

FEATURES OF ENDOSCOPIC DIAGNOSIS OF DIFFUSE GASTRIC CANCER

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ABSTRACT

Relevance: *Linitis plastica denotes a diffuse type of carcinoma, which accounts for 3-19% of gastric adenocarcinoma. It is characterized by rigidity of most or all of the stomach without a filling defect or extensive ulceration.*

The article describes the experience of endoscopic diagnostics of patients diagnosed with Linitis Plastica during 2019-2022 and the 1st half of 2023 at the Center for Expert Endoscopy and Interventional Radiology of the National Research Oncology Center (NROC), Astana, Kazakhstan.

The study aimed to evaluate the features of the use of endoscopic diagnostic methods in diagnosing diffuse gastric cancer.

Methods: a retrospective analysis of diagnosed cases of diffuse gastric cancer in the center of expert endoscopy was carried out from 2019 to the 1st half of 2023.

Results: All patients were initially examined in polyclinics at their place of residence by computed tomography gastroscopy with biopsy and, upon receiving a negative morphological examination, were sent to us for expert examination and repeated biopsy. The cohort included seven patients (2 men and five women) with an average age of 54.6 years (33 to 71 years). Expert gastroscopy and a special technique for taking biopsy material from the gastric mucosa helped make the correct morphological diagnosis for all seven patients with suspected diffuse gastric cancer. Considering the local and generalized metastases and concomitant pathologies, only four patients underwent surgery, and three were administered only chemotherapy. Five patients have died, and two continue palliative chemotherapy.

Conclusion: Plastic gastritis is a form of adenocarcinoma that usually manifests itself at an advanced stage when drug therapy is usually unsuitable. The prognosis can be improved with complete resection. Surgical intervention should be performed only in cases where complete resection is expected. Expert gastroscopy and the use of a special technique for taking biopsy material (according to J. Rohl) from the gastric mucosa increases the morphological value of biopsies and gives a chance to confirm the diagnosis of diffuse gastric cancer and quickly begin surgical treatment or palliative chemotherapy.

Keywords: Linitis Plastica (LP), diffuse gastric cancer, gastrointestinal cancer, Bormann IV, endoscopy.

Introduction: Linitis Plastica (LP) is a diffuse form of gastric cancer and accounts for about 10% of all cases of gastric adenocarcinoma; its exact distribution in the general population is unknown. LP affects women more often than men and is more common for Asians than Caucasians. The age group of patients is lower than in classic gastric adenocarcinoma, and the disease often begins below 40 years, sometimes among very young patients (20 to 25 years old). There are no distinctive or specific indicative symptoms; the symptoms are similar to other forms of gastric cancer and can include fullness after eating, nausea and vomiting, epigastric pain, weight loss, and progressive dysphagia [1]. LP is characterized by malignant glandular proliferation of cricoid cells in the fibrous stroma, ultimately leading to thickening and rigidity of the stomach wall. There are two types of LP: the 1st type of lesion begins from the proximal part of the stomach (body) in the folds thickening form; the 2nd type, the so-called "flat," begins from the antrum and is characterized by the folds flattening and stiffness (Figure 1).

These methods of radiation diagnostics give the right to suspect the presence of a diffuse process in the stomach wall but also require morphological verification. Thus, with this disease, the stomach fluoroscopy reveals a decrease in the stomach size, walls thickening, loss of motility, and pylorus ostium (Figure 2).

Computed tomography of the stomach shows diffuse walls thickening, decreased stomach lumen, and lymphadenopathy of paragastric lymph nodes (Figure 3).

The gastric endosonography reveals the thickening and blurring of the first three sonographic layers and a significant thickening of the 4th layer (Figure 4). The endosonographically guided needle biopsy (EUS with FNA) ensures a sensitivity below 30% since the cells are located in the fibrosis thickness both in a chain and alone.

Unlike other gastric cancers, LP often and quickly leads to lymphatic and peritoneal dissemination. Gastric LP can be primary or secondary due to infiltrating lobular breast carcinoma. LP is commonly sporadic, but family cases have also been reported [2].

