BLOODCENTER of WISCONSIN™

ADAMTS13 EVALUATION: ACTIVITY, INHIBITOR AND ANTIBODY

BloodCenter of Wisconsin's Hemostasis Reference Laboratory offers comprehensive testing for ADAMTS13.

BACKGROUND:

Thrombotic thrombocytopenic purpura (TTP) is a rare life-threatening condition characterized by consumption of platelets, hemolytic anemia, and varying degrees of organ dysfunction. Diagnosis of TTP is made clinically, and its diagnosis and differentiation from other thrombotic microangiopathies is often difficult.[1,2]

ADAMTS13 is a plasma protein that regulates the interaction of platelets with von Willebrand factor. Absent or low ADAMTS13 activity allows formation of platelet microthrombi, which in turn obstruct arterioles and capillaries, generating the clinical sequelae of TTP.

The majority of adults with idiopathic TTP have a severe deficiency of ADAMTS13 with activity levels <10%.[1,2] The low levels are often due to autoantibodies that inhibit or clear ADAMTS13. Patients with idiopathic TTP usually require therapeutic plasma exchange to achieve clinical remission.[2,3] Patients with idiopathic TTP and severe ADAMTS13 deficiency are more likely to respond to plasma exchange therapy than patients without severe deficiency. Persistence of ADAMTS13 deficiency or an inhibitor/antibody during clinical remission suggests an increased risk for recurrence of symptomatic TTP.[2,4-6] Identification of an autoimmune mechanism in idiopathic TTP explains the rationale for immunotherapy.[1,2]

Congenital severe ADAMTS13 deficiency is an autosomal recessive disorder (Upshaw-Schulman syndrome). Patients may present as children or adults, and are at risk for recurrent episodes of TTP. Antibody to ADAMTS13 is usually not detected, and patients generally improve with plasma transfusion therapy for ADAMTS13 replacement.

REASONS FOR REFERRAL:

- Test results may assist in diagnosis of congenital or idiopathic TTP, and may have prognostic value regarding likelihood of relapse.[1,2,4,5]
- Severe deficiency of <10% appears to be a relatively specific finding in patients with a clinical diagnosis of idiopathic TTP or Upshaw-Schulman syndrome.
- Low activity with inhibitor/antibody has increased specificity for idiopathic TTP.

METHOD:

ADAMTS13 activity is measured by Fluorescence Resonance Energy Transfer (FRET) with a synthetic substrate.[7] ADAMTS13 inhibitor is determined using mixing studies; one inhibitor unit is defined as the concentration of inhibitor able to reduce the ADAMTS13 activity of an equal volume of normal pooled plasma by half.[8] The ADAMTS13 antibody assay detects IgG antibody serologically by ELISA.

TURNAROUND TIME:

ADAMTS13 Activity and Inhibitor: 2 - 4 days
ADAMTS13 Antibody: 7 - 10 days

CPT CODES:

ADAMTS13 Activity	85397
ADAMTS13 Inhibitor	85335
ADAMTS13 Antibody	83520

PO Box 2178
Milwaukee, WI 53201-2178
Location/Sample Deliveries:
638 N. 18th St. Milwaukee, WI 53233-2121
p800-245-3117 | f414-937-6202 | www.bcw.edu

REPORTABLE RANGE/NORMAL VALUES:

ADAMTS13 Activity	≥ 67%
ADAMTS13 Inhibitor	≤ 0.4 Inhibitor Units
ADAMTS13 Antibody	≤ 18 Arbitrary Units

LIMITATIONS:

- Not all patients with idiopathic TTP have abnormal ADAMTS13 laboratory results. The reported prevalence of severe deficiency in patients presenting with idiopathic TTP varies from 33 to 100%.[1, 2] Prevalence of inhibitors ranges from 44% to 93%[6,8] with a somewhat higher reported prevalence of antibody detected by ELISA.
- Severe deficiency of ADAMTS13 has been proposed as a relatively specific laboratory marker of TTP. Whether severe deficiency occurs in other conditions is debated.[5] Mild to moderate deficiency has been observed in multiple medical conditions including inflammation, hepatic dysfunction and pregnancy.[1]
- Recent plasma exchange therapy may affect ADAMTS13 assay findings.
- Hemolysis with plasma free hemoglobin >2 gm/L or an elevated bilirubin level can cause artifactually low ADAMTS13 activity and false positive inhibitor results.[9]
- ADAMTS13 Antibody assay is less specific than the functional inhibitor assay, and positive results have been observed in people without severe ADAMTS13 deficiency, including healthy individuals and patients with other immunologic disorders.[6]

REFLEX ALGORITHM:

ADAMTS13 Evaluation is a reflexive testing algorithm. ADAMTS13 Activity is always performed. If activity is ≤ 30%, the inhibitor assay is performed. If the inhibitor is ≤ 0.7 Inhibitor Units, testing for ADAMTS13 Antibody is performed. Charges reflect assays performed. Each test is available for individual order.

SPECIMEN REQUIREMENTS:

Citrated plasma, frozen in plastic tubes

ADAMTS13 Evaluation: 3 aliquots (0.5 ml each)

ADAMTS13 Activity or Inhibitor or Antibody: 0.5 ml for each test ordered

SHIPPING REQUIREMENTS:

Place the frozen specimen and the test requisition form into plastic bags, seal and place in an insulated container. Surround with at least 5 pounds of dry ice. Seal the insulated container, place in a sturdy cardboard box and tape securely. Ship the package in compliance with your overnight carrier guidelines. Label with the following address:

Client Services/Hemostasis Reference Laboratory
BloodCenter of Wisconsin
638 N. 18 St.
Milwaukee, WI 53233
800-245-3117, ext. 6129

REFERENCES:

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