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Case Report

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Combined Treatment for Locally Advanced Cardioesophageal Cancer in a Comorbid Patient with Internal Carotid Artery Stenosis

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AIM OF THE STUDY was to present a case of combined, staged surgical treatment for locally advanced cardioesophageal cancer complicated by esophageal stenosis in a comorbid patient with a significant lesion of the internal carotid artery, and to summarize the data of scientific literature on the methods for its diagnosis and treatment.

MATERIAL AND METHODS A 65-year-old patient came to the Moscow Clinical Research and Practice Center named after A.S. Loginov in August 2020 with complaints of difficulty in passing solid food through the esophagus. During the examination at the Center, Siewert II cType 3 T4bN2M0 G3 cardioesophageal junction cancer was diagnosed. Taking into account the results of comprehensive diagnostics, the patient was found to have asymptomatic stenosis of the internal carotid artery up to 75%. Step-by-step surgical treatment of the patient was performed.

DISCUSSION In the presented clinical observation for prevention of intra- and postoperative ischemic complications, at the first stage the patient underwent carotid endarterectomy followed by surgical treatment for the underlying pathology. The presented observation is of interest due to the rare occurrence of such a combination of surgical interventions and the lack of consensus regarding the treatment tactics for this category of patients.

CONCLUSION Combined staged treatment of a patient with cardioesophageal cancer and internal carotid artery stenosis reduces the risk of perioperative complications and improves the prognosis of further treatment for the underlying disease.

Keywords: cardioesophageal cancer, internal carotid artery stenosis, carotid endarterectomy

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ACVA — acute cerebrovascular accident
CEA — carotid endarterectomy
CEC — cardioesophageal cancer
ICA — internal carotid artery
IS — ischemic stroke
MSCT — multislice computed tomography

INTRODUCTION

The term of "cardioesophageal junction cancer" includes tumors with an epicenter within 5 cm distal and 5 cm proximal to the Z-line, according to one of the most common classifications, which was proposed by R. Siewert in 1987. According to the US population-based cancer registry, from 1973 to 2015, the incidence of true cardioesophageal cancer (CEC) became equal to that of distal esophageal cancer, and the cumulative increase in the incidence of CEC from 1970 to the present has amounted to 350% [1, 2].

In this regard, prevention, diagnosis and treatment of CEC are of increasing scientific and practical interest. Despite significant global experience in the treatment of CEC, the approaches and treatment algorithms of the leading global associations continue to differ. In Western European countries and the USA, the concept of perioperative chemo- and chemoradiation therapy in combination with surgery prevails [3–5], while our Asian colleagues prefer surgery and supplement it with adjuvant chemotherapy only in the presence of compelling oncological indications [6].

In domestic clinical practice, we often encounter locally advanced forms of cardioesophageal junction tumors, the first signs of which are already manifested by the development of complications of the disease, most often in the form of dysphagia and (or) pain syndrome. In such cases, we adhere to the approach of the American and European oncological societies, giving preference to neoadjuvant chemotherapy with subsequent consideration of the issue of resection. It is important to understand that complicated course of the disease often requires correction of treatment tactics; the patients in most cases have severe nutritional status disorders (electrolyte imbalance, protein-energy deficiency), increasing the risk of developing postoperative complications and mortality [7]. With that said, clinical observations reflecting a multidisciplinary approach in comorbid patients with complications of locally advanced cardioesophageal junction cancer are of practical interest and deserve attention.

The presence of clinically significant atherosclerotic lesions of the major arteries of the head in patients whose main problem is another

pathology requiring surgical treatment deserves considerable interest due to certain risks of developing ischemic complications during surgical intervention and anesthetic care for the underlying disease [8, 9].

Ischemic stroke (IS) is a serious medical and social problem of modern society, as it is one of the main causes of disability of the working population. According to the Russian Ministry of Health for 2016, 950.9 cases out of 100,000 people over 18 years of age are annually affected by diseases of the major arteries of the head, 25% of whom suffer IS. According to WHO estimates, stroke ranks second among all causes of death in the world. In the Russian Federation, strokes account for approximately 21.4% of overall mortality [10].

