

## CASE REPORT

# Synchronous intestinal tumors: aggressive jejunal carcinoid and sigmoid malignant polyp

SIMONA GURZU<sup>1)</sup>, T. BARA JR<sup>2)</sup>, T. BARA<sup>2)</sup>, I. JUNG<sup>1)</sup>

<sup>1)</sup>Department of Pathology

<sup>2)</sup>Department of Surgery

University of Medicine and Pharmacy of Targu Mures

## Abstract

Association of aggressive jejunal carcinoid tumors and other primary gastrointestinal neoplasms are rarely observed. We describe the case of a synchronous jejunal carcinoid tumor and two colorectal polyps in a 78-year old woman. Surgical intervention was performed for the colorectal tumors and the carcinoid was incidentally found. It was well differentiated but was accompanied by lymph node metastasis and peritoneal carcinomatosis. In this case, the prognosis was not depending by the colorectal tumors but the aggressive feature of jejunal carcinoid lead to patient's death.

**Keywords:** jejunal carcinoid tumor, synchronous intestinal tumors, peritoneal carcinomatosis.

## □ Introduction

Carcinoids are usually slow growing tumors with relatively favorable prognosis. They represent 0.49% from all malignancies but the incidence is increasing [1]. Most of them are incidentally diagnosed in the gastrointestinal tract, at laparotomy or autopsy [2]. A recent comprehensive study showed that 41.8% from all carcinoids of the gastro-intestinal tract were located in the small intestine [3]. In 1867, Langhans first described the intestinal carcinoid as an adenomatous polyp [4] but the term "Karzinoide" was introduced by Oberndorfer in 1907 [5].

Regarding the small intestine, most of studies revealed the highest frequency of carcinoids in the ileum (47–52% from all gut carcinoids) [6]. A small proportion of them (10%) are located in jejunum [3], the others involving the duodenum and appendix.

About 20–29% of carcinoid tumors of the small intestine are associated with non-carcinoid tumors [7]. In all reported cases, as our best knowledge, the authors presented synchronous tumors located in the ileum [6, 8]. We did not find case reports about synchronous tumors with jejunal carcinoids.

We present a case of a 78-year old woman who had one jejunal carcinoid tumor and two synchronous colorectal tumors: one malignant polyp and one adenomatous polyp with dysplasia.

## □ Patient, Methods and Results

A 78-year old woman presented with left lower abdominal quadrant pain. She related that her mother was diagnosed with breast cancer and her niece presented uterine cervical cancer. Regarding her medical history, she reported that 15 years ago a uterine

leiomyoma was surgically removed. Seven years ago, she underwent colonoscopic examination and one polyp of the sigmoid segment was identified and biopsied. The biopsic specimen revealed an adenomatous polyp with minimal dysplasia. It was not followed by surgical intervention.

At the present hospital admission, she related two-year history of left-sided abdominal pain accompanied by weight loss and episodes of changing of the bowel habit but diarrhea was denied. No other symptoms have been reported. The colonoscopy confirmed the presence of colorectal polyps and the surgical intervention – left hemicolectomy – was performed. Intraoperatory, inspection of the abdominal cavity showed peritoneal carcinomatosis with tumoral implants over the greater omentum and the parietal peritoneum and minimal ascites. At intestinal palpation, a jejunal stenosing tumor was incidentally identified and was resected together with the regional lymph nodes.

