## Differential diagnosis between TTP and atypical HUS

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Thrombocytopenia and microangiopathic hemolytic anemia are the hallmark of the thrombotic microangiopathies (TMAs) thrombotic thrombocytopenic purpura (TTP) and hemolytic uremic syndrome (HUS). TTP, inherited or autoimmune, is mainly caused by the plasma deficiency of the von Willebrand factor cleaving protease ADAMTS13, owing to gene mutations or autoantibodies. Typical HUS is often caused by infections with Shiga-toxin-producing Escherichia coli and thus is called STEC-HUS. The rarer atypical forms of HUS are often associated with complement dysregulation, owing to the inherited deficiency or dysfunction of factor H or other complement proteins. In the past the distinction between these TMAs was almost exclusively based on clinical grounds, the term TTP being used for cases with predominant neurological involvement, STEC HUS for cases presenting with bloody diarrhea and atypical HUS identifying patients with severe renal damage. However the clinical presentation may not easily distinguish TTP from atypical HUS. A more accurate differential diagnosis has now clinical implications, because plasma exchange (the treatment of choice in TTP) is much less effective in atypical HUS, which shows dramatic short- and long-term therapeutic benefits from eculizumab, a monoclonal antibody that inhibits complement activation. The measurement of ADAMTS13 is able to diagnose accurately the majority of TTP cases, but very simple tests such as the platelet count and serum creatinine values can predict the deficiency of the protease with a good degree of accuracy. In atypical HUS, new methods were recently developed that not only demonstrate the activation of the complement system, i.e., the main disease mechanism, but also help to tailor the short- and long-term treatment with eculizumab.