Modern Clinical and Morphological Approach to Early Stomach Cancer

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Abstract: The article presents the results of histological examination of early gastric cancer removed by endoscopic sub mucosal dissection. The algorithm of morphological research is given: methods of histological, histochemical and immunohistochemical processing of tissue samples, the sequence of morphological analysis with the conclusion and conclusions about the effectiveness of endoscopic surgery is analyzed.

Keywords: early gastric cancer, clinical and morphological examination, endoscopic sub mucosal resection.

Annually, more than 4000 newly diagnosed oncological diseases are registered in Uzbekistan [1, 3, 5]. Moreover, there is a stable tendency to increase the number of this category of patients. Oncological diseases in the structure of causes of death in Uzbekistan are in second place after diseases of the circulatory system and are ahead of external causes of death. The incidence of stomach cancer in Uzbekistan among all neoplasms is at a high level (in third place from the total number of neoplasms and in fifth place in terms of 2800 population). Moreover, mortality and morbidity are approximately at the same level.

The difficulties of timely diagnosis and treatment of this disease remain a serious problem both in Uzbekistan and around the world. There is still a high level of tumor detect ability already at the late clinical stages, when there are practically no opportunities for a complete cure [4,12]. Japan's healthcare has achieved quite serious and visible success in this direction (the death rate from stomach cancer is almost 2 times lower than the incidence), where the main efforts are aimed at detecting stomach cancer at early clinical stages [9, 10, 11]. The key to solving this problem is the oncological alertness of doctors, primarily primary care, modern endoscopic capabilities and competent histological examination [13, 14, 16]. Unfortunately, the possibilities of organ-preserving endoscopic surgery are still not widely used in our country. There are several methods of endoscopic removal of early gastric cancers, the most relevant of them are: endoscopic resection of the mucous membrane and endoscopic dissection of the sub mucosal layer [7, 8, 15]. An important point when performing these interventions is the removal of the formation as a single block within healthy tissues. This allows for a full-fledged histological examination, which will determine the subsequent treatment tactics and has significant long-term results.

The concept of "early gastric cancer" includes cancer within the mucous membrane and sub mucosal basis, regardless of the presence of regional metastases in the lymph nodes. At the same time, the presence of regional metastases in the lymph nodes is the most significant prognostic factor for patients with early gastric cancer. Regarding the TNM classification of malignant tumors (7th edition), early gastric cancer includes [16, 18, 21, 34]:

- Tis - intraepithelial tumor without invasion into its own plate of the mucous membrane, severe dysplasia
- T1 - the tumor grows into its own plate of the mucous membrane, the muscular plate of the mucous membrane or the sub mucosal base
- T1a - the tumor grows into its own plate of the mucous membrane or muscle plate of the mucous membrane
- T1b - the tumor grows into the underlying mucosal base

Materials and methods

The work was performed on the basis of the endoscopic and path anatomic departments of the GBUZ "GKB No. 31 DZM". For histological examination, a sample of stomach tissue was taken, removed by endoscopic dissection of the sub mucosal layer in a single block. For morphological examination, after macroscopic description and excision, stomach tissue samples were fixed with a 10% solution of neutral formalin, passed through alcohols of ascending strength according to the generally accepted method and poured into paraffin. Tissue sections prepared from paraffin blocks with a thickness of 4 microns were stained with hematoxylin and eosin, a CHIC reaction in combination with alcyan blue and picrofuxin according to van Gieson. An immunohistochemical study (hereinafter referred to as IHC) was carried out on the Bond immunostainer using ready-made monoclonal antibodies Desmin, CK8/18, CK7, Mucin-1, p53, CD34 and D2-40.

