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CASE REPORT

RARE COINCIDENCE OF GASTRIC CANCER AND LARGE MYOFIBROBLASTIC TUMOR OF THE SPLEEN

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Abstract. *Although its incidence has been decreasing during the last decades, gastric cancer remains a common disease and a global health problem. Conversely, inflammatory myofibroblastic tumors, especially the splenic ones, are extremely rare neoplasms. A female patient in her 50s was hospitalized due to upper gastrointestinal bleeding after a recent coronary stenting. Gastroscopy with a biopsy established an ulcer-type gastric adenocarcinoma. Contrast-enhanced computer tomography (CT) detected additionally an enlarged spleen with a hypodense, well-marked tumor inside. Neither CT, ultrasound, nor PET-CT imaging were conclusive about its type. Gastrectomy, omentectomy, splenectomy and lymphonodal dissection were performed. Histological and immunohistochemical studies proved a gastric adenocarcinoma and a synchronous splenic inflammatory myofibroblastic tumor resected in negative margins. After receiving chemotherapy, the patient is without any data for recurrence. The splenic inflammatory myofibroblastic tumor remains a diagnostic challenge due to the lack of specific clinical and imaging signs, especially in a case with a synchronous abdominal tumor. So, histopathological examination with immunohistochemistry performed by an experienced pathologist is crucial. This paper presents a unique coincidence of epithelial malignant and mesenchymal tumor–gastric cancer and splenic inflammatory myofibroblastic tumor. Hopefully, this report will be valuable in future investigations about these neoplasms' genesis, diagnosis, and treatment.*

Key words: *gastric cancer, splenic myofibroblastic tumor, inflammatory pseudotumor, surgical resection, immunohistochemistry*

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INTRODUCTION

Although its incidence has been decreasing during the last decades, gastric cancer (GC) remains a global health problem [1, 2]. In 2020, it was reported as the fifth most common cancer and the fourth leading cause of cancer death worldwide [3, 4]. Geographically, it is more common in East Asia (China and Japan), Eastern Europe (including Bulgaria), and Central and South America [3, 4]. Conversely, inflammatory myofibroblastic tumors (IMTs), also known as inflammatory pseudotumors, are rare solid mesenchymal tumors with a predilection for the lungs, orbit and abdominopelvic tissues [5]. Splenic IMTs are extremely rare, as their incidence is about 0.0007%, including all surgical and autopsy series

[6]. This article presents the case of a patient with the coexistence of the described tumors, which is quite unusual and unique.

CASE PRESENTATION

A female patient in her 50s was admitted to a regional hospital due to upper gastrointestinal bleeding three months after placement of a coronary stent for an acute myocardial infarction. The suspected cause of the hemorrhage was the dual antiplatelet therapy the patient has been taking. The performed gastroscopy established an ulcer-type tumor of lesser gastric curvature. The biopsy proved a well-differentiated adenocarcinoma, intestinal type. Contrast-enhanced computer tomography (CT) detected an enlarged spleen (126/88 mm) with a hypodense, well-marked tumor formation with a diameter of 66 mm (Fig. 1). The tumor showed rapid contrast enhancement during the early contrast phase with subsequent fast wash-out. The radiologist's conclusion was a possible hydatid cyst or a metastatic lesion. Due to these findings, the patient was referred to our Department of General and Hepato-pancreatic Surgery. The patient complaints included pain in the upper part of the abdomen and weight loss (about 15 kg). The physical examination of the abdomen did not reveal any pathological findings. The laboratory tests revealed mild anemia (Hemoglobin 115 g/l) and slightly elevated CRP – 13.6 mg/l, and fibrinogen – 5 g/l. Serological tests for hydatid disease were negative. The ultrasound examination also detected the known splenic mass, described as cystic, with internal septs. In addition, a positron-emission tomography (PET-CT) was performed to improve the preoperative diagnosis of the splenic lesion. The images revealed: (1) an area of moderately increased metabolic activity (SUVmax 5.5) along the lesser gastric curvature, corresponding to the location of the known tumor; (2) solitary nodules between greater curvature and spleen, as well as of smaller size in subsplenic adipose tissue, without significantly increased size or metabolic activity; (3) diffuse and moderately heterogeneous increased metabolic activity (SUVmax 6.6) in the CT-known lesion in the splenic parenchyma, which cannot be unambiguously interpreted.

The patient comorbidities included recent myocardial infarction (already mentioned) and posttraumatic epilepsy.

The intraoperative exploration revealed: (1) a tumor (about 4/5 cm) located in the gastric corpus, mainly along the lesser curvature of the stomach with visible transmural infiltration; (2) multiple enlarged locoregional lymph nodes, as well as in the hilus of the spleen and along the upper edge of the pancreas; (3) lobulated tumor (about 8/9 cm in size) in the lower pole of the spleen. The liver was found without macroscopically visible or palpable pathological changes. Gastrectomy, omentectomy, splenectomy and lymph node dissection were performed (Fig. 2).

