CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Synchronous adenocarcinoma and gastrointestinal stromal tumor in the stomach – report of two cases

Dragoš Stojanović1,2, Nebojša Mitrović1,2, Dejan Stevanović1,2, Damir Jašarović1,2, Zorana Bokun-Vukašinović1, Marija Nikolić2

1University of Belgrade, Faculty of Medicine, Belgrade, Serbia; 2Zemun Clinical Hospital Center, Belgrade, Serbia

INTRODUCTION

A gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumor that occurs in the gastrointestinal tract, most commonly in the stomach or the small intestine. The surgery of the stomach is the dominant way of treatment of these tumors. The synchronous detection of adenocarcinoma and gastric GIST is not a very common condition, which is often diagnosed intraoperatively and has a significant impact on the prognosis of these patients.

OUTLINE OF CASES

We herein report two cases of gastric GIST with synchronous adenocarcinoma tumors, which were detected incidentally, intraoperatively, while the patients were undergoing surgery for a primary gastric adenocarcinoma.

The first case was of a 76-year-old female patient. The histopathological analysis of the operative specimen firstly showed a poorly differentiated advanced gastric adenocarcinoma. The second tumor, from the gastric serosa, was a spindle cell GIST of low risk. It was diffusely positive for DOG1, CD34, and CD117. Its proliferative index was established using the Ki67 antibody. The number of mitoses was one per 5 mm². The second case was of a 65-year-old male patient. The histopathological analysis revealed an early, well-differentiated, intestinal type adenocarcinoma of the gastric mucosa. The synchronous tumor from the serosa of the stomach was a spindle cell gastrointestinal stromal tumor (CD34, DOG1, and CD117 diffusely positive) of low risk. The proliferative index of this tumor, labeled with the Ki67 antibody, was very low. Necrosis was not present, nor was mitosis.

Conclusion: Synchronous adenocarcinomas and GIST of the stomach are not very commonly associated, and are usually detected intraoperatively and after an immunohistochemical analysis. Recognition of this condition has a very important role in a differential diagnosis and the exclusion of metastases of malignant tumor deposits. Based on the tumor severity, the radicalness of the surgical intervention is determined, which affects the outcome of these patients.

Keywords: gastrointestinal stromal tumor; gastric adenocarcinoma; synchronous tumor
REPORT OF CASES

We herein report two cases of gastric GIST with synchronous adenocarcinoma tumors which, while the patients were undergoing surgery for a primary gastric adenocarcinoma, were incidentally, intraoperatively detected to have a synchronous gastric GIST.

The first case is of a 76-year-old female patient. She was evaluated for her complaints of fatigue and upper epigastric pain. Laboratory test results showed low levels of iron. Ultrasonographic examination of the abdomen did not verify significant deviations from normal findings. Computed tomography examination of the abdomen, on the fundus of the stomach along with the large curvature, showed a soft-tissue tumor, with no significant post-contrast opacification, measuring up to 20 mm, which contained small calcifications (Figure 1).

Esophagastroduodenoscopy revealed on the large curve in the distal part of the corpus of the stomach the circular recess with irregular edges about 3 cm in diameter, on the wide basis, which had infiltrative changes. On the same level, but along the rear wall, gastroduodenoscopy showed a submucosal nodule, about 20 × 15 mm in diameter. The patient was treated surgically; the operation of choice was subtotal gastrectomy with D2 lymphadenectomy. Intraoperatively, changes on the large curvature of the stomach were verified – a nodule 3 cm in diameter, penetrating the serosa and the omentum. A 1 cm in diameter nodule was verified on the serosa of the gastric fundus. The histopathological analysis of the specimen primarily showed a poorly differentiated advanced gastric adenocarcinoma (histological grade 3) that infiltrated half of the stomach muscular wall thickness (Figure 2).

