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Case Report

Immunohistochemical Study on HER-2 Receptor Activity in the Patient with Signet Ring Cell Gastric Carcinoma as Well as its Prognostic and Therapeutical Significance. Case Report and Review of the Literature

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Abstract

Human epidermal growth factor receptor-2 (HER-2) is related to pathogenesis and poor outcome of numerous types of carcinomas, including gastric carcinoma. Gastric cancer patients with HER 2 positivity have become potential candidates for targeted therapy with trastuzumab, that has been confirmed by this case.

Keywords: *Signet Ring Cell Carcinoma; HER-2; Histology; Mucins; Immunohistochemistry; Therapy*

Introduction

Diffuse type of gastric carcinoma, in which glandular formation is extremely poor, is characterized by infiltration of solitary or small clusters of cancer cells into the stroma [1-5]. Tumor cells produce large amounts of the intracellular mucin and in the advanced stage, infiltrating cancer cells are quite often accompanied by dense fibrous connective tissue, giving a scirrhous appearance [4-9].

The reports that signet ring gastric carcinoma has the poorest prognosis, that the prognosis depends from the ultrastructural type of mucous granules have induced numerous researches. So, research on Her-2 receptors of the signet ring cell gastric cancer, explains its specific characteristics, rarely reported [1-5].

Case History

The patient was a 52-year-old Serbian female who presented with a history of waxing and waning abdominal complaints, associated with vomiting, more than twice each day, during one month. She also had some episodes of fever with loss of weight. The liver, the pancreas and the spleen were normal.

Having in the mind that there are only few reports on both presence of HER-2 receptors in signet ring cells and their inhibition by trastuzumab, we aimed to clarify the prognostic significance of HER-2 positivity in advanced gastric cancer of signet ring cell type.

Materials and Methods

The biopsy material (five biopsies from the stomach) was obtained by endoscopically. The specimens were fixed in 4% buffered formaldehyde and in paraffin - embedded. The sections were stained with HE, AB - PAS and LSAB2 method, by using HER- 2 antibody.

Results

Histologically, the authors have discovered the diffuse type of gastric carcinoma, consisted of poorly cohesive cells diffusely infiltrating the gastric mucosa, with no gland formation. The cells appear round and small, arranged as single cells. The mitotic rate is lower than in intestinal type (Figure 1). Superficially, SRC lie scattered in the lamina propria, widening the distances between the pits and glands. These cells push nuclei against cell membranes creating a classical signet ring cell appearance, due to an expanded, optically clear cytoplasm and small, arranged as single cells (Figure 1). They contained acid mucin, staining with Alcian blue at pH 2.5 (Figure 2).

