

An unusual case of synchronous lymphoma and adenocarcinoma occurring as a collision tumour in the stomach – a case report

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SUMMARY

The occurrence of malignant gastric lymphoma and adenocarcinoma in the same patient is very rare. Here we report a case of synchronous gastric carcinoma and gastric lymphoma with a follicular growth pattern associated in a 73-year-old man. Preliminary diagnosis gastric tumour was suggested so laparotomy was performed for the purpose of treatment resection of the stomach. In the operation field, there was a main lesion spreading through the whole of the stomach and additional multiple lymph node enlargements at the hepato-duodenal, retro-pancreatic and the para-aortic lymph nodes. A short-term intraoperative examination of one of the metastatic lymph nodes showed lymphoma of the stomach. Palliative total gastrectomy Roux-en-Y was performed. Finally the pathology of the specimen revealed two different collided tumours: adenocarcinoma solidum and non-Hodgkin's lymphoma malignum with follicular growth pattern. Following surgery and chemotherapy, the patient is now in a disease progress state.

KEY WORDS: synchronous tumours, gastric cancer, lymphoma, adenocarcinoma

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BACKGROUND

The occurrence of malignant gastric lymphoma and adenocarcinoma in the same patient is very rare [1, 2]. Adenocarcinoma of the stomach is still one of the most common malignancies whereas primary gastric lymphoma is relatively uncommon, occurring in only 1–7% of all malignant neoplasms of the stomach [1]. In the literature in such synchronously observed cases the following lymphomatous components were reported: superficial spreading low grade mucosa associated lymphoid tissue (MALT), mass-forming immunoblastic lymphoma, diffuse infiltrating T-cell pleomorphic small cell lymphoma and diffuse large cell type of B cell origin lymphoma [1]. *Helicobacter pylori* infection is considered to be associated with development of these double malignancies [3–8]. In many such synchronously observed cases lymphomas may precede carcinogenesis, while prognosis appears to be more closely associated with the adenocarcinoma than the lymphoma [1]. This phenomenon is probably connecting with the fact that more of the lymphomas are usually histologically low grade. Only a few reports have described cases of synchronous adeno-

carcinoma associated with low grade B-cell lymphoma of mucosa-associated lymphoid tissue (MALT) of the stomach [8–23]. However, reports of other types of malignancies synchronously discovered with gastric carcinoma are rather unique. Sung Ha Park et al. [24] reported a single case of gastric carcinoma with a synchronously discovered non-Hodgkin's lymphoma diffuse large cell type (B-cell) but not involving the gastrointestinal tract. Nishino N et al. [25] reported synchronously non-Hodgkin's diffuse large cell type (B-cell) and adenocarcinoma occurring as a collision tumour in the stomach.

AIM

Here we report our observations regarding an unusual case of synchronous gastric carcinoma and gastric lymphoma with a follicular growth pattern associated.

CASE REPORT

In February 2004, a 73-year-old man was admitted to the Great Poland Cancer Centre at the 2nd Department of Oncological Surgery, Poznań. Before that he had suffered from periodic epigastric pain, weakness, periodic vom-

iting, loss of appetite and tiredness, but he did not complain of fever or night sweats. In the preliminary diagnosis a gastric tumour was suspected and appropriate diagnostic procedures were applied. Gastrofibroscopy showed a lesion infiltrating the corpus of the stomach. Histological examination revealed carcinoma solidum ventriculi. X-ray of the upper digestive tract showed an ulcero-infiltrative mass lesion in the corpus of the stomach; the cardiac region, fornix and antrum were normal. The patient was directed to surgery. After he was admitted to the 2nd Department of Oncological Surgery presurgical exams were ordered. Haematological and biochemical tests and x-ray chest examination were normal. Abdominal ultrasound showed enlargement of the lymph nodes in the epigastric region and enlarged infiltrated stomach wall. There were no signs of metastatic disease in the abdomen. We recommended laparotomy and consequently, after the patient had agreed, he underwent an operation. In the operation field, there was no evidence of metastatic lesions in the liver or peritoneum. The main lesion of the stomach was an ulcero-infiltrative mass tumour spreading through the whole of the stomach and there were also multiple lymph node enlargements at the hepato-duodenal, retropancreatic and the para-aortic lymph nodes. A short-term intraoperative examination of one of the metastatic lymph nodes suggested lymphoma. Palliative total gastrectomy Roux-en-Y oesophago-jejunostomy with end-to-side anastomosis, and distal jejuno-jejuno anastomosis and lymphadenectomy of the remaining enlarged lymph nodes was performed (D2 dissection). The postoperative course was uneventful and the patient was discharged on the 13th day after the surgery.