The final diagnosis was made by the immunohistochemical analysis, and the tumor was positive for cytokeratins. The second tumor, from the gastric serosa, was a spindle cell GIST of low risk. It was diffusely positive for DOG1, CD34, and CD117. Its proliferative index was established using the Ki67 antibody (+ in less than 3% of the tumor cells). The number of mitoses was one mitosis per 5 mm² (Figures 3 and 4).

The second case was of a 65-year-old male patient evaluated for his complaints of dysphagia, loss of appetite, pain in the upper abdomen and two episodes of melena. Laboratory test results showed low levels of hemoglobin.

Figure 1. Computed tomography findings of the 76-year-old female patient: a soft tissue tumor, with no significant post-contrast opacification along the large curvature of the stomach fundus (arrow)

Figure 2. The 76-year-old female patient: adenocarcinoma of the stomach, poorly differentiated, intestinal type (H&E, ×100)

Figure 3. The second tumor, from the gastric serosa in the 76-year-old female patient: gastrointestinal stromal tumor, spindle cell type (H&E, ×200)

Figure 4. The second tumor, from the gastric serosa in the 76-year-old female patient: gastrointestinal stromal tumor, spindle cell type, antiDOG1 antibody (×400)
Esophagogastroduodenoscopy verified hyperemic mucosa of the antrum, with subepithelial polypoid tumor, with central recess, about 3–4 mm in diameter. Biopsy was taken and histopathological examination showed a high degree of dysplasia. The patient was treated surgically; the operation of choice was subtotal gastrectomy. Intraoperatively, a small tumor was verified on the serosa of the stomach corpus, 10 × 13 mm in diameter, and a tumor on the stomach antrum, 5 mm in diameter, which did not penetrate the serosa.

The gastric tumor was located in the fundic part of the stomach. It was an ulcerative lesion, 5 mm in diameter. The serosal tumor weighed 0.6 grams, measuring 13 × 10 × 10 mm.

The histopathological analysis revealed an early, well-differentiated, intestinal type of adenocarcinoma of the gastric mucosa that superficially invaded the lamina propria. Signs of chronic atrophic gastritis with intestinal metaplasia in the surroundings of the above-mentioned tumor were noted.

The tumor from the serosa of the stomach was a spindle cell GIST (CD34, DOG1, and CD117 diffusely positive) of low risk. The proliferative index of this tumor, labeled with the Ki67 antibody, was very low (about 1% of Ki67 positive tumor cells). Necrosis was not present, nor was mitosis (0 mitoses / 50 high power fields, or 0 mitoses / 5 mm²).

**DISCUSSION**

The emergence of two histologically different neoplasms in the same organ is not very common. Adenocarcinoma is the most common malignant stomach tumor, while GIST is a stromal tumor of the digestive tract that occurs in less than 1% of all gastrointestinal malignancies [7]. Synchronous tumors are not a very common tumor association, and are usually detected only during the histopathological evaluation [8]. When the GIST is submucosal or subserosal, the gastric mucosa may not be invaded and the endoscopic biopsies can be normal. In most of the reported cases of synchronous gastric adenocarcinoma and GIST, the preoperative biopsy fragments showed only adenocarcinoma, and the GISTs were detected only following laparotomies and examinations of the resected stomachs [9]. In our first case, gastroduodenoscopy showed submucosal nodule, about 20 × 15 mm in diameter. In our second case, total gastrectomy was performed primarily for the gastric adenocarcinoma, and a small GIST was incidentally found with the histopathological examination of the specimen. The coexistence of the primary gastric adenocarcinoma and a GIST has often been detected incidentally on the gastric mucosa or serosa, or occasionally intramurally, at surgery or gastroscopy for other reasons [10]. Some authors have found that 10% of GISTs are in association with other neoplasms, usually cancer [11]. The incidence of synchronous occurrence of adenocarcinoma and GIST is 0.25%. According to the literature, co-existence of GISTs with other tumors ranges from 4.5% to 33%. Maiorana et al. [12] found that out of 52 patients there were six cases of GIST in association with other tumors (five with adenocarcinoma and one with carcinoid) [13]. GIST is most common in the stomach (60%), jejunum and ileum (30%), duodenum (5%), and colorectum (< 5%), while in a few individual cases a GIST was found in the esophagus and the appendix (< 1%) [14].