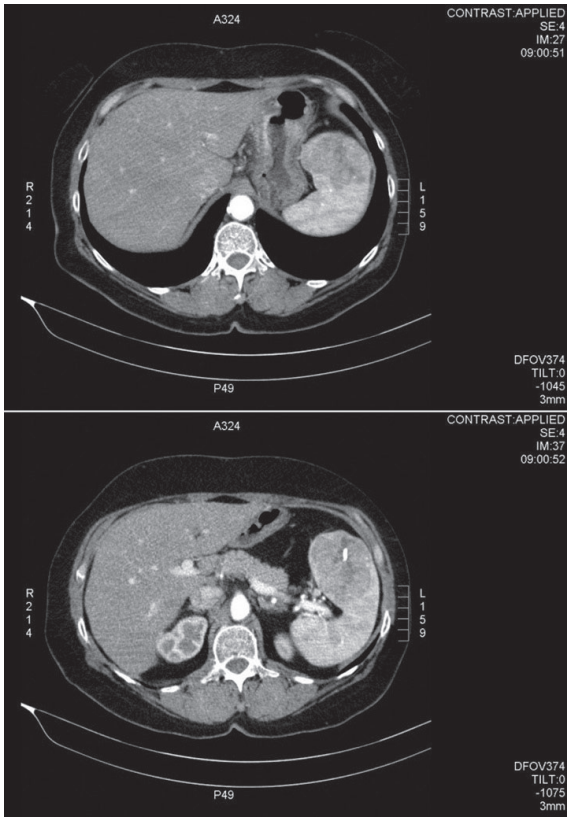

Fig. 1. CT images of a thickened gastric wall (the lesser curvature) and the presence of a splenic mass

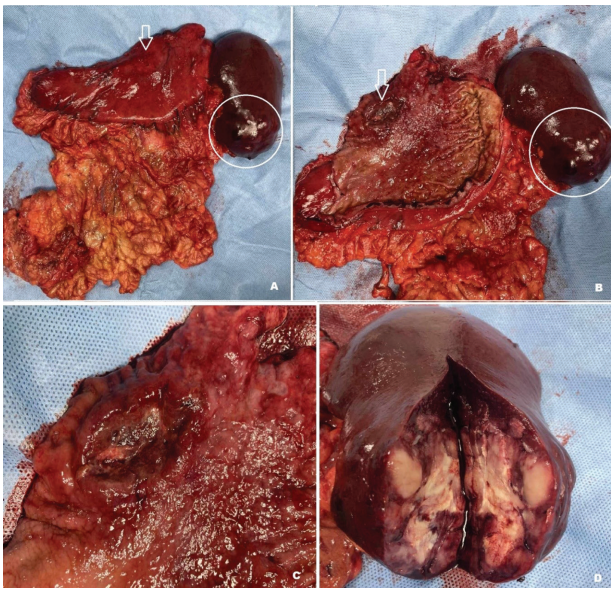

Fig. 2. The view of the specimen before (A) and after the section across the lesser curvature (B); Gastric tumor is marked with an arrow, while the splenic mass – with a circle; (C): Closer macroscopic view of the ulcer-type gastric cancer; (D): Macroscopic view of the cut surface of the splenic lesion

The histological and immunohistochemical studies proved a moderately differentiated tubular adenocarcinoma of the gastric corpus with transmural infiltration and serosal breakthrough and the presence of a signet-ring cell component – about 30% of the examined tumor tissue. Disseminated tumor emboli in lymphatic capillaries were found. A total of 57 lymph nodes were isolated, 8 of which had metastases and extranodal extension. The resection margins were negative. The splenic lesion was diagnosed as an inflammatory pseudotumor (myofibroblastic tumor) – spindle cells with characteristics of fibroblasts and myofibroblasts (SMA-positive/ALK-negative/CD30-negative/CD23-negative) were found, which partially displaced the structures of the spleen; without metastases.

The postoperative period was uneventful. The patient received adjuvant chemotherapy. A regular follow-up was performed. Nineteen months after the operation, the patient was in good health without any clinical, ultrasound, endoscopy, or PET-CT imaging data for the recurrent disease.

DISCUSSION

Gastric cancer is a common and aggressive malignant neoplasm with epithelial origin. According to GLOBOCAN data from 2020, about 1.1 million cases of gastric cancer were diagnosed worldwide, and 770,000 deaths were due to the same disease [1, 3]. The latest statistics for Bulgaria showed a GC incidence of 19.7/100,000 (almost 1400 new cases per year) and a GC-related mortality rate of 16.1/100,000 (about 1100 deaths per year) [4]. A variety of factors, including infectious, environmental, and genetic ones, have an impact on the development of this tumor [1, 2]. The Helicobacter pylori infection, also found in the presented case, was proven to be a carcinogen, even though the detailed mechanisms are not fully understood [1]. The H. pylori effect on oncogenesis has been described through two main mechanisms: indirect inflammatory response to the infection on the gastric mucosa and direct epigenetic effect of H. pylori on the stomach epithelial cells [2, 7]. Another microorganism related to GC is the Epstein–Barr virus (EBV). However, only 10% of GCs are associated with such an infection, and specific features characterize these cases – it typically presents a lump or ulcer with lymphocyte infiltration in the proximal stomach. The lesion has a lower tendency of lymph node metastasis but a greater rate of submucosal invasion. However, the overall prognosis is better [1, 2, 8].

