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CASE REPORT

"Duodenal Adenocarcinoma Giving Rise to Rectal Metastasis" a Rare Disease with an Extremely Rare Metastatic Pattern

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Introduction

Adenocarcinoma of the duodenum is relatively rare. We present a case of a patient with a local recurrence of an adenocarcinoma localized in the duodenum, with a rectal intraluminal metastasis.

Case Report

A 65-year-old woman with no previous relevant medical history was diagnosed with an anaplastic ovarian carcinoma stage IA (Fig. 1). She underwent surgery and was treated with 6 cycles of adjuvant carboplatin and paclitaxel, despite the tumor being stage IA. Seven years later, she developed mediastinal lymphadenopathy, which was cytologically consistent with a metastasis of the ovarian cancer. She was treated again with 6 cycles of carboplatin and paclitaxel, which resulted in a persistent complete remission. After another 5 years, she presented with jaundice and cholestasis accompanied by abdominal pain, nausea, vomiting, and weight loss. The diagnosis was of a stenosing duodenal tumor with no signs of metastasis. Histological biopsy of the tumor showed an adenocarcinoma (Fig. 2) and DNA sequencing (involving examination of copy number variation using single nucleotide polymorphisms (SNPs) from a large number of genomic regions) confirmed this to be a secondary malignancy. Next generation sequencing (NGS) showed a mutation in the TP-53 gene exon (c.797G>T; p.G266V) in the ovarian tissue and lymph nodes; this mutation was absent in the duodenal tumor. The duodenal tumor carried mutations in the KRAS-gene exon 2 (c.35G>A; p.G12D), CDKN2A-gene 2 (c.330G>A; p.W110*), and SMAD4-gene exon 9 (c.1081C>T; p.R361C). These mutations were also absent in the ovarian tumor and lymph node metastases. Analysis of the SNPs showed the same loss of pattern in a large number of different chromosomal regions in the ovarian tumor and lymph node tumor, which did not correspond with the duodenal tumor.

A Whipple procedure was performed; the final conclusion of which was a moderately differentiated pT4N1 adenocarcinoma of the duodenum. One year after surgery, the patient presented with abdominal pain, rectal blood loss, and constipation. A CT-scan of the abdomen showed a local recurrence in the hepatoduodenal ligament, retroperitoneal lymphadenopathy, and a rectal mass. On rectal endoscopy, an intraluminal stenosing tumor was found to be present, located approximately 15 cm from the anal margin (Fig. 3). Biopsy of the rectal mass showed an adenocarcinoma with identical molecular abnormalities as the previous duodenal tumor. The patient was therefore diagnosed with a local recurrence of the adenocarcinoma localized in the duodenum, with a rectal intraluminal metastasis. Palliative treatment with capecitabine and oxaliplatin (CAPOX) was initiat-

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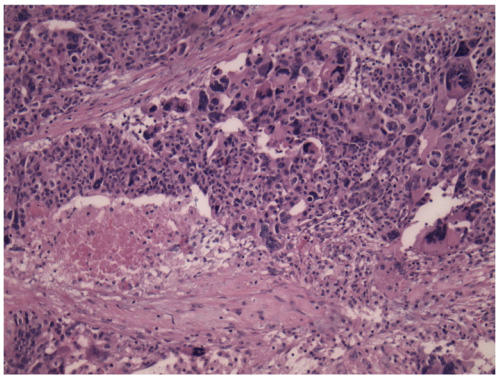

Fig. 1 Anaplastic carcinoma of the ovary: solid sheets of large atypical multinucleated tumor cells with strong nuclear atypia and atypical mitosis

ed, resulting in a radiological response. Currently, this treatment is ongoing. Genetic counseling was performed and did not reveal any known germline genetic aberrations corresponding with an increased risk of solid tumors.

