

The new proof of neuro-endocrine-immune network—expression of islet amyloid polypeptide in plasma cells in gastric mucosa of peptic ulcer patients

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Subject headings peptic ulcer; plasma cells; gastric mucosa; islet amyloid polypeptide (IAPP); neuro-endocrine-immune network

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INTRODUCTION

Peptic ulcer, as a common disease, seriously affected people's work and life. Its occurrence, development and change have close relationship with the change of people's moods. Animal experiment proved that significant changes occurred in the endocrine system of the gastric ulcer rats^[1]. Recent study also showed that the number of lymphocytes increased markedly in the gastric mucosa of peptic ulcer patients^[2]. All the above indicated that peptic ulcer is closely related neuro-endocrine-immune system. IAPP, a novel islet hormone, not only takes part in the regulation of blood glucose^[3], but also protects gastric mucosa^[4] and regulates gastrointestinal movements^[5]. On the basis of previous studies, we observed the expression change of IAPP and explored the relationship between the endocrine and the immune system in gastric mucosa of peptic ulcer patients, so as to provide morphologic data on the existence of neuro-endocrine-immune network and the changes in peptic ulcer.

MATERIALS AND METHODS

Twenty-one samples, including 6 cases from normal human stomach, 15 cases from gastrectomy of gastric ulcer patients, were collected. The paraffin

sections were prepared as usual. Immunohistochemical PAP method was used to show IAPP-IR cells. Briefly five-micron sections were placed on glass slides deparaffinized in xylene, rinsed in ethanol, and brought to PBS through a series of descending concentration of ethanol; endogenous peroxidase activity was blocked with methanol-H₂O₂ at room temperature for 30 min; rabbit anti-IAPP serum (peninsula, USA) was diluted 1/6000 with PBS, and the sections were incubated overnight at 4 °C. Goat anti-rabbit IgG (Huamei, Beijing) (1/50), peroxidase-anti-peroxidase (Capital Medical University) (1/100) and DAB kit (Zhongshan, Beijing) were used for staining. As the negative control, the primary antiserum was replaced by PBS and other steps were the same as stated above. All the sections were counterstained with Mayer hematoxylin.

RESULTS

The IAPP-IR cell was not observed in the gastric mucosa of normal subject (Figure 1A). In comparison, a great number of plasma cells IAPP-IR were found in the gastric mucosa of peptic ulcer patients (Figure 1B,C). Most of IAPP-IR plasma cells were weak and only a few were strong for IAPP staining (Figure 1D). Of the negative control sections, no immunoreactive product to IAPP was found in plasma cells (Figure 1E).

DISCUSSION

The gastric mucosa, in which there are a lot of neurons, endocrine cells and immunocytes that may interact with each other, is an important field for the study of neuro-endocrine-immune network. It will undoubtedly provide valuable data for the study on this network by exploring the change of immune-endocrine of gastric mucosa of peptic ulcer patients. Based on the observation of T and B lymphocytes which increase obviously in the gastric mucosa of peptic ulcer patients^[2] and the action of IAPP, a novel islet hormone, which inhibits gastric acid secretion^[6] and protects gastric mucosa^[4], we further studied the expression change of IAPP in the gastric mucosa. Unexpectedly, it was found that the plasma cells of gastric mucosa increased in number, moreover most of them expressed IAPP to some degree.