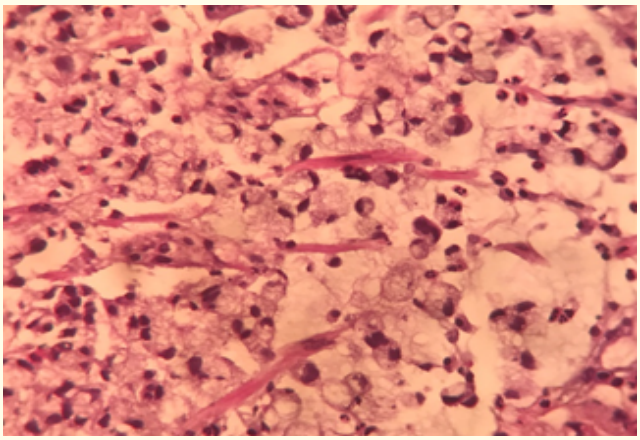

Figure 1: *Optically clear cytoplasm (HE x 400).*

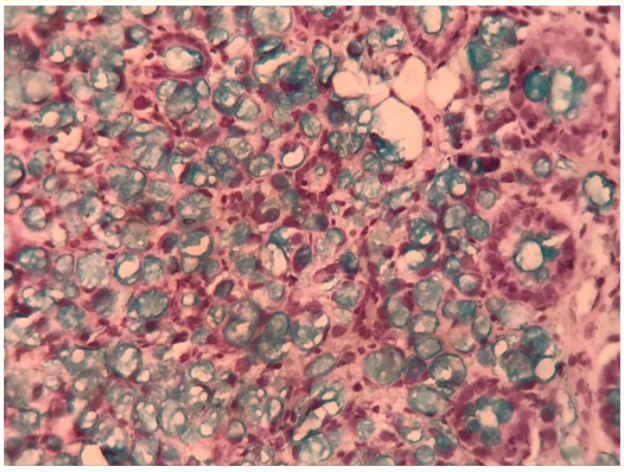

Figure 2: *Signet ring cell gastric carcinoma: hypersecretion of intestinal (acid) mucin (AB, ph = 2.5 x 400).*

New immunohistochemical results on Human Epidermal growth factor Receptor-2 (HER-2) have pointed out that HER-2 is related to pathogenesis and poor outcome of numerous types of carcinomas (especially breast cancer), as well as gastric signet ring carcinoma, that we also have discovered (Figure 3).

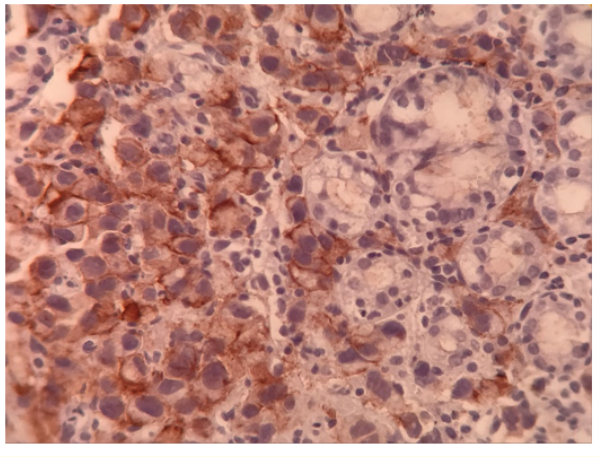

Figure 3: *Heterogeneity of HER-2 positivity in signet ring cell type gastric cancer (LSAB 2 x 400).*

Having in the mind that HER-2 positive cancer, in any type of organ, has opened the door to new type of treatment, based on treatment with trastuzumab, well known that it shows antitumour activity of pan-HER inhibitors in HER-2 positive gastric cancer.

Discussion and Conclusion

Endoscopical biopsies from our patient with signet ring cell gastric carcinoma were studied. Comparing with other types of gastric cancer, signet ring cell (SRC) type has a tendency to involve the entire stomach and to extend directly into neighboring organs [6-9]. It has the poorest prognosis, is more common in females than males and occurs at a comparatively younger age [1]. Tumor cells produce large amounts of intracellular mucin and in the advanced stage, infiltrating cells are quite often accompanied by dense fibrous connective tissue, giving a scirrhous appearance [10-15].

Human epidermal growth factor-2 (HER-2) overexpression has prognostic value in breast cancer. However, the significance of HER-2 positivity in gastric cancer is controversial in this study. We have investigated the frequency of overexpression of HER- and its relation to prognosis.

Recent progress of molecular biology has revealed genetic alterations in gastric carcinomas [4-8]. Positive HER-2 finding was found in 53,9 patients with poorly differentiated grade, with depth of invasion and with the increased number of lymph-node metastasis.

In contrast to many articles regarding the bad prognosis of the signet ring cell carcinoma, via HER2, we suggest that the discover of HER-2 receptors in cancerous signet ring cells in the stomach, has opened the door for trastuzumab therapy of the signet ring cell carcinoma in the stomach, blocking the effects of both HER-2 receptors and catherin [13-15].

In contrast to many reports on the prognosis of SRCC, that is well known, we suggest that the HER-2 positive receptors induce new anti HER- therapy with trastuzumab.

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