Discussion

Despite the fact it compromises 75% of the length of the digestive tract, the small bowel is infrequently the site of cancer. Data from the United States Surveillance, Epidemiology, and End Results (SEER) program of 1973–2000 revealed the incidence of carcinoma of the small bowel to be 5.9 cases per million, with a male predominance with a male to female ratio of 1:4. Of these carcinomas, 49% are localized in the duodenum [1]. A French population-based study, performed between 1976 and 2001, showed the incidence of cancer in the small bowel to be 1.8 per 100,000 in men versus 1.5 per 100,000 in women. Adenocarcinoma was the most common histological type, representing 40.4% of the cases, and the median age of diagnosis is between 50 and 70 [2]. In a nationwide population-based assessment conducted in Denmark between 1994 and 2010, 28% of the patients with a duodenal adenocarcinoma presented with a stage I/II, 24% with stage III, and 27% with stage IV. The incidence of small-bowel cancers is increasing, mainly because of a large increase in the incidence of duodenal adenocarcinomas [3]. The exact etiology is unknown, but most adenocarcinomas from the small bowel arise from adenomas, most likely through a multistep process involving specific genetic changes. Predisposing factors are chronic mucosal inflammation as seen in Crohn's disease and Coeliac disease, and possibly various dietary factors such as intake of alcohol, refined sugar, red meat, and smoked food. An increased risk is also present in some hereditary cancer syndromes such as familial adenomatous polyposis (FAP), Peutz-Jeghers syndrome, and Lynch syndrome [4, 5]. Metastases of duodenal adenocarcinoma are often seen in regional lymph nodes, the liver, and the lungs [6]. There have been no prior reports of intraluminal metastasis of duodenal cancer. Data regarding the optimal systemic treatment for metastatic small-bowel carcinoma is scarce. When colorectal metastatic lesions are found, the areas of greatest suspicion regarding primary origin are melanoma and lobular breast cancer; however, these are hematogenous metastasis, and not intraluminal [7, 8]. A recent case report was published describing a patient with small-bowel metastasis from primary rectal cancer. The hypothesis of the authors concerning the mechanism of metastasis included hematogenous and peritoneal spread and translocation of tumor cells [9]. Literature describes a higher incidence, in patients with an adenocarcinoma of the small bowel, of secondary malignancies localized in the colon, rectum, the ampulla of Vater, endometrium, or ovary—suggestive that genetic pre-disposition may have a role [4]. The prognosis for small-bowel adenocarcinoma is poor for all stages, with a 5-year overall survival rate ranging from 14 to 33% [5].

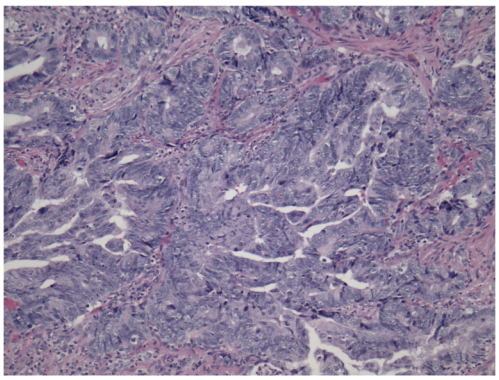

Fig. 2 Duodenal adenocarcinoma: atypical glands with cribriform growth pattern and nuclear atypia. No tumor giant cells present

Conclusion

Intraluminal metastasis can be caused by the rare duodenal cancer type. Next generation genome evaluation is very helpful for discriminating between primary and secondary tumors.

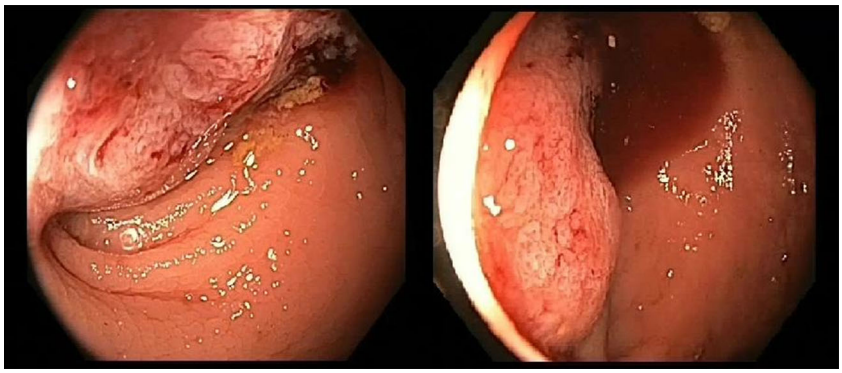

Fig. 3 Rectal endoscopy shows an intraluminal stenosing tumor

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Consent Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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