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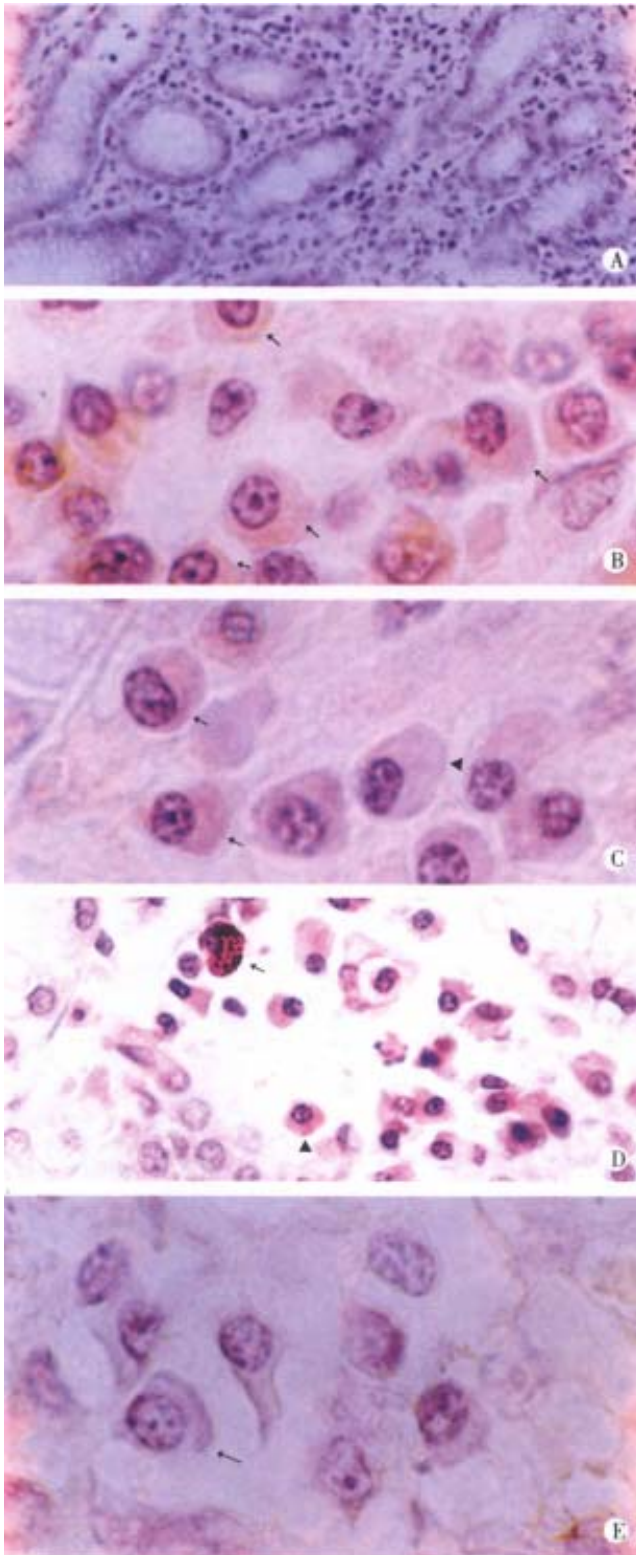


Figure 1 Immunohistochemical PAP method, Mayer Hematoxylin counterstained showing IAPP-IR cells.

A. The gastric mucosa of normal human, no IAPP-IR cell was found. $\times 200$

B-E. The gastric mucosa of peptic ulcer patients.
B. The more IAPP-IR plasma cells (↑). $\times 1000$

C. The weak positive (↑) and negative (▲) plasma cells. $\times 1000$

D. The strong (↑) and weak (▲) positive IAPP-IR plasma cells. $\times 400$

E. The negative control section in which IAPP antiserum was replaced by PBS. (↑) showing plasma cell. $\times 1000$

Firstly, the specificity of the above findings should be confirmed because there was no IAPP expression in the plasma cells on the negative control sections; and there were also IAPP-IR negative plasma cells around the positive ones. Secondly, the significance of IAPP expression in plasma cells should be studied. IAPP is mainly secreted by islet B cells^[7]. Recent study indicated that besides regulating blood glucose, IAPP could inhibit gastric acid secretion^[4], and protect gastric mucosa^[5]. IAPP-IR cells of islet were markedly increased during the healing process of rat gastric ulcer^[8]. The above-mentioned studies all suggested that IAPP is beneficial to ulcer healing. As it is known, the plasma cells of gastric mucosa come from B lymphocytes and they respond by synthesizing and secreting IgA. It is observed, for the first time, that plasma cells in gastric mucosa of peptic ulcer patients not only increased in the number, but also expressed IAPP. Combined with our previous observation that T and B lymphocytes of gastric mucosa increased in peptic ulcer patients, it is reasonable to infer that some plasma cells in gastric mucosa of peptic ulcer patients may transform to ones expressing IAPP so as to maintain the high level of IAPP in the gastric mucosa and help promote ulcer healing just as a growth factor^[9].

CONCLUSION

It is found, for the first time, that IAPP was expressed in plasma cells of gastric mucosa of peptic ulcer patients, which provides morphologic evidence for the existence of neuro-endocrine-immune network.

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