Results and their discussion

To the clinic of endoscopic surgery, patient M., 78 years old, on an outpatient basis, when performing esophagogastroduodenoscopy (EGDS), a lumpy, easily fragmenting formation of 1.5-1.7 cm of dense consistency was found in the area of large curvature of the stomach. A biopsy was taken. Histological examination revealed a tubular-fibrous adenoma with severe dysplasia and areas of highly differentiated adenocarcinoma. Next, patient M. enters GKB No. 31 for routine EGDS. The EVIS GIF- Q160Z endoscope is freely passed into the esophagus, then into the stomach. Gastric mucosa in all departments with signs of focal atrophy, in the antrum mainly by large curvature - foci of intestinal metaplasia in the form of areas of elevated mucosa of whitish color and light blue color when examined in the NBI mode, gastric fields are edematous, clearly outlined, the mucous membrane acquires a granular appearance. In the anal part of the stomach, a flat-raised epithelial formation of irregular oval shape in the form of a comma with a size of about 25x28 mm is determined by a large curvature, its surface is uneven, lobed, with a hill-shaped elevation in the central part up to 8-10 mm in diameter and up to 4-5 mm high, along the edges the height of the formation is not more than 2.5 mm (type 0-IIa+Is according to the Paris classification). The edges of the formation are uneven, clear for a longer distance, but its edge on the side of the anterior wall is more gentle, the border with the surrounding mucosa is less clearly visualized here. The formation has a light pink color, whitish compared to the surrounding mucous membrane, palpation ally soft, displaced. When examined in the NBI, zoom mode (115-fold increase) and chromos copy (0.2% indigo carmine solution): the edges of the formation are clearly defined, the surface is lobed, uneven, the dimple pattern is heterogeneous throughout the formation. On the surface of the central hilly raised area, the dimple pattern is distinctly heterogeneous in size and shape, at individual loci it is strongly crushed, indistinctly traced, micro vessels here have the appearance of an angular mesh network; as part of large pits having the appearance of papillae, defomated, convoluted micro vessels of different diameters are determined (irregular intracellular capillary loops), some vessels are pronounced unevenly dilated, convoluted. Throughout the flattened part of the formation,

whitish pits of the mucous membrane, somewhat wavy in shape, enlarged in size, densely adjacent to each other, are uniformly traced, capillaries repeat their contours, convoluted, angular, in some areas various pits in shape and size are determined *(Fig. 1).*

Fig. 1. Esophagogastroduodenoscopy. Stomach formation

Endoscopic diagnosis: superficial epithelial formation of type O-Pa+Is (early cancer). Endoscopic signs of mixed gastritis with multiple foci of intestinal metaplasia.

The course of the operation: the border of the cancerous tumor is circularly marked with electro coagulation marks at a distance of 3-4 mm from the visible edge. A sterile saline solution with the addition of epinephrine was gradually infiltrated under the base of the tumor (a total of 1 ml of 0.1% epinephrine was used), the tumor tissue was uniformly well raised throughout its entire length. A circular incision of the mucosa around the neoplasm was made. A gradual excision of the tumor in the sub mucosal layer was performed (electrosurgical unit ERBE mode Forced effect 4 Coag 80 W) with preliminary electro coagulation of the perforant vessels with an end ographer (Coag mode. soft effect 4, 80 W). The neoplasm was removed in a single block. During dissection, there were no signs of tumor invasion into the sub mucosal or muscular layers. The resulting mucosal defect is 35x35mm in size, its bottom is an even muscle layer with remnants of the sub mucosal. Hemostasis was performed by coagulation of small thrombosed vessels in the bottom of the defect using an endographer. The material was extracted for histological examination. Hemostasis control - dry.

A fragment of a lamellar type was sent for histological examination in a single block measuring 3.7x3.0x0.2 cm with a bumpy surface. After macroscopic examination, the edges of the resection and the rest of the tissue of the sent fragment were marked and taken separately for subsequent histological wiring. Routine staining with hematoxylin and eosin, CHIC reaction with alcyan blue, picrofuxin according to van Gieson were performed, and an immunohistochemical study was performed using ready-made monoclonal antibodies Desmin, CK8/18, CK7, Mucin-1, p53, CD34 and D2-40.

The morphological analysis included the following steps:

1. Determination of the pathological process in the sent object.

For this purpose, the histological classification of epithelial tumors of the stomach was used (WHO, 2010). Conclusion: tubular-villous gastric adenoma with severe dysplasia and areas of malignancy by the type of highly differentiated papillary adenocarcinoma *(Fig. 2).*

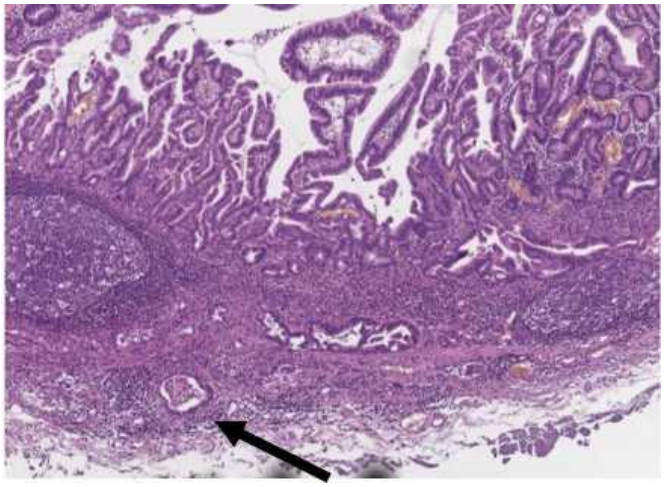

Fig. 2. A section of the mucous membrane and adjacent parts of the sub mucosal base of the stomach with the presence of highly differentiated papillary adenocarcinoma with a site suspected of invasion into the sub mucosal base (arrow). Color: hematoxylin and eosin. X 100)