Many studies on the genetics and molecular biomarkers of GC have been performed. Hereditary cancer of the stomach could be related to mutations in CDH1, BRCA2, STK11, ATM, SDHB, PRSS1, MSR1, CTNNA1 and PALB2 genes [2]. However, the patient presented in this article is the first in her family to have GC. Critical signatures for GC development encompass HER2 expression modules, factors regulating apoptosis, cell cycle regulators, factors affecting cell membrane properties, multidrug resistance proteins, and microsatellite instability [2].

In general, the diagnosis of GC (as in the presented case) is based on gastroscopy with a biopsy performed due to complaints such as dysphagia, reflux, weight loss, gastrointestinal bleeding, anemia, or vomiting [9]. CT and MRI are comparable and often sufficient for imaging and GC staging. PET-CT is not ideal for T-stage evaluation but can be considered for specific clinical indications such as further evaluation of indeterminate lesions and the preoperative chemotherapy response [1, 2, 9]. This diagnostic algorithm was adopted in the case shown in this article – CT and ultrasound examinations were performed after the GC detection through gastroscopy, and subsequent PET-CT was conducted because of the unexpected finding in the spleen. However, none of these imaging tests could prove the type of splenic mass preoperatively.

Inflammatory myofibroblastic tumors (IMTs) are rare, typically intermediate malignant neoplasms with potential local recurrence and a low risk of metastases (< 5%) [10]. They could be found in various organs and tissues with a predilection for lungs and orbits [10, 11]. Localization in the spleen is extremely rare. Until 2019, only 120 cases of splenic IMT have been reported in the literature [6]. According to the current review of the medical scientific data, the case of coexistence of gastric cancer and IMT described in this article is the first presented in the literature.

The etiology of IMT remains unclear [5, 6, 10, 11]. According to several studies, it represents an immunological response to an infectious or non-infectious agent. The reported triggers could be EBV, HIV and HHV-8 infections, surgery, trauma, hemangioma bleeding or rupture, or immunologic disorders [6, 10, 12, 13]. EBV could be part of the gastric cancer pathogenesis, too [1, 2, 8]. However, such a kind of infection has not been proved in the case presented in this article.

Preoperatively, the splenic IMTs present a diagnostic challenge because the clinical signs are pretty unspecific [5, 6, 10, 14]. Left upper quadrant abdominal pain, fever, splenomegaly, anemia, weight loss, or a discrete splenic mass could be part of the clinical picture of the disease [10]. However, most of these

symptoms could be related to any other benign or malignant splenic disease [10]. Alternatively, as in the presented case, they could be a result of gastric cancer, and it might be suggested that the splenic IMT was an incidental finding on imaging tests. Ultrasonography, CT and MRI are commonly used as diagnostic tools [6, 10, 12, 15]. Imaging characteristics of IMT also vary, so the differential diagnosis remains quite broad [16], especially in cases such as the one presented in this article – the splenic mass should be distinguished not only between the primary splenic tumors but also the metastatic lesions and hydatid disease. In an ultrasound examination, IMTs are generally shown as well-defined hypoechogenic masses with partial calcification and unspecific vascularization [10-16]. CT typically reveals a hypo- or isodense lesion with variable contrast enhancement due to the fibrous component [10-16]. As in the presented case, PT-CT usually shows irregular metabolic activity, with occasional intense FCG uptake [10-16]. So, the IMT should be distinguished from a lot of diseases, such as lymphoma, hamartoma, plasmacytoma, inflammatory pseudotumor-like follicular dendritic cell sarcoma, malignant fibrous histiocytoma, hemangiomas, sclerosing angiomatoid nodular transformation (SANT), age-related EBV-associated lymphoproliferative disease and metastatic lesion [10]. Because of that, the histopathological examination with immunohistochemistry analysis performed by an experienced pathologist is crucial [10, 12]. Microscopically, IMTs comprise a proliferation of spindle cells in an inflammatory stroma, mainly consisting of mature plasma cells, histiocytes and lymphocytes, and rarely neutrophils and eosinophils [6, 10, 11, 17]. Immunohistochemical staining typically shows positivity for smooth muscle actin (SMA), desmin and vimentin, but CD21, CD23, CD35, CD15 and CD30 negativity [10]. The positive rate range of ALK (anaplastic lymphoma kinase) is 30%-65%, which is more frequent in younger patients [6, 10, 18].

Surgical resection is the golden standard for treatment [5, 6, 10]. The prognosis of splenic IMT has been reported to be favorable after splenectomy [5]. Steroids, radiotherapy, and chemotherapy could be initiated in unresectable cases [19].

CONCLUSIONS

The splenic inflammatory myofibroblastic tumor is extremely rare and remains a diagnostic challenge due to the lack of specific clinical and imaging signs. This article presents the case of a patient with an unusual and unique coexistence of malignant epithelial (glandular) and mesenchymal tumor (IMT) in the stomach and spleen, respectively. So, hopefully, this case report will be valuable in future investigations about the genesis, diagnosis, and treatment of these types of neoplasms.

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