The literature describes the phenomenon of synchronous GIST with different tumors, adenocarcinoma, lymphoma, leukemia, lung cancer, prostate cancer, pancreatic cancer, adrenal adena [15, 16, 17]. In most cases, GIST and adenocarcinoma are described in different parts of the stomach, but in the literature there are few cases where they are in collision [18]. Patients treated for synchronous tumour should receive adjuvant therapy for the more advanced or aggressive tumour type [19]. Synchronous adenocarcinomas and GIST of the stomach are not a very common association of the two tumors, usually detected intraoperatively and after an immunohistochemical analysis. Recognition of this condition is very important in differential diagnosis and the exclusion of metastases of malignant tumor deposits. Based on the tumor severity, the radicalness of the surgical intervention is determined, which affects the outcome of these patients [18, 19].

GIST is positive for CD117, CD34, and occasionally for actin, but always negative for desmin and S100 protein [20]. In our cases, GIST is from the category of low risk, with spindle cells, with no signs of atypia, necrosis, or bleeding. Immunohistochemical staining was positive for the DOG-1, CD34, CD117, and Ki67 (1–3% of the tumor cells). Many studies highlight the positivity of CD117 and CD34 in GIST tumors. According to the literature, CD117 is expressed in 80–95% of the tumor cells. The definitive diagnosis is not possible if the tumor is negative for CD117, CD34, SMA, and S100 [20]. A novel marker DOG-1 has been found in GIST tumors, which can be used for definitive diagnosis. DOG-1 is a membrane calcium-dependent chloride channel expressed specifically and strongly at GIST [21, 22]. In our cases, definite diagnosis of GIST was possible because the tumour cells were diffusely and strongly positive for DOG1, CD34, and CD117.
Синхрони аденоакарцином и гастроинтестинални стромални тумор желуца – приказ два случаја

Драгош Стојановић1,2, Небојша Митровић1,2, Дејан Стевановић1,2, Дамир Јашаровић1,2, Зорана Бокун-Вукашиновић2, Марија Николић2

1Универзитет у Београду, Медицински факултет, Београд, Србија; 2Клиничко-болнички центар Земун, Београд, Србија

САЖЕТАК
Увод Гастроинтестинални стромални тумори (ГИСТ) најчешћи су мезенхимални тумори који се јављају у гастроинтестиналном тракту, најчешће у желуцу и танком цреву. Операција је доминантан начин лечења ових тумора. Синхронни аденокарциноми и ГИСТ желуца су честа асоцијација два различита типа тумора, који се често јављају интраоперативно и имају значајан утицај на прогнозу болесника. Позната је веома низак, а некроза и митозе нису биле присутне. Пролиферативни индекс је установљен антителима CD34 и CD117 дифузно.

Приказ болесника У овом раду дат је приказ два случаја синхроних аденоакарцинома и гастроинтестиналних тумора желуца, који су дијагностиковани случајно у току операције. Пациенткиња стара 76 година, код које је хистопатолошка депозита малигног тумора. На основу узнапредовалости уврште се као гастроинтестинални стромални тумор вретенастих ћелија желуца, ниска позитивност на DOG1, CD34 и CD117, а пролиферативни индекс је 1/5 mm². Други случај је болесник стар 65 година оперисан због раног доброго диференцираног аденоакарцинома интестиналног типа, код којег је интраоперативно установљен синхронни ГИСТ вретенастих ћелија. Закључак Синхрони аденокарциноми и ГИСТ желуца су не тако честе асоцијације димензију различита типа тумора, који се обично откривају интраоперативно и после имунохистохемијске анализе. Позната је веома низак, а некроза и митозе нису биле присутне. Синхрони аденокарциноми и ГИСТ желуца су са нижим ризиком. Пролиферативни индекси био је веома низак, а некроза и митозе нису биле присутне..

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