2. Determination of the integrity of the muscle plate of the mucous membrane. In addition to the use of routine colorings, IHC (Desmin) was used to accurately verify the muscle plate. Conclusion: a violation of the integrity of the muscle plate of the mucous membrane is determined with the growth of a tumor into it and in growth into the sub mucosal base *(Fig. 3).*

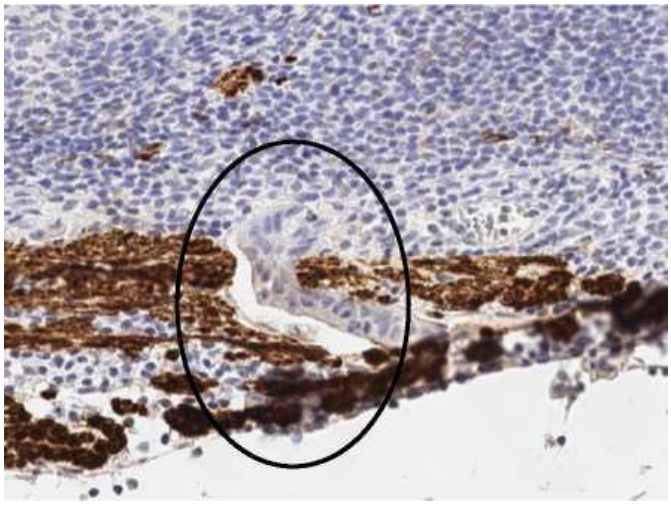

Fig. 3. Tumor germination of the muscle plate of the mucous membrane of the stomach wall (marked with an oval). IHC - Desmin. X 200

3. Assessment of the depth of tumor invasion.

Assessment of the depth of invasion of early gastric cancer is carried out from the muscle plate of the mucous membrane to the deepest point of invasion of the tumor. The fundamental point is to identify the depth of invasion of more than 500 microns!

Conclusion: the depth of maximum invasion into the sub mucosal base is 100 microns *(Fig. 4).*

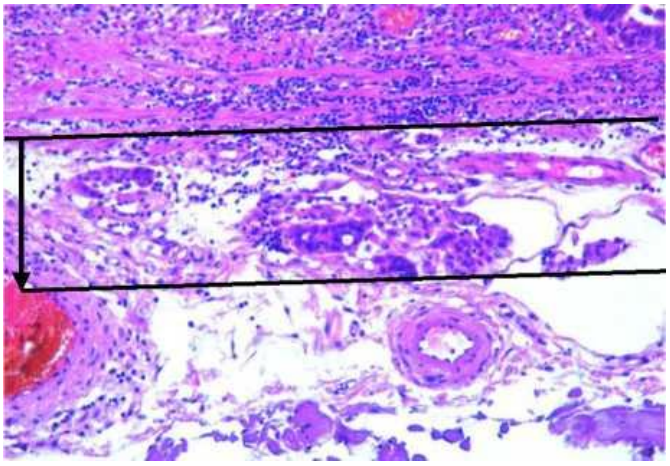

Fig. 4. The maximum depth of invasion into the submucosal base of the stomach wall (arrow). Color: hematoxylin and eosin. X 100

4. Determination of cancer emboli in the lumen of blood and lymphatic vessels.

CD34 expression with parallel expression of cytokeratin 8/18 was used for reliable determination of blood vessels (often they are "simulated" by stromal slits in the submucosal base). Antibody D2-40 was used to detect lymphatic vessels.

Conclusion: cancer emboli are visualized in the lumen of many blood vessels *(Fig. 5)*, no tumor emboli were detected in the lumen of lymphatic vessels.