The pathological analysis of the specimen described the lesion of the stomach as a poorly differentiated adenocarcinoma infiltrating the whole gastric wall and extending to the serosa and perigastric lipid tissue. The pathology also showed the collision areas of the two neoplastic components. Near the infiltrated poorly differentiated adenocarcinoma there were massive lymphocyte components consisting of small cells with a follicular growth pattern. It was revealed to be a lymphoma infiltrating the perigastric lipid tissue. Regional lymph node examination revealed lymphoma in 12 of 102

nodes. There was no evidence of adenocarcinoma metastases. An immunohistochemical study on paraffin-embedded tissue showed: CAM 5.2+, CK7+, CK20-, and Ki67 positive in 60% of nuclei of the adenocarcinoma cells. The pattern of lymphoma immunohistochemical staining was: CK-, CD20+, CD79a+, bcl2+, CD3-, CD30- and finally Ki67 positive in a few nuclei of the lymphoma cells. The final histopathological diagnosis was: 1) Carcinoma solidum adenoides (CAM 5.2+, CK7+), 2) Lymphoma malignum folliculare G1 (CD20+, CD79a+, bcl2+).

The patient was directed to radical COP chemotherapy course with Encorton p.o., Endoxan i.v. and Vincristin i.v. according to standard procedure at the Department of Chemotherapy, Great Poland Cancer Centre. After that he underwent a bone marrow biopsy which revealed 30% of lymphoma cells in bone marrow. There were palpable inguinal nodes. The patient completed 8 cycles of COP chemotherapy for treatment of the lymphoma. In September 2004 during examining of the abdomen direct [RA1] tenderness of the epigastric area was noted. There were no palpable lymph nodes in the cervical, supraclavicular, axillary or inguinal areas. The computer tomography showed a solid heterogeneous tumour localized near the visceral trunk. There was evidence of invasions of the tumour to the pancreas, spleen, spleen vein, transverse colon, ileum bowels and the upper part of the right kidney. Gastrofibroscopy showed no evidence of disease recurrence. The patient underwent fine needle biopsy under computer tomography control. Microscopic examination revealed poorly differentiated adenocarcinoma cells. Next the patient underwent palliative 5FU+Leucovorin LF1 chemotherapy course with Fluorouracil i.v. and Leucovorin i.v. in standard doses (Fluorouracil 3750, Leucovorin 185 mg in 1 week cycle). The patient finished 4 cycles of palliative chemotherapy for treatment of the recurrent adenocarcinoma. The patient was under symptomatic and palliative treatment and he is still being treated at the Great Poland Cancer Centre as an outpatient. The last checkup was noted in April 2005. Systematic progress of recurrent carcinoma and consistent worsening of living conditions have been observed.

DISCUSSION

The occurrence of primary multiple malignancies arising from different tissue in the same organs and patients is very rare [2]. There have not been many case reports of other types of malignancies synchronously associated with gastric adenocarcinoma, especially occurrences in the same organs. In the reported synchronously observed cases we found in the literature such lymphomatous components as: superficial spreading low grade mucosa associated lymphoid tissue (MALT), mass-forming immunoblastic lymphoma, diffuse infiltrating T-cell pleomorphic small cell lymphoma, diffuse well-differentiated lymphocytic lymphoma and diffuse large cell type of B cell origin lymphoma (non-Hodgkin's lymphoma) [1, 9, 8, 24, 26, 27]. There is only one non-Hodgkin's lymphoma (diffuse large cell type (B-cell)) [24]. Non-Hodgkin's lymphomas have been classified by several different systems over the past 30 years. The newer system is called the Revised European American Lymphoma (REAL) classification and has been recommended for use [28]. In our case the synchronously-discovered malignant lymphoma involved the stomach, the lymph nodes of gastric curvatures and localized near the visceral trunk. Bone marrow biopsy showed 30% malignant lymphoma cells. Chest examination showed that the lymphoma did not involve the lung or the mediastinum. The pathology revealed a low-grade lymphoma but the 'stage' was described as CS IV_E because of extranodal standed for and affected the bone marrow (Lugano staging system). A controversy concerned the diagnosis of undifferentiated small cells that frequently turn out to be undifferentiated carcinoma or high grade malignant lymphomas. An immunohistochemical study showed positive staining for CD20, CD79a, bcl2 and negative for CK, CD3 and CD30 in the lymphoma cells. Some cases of anaplastic cell lymphoma and Hodgkin's disease express keratin but in most cases (like this one) keratin antibodies distinguish lymphoma and anaplastic carcinoma [24, 29]. In our case, expression of keratin was observed in cells from the part of the mass with adenocarcinoma infiltrating (CAM 5.2, CK7) but not in cells from lymph nodes and tumour lymphoma. Moreover, in lymph cells, only B-cell specific surface markers such as CD20

