Synchronous gastric tumours (carcinoid and adenocarcinoma) - Report of two cases

Blanka Kupková[1], Stanislav Rejchrt[1], Jan Nožička[2], Rudolf Repák[1], Marcela Kopáčová[1], Stanislav Filip[3], Jan Bureš[1]

[1] Clinical Centre, 2nd Department of Internal Medicine, Charles University Teaching Hospital, Hradec Králové, Czech Republic

[2] Fingerland Department of Pathology, Charles University Teaching Hospital, Hradec Králové, Czech Republic

[3] Department of Oncology and Radiotherapy, Charles University Teaching Hospital, Hradec Králové, Czech Republic

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Abstract. *Synchronous gastric tumours have rarely been reported in literature. They can grow separately within a stomach or be a merging of two originally separate neoplasms (collision tumour) or be mixed to form a composite tumour. We report two cases of synchronous gastric carcinoid and carcinoma. In the first case of a 79-year-old woman, three separate polypoid gastric tumours were found (adenocarcinoma and two carcinoid tumours). There were marked intestinal metaplasia of the prepyloric antrum and focal chronic atrophic gastritis, with increased serum gastrin, Helicobacter pylori negative. Autoantibodies against parietal cells of the stomach were positive. There were no distant metastases. Carcinoid syndrome was absent. In the second case of a 77-year-old man, tumorous triplicity was found: gastric adenocarcinoma and carcinoid of the stomach as well as cutaneous non-Hodgkin B-cell lymphoma originating from the patient's face. Helicobacter pylori was negative at histology, there were no signs of atrophic gastritis. Carcinoid syndrome was absent.*

Key words: *synchronous gastric tumours, adenocarcinoma, carcinoid.*

Kupková B, Rejchrt S, Nožička J, Repák R, Kopáčová M, Filip S, Bureš J. Synchronní nádory žaludku (karcinoid a adenokarcinom) - popis dvou případů. Folia Gastroenterol Hepatol 2004; 2 (1): 46 - 52.

Souhrn. *Synchronní nádory žaludku jsou v literatuře popisovány zřídka. Mohou růst odděleně nebo dosahovat jeden druhého (tzv. kolizní nádor) nebo vytvářet smíšený (kompozitní) tumor. Autoři popisují dva případy synchronních nádorů žaludku. V prvním případě byly u 79-leté ženy zjištěny v žaludku tři polypoidní tumory (adenokarcinom a dva karcinoidy). Dále byla zjištěna výrazná intestinální metaplázie žaludečního antra, fokální chronická atrofická gastritida se zvýšeným sérovým gastrinem. Helicobacter pylori byl negativní, autoprotilátky proti parietálním buňkám žaludečního těla byly pozitivní. Nebyl vyjádřen karcinoidový syndrom. Ve druhém případě byla u 77-letého muže zjištěna nádorová triplicita: žaludeční adenokarcinom a karcinoid a kožní non-Hodgkinův B-lymfom tváře. Nebyla zjištěna atrofická gastritida, Helicobacter pylori byl negativní. Ani v tomto případě nebyl vyjádřen karcinoidový syndrom.*