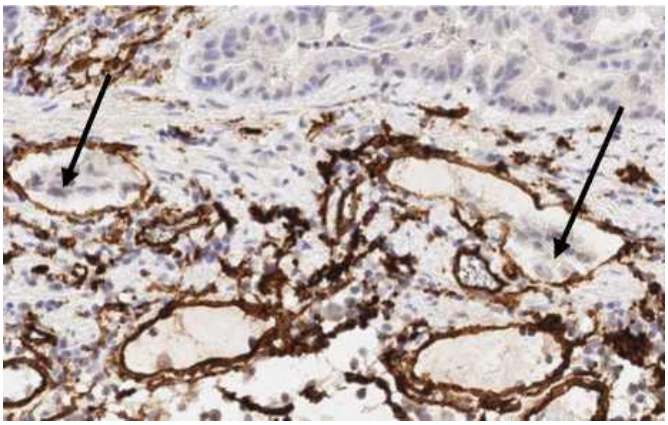

Fig. 5. Determination of blood vessels containing tumor emboli (arrows). IHC - CD34. X 200

5. Determination of the expression level of p53, muc-1, SK8/18, SK7.

To clarify the type of tumor, as well as the level of expression of the "wild" type of p53, IHC was performed. Moderate expression of bcl-2, p53, muc-1, SC7, and pronounced expression of SC8/18 are detected in tumor cells.

Conclusion: Intestinal adenocarcinoma with moderate expression of p53.

6. Assessment of the horizontal edge of the resection.

To accurately determine the absence of tumor growth in the edges of resection, the main point is the correct cutting of the material. There are 2 possible options: either the edges of the resection are taken and marked separately along the perimeter of the formation, or (which is more preferable), the material is cut into thin plates in 2 mm increments, each of which is marked and placed in a separate cassette. The material is taken for research entirely without an archive.

Conclusion: moderate chronic inflammation, foci of colonic metaplasia were detected in the horizontal edges of resection; no tumor growth was detected.

7. Evaluation of the vertical edge of resection.

With a negative vertical edge of resection, the tumor in the deep compartments covers the stomach tissue. To accurately determine the presence of tumor complexes in the resection margin, IHC with cytokeratins 7 is performed.

Conclusion: there is no tumor growth in the vertical edge of resection *(Fig. 6)*.

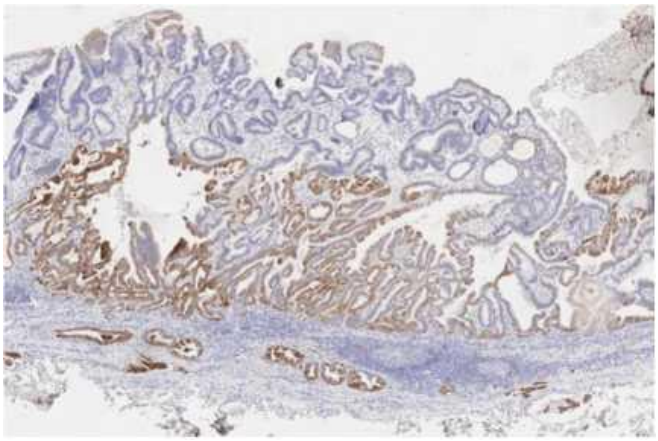

Fig. 6. Assessment of the vertical edge of resection. IHC - SK7. X 100

General conclusion: tubular villous adenoma of the antrum of the stomach with severe dysplasia; malignancy by type of highly differentiated papillary adenocarcinoma, intestinal type, O-IIa-Is, size 2.5x2.8cm, with foci of invasion into the subcutaneous layer up to 100 microns deep; with the presence of cancer emboli in blood vessels; horizontal and vertical edges of resection are negative; pTlbNxMx.

Conclusions

The obtained results are analyzed in accordance with the criteria of the effectiveness of the performed EGDS:

1. The degree of differentiation is a highly differentiated cancer;

2. Resection of education as a single unit;

3. Dimensions larger than 2.0 cm, but smaller than 3.0 cm (2.5x2.8 cm);

4. Invasion of blood vessels - identified;

5. Invasion of lymphatic vessels - not detected;

6. Ulceration - absent;

7. Invasion depth - less than 500 microns (100 microns);

8. The horizontal edge of the resection is negative;

9. The vertical edge of the resection is negative;

10. Classification by pTNM - pTlbNxMx.

Thus, according to points 1, 2, 510 - performed endoscopic submucosal resection can be considered successful. However, paragraph 3 makes the operation conditionally successful (extended indications for EGDS), and paragraph 4 puts it into the category of ineffective and requires further surgical treatment in an expanded volume.

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