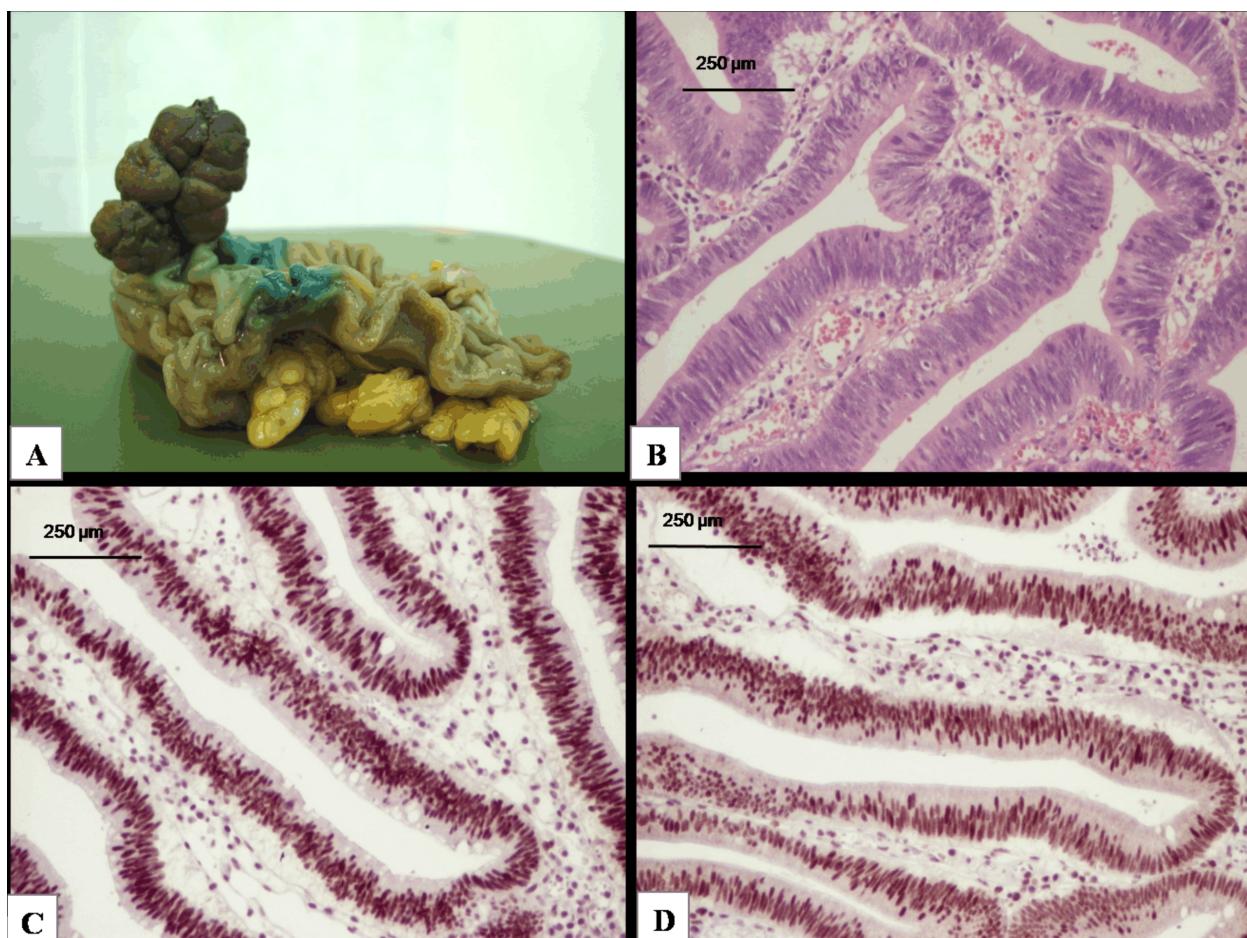
Pathological assessment of the colorectal segment showed a 20×15 mm sigmoid polyp (Figure 1) and a small rectal polyp (5×5×3 mm). Histologically, the sigmoid polyp presented malignant transformation (Figure 1) with invasion limited to the mucosa (pT1), without invasion of the stalk or the polyp basis. No lymph node metastases were identified in the three regional lymph nodes, including the sentinel lymph node, colored *in vivo* with submucosal peritumoral injection of blue dye substance (pN0). The rectal adenomatous polyp presented minimal dysplasia.

Regarding the jejunal specimen, a 25×20 mm stenosing white-yellowish tumor mass was observed. Histologically, it was a carcinoid tumor with an unusual aggressive feature. The tumor cell proliferation was observed in all jejunal layers, crossing the serosa. The

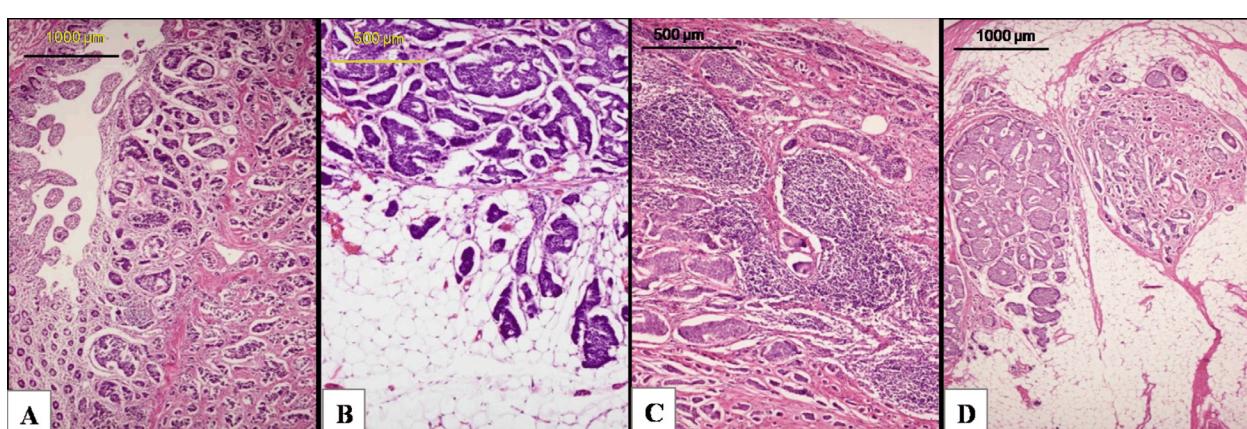
tumors cells constitute, in the main part, solid islands but rare acinar structures have also been present. At high power view, a well-differentiated carcinoid tumor, with a small number of mitoses (<2 mitoses/10 high-power view microscopic fields) was identified (Figure 2). The tumor cells were stained with synaptophysin and chromogranin A. The Ki67 index was under 2% but more than 70% of nuclei were p53 positive (Figure 3). In all tumor implants and lymph node metastasis, the tumor cells presented same features as in the primary carcinoid tumor (Figure 2). Based on these data, the final tumor stage was pT4N1M1.

