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A case of multi-focus gastric adenocarcinoma occurring synchronously with an associated gastric GIST

Authors' Contribution:

- A** Study Design
- B** Data Collection
- C** Statistical Analysis
- D** Data Interpretation
- E** Manuscript Preparation
- F** Literature Search
- G** Funds Collection

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Summary

Background

The occurrence of multiple primary malignancies in the same patient is rare but, in order to improve prognoses among gastric cancer patients, the early identification of further cancers is considered to be of crucial clinical importance.

Aim

In this paper we have presented our observations relating to a case of multi-focus gastric adenocarcinoma occurring synchronously with an associated gastric Gastro-Intestinal-Stromal-Tumour (GIST).

Case Report

We report a case of multi-focus gastric adenocarcinoma occurring synchronously with an associated gastric GIST in a 78-year-old man treated in the Great Poland Cancer Center.

Conclusions

We conclude, in common with other authors, that in order to increase the incidence of early diagnosis in cases of early stage carcinoma, and thus prolong the patients' lives, or even cure them completely, it is essential to identify high risk patients, especially in the case of primary carcinoma recognition during the actual diagnosis or in the past. Diagnosis must be thorough and precise, while treatment applied should be adequate. After surgery, the patient should be continuously monitored.

Key words

synchronous gastric carcinoma • Gastro Intestinal Stromal Tumour

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BACKGROUND

The occurrence of multiple primary malignancies in the same patient is rare. Such cases are described as synchronous or metachronous cancers. Such cases may arise from different organs or different types of tissues. Synchronous tumours are defined as entities which are diagnosed within 6 months of the diagnosis of a primary malignancy. Synchronous tumours are characterized by the presence of different histological features with no physical connection between the two or evidence of metastatic disease [1]. Improvements in prognosis have led to an increased incidence of second primary cancers, since patients with primary malignancies have an increased risk of developing a second primary cancer. This has had a negative influence on the overall prognosis for these patients [2].

Many authors have presented synchronous malignancies localized in different organs [2–6] including gastric cancer. Synchronous or metachronous primary malignancies have been detected in organs other than stomach or in cases of multi-focus gastric adenocarcinoma [7,8]. The occurrence of both malignant gastric carcinoma and gastric malignancies arising from other tissues in the same patient is very rare. In the synchronously observed cases which have been described, gastric lymphoma was reported more frequently than gastric adenocarcinoma [9].

AIM

In this paper we present our observations regarding a case of synchronous multi-focus gastric adenocarcinoma with an associated gastric GIST. This is probably the first publication in which these two malignancies have been reported synchronously in the stomach.

CASE REPORT

In January 2005, a 78-year-old Polish man was admitted to the 2nd Surgical Oncology Department of the Great Poland Cancer Centre, Poznań. The patient complained of weakness and periodic vomiting and had been diagnosed as suffering from ischemia. A gastric tumour was suspected. Gastroscopy showed: i) in the sub-cardiac region: a polyp, 3cm in diameter, with a wide base and covered by normal mucosal epithelium and ii) in the pre-pyloric region: a polyp of non-uniform shape, 3.5cm in diameter and covered by “dysplastic” mucosa with white plaques, iii) in the corpus

of the stomach there were small solitary polyps covered by normal mucosa. Histological examination revealed: 1) *polypus adenomatosus*; 2) *dysplasia epithelii gradu majoris*. The biopsy material was insufficient for pathological diagnosis and examination of the whole tumour was suggested. X-ray examination of the upper digestive tract showed a small peri-cardiac hernia and a well dissociated shadow of a 4×5cm tumour resembling a calcified cyst in the stomach. Laboratory analysis showed aniso-erythrocytes and poikilocytosis, carcino-embryonic antigen (CEA): 0.7ng/ml and alpha-fetal protein (AFP): 3.64ng/ml. Clinical data (weight loss, weakness) correlated with the results of gastroscopy (gastric tumours with dysplastic mucosa), and though there was no pathological verification, ischaemia suggested a diagnosis of gastric carcinoma and the patient was referred for surgery. After the patient was admitted, pre-surgical exams were ordered. Haematological and biochemical tests, an X-ray examination of chest and abdominal ultrasound were normal. There was no evidence of metastatic disease in the abdomen. We recommended laparotomy, gastrotomy and wide local excisions of the tumours. Consequently, after obtaining the patient's consent, an operation was carried out on the 26th of January 2005. A hard tumour, 5cm in diameter was discovered in the gastric sub-cardiac region during the laparotomy. There was a soft 3×2cm diameter tumour in the pre-pyloric region. Both tumours were excised. We performed gastrotomy for access and wide local excisions. The postoperative course was uneventful and the patient was discharged on the fourteenth day after the surgery.

Histological examination revealed: i) a 3 calcified tumour of 3cm in diameter in the sub-cardiac region and partially covered by mucosa, initially diagnosed as: *Neoplasma nonepitheliale fusocellulare probabiliter benignum*; in the differential diagnosis GIST and *leiomyoma* were suggested. Immunohistochemical studies on the paraffin-embedded tissue showed positive staining for CD117(+), CD34(+), S-100(±) and negative for SMA(-), desmin (-), AE1/AE3(-) and Ki67(-), which did not suggest proliferative activity. The complete pathologic examination revealed: *tumour stromalis tractus digestivi benignus (GIST)*; ii) in the pre-pyloric region was a tumour measuring 2.5×2.5×1.5cm, diagnosed as: *Adenocarcinoma tubulare G3 exulcerans in adenomate*. There was no certainty about free margins.

