Patagonfibrase Disturbs Protein Expression of Tissue Factor and Protein Disulfide Isomerase in skin

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Introduction: Patagonfibrase is a P-III metalloproteinase isolated from the venom of the South American rear-fanged snake Philodryas patagoniensis. Local lesions are usually described in snakebites inflicted by this species. Thus, this study was performed to determine whether patagonfibrase affects the local expression of two proteins having important roles in hemostasis and inflammation: tissue factor (TF) and protein disulfide isomerase (PDI). Material and Methods: Male Wistar rats were s.c. injected with patagonfibrase (60 µg/kg). Animals injected with saline were used as negative controls. After 3 h, animals were anesthetized, and blood was collected to evaluate hemostasis parameters. Skin fragments of 4 cm in diameter – whose centers correspond to the injection site - were also taken and used to evaluate the expression of TF and PDI by Western blotting (WB) and immunohistochemistry, using anti-TF and anti-PDI monoclonal antibodies. Results and Discussion: Patagonfibrase altered neither the number of blood cell counts nor plasma fibrinogen levels. In addition, it did not modify levels of TF activity in plasma. By semiquantitative WB, patagonfibrase increased the TF expression by 2-fold, but decreased the PDI expression by 3-fold in skin samples. Immunohistological detection of TF in routinely fixed paraffin sections of rat skin showed prominent TF expression in the subcutaneous tissue, where fibroblasts and mononuclear inflammatory cells were the main elements reacting with anti-TF antibodies. Conclusions: To our knowledge, we report for the first time a high expression of TF and a low expression of PDI induced by a snake venom metalloproteinase at the local of metalloproteinase injection. The increased expression of TF may contribute to the local inflammatory reactions that characterize snakebites. Therefore, modulation of TF activity could become a tempting strategy in therapy of snake envenomation.

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