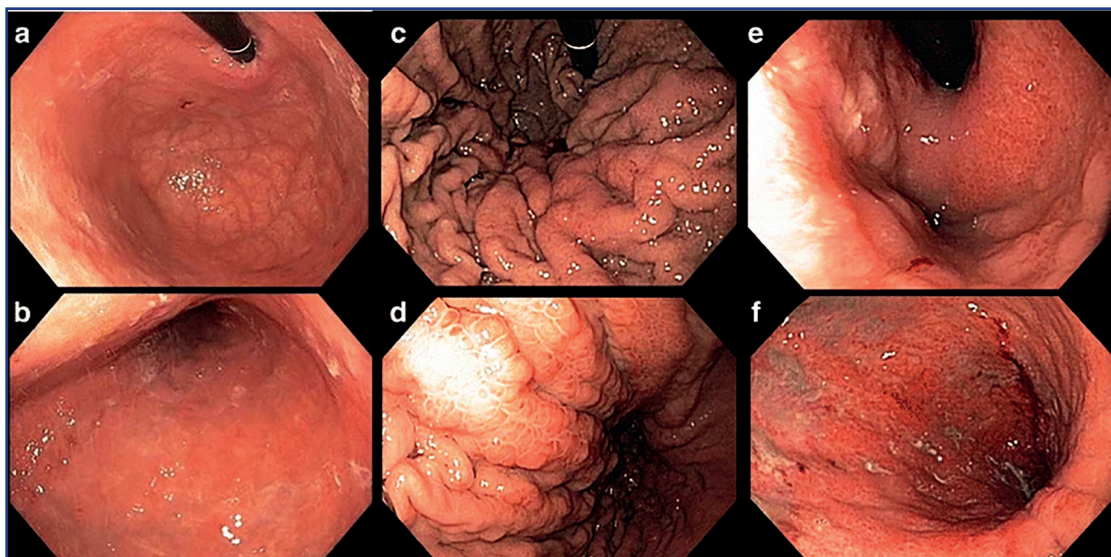


Figure 1 – Endoscopic types of diffuse gastric cancer: a-b – normal gastric mucosa, c-d – type 1 diffuse gastric cancer, e-f – type 2 (flat) diffuse gastric cancer [1]



Figure 2 – X-ray picture of diffuse gastric cancer [1]

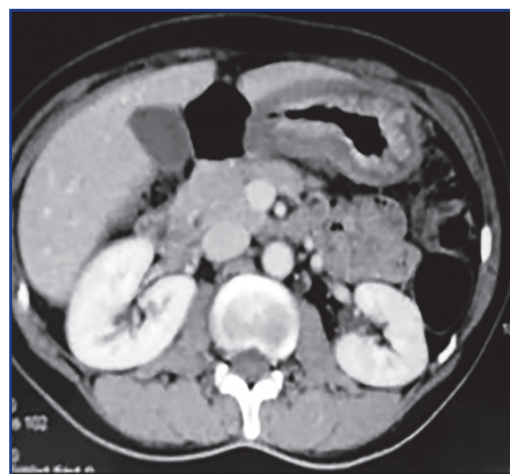


Figure 3 – Computed tomography of the stomach in diffuse gastric cancer [1]

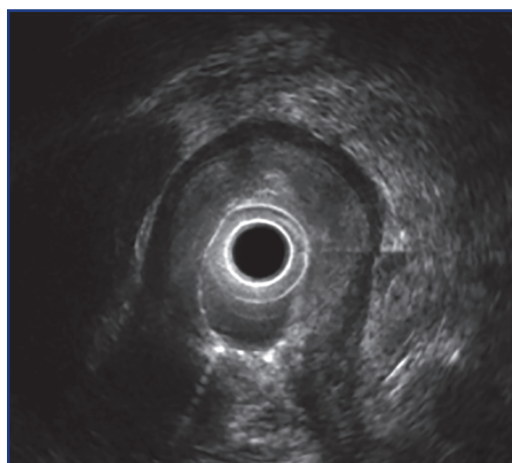


Figure 4 – Endosonographic picture in diffuse gastric cancer [1]

Materials and methods: This study is part of a single-center retrospective study evaluating the effectiveness of endoscopic technologies in diagnosing

diffuse gastric cancer. The case histories of 7 patients with diffuse gastric cancer, diagnosed and treated in the clinic of the National Research Oncology Center

(NROC, Astana, Kazakhstan), have been retrospectively analyzed. Patients diagnosed with LP were identified from the cancer database, and their clinical and pathological data have been extracted from relevant case histories. All cases were discussed in a multidisciplinary group, and their clinical progress and outcome have been noticed.