Klíčová slova: *synchronní nádory žaludku, adenokarcinom, karcinoid*

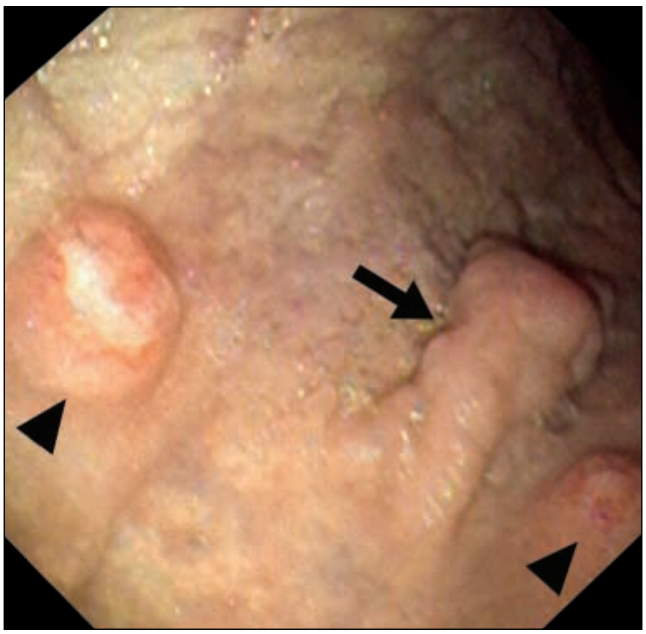

Fig. 1
A 79-year-old female investigated because of microcytic sideropenic anaemia. Three polypoid tumours were found at the middle part of the major curvature and the anterior wall in the gastric body (30 mm, 15 mm and 7 mm in diameter). Adenocarcinoma is marked with an arrow, carcinoids are indicated by arrowheads.

Synchronous gastric tumours have rarely been reported in literature. They can grow separately within a stomach or be a merging of two originally separate neoplasms (collision tumour) or be mixed to form a composite tumour (43).

Gastric carcinoids may constitute 2 - 10 % of all carcinoid tumours. Type 1 gastric carcinoids are associated with hypergastrinaemia and chronic atrophic gastritis, type 2 carcinoid tumours occur in MEN-1 (multiple endocrine neoplasia 1) combined with Zollinger-Ellison syndrome, and type 3 carcinoids lack any relation to hypergastrinaemia (6,8,14,16,31,33). Gastric carcinoid tumours can be multiple and/or associated with other synchronous gastric neoplasms (5,15,17,20,32,34,35,38,44). Similarly, gastric adenocarcinoma, especially early cancers, can also be multifocal (22,25,27,37,40,46) and/or simultaneously associated with other tumours of the stomach (2,10,19,21,42). We report two cases of synchronous gastric carcinoid and carcinoma.