The relationship between acute cerebrovascular accident (ACVA) and atherosclerosis of the internal carotid artery (ICA) was identified in the mid-20th century, and at that time, the concept was put forward that removal of atherosclerotic plaque could prevent stroke [11].

Currently, the risks of developing IS, depending on the degree of ICA stenosis, have been determined. Based on this knowledge, indications for surgical treatment were proposed. Carotid endarterectomy (CEA) is indicated for patients with symptomatic ICA stenosis greater than 60%, and asymptomatic stenosis greater than 70%. Surgical treatment was proven to reduce the risk of stroke in this category of patients [8, 12].

A special group consists of patients with comorbidity. Thus, in patients preparing for surgical treatment of coronary pathology, a history of critical stenosis of the ICA increases the risk of developing IS from 6 to 14%, when compared with patients without atherosclerotic lesions of the carotid arteries, 2% [13].

In patients with oncological pathology, the incidence of ICA stenosis does not differ from the known incidence of atherosclerosis in the population [14].

The question of the effectiveness of CEA in comorbid patients remains open, since the effectiveness of secondary prevention of IS is assessed within 5 years after revascularization surgery. This is especially true for patients with oncological pathology, for whom 5-year survival rates are critical. However, in order to reduce the perioperative risks of cerebral ischemic complications during the treatment of the underlying pathology, CEA is recommended as the first stage.

In our article, we present a case of combined stepped therapy of locally advanced Siewert type II cardioesophageal cancer, complicated by esophageal stenosis in a patient with concomitant hemodynamically significant ICA stenosis, which required surgical correction.

MATERIAL AND METHODS

A 65-year-old female patient came to the Moscow Clinical Research and Practice Center named after A.S. Loginov (the Center) in August 2020 complaining of difficulty in passing solid food through the esophagus. According to the patient, since November 2019, she had been experiencing periodic general weakness and nausea, but did not seek medical help. In May 2020, dysphagia, periodic vomiting when eating solid food, appeared for the first time. During examination at the Center, Siewert II cType 3 T4bN2M0 G3 cardioesophageal junction cancer was diagnosed.

Esophagogastroduodenoscopy data from 08.2020: endoscopic picture of infiltrative changes in the lower third of the esophagus with luminal stenosis (impassable for a standard endoscope), a nasal endoscope was inserted into the lumen of the stomach with difficulty, the length of the tumor stenosis was 2 cm, the tumor extended circularly to the body of the stomach. Multislice computed tomography (MSCT) data from 08.2020: uneven circular thickening of the gastric wall up to 14–16 mm at the level of the cardioesophageal junction, extending along the lesser curvature to the border of the middle and lower third of the body, along the greater curvature to the cardiac section, and also to the lower third of the esophagus (for about 30 mm

proximal to the esophageal opening of the diaphragm); the wall contour was somewhat bumpy with stenosis of the lumen and dilation of the lumen of the esophagus up to ~30 mm), with contrast enhancement it increasingly accumulated contrast medium.

The cellular tissue at this level was infiltrated with changes spreading to the crura of the diaphragm (the border with them was not traced), locally on the left lobe of the liver and the upper pole of the spleen, as well as the orifice of the celiac trunk. The following lymph nodes were visualized along the regional lymph drainage pathways: in the lower mediastinum, para-aortic ones up to 6×7 mm (with increased accumulation of contrast agent), lower paraesophageal ones up to 3 mm; cardiac ones, along the lesser curvature and along the left gastric artery, including those merging with the tumor with a thickness of about 8-10 mm; along the greater curvature and pyloric ones were not enlarged; along the common hepatic artery up to 6×9 mm and the celiac trunk up to 5×9 mm, along the splenic vessels and in the splenic hilum up to 5 mm. Lymph nodes of the abdominal cavity and retroperitoneal space (except for those described above): in the hepatoduodenal ligament up to 7×13 mm, aortocaval and paraaortic ones up to 5×8 mm, mesenteric ones 2–3 mm (the density of the mesentery is increased).