Results: All patients were initially examined at their local polyclinics and referred for CT and esophagogastroduodenoscopy with biopsy. Upon receiving a negative morphological examination, patients were sent to the NROC for expert examination and repeated biopsy. Their demographics, symptoms, endoscopy results, treatment details, and survival statistics are summarized in Table 1. The cohort included seven patients (2 males and five females) with an average age of 54.6 (33 to 71 years). The main manifested signs and symptoms were dysphagia and weight loss. The stomach was affected in 100% of cases. LP was detected in 100% of cases after a second biopsy by J. Rohl method, performed at the NROC. Primary and repeated biopsies were negative in all patients, and chronic hyperplastic gastritis was concluded.

In order to improve the accuracy of subsequent morphological examination, all patients referred to NROC with suspected diffuse gastric cancer during expert gastroscopy were biopsied using a special technique (according to J. Rohl, 2013). Namely, the biopsy material from the gastric mucosa has been taken polytopically from several points, step by step, using the Adson forceps. Besides, for reliability, the protruding part of the mucous membrane was resected using the diathermic loop and subsequent sampling of the biopsy specimen from the resected bed. One patient (case 1) was examined thrice since the first endoscopy revealed diffuse mucosa inflammation, and the biopsy showed only chronic inflammation without dysplasia signs. CT scan suspected LP but without a histological verification. A second endoscopy and biopsy were negative. Surgery was not offered to two patients with metastatic disease and one with extensive local organ involvement. Only four patients had local lymph node damage and no serious comorbidities, making performing a gastrectomy and subsequent chemotherapy possible. Five of 7 patients died within 2-7 months of follow-up period. At this point, the maximum survival rate recorded in that patient cohort was seven months.

Table 1 – Details of patients with diffuse gastric cancer

Nº	Age, gender	Symptoms	Endoscopic picture	No. of negative biopsies	Morphology	Treatment	Outcome at data collection time	Survival time
1	66 (female)	Dysphagia, weight loss	Type 2 (squamous)	3	Colloid cancer	Gastrectomy + 6 courses of neoadjuvant PCT	Death	6 months after gastrectomy
2	58 (female)	Dysphagia, loss of appetite, rapid food saturation	Type 1	1	Colloid cancer	4 courses of neoadjuvant PCT	Death	4 months after diagnosis
3	33 (female)	Dysphagia, vomiting of food, rapid food saturation	Type 1	2	Colloid Cancer Foci	3 courses of palliative PCT	Death	7 months after diagnosis
4	41 (female)	Dysphagia, weight loss, vomiting of food, loss of appetite, vomiting of food	Type 1	2	Diffuse undifferentiated adenocarcinoma with colloid cancer foci	Gastrectomy by Billroth-2	Death	2 months after gastrectomy
5	55 (male)	Dysphagia, loss of appetite, weight loss	Type 1	1	Non-differentiated cancer	2 courses of palliative PCT	Death	3 months after diagnosis
6	71 (female)	Dysphagia, loss of appetite, rapid food saturation	Type 1	2	Colloid cancer	Gastrectomy + 3 courses of adjuvant PCT	Alive	3 months after surgery
7	58 (male)	Dysphagia, loss of appetite, rapid food saturation	Type 1	1	Colloid cancer	Gastrectomy + 4 courses of adjuvant PCT	Alive	2 months after surgery

Note: PCT - polychemotherapy

Discussion: Gastric carcinoma is notorious for its inability to cause early symptoms, so patients do not seek care until the late stage of the disease. Due to the abundant lymph supply, the cancer quickly spreads beyond the reach of surgical resection. Consequently, the patients with symptoms tend to have a far-reaching malignant tumor. Diagnosing diffuse cancer is often challenging because there are endoscopically inactive and

endoscopically active phases. In the endoscopically inactive phase, there are complaints on dysphagia, but there are no visually visible changes in the endoscopic picture, such as the folds thickening or flattening and the rigidity of the walls. In the endoscopically active phase, the folds thinning, walls rigidity, and absence or weakening of peristalsis are already observed, but multiple superficial biopsies are often negative, and by that

time, the peritoneal and lymphogenous dissemination is manifested [3]. Therefore, a deep sequential biopsy with morphological verification of colloid cells in the fibrous stroma of the stomach wall is required. X-ray of the stomach with contrast is one of the final stages of diagnosis and gives a distinctive picture of the lumen narrowing, reduction of stomach size, folds thickening, and lack of peristalsis. Endosonography reveals blurring and thickening of the first three layers and a significant thickening of the 4th layer of the stomach wall to 10-20 mm. Computed tomography and endosonography may be useful for diagnosing and assessing the local spread. The differential diagnosis should include malignant diseases (adenocarcinoma and lymphoma) and some benign diseases with thickening of the stomach wall (Menetrier's disease, lymphoid hyperplasia, and amyloidosis).