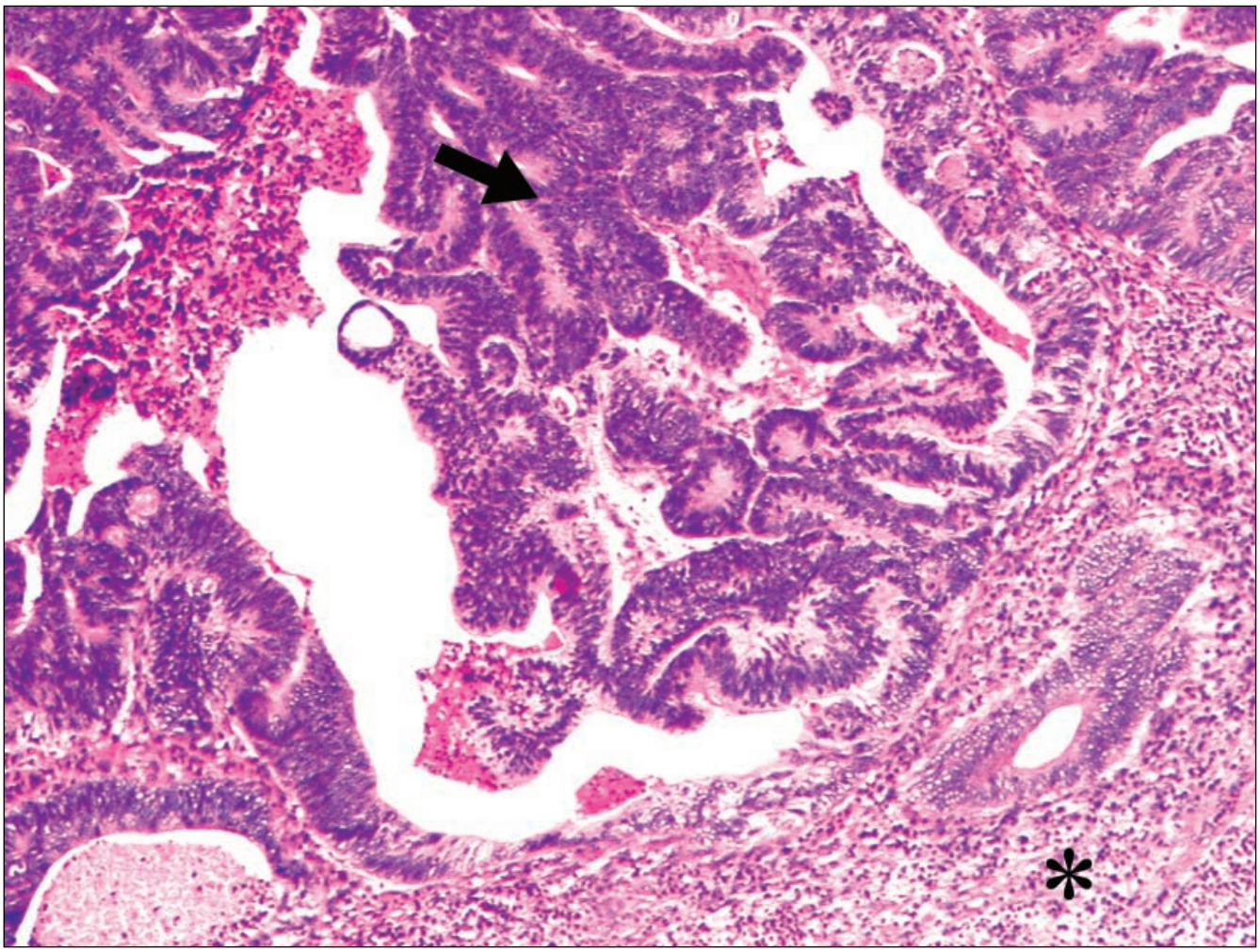

Fig. 2
The same patient as seen in Fig. 1. Adenocarcinoma of the stomach with its differentiation into an intestinal type (arrow) and a diffuse type (asterisk). Haematoxylin-eosin.

