fevers, chills, dyspnea, chest pain, cough, abdominal pain, melena, BRBPR, gross hematuria, active arthritis, headaches, or fatigue.

His past medical history is also significant for thyroid cancer s/p thyroidectomy and allergic rhinitis. He has no drug allergies. His social history is remarkable for being a non-smoker. He reports 1-2 alcoholic drinks each evening and stays quite active. He attends a local gym regularly and exercises for 60 minutes about 5 times per week. His family history is remarkable for CAD and thyroid disease.

His medication list includes Omeprazole, Levothyroxine, Allopurinol, Pravastatin, Olmesartan, Hydrochlorothiazide, Metoprolol, Quinipril and Aspirin.

His physical examination revealed a blood pressure of 105/60 mm hg., pulse of 70, and temperature of 36.6 C. His physical examination was remarkable for petechiae on his lower extremities and the aforementioned epistaxis.

Laboratory evaluation revealed a platelet count of 2000 per uL. His CBC was otherwise unremarkable. His chemistries were also unremarkable

General Discussion and Historical Context

Idiopathic thrombocytopenia purpura is an immune-mediated hematologic process that results in significant thrombocytopenia[1]. In some cases, clinical manifestations are often subtle or asymptomatic[2]. In other cases, manifestations can be quite severe sometimes resulting in very poor outcomes. ITP was first reported in 1556 by Portuguese physician Amato Lusitano and more fully described in 1735 by German physician Paul Gottlieb Werlhof. Interestingly, the disorder was previously called "Werlhof's disease" before the pathophysiology of the disease was elucidated.

Epidemiology

The incidence of ITP is estimated to be about 100 new cases per million with cases being evenly split between children and adults[3]. Childhood ITP is equally common in males and females while adult ITP is more common in females especially for those diagnosed later in life[4]. The median age of diagnosis for adults is 55-60 years[5].

Diagnosis and Pathogenesis

Idiopathic thrombocytopenic purpura (or immune thrombocytopenia) has two diagnostic criteria[6]. First, an isolated thrombocytopenia is noted with no other hematologic abnormalities. Second, no other disorders are present that can result in secondary thrombocytopenia. Thus, other hematologic disorders, medication effects, hepatitis B or C, HIV, liver disease, lupus erythematosis, and other disorders must be ruled out. Splenomegaly is usually not noted on exam despite the fact that splenic macrophages are believed to be responsible, in part, for the thrombocytopenia[7].

If the diagnosis remains in doubt, a bone marrow biopsy can be performed. There is no consensus on the reliability of serologic testing for platelet antibodies[8]. The pathogenesis of ITP is believed to be a B-cell and T-cell autoimmune destructive hematologic process that targets platelets. The antibodies are usually IgG that target the platelet membrane glycoproteins Iib-Iia or Ib-IX leading to opsonization and phagocytosis by white blood cells[9]. Other damaging effects include direct damage to megakaryocytes and a reduction in the platelet stimulating hormone thrombopoietin[10].

Clinical Features and Outcomes

Most patients with ITP present with purpura and/or petechiae most commonly on the extremities[11]. Epistaxis, gross hematuria, hematomas, or menorrhagia are common. Clinical findings are typically only seen when the platelet count drops below 10-20,000 per uL. More serious problems such as intestinal bleeding or CNS bleeding are potentially life-threatening complications of ITP. The prognosis for childhood ITP is generally excellent with about 65% of cases remitting spontaneously within six months[12]. Another 10% will resolve spontaneously by twelve months while another 10% will remain stable over time with mild thrombocytopenia without overt clinical problems[13]. Adults generally have worse outcomes with sustained remission only occurring in about 25% of cases[14]. The mortality rate for ITP is approximately 4% among both male and female patients. The elderly are particularly prone to poor clinical outcomes with the vast majority of deaths (most due to bleeding or infections) occurring in those over the age of fifty[15].

Treatment and Prognosis

Treatment is usually indicated when the platelet count falls below 20,000 per uL or if there is active bleeding and the platelet count is between 20,000-50,000 per uL[16]. Hospitalization and management under the direction of a hematologist is usually required when counts get very low given the risk of potentially life-threatening CNS bleeding. The first line treatment modality is typically steroids (usually dexamethasone or methylprednisolone) with the dosage being tapered as dictated by clinical improvement[17]. Tapering can take an extended period of time as relapses are common as the steroid dose is reduced[18]. In addition, steroid-sparing agents can have some degree of effectiveness in certain patients[19]. Intravenous immunoglobulins are administered in some patients although the effectiveness tends to be short-lived[20]. For this reason, IVIG is sometimes used prior to surgery. Rho-D immunoglobulin (anti-D) is also sometimes used for this purpose and its effect can also, unfortunately, be short-lived[21]. Despite the potential side effects, immunosuppressants such as vincristine or azathioprine are also used in select cases. Thrombopoietin receptor agonists, which stimulate the production of platelets are also considered in some patients[22]. Romiplostim and eltronbopag are two such agents approved by the FDA for treatment of ITP[23].

When medical treatments are not effective or bleeding continues despite medical therapy, splenectomy is sometimes considered with the hope that this will control splenic phagocytosis of opsonized platelets[24]. Splenectomy can resolve the ITP in 60% of cases but the peri-operative and post-operative bleeding risks are significant[25]. Transfusions of platelets are sometimes used as a temporizing measure, but rarely result in long-term resolution of the thrombocytopenia[26]. Novel therapies include treating H. pylori infection[27], as well as medications such as dapsone and rituximab[28]. Prognosis for patients with ITP varies widely and is generally better for younger patients[29].

Clinical Course and Follow-Up

The 87-year old patient was hospitalized with a platelet count of 2,000 per uL and unrelenting epistaxis. He was treated with numerous agents including steroids and steroid-sparing agents. He also received numerous platelet transfusions. Unfortunately, his platelet count did not respond to the treatments and he eventually underwent a splenectomy. Despite all of these therapies, his platelet count remains essentially undetectable. His clinical course declined gradually over time and the patient was eventually placed on hospice by his family.

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