We recommended a second laparotomy and total gastric resection. After the patient had agreed,

he was again re-admitted for this further surgery. X-ray images of the upper digestive tract showed: narrowings in the pre-pyloric region with pre-stenotic high gastric movements. The mucosa and gastric folds were normal. Surgery was performed in April 2005. Total gastric resection was performed by the Roux-Y method. Histological examination revealed: in macroscopic examination i) cicatrices with omental adhesions in the anterior wall of the gastric corpus, ii) a field of abnormal mucosa in the pre-pyloric region, measuring 0.5×0.5cm and lying 1.5cm from the distal excision margin and iii) a lack of mucosa on the posterior wall of the gastric corpus. Microscopic examination revealed: i) *cicatrix* on the anterior wall of the gastric corpus, ii) *adenocarcinoma tubulare* – carcinoma infiltrated muscular membranes of the mucosa in the pre-pyloric region and iii) on the posterior wall of the gastric corpus: *adenocarcinoma tubulare G2 typus intestinalis s. Lauren*, carcinoma infiltrated muscular membranes of the mucosa and submucosa. In another part of stomach, histopathological examination revealed: *metaplasia intestinalis completa diffusa, gastritis chronic*. Examination of the regional lymph nodes of the greater curve revealed adenocarcinoma metastasis in only one node. The final histopathology result was: *Status post resectionem tumoris corporis ventriculi et polypi regionie pylori ventriculi. Adenocarcinoma tubulare bifocale (regionie pylori et curvaturae maioris corporis) ventriculi. Metastases carcinomatosae in uno lymphonodo. G2,pT1,pN1. tumour stromalis tractus digestivi (GIST) benignus.*

The postoperative course was uneventful and the patient was discharged on the thirteenth day after surgery. The patient was observed further on an outpatient basis and underwent a metastatic work-up. To date, no metastatic disease has been observed.

DISCUSSION

In this study two kinds of synchronous malignancy were recognized: a multi-focus gastric adenocarcinoma and an associated gastric GIST. These arose from different tissue types. The occurrence of primary multiple malignancies originating from different tissues and arising in the same organ is very rare. In this case, nonspecific symptoms delayed and disturbed proper recognition. Both malignancies were detected as polypoid lesions, in one case the lesion was covered by normal mucosal epithelium and in the other it was covered by dysplastic mucosa with white

plaques. Endoscopic biopsy material was inadequate for pathological diagnosis. Histological examination after the endoscopy and local surgical excision was recommended. This kind of treatment, which depends on histological diagnoses and free margins, could be defined as final operation. In this case, both malignancies were detected after local surgical excision but subsequent total gastrectomy led us to recognize another focus of gastric adenocarcinoma. This focus of gastric adenocarcinoma had been asymptomatic in prior examinations. Intra-operative histological examination was not carried out, in order to avoid the loss of, or damage to, this unusual specimen. Fortunately for this patient, the histological examination showed involved surgical margins and further surgery was performed. According to many authors, a one-stage operation to excise both malignant tumours at the same time is an efficient and safe method of treatment [2,5]. In our case, however, this kind of treatment was not possible owing to the lack of earlier diagnosis.

The second malignancy was also detected as a polyp. Gastrointestinal stromal tumors were defined as one of the most common mesenchymal neoplasms of the abdominal cavity. GIST is thought to arise from precursors shared with the intestinal gut pacemaker cells (Cajal cells). Pre-surgical knowledge of the tumour is very important in treatment planning. For local advanced GIST, wide local excision of the primary focus or complete excision of invaded organs should be performed, if it is possible without damaging the tumour [10]. In total resections of tumours, with intent to cure, the presence of clear resection margins is of crucial importance for patient survival. It has been suggested that the results of treatment are influenced mainly by the adequacy of surgical procedure [11]. Imatinib mesylate is an effective nonsurgical treatment for patients with advanced metastatic or inoperable GIST. Several clinical trials have confirmed the efficacy of imatinib in the treatment of metastatic/inoperable GIST [12,13] though it should be underlined that for patients with longer follow-up times, the rate of disease progression or resistant increases and complete remission is rare [14–16]. The quality of GIST surgery therefore has a crucial role in patients' prognosis.

In the presented case, the size of the primary tumour and the histological type of GIST were found to be characteristic features of a tumour of lower recurrence potential. There were clear resection margins around the primary tumour. We had no

doubts concerning the extent of surgery after the first operation. Even before the second operation, the prognosis of the patient was good.

CONCLUSIONS

The advisability of surgical treatment for multiple primary carcinomas seems to be indisputable. Radical surgery to excise both malignant tumours at the same time is recommended but, in many cases, there may be problems associated with early diagnosis [17]. In our opinion, which is shared by many authors, in order to increase the likelihood of carcinoma diagnosis at an early stage, and thus prolong patients' lives, or even cure them completely, it is essential to identify high risk patients, especially in the case of primary carcinoma recognition during the actual diagnosis or in the past. Diagnosis must be thorough and precise, while treatment applied should be adequate. After surgery, the patient should be continuously monitored. Many authors stress the fact that the risk of postoperative complications does not depend solely on the course of the operation. The stage and clinical advancement of the carcinoma is the decisive factor and good results depend primarily on early diagnosis.

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