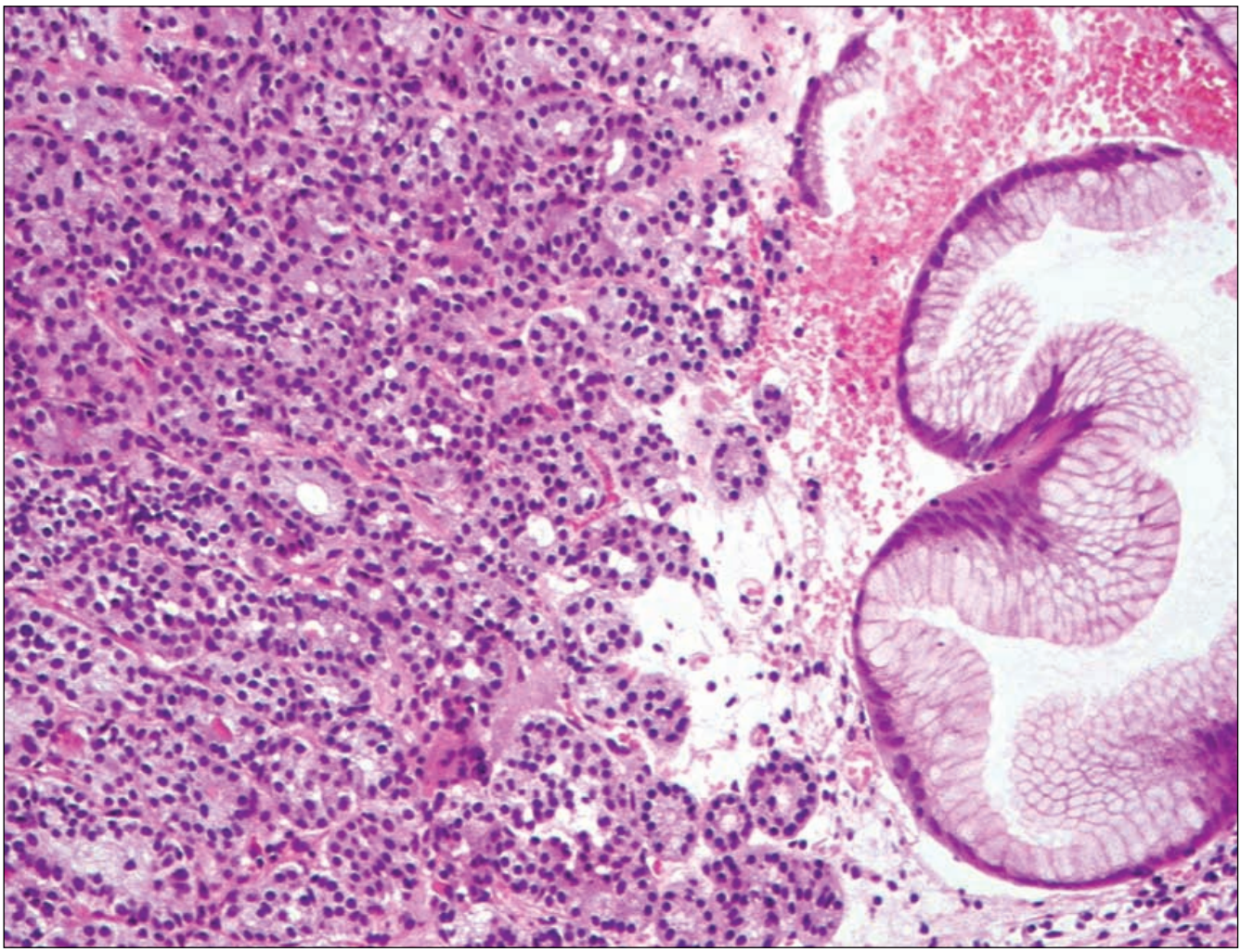

Fig. 3
The same patient as seen in Figs. 1 - 2. Typical carcinoid growing within the lamina propria mucosae with the predominantly trabecular type of growth. Haematoxylin-eosin.

Case No. 1

A 79-year-old female was admitted to hospital because of heart failure. Upper GI endoscopy was carried out for microcytic hypochromic anaemia (haemoglobin 71 g/L). Three polypoid tumours were found at the middle part of the gastric corpus (30 mm, 15 mm and 7 mm in diameter), Fig. 1. Histology of the largest tumour revealed moderately differentiated adenocarcinoma, Fig. 2. Histology of the remaining two polypoid tumours found carcinoid in both (Fig. 3). There was a positive immunohistochemical reaction with chromogranin A and synaptophysin antibodies (Fig. 4). Biopsy specimens showed marked intestinal metaplasia of the prepyloric antrum and focal chronic atrophic gastritis. There were no distant metastases. Carcinoid syndrome was absent, urine 5-hydroxy-indole-acetic acid output was normal (21.0 μmol per 24 hours), serum gastrin level was increased (2,200 pg/mL). Helicobacter pylori was negative (by means of 13C-urea breath test). Autoantibodies against parietal cells of the stomach were positive.

Considering the patient's status and her polymorbidity (not fit for surgery) and according to her wish we chose endoscopic therapy. We removed visible tumorous mass by means of endoscopic resection followed by argon-plasma coagulation. Regular laboratory controls and gastroscopy with repeated further argon-plasma coagulation were done. Now, 12 months later, the patient is still symptom free, with no liver metastases, however with significant local progression of gastric adenocarcinoma.

Case No. 2

A 77-year-old man had been treated (surgery followed by radiotherapy) and followed-up for cutaneous follicular centroblastic malignant B cell lymphoma of his left face for three years. At the moment he has lost his appetite and body weight (8 kg within 3 months)