Based on her family medical history – mother's breast cancer and niece's uterine cervical cancer – immunohistochemically stains were performed with MLH-1 and MSH-2 in order to exclude the possibility of hereditary cancer. Both antibodies were positive in polyps and the carcinoid tumor (Figures 1 and 3).

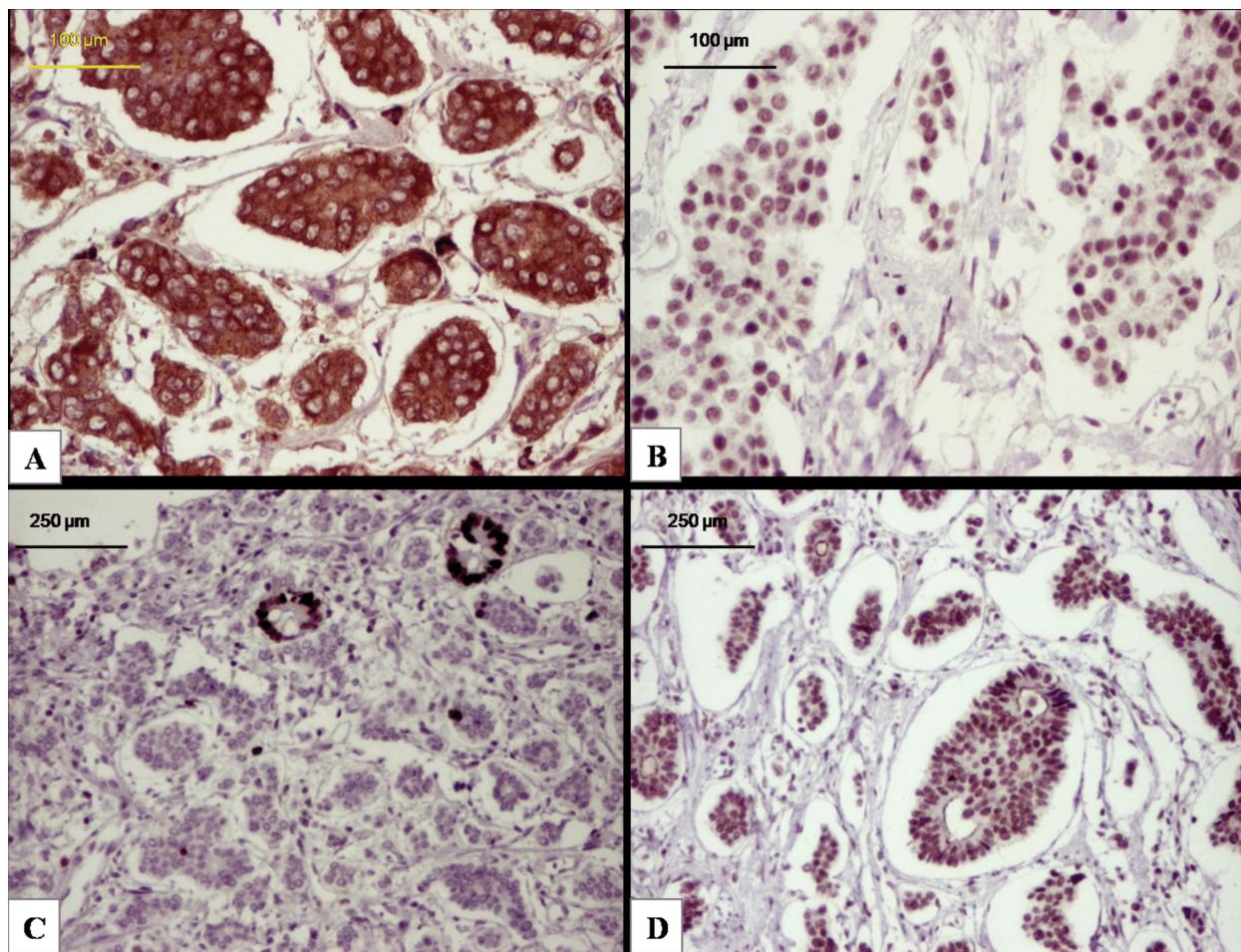
The post-operative evolution was unfavorable, a further laparotomy was performed but our patient died at two weeks after surgical intervention, due to peritoneal carcinomatosis and adhesional intestinal obstruction.