The surgical treatment is possible only in 20-25% of cases of that disease due to observed early peritoneal dissemination and distant metastases. The surgery in the volume of total gastrectomy is indicated only in case of localized lesions.

In most cases, LP chemotherapy is the only alternative to treatment, but its effectiveness in this form of cancer is very low. Even with complete surgical removal of the tumor, adjuvant chemotherapy does not have such a positive effect as observed in the case of classical gastric adenocarcinoma [4]. Consequently, the average survival rate is 6 months without gastrectomy and 14 months with gastrectomy. Due to early peritoneal dissemination, lymphatic invasion, and metastasis to neighboring organs, the prognosis for this disease is unfavorable. In Europe and Japan, the 5-year survival rate amounts to only 10-20% [5].

Recently, much attention has been paid to the use of preoperative hyperthermic intraperitoneal chemotherapy (Hyperthermic Intraperitoneal Chemotherapy, HIPEC) in gastric cancer, both for prevention and treatment of peritoneal diseases, and several randomized trials are currently underway [6]. Given the strong peritoneal tropism of cirrhosis and LP tumors, HIPEC may come to the forefront soon as routine management of this patient subgroup.

It is known that the neoadjuvant therapy has many theoretical advantages. Among them, a higher degree

of treatment adherence compared to postoperative therapy and the possibility of reducing the tumor stage or size [7]. Since LP tumors are often advanced, neoadjuvant therapy may be of prime importance for improving local control and increasing the incidence of potentially curative gastrectomy.

Primary plastic gastric cancer is a diffuse carcinoma with a scirrhous stroma that invades the submucosa, occupying more than 1/3 of the stomach surface. Pre- or postoperative HIPEC may represent an alternative strategy, especially given this tumor's high peritoneal spread rates. Further progress is required in developing targeted therapies that will affect the cancer cells and their stroma.

Conclusion: Early diagnostics of diffuse gastric cancer is challenging. However, thickened folds, wall rigidity, and peristaltic movement deficiency shall alert the doctor. Multiple biopsies and loop resection of the affected area by the J. Rohl method increase the morphological value of the biopsy material, help verify the diffuse gastric cancer diagnosis, and quickly start surgical treatment or palliative chemotherapy.

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АНДАТПА

ДИФФУЗДЫ АСҚАЗАН ҚАТЕРЛІ ІСІГІНІҢ ЭНДОСКОПИЯЛЫҚ ДИАГНОСТИКАСЫНЫҢ ЕРЕКШЕЛІКТЕРІ

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Өзектілігі: *Linitis plastica* асқазан аденокарциномасының 3-19% құрайтын карциноманың диффузды түрін білдіреді. Ол асқазанның көп бөлігінің немесе бүкіл бөлігінің қаттылығымен сипатталады, толтыру ақауы немесе кең жаралар жоқ. Мақалада ұлттық ғылыми онкологиялық орталығының (ҰҒОО) сараптамалық эндоскопия және интервенциялық радиология орталығында 2019-2022 жылдар және 2023 жылдың I жартысы ішінде пластикалық линит диагнозы қойылған пациенттерді эндоскопиялық диагностикалау тәжірибесі сипатталған, Астана, Қазақстан.

Зерттеудің мақсаты: – диффузды асқазан обырын диагностикалау кезінде эндоскопиялық диагностика әдістерін қолдану ерекшеліктерін бағалау.

Әдістері: 2019 жылдан бастап 2023 жылдың 1-ші жартыжылдығына дейін сараптамалық эндоскопия орталығында асқазанның диффузды қатерлі ісігінің диагностикалық жағдайларына ретроспективті талдау жүргізілді.

