A CASE OF MENETRIER'S DISEASE ASSOCIATED WITH PROTEIN-LOSING GASTROPATHY AND ABNORMAL SERUM COMPLEMENT PROFILE

Motoharu KONDO, M.D., Hidetsugu NISHIBORI, M.D., Minoru IKEZAKI, M.D., Shuhei TAKEMURA, M.D. and Masasuke MASUDA, M.D.

Department of Medicine, Kyoto Prefectural University of Medicine, Kamikyo-ku, Kyoto 602

Summary

A 44-year-old man with Menetrier's disease associated with protein-losing gastropathy and with abnormal serum complement profile is reported. He was treated by an antifibrinolytic compound tranexamic acid (trans-AMCHA) since he was found to have elevated fibrinolytic activity in the biopsied gastric mucosa. The therapy brought his serum protein from 3.8g/dl to 5.6g/dl, however could not reduce his mucosal disorder. Substitution of a placebo for trans-AMCHA resulted in marked depression of his serum protein to 3.7 g/dl. It was concluded that trans-AMCHA was effective in raising his serum protein to a certain extent but failed to block the vicious circle of "mucosal disorder", "increased tissue fibrinolysis" and "hypoproteinemia" (Kondo, M. et al. Gastroenterology 70, 1045, 1976). Abnormal serum complement profile seen in this patient was found to be due to cold activation of the classical complement pathway (Kondo, M. et al. J. Immunol. 117, 486, 1976). Although no correlation between the phenomenon and Menetrier's disease has been clarified yet, the appearance of wheezing as in asthma when exposed to cold suggested that cold activation of complement occurred in vivo and resulted in increasing of the vascular permeability in the lungs.

Key Words: Menetrier's disease.

Diffuse thickening of the gastric wall caused by excessive proliferation of the mucosa was first described by Menetrier in 1888, and the variety of names such as "Menetrier's disease", "giant rugal hypertrophy", "giant hypertrophic gastritis" etc are used by different authors. Association of hypoproteinemia was demonstrated by Citrin1) and a loss of albumin in the gastric juice was documented. No specific treatment for this condition was indicated except for gastrectomy, until atropine2) or tranexamic acid3) was introduced to have favorable clinical results.

Abnormal serum complement profile have been shown in patients with immunological disorders such as SLE (systemic lupus erythematosus)4), deficiencies of individual complement components or control proteins in the complement pathway5), or in disseminated intravascular coagulation (DIC)6). In vitro activation of the complement after obtaining serum samples, including "cold activation of complement", has recently attracted attentions since those changes let us confuse in the understanding of hemolytic complement assay in

Received April 10, 1978. Accepted May 8, 1978.

Address requests for reprints to: Dr. Motoharu Kondo, M.D., The First Department of Internal Medicine, Kyoto Prefectural University of Medicine, Kawara-machi, Kamikyo-ku, Kyoto, 602 Japan.

The authors are grateful to Dr. T. Bamba, Dr. T. Tsukamoto, Miss M. Nagai, Mrs. K. Hirano and Miss C. Tsujigiwa for their help.
the clinical field. Cold activation of complement was first noted by the dissociation of hemolytic complement activity (CH50) in serum and plasma;⁷) that was, sera from certain patients with chronic hepatitis or liver cirrhosis showed a decrease of CH50 and the early components of complement (C1, C4, C2) while their EDTA-treated or heparinized plasma maintained a normal complement level. This phenomenon was reported later to be due to activation of the classical pathway by an unknown factor present in their sera in a cold environment⁸).

The present paper intends to report a case of Menetrier's disease associated with hypoproteinemia and bronchial asthma, whose serum complement revealed cold activation.

**Materials and Methods**

Standard fibrin plates were prepared with the use of plasminogen rich fibrinogen (Nakarai Chem. Co., Kyoto) and bovine thrombin (Mochida Pharm. Co., Tokyo) according to the method of Astrup and Müllertz⁹).

The fibrinolytic activity of the tissue was measured by the area of lysis in a standard plate after incubation with a mucosal specimen at 37°C for 18 hours. Activity was expressed as square millimeters of the area of lysis (mm²). Normal values for tissue fibrinolytic activity in biopsied gastric mucosa from 30 volunteers were 28.4±10.2 mm².

Titration of hemolytic complement activity CH50, and complement components C1, C4 and C2 was performed, using intermediate cells EA¹¹), EAC4¹²), EAC1¹³) and EAC14¹⁴), respectively.

**Case Report**

A 44-year-old man with long history of nausea, vomiting and epigastric distress was admitted to our hospital on January 1977. He was well until 1968 when he first noted epigastric fullness. At that time he was pointed out the presence of giant rugal hypertrophy of the gastric mucosa by upper G.I. series, and a subsequent gastric endoscopy revealed erosive gastritis with giant folds. In 1974, symptoms developed and he admitted to a hospital in 1975, where he was pointed out the presence of hypoproteinemia of 3.8 g/dl with albumin 2.1 g/dl. He was then referred to us because nausea, vomiting, emaciation and generalized edema.

Physical examination revealed anemia, tenderness at the epigastric region, and pitting edema at the legs. Chest was normal and there was no evidence of ascites. Abnormal laboratory findings were, RBC 318x10⁴, Hct 29%, WBC 8700 with eosinophilia of 12%, positive stool occult blood, serum cholesterol 98 mg/dl, serum Fe 35 µg/dl, and serum protein 3.8 g/dl with albumin 1.8 g/dl. Urinalysis was normal, and liver function tests were also normal.¹³¹-I-polyvinyl pyrrolidone (PVP) fecal clearance was 4.8% (normal less than 1.5%), indicating leakage of plasma proteins into the digestive tract. ¹²⁵I-albumin half-life was reduced to 4.1 days (normal 15 to 30 days) revealing increased catabolic rate of albumin. His gastric juice revealed achlorhydria, and contained proteins mainly albumin and IgG.

Upper G.I. series demonstrated a tumor-like thickening of the gastric wall at the corpus which could not be distended by infusion of air, and significant giant gastric folds extending from the cardia to the fundus (Fig. 1). By endoscopy, irregularly distorted giant folds with eroded mucosa was observed in the fundus, and the lumen of the corpus was narrowed by the coarse gastric mucosa. There was no evidence of ulceration nor malignancy. By computed tomography this thickened gastric wall was also demonstrated (Fig. 2).