**Figure 1 – The malignant sigmoid polyp, macro- (A) and microscopically aspect in Hematoxylin–Eosin stain (B), with positivity for MLH-1 (C) and MSH-2 (D).**



**Figure 2 – The primary jejunal carcinoid tumor infiltrates all layers, crossing the serosa (A and B) and produces metastases in the lymph nodes (C) and the great omentum (D). Hematoxylin–Eosin stain.**



**Figure 3 – The immunohistochemical aspect of the carcinoid tumor: (A) positivity for chromogranin A; (B) high expression of p53; (C) negativity of Ki67 with preserved positivity in normal intestinal glands; (D) positivity for MLH-1.**

## Discussion

In the small intestine carcinoids, the lymph node metastasizing rate seems to be related to the tumor size and degree of differentiation [1]. In our case, although the tumor was well differentiated with a low mitotic rate, it was highly aggressive. In this case, p53 was more important than Ki67 in predicting aggressiveness.

Peritoneal metastasis or carcinomatous ascites are rarely associated with carcinoid tumors [9]. Twenty-seven percent of ileal carcinoids present peritoneal carcinomatosis [9] but no data about jejunal tumors have been reported. Even general opinion is that the five-year survival rate in intestinal carcinoids is independently by peritoneal carcinomatosis, one of the recent studies revealed that peritoneal carcinomatosis was direct cause of death in 40% of patients [10]. In our case, the main cause of death was also peritoneal carcinomatosis.

Commonest symptoms of patients with intestinal carcinoids are either carcinoid syndrome or they may be related to mesenteric ischemia, intestinal infarction or obstruction [11]. In our case, no clinical signs have been associated.

Intestinal carcinoids may be associated with other carcinomas, one-third of the second cancers being also located in the gastrointestinal tract [1, 7]. In synchronous

tumors, the prognosis is usually depending by the non-carcinoid tumor, in only one of the 270 cases analyzed by Berner M, the carcinoid itself changing the prognosis [12]. In our case, the malignant polyp was diagnosed in a very early stage (pT1N0) and the survival was directly related to the carcinoid tumor associated with peritoneal metastasis.

Although synchronous carcinoids may present genetic familial predisposition, in our case both carcinoid tumor and malignant polyp expressed MLH-1 and MSH-2, according to the literature data which revealed that all carcinoids presented a microsatellite-stable phenotype, with increasing of MLH-1 and MSH-2 immunohistochemical expression, although 20% of carcinomas of the small intestine may be microsatellite instable tumors [13].

There are studies, which showed an increase risk for prostate carcinoma in males with intestinal carcinoid tumors, and for melanomas, other skin tumors and endocrine malignant tumors in both genders [14] but other locations have been reported [8].

There are some hypotheses about association between carcinoid and non-carcinoid tumors. Some authors admit that the carcinoid tumors secrete different growth factors and proliferative peptides, which may determine tumor growth or neoplastic transformation in other sites [3].

It was reported that gastrin and cholecystokinin, both of them being secreted by carcinoid tumors, are regulating growth factors of colorectal carcinoma [15]. Genetic predisposition, association of Crohn's disease or ulcerative colitis and failure of immunologic surveillance may be also implicated. Further studies are necessary to elucidate the pathogenesis of second-associated tumor in patients with carcinoid tumors.

Due to non-specific symptoms of these patients, absence of carcinoid syndrome in some cases and incidentally reported findings, examination of the entire gastro-intestinal tract is necessary in presence of any non-carcinoid tumors of the gastrointestinal tract. Somatostatin scintigraphy and serum level of chromogranin A may be helpful in these cases.

## Conclusions

Our case underlines two aspects. On the one hand, it emphasizes the major importance of postoperative follow-up for synchronous or metachronous cancers in the patients with benign or malignant gastrointestinal tumors. On the other hand, in our case, despite the few number of mitoses and low Ki67 index, the incidentally finding jejunal carcinoid was highly aggressive leading to patient's death. It proves that new criteria seem to be necessary to predict aggressiveness of the intestinal carcinoid tumors.

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## Corresponding author

Simona Gurzu, Lecturer, MD, PhD, Department of Pathology, University of Medicine and Pharmacy of Târgu Mureş, 38 Gheorghe Marinescu Street, 540139 Târgu Mureş, Romania; Phone +40745–673 550, e-mail: simonagurzu@yahoo.com

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