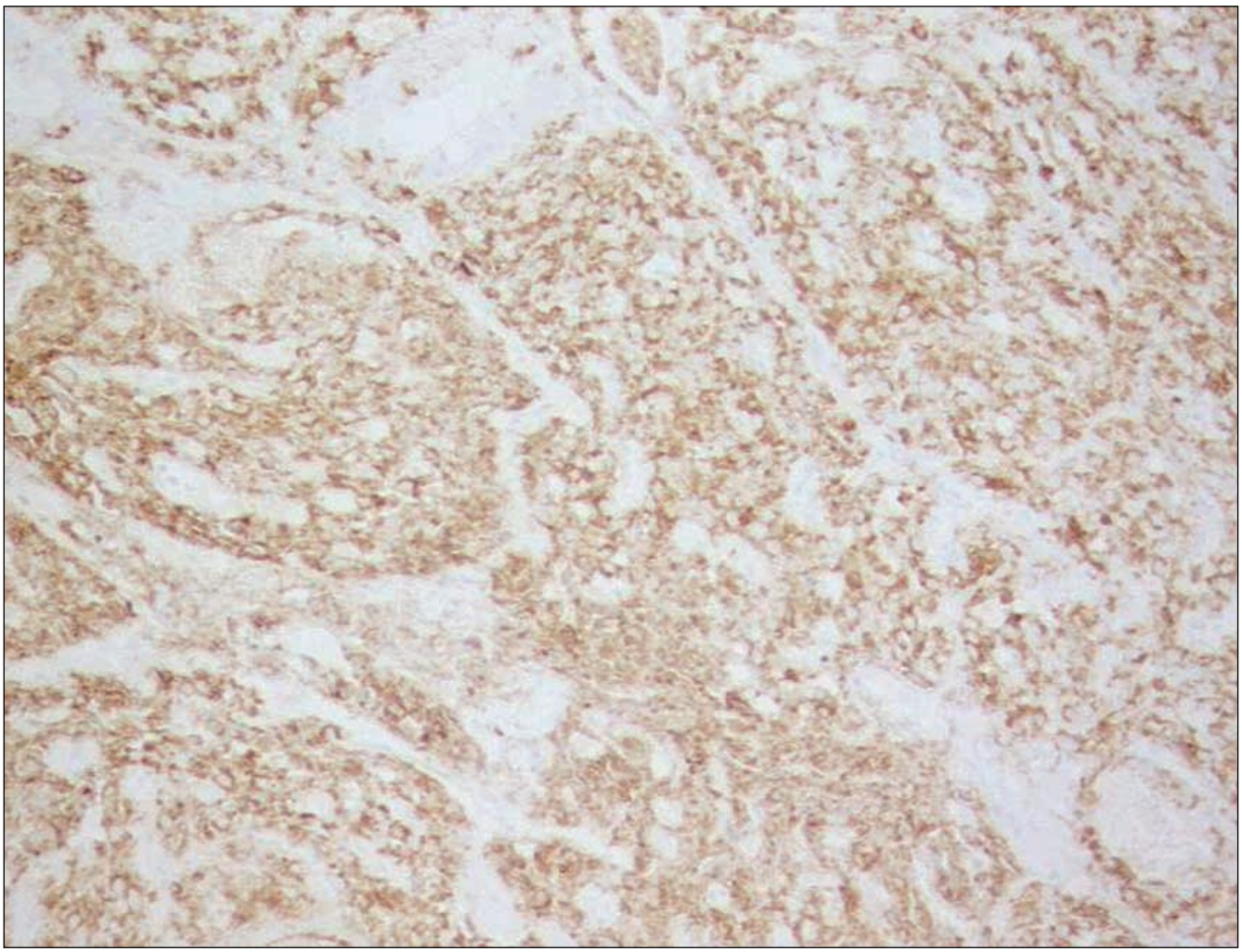

Fig. 4
The same patient as seen in Figs. 1 - 3. Immunohistochemical distinct positivity of synaptophysin of carcinoid tumorous cells. Synaptophysin - diaminobenzidine.

and has suffered from upper right dull abdominal pain. Multiple liver metastases were found by ultrasonography and CT scan (comprising about 50 % of liver parenchyma). The oncologist referred the patient for upper GI endoscopy. There was a tumour (3 to 4 cm in size) found in the distal third of the gastric major curvature, Fig. 5. Adenocarcinoma was found at histology. There was another tiny sessile polyp (3 mm in diameter) growing next to the previous one at the middle part of the major gastric curvature, too, Fig. 6. Histology revealed carcinoid. There were no symptoms of carcinoid syndrome. Helicobacter pylori was negative at histology, there were not any signs of atrophic gastritis. Because of generalised malignant disease, systemic palliative chemotherapy was administrated (leucovorin, fluorouracil and etoposid). Investigation of serum gastrin and urine 5-hydroxy-indole-acetic acid output was not managed. Three days after chemotherapy was started, the patient suddenly died of heart failure. Generalised adenocarcinoma was proved at autopsy (including liver multiple metastases). There was a tumorous triplicity in this particular case: gastric adenocarcinoma and carcinoid of the stomach and cutaneous non-Hodgkin B-cell lymphoma originating from the patient's face.

