Differential Diagnosis and Secondary Causes of Immune Thrombocytopenia (ITP)

Variable	Clinical and Laboratory Findings	Other Tests and Findings to Confirm Diagnosis
Differential diagnosis of ITP		
Pseudothrombocytopenia	No symptoms, in vitro phenomena	Platelet aggregation on peripheral-blood smear, repeat platelet count in citrated blood
Renal or liver disease	Symptoms, signs, and clinical history	Renal function and liver-function tests and imaging of abdomen, including liver and spleen
Myelodysplastic syndrome, acute leukemia	Other cytopenias and abnormal peripheral-blood smear	Peripheral-blood smear, bone marrow aspirate and biopsy, with flow cytometry and cytogenetic testing
Aplastic anemia	Pancytopenia	Bone marrow aspirate and biopsy with cytogenetic testing
Genetic diseases that cause thrombocytopenia (e.g., Bernard–Soulier syndrome and *MYH9*-related disorders)	Young age at presentation, family history of thrombocytopenia, abnormal size and morphologic features of platelets or abnormalities seen in neutrophils on peripheral-blood smear, other clinical abnormalities (e.g., renal disease and deafness in patients with *MYH9*-related disorders)	Peripheral-blood smear, mean platelet volume, genomic testing
Thrombotic thrombocytopenic purpura	Neurologic or cardiac symptoms	Schistocytes on peripheral-blood smear, elevated LDH level, low haptoglobin and ADAMTS13 levels, direct antiglobulin test–negative hemolytic anemia
Heparin-induced thrombocytopenia	Venous thrombosis, previous exposure to heparin	Platelet factor 4–heparin antibody tests, platelet-activation assays

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Secondary causes of ITP		
Use of certain drugs	Sudden onset after initiation of new medication (common drugs include quinine or quinidine, acetaminophen, abciximab, carbamazepine, rifampicin, and vancomycin)	Tests to detect drug-dependent antibodies, if available
Lymphoproliferative disorder (e.g., chronic lymphocytic leukemia and Hodgkin's lymphoma)	Weight loss, night sweats, lymphadenopathy or splenomegaly	Complete blood count; peripheral-blood flow cytometry, bone marrow flow cytometry, or both; bone marrow aspirate and biopsy; protein electrophoresis imaging of abdomen, chest, and neck to assess lymphadenopathy and spleen size (as appropriate)
Immunodeficiency syndrome (e.g., common variable immunodeficiency and autoimmune lymphoproliferative syndrome)	Hypogammaglobulinemia, cytopenias, frequent infections (especially chest or sinus infections), colitis, lymphadenopathy, splenomegaly	Immunoglobulin quantification, lymphocyte subset count, genetic testing
Infection (e.g., HIV and AIDS, HBV, HCV, cytomegalovirus, EBV, and *Helicobacter pylori*)	Other suggestive symptoms and signs; at-risk populations	Serologic and PCR tests for HIV, HBV, HCV, cytomegalovirus, and EBV; breath or stool antigen tests for *H. pylori*
Other autoimmune disease (e.g., systemic lupus erythematosus, rheumatoid arthritis and antiphospholipid syndrome)	Arthralgias or arthritis, hair loss, sun sensitivity, mouth ulcers, rash, thromboembolism	Tests for antinuclear antibodies, rheumatoid factor, anti–cyclic citrullinated peptide antibodies, antiphospholipid antibodies
Evans syndrome	Thrombocytopenia and direct antiglobulin test–positive hemolytic anemia	Peripheral-blood smear; measurements of haptoglobin and LDH levels; direct antiglobulin test

* ADAMTS13 denotes a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13; AIDS acquired immunodeficiency syndrome; EBV Epstein–Barr virus; HBV hepatitis B virus; HCV hepatitis C virus; HIV human immunodeficiency virus; LDH lactate dehydrogenase; *MYH9* gene encoding nonmuscle myosin heavy chain 9; and PCR polymerase chain reaction.

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