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Endocrine tumours of the hindgut

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Neuroendocrine tumours of the colon and rectum are rare but distinct with regard to clinical symptoms, diagnostic and therapeutic management and prognosis compared to other neuroendocrine tumours of the gut as well as ordinary colorectal cancer. Therapeutic algorithms are proposed depending mainly on analogous TNM categories and grading considering conventional and experimental surgical and non-surgical therapy. Colonic neuroendocrine tumours are often misdiagnosed as undifferentiated adenocarcinoma and are therefore not properly treated with adjuvant and additive chemotherapy. As most rectal neuroendocrine tumours are benign because of submucosal extension only, the size and infiltration depth correlates with lymph-node and distant metastases and therefore with the prognosis. It is unknown whether endoscopic ultrasound can improve the diagnostic accuracy compared to size-related conclusions, and therefore whether it can change therapeutic strategies and improve survival by modern rectal surgery.

Key words: neuroendocrine tumour; colon; rectum; diagnostics; surgery; chemotherapy; radiotherapy.

Neuroendocrine cells, generally spread all over the body, are focused in the respiratory and gastrointestinal tracts. According to the vascular supply during embryogenesis, three major areas are differentiated: foregut (respiratory system and upper gastrointestinal tract, coeliac artery), midgut (gastrointestinal tract, superior mesenteric artery) and hindgut (gastrointestinal tract, inferior mesenteric artery).[1] As the colon is part of the mid-gut up to the left splenic flexure, the distal colon beyond the flexure is associated with the hindgut, as is the whole rectum.

Cells with the capability to produce neuroendocrine hormones have a varying morphological phenotype as well as biological potential to progress, invade and metastasize. Histopathological classification of neuroendocrine tumours (NETs)

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reflects the morphology and biology of the tumour cells. There are highly differentiated NETs and poorly differentiated neuroendocrine carcinomas, including small cell carcinoma. The former refers to NETs with little proliferation and a size up to 2 cm (typical carcinoid) as well as highly differentiated neuroendocrine carcinomas (atypical carcinoid) showing significant proliferation with a size frequently more than 2 cm.

Large cell neuroendocrine carcinomas are rare and insufficiently described and tend to be associated with the poorly differentiated neuroendocrine carcinomas.[2]

Histopathological classification and biological characteristics are associated with clinical phenotype and prognostic outcome. This allows a decision to be made on how radical the therapeutic interventions should be. NETs of the colon present as locally advanced symptomatic tumours resembling adenocarcinoma, and are therefore initially very often misdiagnosed as ordinary colonic cancer. Most NETs of the rectum are small and asymptomatic and are well characterized by macroscopic and histological morphology.

EPIDEMIOLOGY

Colon

Incidence is 0.1–0.31 per 1 00 000 per year, with a higher incidence in Afro-Americans compared to Caucasians.[3,4] In post-mortem analysis incidence is up to 8 times higher compared to surgical incidence.[5] The percentage of NETs relative to the overall number of colonic tumours is 0.33–0.99.[6,7] By retrospective analysis of poorly differentiated and undifferentiated colonic cancers with immunohistochemistry, the percentage of neuroendocrine carcinomas rose to 3.9%.[7] About 5.8–8.7% of the NETs are NETs of the colon. Regarding gastrointestinal NETs, the percentage of colonic NETs is 8.22–11.7%.[4,8]

The average age is about 65 years, younger than for colonic adenocarcinomas (about 70 years),[3,4,9] and the female/male ratio is 1.4/2.[4,10,11]

Rectum

Incidence is 0.1–0.14 per 1 00 000 per year.

The percentage of NETs relative to the overall number of adenocarcinomas of the rectum is 0.9–1.3%; 12.5–15.8% of NETs are NETs of the rectum, which is 15–18% of the gastrointestinal NETs.[4,8] NETs of the rectum are third amongst gastrointestinal NETs, following appendiceal and small bowel NETs. NETs smaller than 2 cm have been found in 1/1400 sigmoidoscopies.[12] Average age is 52–59.5 years compared to 62–68 years for adenocarcinomas. Female/male ratio is even.[4,6,13,14]

CLINICAL ASPECTS

Colon

Localization

About 50% are localized in the caecum, another 15% in the ascending colon; 10–15% each can be detected in the transverse, descending and sigmoid colon. Favourite