Нәтижелері: Барлық пациенттер бастапқыда тұрғылықты жеріндегі емханаларда компьютерлік томография (КТ), биопсиялық гастроскопия арқылы тексерілді және морфологиялық зерттеудің теріс нәтижесін алғаннан кейін бізге сараптама мен қайталама биопсияға жіберілді. Когортқа орташа жасы 54,6 (33-тен 71 жасқа дейін) жеті пациент (2 ер адам және бес әйел) кірді. Асқазанның шырышты қабығынан биопсиялық материалды алудың білікті гастроскопиясы мен арнайы әдістемесі диффузды асқазан қатерлі ісігіне күдікті барлық жеті науқасқа дұрыс морфологиялық диагноз қоюға көмектесті. Жергілікті және жалпыланған метастаздар мен ілеспе патологияларды ескере отырып, тек төрт пациентке операция жасалды, ал үшеуіне тек химиотерапия тағайындалды. Бес науқас қайтыс болды, ал екеуі паллиативті химиотерапияны жалғастыруда.

Қорытынды: Қорытындылай келе, пластикалық гастрит аденокарциноманың бір түрі болып табылады, ол әдетте көп жағдайда дәрі-дәрмекпен емдеу мүмкін болмаған кезде кейінгі кезеңде көрінеді. Толық резекция кезінде болжамды жақсартуға болады. Хирургиялық араласу толық резекция қажет болған жағдайда ғана жасалуы керек. Сараптамалық гастроскопия және асқазанның шырышты қабығынан биопсиялық материалды алудың арнайы әдісін қолдану (J. Rohl бойынша) биоптаттардың морфологиялық құндылығын арттырады және диффузды асқазан обырын растауға және хирургиялық емдеуді немесе паллиативті химиотерапияны тезірек бастауға мүмкіндік береді.

Түйінді сөздер: Пластикалық линит, асқазан қатерлі ісігінің диффузды түрі, асқазан-ішек қатерлі ісігі, Борман IV, эндоскопия.

АННОТАЦИЯ

ОСОБЕННОСТИ ЭНДОСКОПИЧЕСКОЙ ДИАГНОСТИКИ ДИФFUЗНОГО РАКА ЖЕЛУДКА

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Актуальность: Linitis plastica обозначает диффузный тип карциномы, на долю которого приходится 3-19% аденокарцином желудка. Он характеризуется ригидностью большей части или всего желудка при отсутствии дефекта наполнения или обширных изъязвлений.

В статье описан опыт эндоскопической диагностики пациентов с пластическим линитом.

Цель исследования – оценка особенностей применения методов эндоскопической диагностики в диагностике диффузного рака желудка.

Методы: Проведен ретроспективный анализ 7 случаев диффузного рака желудка, диагностированных в Центре экспертной эндоскопии и интервенционной радиологии Национального научного онкологического центра (ННОЦ, Астана, Казахстан) с 2019 по 2023 гг.

Результаты: Все пациенты были первично обследованы в поликлиниках по месту жительства, где были направлены на КТ и эзофагогастроудоденоскопию с биопсией. При получении отрицательного морфологического исследования пациенты были направлены в ННОЦ для экспертного осмотра и повторной биопсии. Когорта пациентов состояла из 2 мужчин и 5 женщин со средним возрастом 54,6 года (диапазон 33-71 год). Для морфологической верификации диффузного рака желудка всем пациентам в Центре экспертной эндоскопии ННОЦ проводилась гастроскопия с биопсией с использованием специальной методики забора биопсийного материала. С учетом наличия местного и генерализованного метастазирования и сопутствующей патологии, оперативное лечение проведено только 4 пациентам, 3 пациентам назначена только химиотерапия. Летальный исход зафиксирован у 5 пациентов, 2 пациента продолжали паллиативную химиотерапию на момент сбора данных.

Заключение: Пластический линит является одной из форм аденокарциномы, которая обычно проявляется на более поздней стадии, когда в большинстве случаев медикаментозное лечение невозможно. Прогноз может быть улучшен при полной резекции. Хирургическое вмешательство следует проводить только в тех случаях, когда предполагается полная резекция. Экспертная гастроскопия и применение специальной методики забора биопсийного материала (по J. Rohl) со слизистой желудка увеличивает морфологическую ценность биоптатов и дает шанс подтвердить диагноз диффузного рака желудка и быстрее начать хирургическое лечение или паллиативную химиотерапию.

Ключевые слова: Пластический линит (ПЛ), диффузный тип рака желудка, рак желудочно-кишечного тракта, Борман IV, эндоскопия.

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