and CD79a were expressed. Bcl-2 protein was positive but differences between adenocarcinomas and lymphomas were not statistically significant in some reports (70% for lymphomas and 30% for adenocarcinomas) [29, 30]. Immunophenotyping markers makes it easy to differentiate lymph node B-cell lymphoma and gastric carcinoma. Immunohistochemically, the Ki-67 labelling indicated (a few percent) significantly lower proliferative activity of the lymphoma than the adenocarcinoma (60%) [1]. This phenomenon was probably due to the fact that the lymphoma in our case was histologically low grade. According to the published data we know that more synchronous and metachronous lymphomas are histologically low grade [1]. Nakamura et al. [1] additionally found that the size of the lymphomas was significantly larger than that of adenocarcinomas and the depth of invasion also tended to be deeper in lymphomas than adenocarcinomas. In conclusion the author suggested that lymphomas preceded the carcinogenesis. Finally in our case the histopathological diagnosis was follicular lymphoma. In the REAL classification, follicle centre lymphomas (follicular centre cell lymphomas with a follicular growth pattern) are one of the more common non-Hodgkin's lymphomas. They afflict almost exclusively adults, particularly the middle-aged and elderly. They are of B-cell lymphocyte origin. Because the small-cleaved cells of follicular lymphomas know how to circulate in the blood, patients usually present with disseminated lymphadenopathy. Nonetheless these lymphomas have a better prognosis than higher grade lymphomas.

Due to the lack of any long-term follow-up observations the prognosis of patients with double primary gastric lymphoma and adenocarcinoma is unknown. Nakamura et al. [1] suggested that the survival probability appeared to be similar to that for gastric adenocarcinoma. These results, in addition to the fact that many of the lymphomas were low grade with lower MIB-1 index, suggest that prognosis depends on the behaviour of the adenocarcinoma rather than the lymphoma. In our case the adenocarcinoma was a poorly differentiated carcinoma in clinical stage II with poor clinical prognosis. Surgical treatment of gastric cancer has been universally recog-

nized as the most effective way of treatment. However, curative resection of cases in stage III and IV and poorly differentiated carcinoma results only in an average survival period, little more than of patients without operation [31].

The advisability of surgical treatment for primary multiple neoplasms seems to be indisputable. A one-stage operation to excise both malignant tumours at the same time is possible. Treatment strategies for extranodal non-Hodgkin's lymphoma are well established, but there still remains controversy regarding the optimal approach, particularly for gastric lymphoma [32, 33]. Surgery, radiotherapy and chemotherapy have been used alone or in various combinations.

In our opinion, which is shared by many authors, in order to increase the early diagnosis of an early stage carcinoma and thus prolong patients' lives, or even cure them completely, it is essential to identify high risk patients, especially with primary carcinoma or other types of malignancies recognized during the actual diagnosis or in the past. This group of patients needs to receive adequate treatment, and ought to be continuously monitored after the surgery. According to the literature data, lymphoma may precede the development of adenocarcinoma in many of the synchronous cases [1]. *Helicobacter pylori* infection is also thought to play an important role in the pathogenesis of these double malignancies [3-8]. Prophylactic endoscopy and *Helicobacter pylori* eradication are necessary in order to increase early diagnosis of the early stage and to identify high risk patients.

CONCLUSIONS

Finally the conclusion is that the stage and clinical progression of the adenocarcinoma and lymphoma are decisive, but results appear to be similar to those for gastric adenocarcinoma.

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