Discussion

Gastric carcinoid tumours are relatively rare. According to a 5-decade analysis of 13,715 carcinoid tumours by Modlin et al., within the gastrointestinal tract, carcinoids occurred in the stomach only in 8.7 % (33). In the Czech National Oncology Register, there were a total of 1,314 carcinoid tumours registered in the period 1984 - 1994 in the Czech Republic, 987 carcinoids (75 %) occurred in the gastrointestinal tract, mostly found in the large bowel (appendix, colon & rectum; 44 %) and small bowel (26 %) (41). Only 65 gastric carcinoids were registered in this peri-

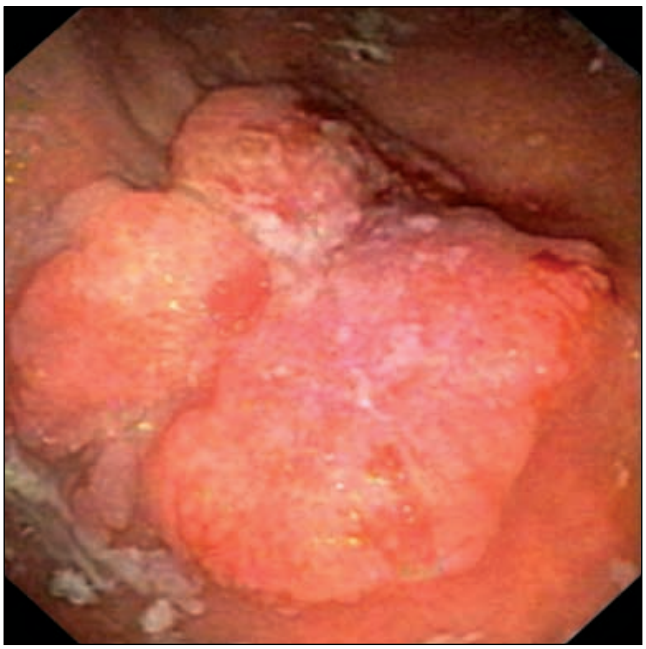

Fig. 5
A 77-year-old man. There was a polycyclic polypoid tumour (3 to 4 cm in size) found in the distal third of the gastric major curvature. The tumour was centrally depressed with a small shallow ulcer. Adenocarcinoma was found at histology.

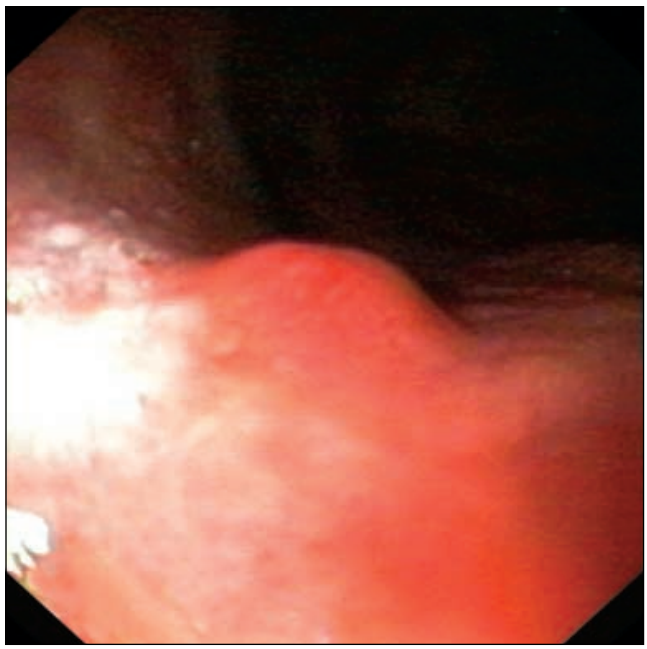

Fig. 6
The same patient as seen in Fig. 5. There was another tiny sessile polyp (3 mm in diameter) growing next to the previous one at the middle part of the major gastric curvature, too. Histology revealed carcinoid.