Pathomorphological examination dated 09.2020: poorly differentiated adenocarcinoma.

Taking into account the results of the comprehensive diagnostics, it was planned to perform diagnostic laparoscopy with peritoneal lavage in order to assess the extent of the tumor process and exclude peritoneal carcinomatosis and free tumor cells; however, during the examination, severe stenosis of the left ICA was revealed, which increased the perioperative risks of IS. In this regard, the patient was referred to the neurosurgeon.

In September 2020, the patient was hospitalized in the neurosurgical department and underwent additional examination. According to the computed tomography angiography data, atherosclerotic stenosis of the left ICA up to 75% was detected (Fig. 1). Ultrasound duplex scanning of the major arteries revealed an unstable nature of the atherosclerotic plaque. The diagnosis was “Asymptomatic stenosis of the left internal carotid artery up to 75%”.

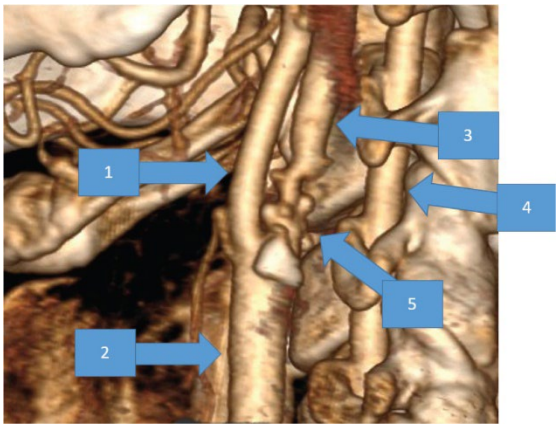

Fig. 1. Preoperative computed tomography angiography: 1. External carotid artery; 2. Common carotid artery; 3. Internal carotid artery; 4. Vertebral artery; 5. Atherosclerotic plaque

In order to prevent the ischemic type ACVA development, the patient underwent eversion CEA on the left through the anterior cervical approach (Fig. 2).

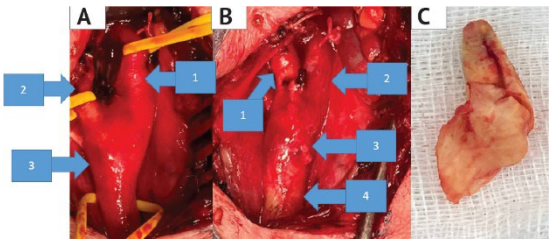

Fig. 2. Intraoperative photographs. A: 1. Internal carotid artery on the left; 2. External carotid artery; 3. Common carotid artery. B: 1. External carotid artery; 2. Internal carotid artery. 3. Vascular suture; 4. Common carotid artery. C — Atherosclerotic plaque

On the 2nd day after surgery, the patient's vital functions were compensated, and her neurological status was without deficit. According to the ultrasound examination of the brachiocephalic arteries, the left ICA was passable along its entire

length. On the 3rd day, she was discharged from the hospital in a satisfactory condition. After the surgical intervention, the patient was re-examined by an anesthesiologist and admitted to surgical treatment of the underlying pathology.

In October 2020, a diagnostic laparoscopy with peritoneal lavage was performed. No signs of peritoneal carcinomatosis or metastatic liver damage were detected. Cytological examination of peritoneal lavage dated 09.10.2020: no elements of malignant neoplasm were found in the provided material. Immunocytochemical study dated 10.09.2020: no malignant cells with antiendomysial antibodies (EMAs) were detected. Given the locally advanced nature of the tumor process, neoadjuvant chemotherapy was planned at the first stage of treatment, however, by this time, dysphagia had reached grade 3, which required urgent stent placement: on October 27, 2020, endoscopic stenting of tumor stenosis of the cardioesophageal junction was performed (metal stent, partially covered with BS 18 mm 120 mm Dist). The postoperative period was uneventful. After the stent was installed, adequate nutrition with gentle food was restored, the nutritional status was corrected, which made it possible to begin neoadjuvant chemotherapy using the FLOT regimen on 02.11.2020.

