Laboratory Testing for TTP: ADAMTS-13 Activity and Antigen Assays

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The discovery of ADAMTS-13 and its interactions with von Willebrand Factor provided insight into the pathogenesis of Thrombotic Thrombocytopenic Purpura (TTP). ADAMTS-13 is directly implicated in TTP: congenital TTP is due to its absence and most forms of acquired TTP result from autoantibodies that adversely affect ADAMTS-13 function. Differentiating between congenital and acquired TTP is important because treatment differs. Therefore the laboratory is looked upon to provide assays for ADAMTS-13 that can provide results in a timely fashion (due to ease of assay performance) and yield useful information regarding the activity of the protease, in the absence or presence of autoantibodies. In one decade, assays for the detection of ADAMTS-13 activity have been developed, improved upon, and are now commercially available. To a large degree this is due to advancements in "miniaturization" of the VWF substrate allowing for development of recombinant fusion peptidyl substrates incorporating various tags for colorimetric or fluorometric visualization/quantification. Use of these substrates has significantly reduced test time and favors introduction of these assays into a clinical laboratory environment. Advancements in ADAMTS-13 activity assays directly impact assays for assessing the inhibitory activity of antibodies to the protease since these assays can be modified by incorporation of a classical mixing study. ELISA assays are commercially available that assess total anti-ADAMTS-13 IgG, however, these quantify both neutralizing and non-neutralizing antibodies to ADAMTS-13. Assays have also been developed to quantify antigenic levels of the protease. Consideration of pre-examination issues relating to these three assays types (activity, modified activity for inhibitory antibodies, and antigen) is in its infancy. Overall the challenge for laboratories and clinicians is to understand the clinical significance of the data that these tests generate and how these do/do not affect outcomes in TTP patients.