

New Approach to Protein-losing Gastroenteropathy

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Summary

Fibrinolytic activity in the biopsied gastrointestinal mucosa was investigated in patients with protein-losing gastroenteropathy, and the increased activity was observed in patients associated with erosive gastritis, Menetrier's disease, atrophic gastritis, or Crohn's disease. However, patients with intestinal lymphangiectasia showed normal mucosal fibrinolysis. Antifibrinolytic therapy with tranexamic acid revealed significant therapeutic effect in the group with increased mucosal fibrinolysis. It is concluded that tranexamic acid appeared to be successful in blocking the vicious circle of "membrane disorder", "increased tissue fibrinolysis", "increased vascular permeability", and "hypoproteinemia" in protein-losing gastroenteropathy.

Excessive loss of plasma protein into the digestive tract is a major cause of hypoproteinemia and defined as protein-losing gastroenteropathy. The mechanism of this enteric protein loss has been attributed to exudation of protein through inflamed or ulcerated mucosa (1, 2), or to passive diffusion between mucosal cells in cases of lymphatic abnormality (3, 4, 5) (Fig. 1). Except for a situation that

plasma protein or lymph leaks because of mechanical reason such as vascular damage or lymphatic fistula, several factors responsible for increasing vascular permeability must be taken in account for this mechanism. However, for a longer period no factor has been shown which will attribute to enhance the vascular permeability.

Based on the evidence that most of the patients with protein-losing gastroenteropathy reveal increased fibrinolytic activity of the digestive mucosa, we (6, 7) have established an antifibrinolytic therapy on this clinical condition. Plasmin, easily activated from plasminogen by an activator released from tissue, can increase vascular permeability by itself, or by activating kinins or complement. Since activated plasmin in the circulating blood is immediately inactivated by several inhibitors present in blood, it is questionable if plasmin in the circulation can enhance vascular permeability in the digestive mucosa and results in enteric protein loss. Therefore,

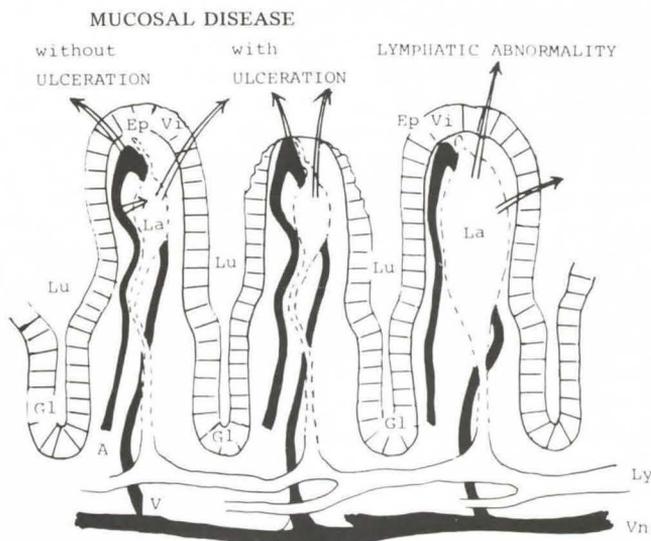


Fig. 1 Mechanism of protein-losing gastroenteropathy

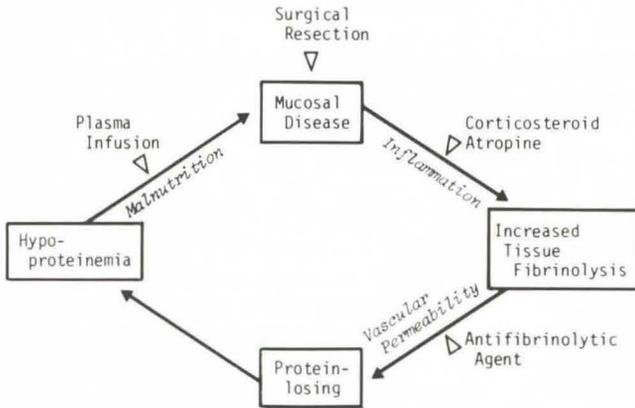


Fig. 2 Vicious circle in protein-losing gastroenteropathy, and its possible therapeutics

it seems reasonable to demonstrate the increased fibrinolytic activity in the digestive mucosa, since mucosal samples are easily available using biopsy forceps under the control of endoscopy and the fibrinolytic activity can be examined repeatedly.

Several patients with protein-losing gastroenteropathy have been treated by antifibrinolytic compound trans-AMCHA (trans-4-aminomethyl cyclohexane carboxylic acid; tranexamic acid). The therapeutic effect was significantly observed in cases with erosive gastritis, giant hypertrophic gastritis (Menetrier's disease), atrophic gastritis, Crohn's disease and intestinal polyposis associated with protein-losing. In cases with lymphatic abnormality, this therapy was initially effective in raising serum protein level in a case with lymphangiectasia to a certain extent, but was not able to cure the disease completely.

These data suggested that antifibrinolytic compound trans-AMCHA appeared to be successful in blocking the vicious circle of "membrane disorder", "increased tissue fibrinolysis", "increased vascular permeability", and "hypoproteinemia" in protein-losing gastroenteropathy. Vicious circle in protein-losing gastroenteropathy and its possible therapeutics are shown in Fig. 2. Ineffectiveness of this hypothesis in the mechanism of protein-losing due to lymphatic abnormali-

ties should further be investigated in a large number of patients. However since there is no definite treatment for these lymphatic abnormality, it seems worth trying this antifibrinolytic therapy on these patients with protein-losing, as well as cases of protein-losing of unknown origin. No specific side effect has been experienced.

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