The patient underwent 9 courses of chemotherapy. The results of the follow-up examination revealed stabilization of the primary tumor with a partial reduction in regional lymph nodes, which allowed for full-scale radical surgical treatment.

Given the initial extent of the tumor, in order to ensure adequate access from the tumor, it was necessary to remove both the esophagus and stomach. On 04.07.2021, esophagogastrectomy with two-zone lymphadenectomy and plastic surgery of the left half of the colon was performed while maintaining nutrition through a. colica sinistra in an isoperistaltic position. The duration of the surgical intervention is 480 minutes (Fig. 3).

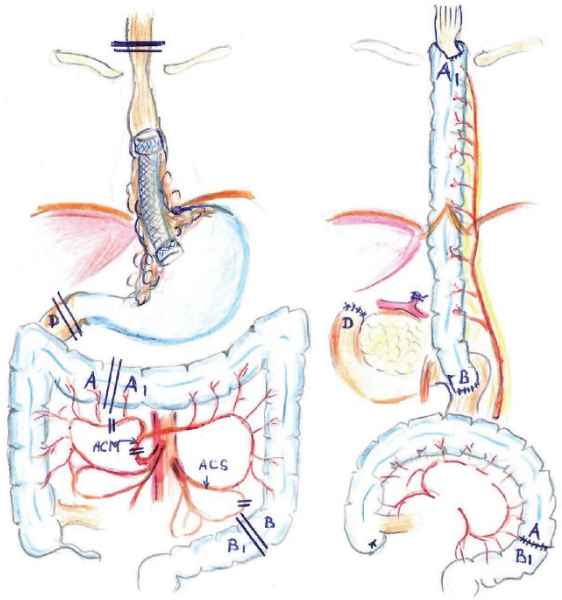

Fig. 3. Esophagogastrectomy with replacement of the transverse and descending colon with preservation of nutrition due to the left colic artery with the location of the graft in an isoperistaltic position
Notes: ACM — a. colica media; ACS — a.colica sinistra; D — duodenum; A1 — oral segment of the graft; B — caudal segment of the graft; || — lines of intersection of organs and vessels

Postoperative pathomorphological examination: Adenocarcinoma of the cardioesophageal junction with invasion into the adventitia of the esophagus and visceral peritoneum of the stomach, foci of perineural growth and lymphovascular invasion, with metastases in 3 regional lymph nodes, with the presence of a tumor embolus in the vein, with weakly expressed morphological signs of tumor regression after neoadjuvant therapy (TRG4 according to the Mandard classification) ypT4a N2 (3/14) L1 V1 Pn1 R0.

After surgical treatment, the patient's body weight decreased to 57 kg. Further, thanks to comprehensive nutritional support and a physiological method of reconstructing the digestive tract, the initial body weight of 67 kg was restored. Dynamic observation was carried out. Until February 2023 - no signs of relapse of the disease. In February 2023, she noted pain in the projection of the left hip

joint. MSCT data from 03.2023: multiple secondary focal lung lesions, left-sided hydrothorax, thickening of the walls of the colon graft (differentiate between inflammatory and neoplastic secondary changes), infiltration of the cellular tissue in the area of the right crus of the diaphragm, along the celiac trunk, common hepatic artery and splenic artery, with involvement of the portal vein confluence, adjacent organs (liver capsule, pancreas), minimal increase in the size of the formation of the lateral pedicle of the left adrenal gland, the appearance of a similar one in the body also on the left (probably of secondary genesis), focal formation in the left ilium and left sacroiliac joint, with probable involvement of surrounding muscles, intra-abdominal and retroperitoneal secondary lymphadenopathy. On 11.04.23, a biopsy of the soft tissue component of the metastatic lesion in the ilium was performed. Morphological examination: metastasis of mucinous adenocarcinoma to the soft tissues of the thigh. Palliative XELOX chemotherapy was initiated, 1 course of treatment was administered. The patient refused further treatment due to the severity of her condition.

