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Pathophysiology of thrombotic thrombocytopenic purpura : the "two-hit" paradigm

Lotta, L.A.

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Author: Lotta, Luca Andrea

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Figures

Figure 1. Panel A: fluctuations of ADAMTS13 activity over time in the healthy individual. Fluctuations are spontaneous or determined by environmental challenges. Infections, traumas, local inflammation may determine small deflections (broken arrow); pregnancy, infections, surgery or other currently unknown factors may constitute stronger challenges and determine great deflections in the activity (full arrow). Broken horizontal line close to 0 indicates the thrombotic thrombocytopenic purpura (TTP)-triggering threshold. Panel B: fluctuations of ADAMTS13 activity over time in individual with severe ADAMTS13 deficiency and relatively high (>6%) residual activity. Minor fluctuations do not result in the onset of TTP, whereas major challenges result in TTP onset. Time to onset is relatively long (horizontal line) and TTP episodes infrequent (arrow). The number on top of the arrow indicates the number of TTP episode. Panel C: fluctuations of ADAMTS13 activity over time in individual with severe ADAMTS13 deficiency and relatively low (<3%) residual activity. Minor fluctuations result in the onset of TTP. Time to onset is relatively short (horizontal line) and TTP episodes frequent (arrows). Numbers on top of the arrow indicate the number of TTP episode.

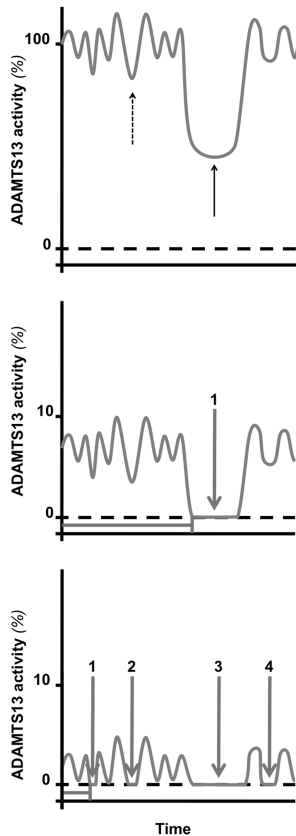


Figure 2. Relationship between age of disease onset and residual plasmatic activity of ADAMTS13 in congenital TTP patients. Areas indicate three different scenarios corresponding to the models reported above the plot. A: low residual ADAMTS13 activity and early age of onset. B: high residual activity and early age of onset. C: high residual activity and late onset.

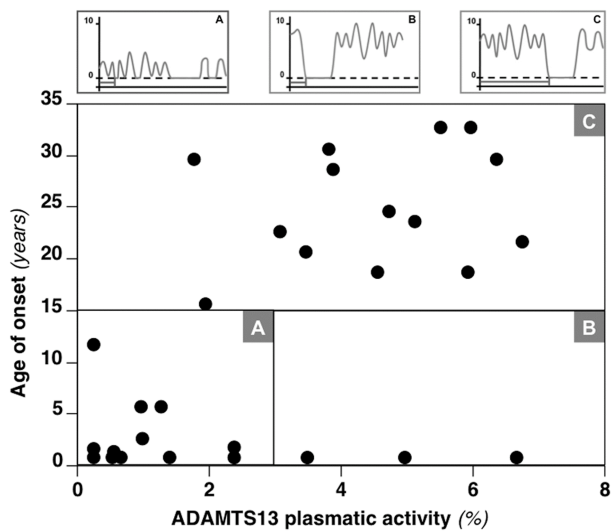


Figure 3. Relationship between frequency of TTP episodes and residual plasmatic activity of ADAMTS13 in congenital TTP patients. Areas indicate two different scenarios corresponding to the models reported above the plot. Dark grey: low residual activity and frequent recurrences. Light grey: high residual activity and infrequent recurrences.

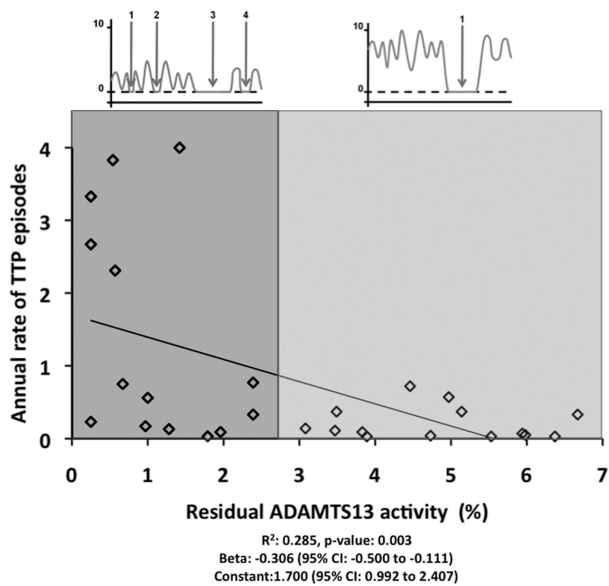


Figure 4. Relationship between risk of TTP recurrence and residual plasmatic activity of ADAMTS13 in acquired TTP patients. Increasing levels of plasmatic activity of ADAMTS13 are associated with exponentially decreasing risk of recurrence. Patients with low residual activity have the highest risk of recurrence (left), patients with high residual activity are at lower risk (middle), and patients with normal activity have virtually no risk (right). This is consistent with observations in congenital TTP patients.