od (6.6 % out of 987), however, there were no synchronous gastric tumours among them (41). We report two cases of synchronous gastric carcinoid and adenocarcinoma of the stomach.

Both gastric carcinoid and gastric adenocarcinoma can be associated with other neoplasms, they can grow separately (4,5,10,21,26,30,36), merge with one another creating a so-called collision tumour (11,24,28) or can form a mixed neoplasm, a so-called composite tumour (1,3,9,18,23,29,39,45). Sometimes distinguishing between collision and composite tumour may be difficult (12,13,47).

Our first case was a type 1 gastric carcinoid tumour associated with hypergastrinaemia and chronic atrophic gastritis, the second patient most likely had type 3 carcinoid but it could not be classified definitely. We did not manage to investigate serum gastrin as the patient had suddenly died of heart failure. The second case represented a tumour triplicity: gastric adenocarcinoma, carcinoid of the stomach and cutaneous non-Hodgkin B-cell lymphoma. In both our cases, gastric tumours grew separately within a stomach not merging. No one had carcinoid syndrome. This syndrome is quite rare, for instance in Modlin's series, it was found only in 4 % of cases (33).

Synchronous gastric tumours have seldom been reported in literature. Gastric carcinoids can be associated with carcinoma of the stomach (1,3,5,9,11, 23,24,29,36,39,45,47). Gastric carcinoid tumours have been also reported together with gastrin-producing tumours and stromal neoplasms (4,26,30,33,35). Gastric carcinoma can be associated also with lymphoma (2,7,10,19,21,42) and stromal tumours of the stomach (21,28,30).

Gastric carcinoids exhibit worse prognosis (overall 5-year survival 49 %) compared to carcinoid tumours of the appendix (86 %) and rectum (72 %) (26). However, in synchronous gastric carcinoma and carcinoid tumours, prognosis of a particular patient seems to be determined by the advanced status of the carcinoma.

Simultaneous finding of gastric carcinoid and carcinoma raises the question if such an occurrence is merely an accidental association or if there is a causal relationship. It is suggested that the longstanding hypergastrinaemia may have played a causative role in the development of multiple carcinoids and cancer. We found high serum gastrin in our first patient. Atrophic gastritis (both autoimmune one in pernicious anaemia or due to Helicobacter pylori infection) has been recognized as a risk factor for malignant development, too (7,10,19,21). Atrophic gastritis was found only in our first case, Helicobacter pylori was negative in both. The possibility that gene mutations might

underlie tumour predisposition in neoplasm duplicity cannot be theoretically discarded (30,37). There was no history of family tumour occurrence in our cases. DNA microsatellite instability might be responsible for multiple gastric neoplasms (22,27,40,46). An interesting hypothesis is that a single carcinogenic agent might induce development of tumours of different histotypes (4,30). This theory is supported by some experimental studies (30). Microallelotyping found different histogenetic and tumorigenetic pathways in gastric adenocarcinoma and carcinoid tumours development (13). However, according to another study carcinoid and adenocarcinoma, the two histologically distinct tumours, appear to be derived from a common multipotent epithelial stem cell (12). Upon these previously discussed studies no definite conclusion concerning aetiology and pathogenesis could be stated. Nevertheless case reports of rare synchronous gastric neoplasms of distinct histotypes may bring new insights into understanding tumorous biology.

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Address to correspondence:
Blanka Kupková, MD, Clinical Centre, 2nd Department of Medicine, Charles University Teaching Hospital,
Sokolská 581, 500 05 Hradec Králové, Czech Republic
E-mail: BlankaKupkova@seznam.cz