Symptomatic therapy was carried out, due to deterioration of the condition, progression of the tumor process, the patient died on June 21, 2023. Overall survival was 2 years 6 months. Relapse-free survival was 2 years 2 months.

DISCUSSION

Atherosclerosis is a progressive degenerative process that affects many vessels in the body. According to scientific research, atherosclerotic lesions detected in one major vessel are certainly found in others; in 10–18% of patients with coronary heart disease, critical damage to the carotid arteries is detected [8, 15].

In patients preparing for coronary artery bypass graft surgery, a history of hemodynamically significant ICA stenosis makes one think about performing preliminary CEA due to the increased risk of intra- and postoperative cerebral ischemic complications [8, 16].

This is supported by statistical data, according to which the incidence of intraoperative cerebrovascular accidents and fatal outcomes during coronary artery bypass graft surgery is 14%. Whereas performing preliminary CEA reduces the risk of developing IS to 4% [17].

Other authors indicate that in patients with combined coronary and carotid atherosclerotic pathology who underwent coronary artery bypass graft surgery, the incidence of IS/fatality was 4% in the group of patients without prior CEA and 1% in patients who had previously undergone surgical treatment for ICA stenosis during the 30-day postoperative follow-up. The 90-day follow-up period showed that the incidence of IS/death in patients who did not undergo preliminary CEA was 9% versus 1% in patients after CEA [18].

Patients undergoing heart valve surgery are no exception. According to the studies cited, ICA stenosis is the cause of intra- or postoperative stroke in mitral valve surgery in 1.84% of cases [19].

This conclusion also applies to all surgical interventions not related to vascular surgery. Thus, in general surgery, the risk of stroke in patients with ICA stenosis is 3.6% [19].

The same applies to patients with oncological pathology. In particular, those who have previously undergone radiation therapy for neoplasms of the head and neck due to the negative impact of radiation on the intima of the ICA, which in turn triggers a cascade of degenerative processes leading to the formation of atherosclerotic plaques [20, 21].

Before surgical treatment of carotid arteries in these patients, it is necessary to weigh the pros and cons, take into account the expected survival of the patient, comorbid pathologies, state of vital functions, and consider the risks of surgical intervention.

Nevertheless, the fact remains that prophylactic CEA performance reduces the risks of intra- and postoperative strokes in cancer patients; the latter is confirmed by repeated successful cases of staged or combined surgical treatment of this category of patients [14, 21, 22].

Treatment of comorbid patients with complicated locally advanced cardioesophageal junction cancer requires a qualified multidisciplinary approach involving oncologists-chemotherapists, surgeons, nutritionists, endoscopic surgeons, and in some cases experts of other specialties in case of severe concomitant pathology that does not allow for full treatment of the underlying oncological disease in the required volume [23].

This clinical observation demonstrates the possibility of a significant increase in the duration and quality of life of a patient with a locally advanced form of cancer diagnosed at IVA stage. Despite the presence of concomitant vascular pathology, the development of tumor stenosis of the cardioesophageal junction, the patient was able to undergo surgical treatment for critical stenosis of the carotid artery, complete a full course of neoadjuvant chemotherapy, radical resection in the R0 volume, as well as achieve long-term control of the disease with the development of relapse only 26 months after the start of treatment.

CONCLUSION

Development of multidisciplinary interaction of experts of various specialties in the conditions of multidisciplinary centers will ensure further improvement of diagnostic and treatment outcomes for difficult patients with comorbidity.

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