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Small cell carcinoma of the rectum

Small cell carcinomas (SCCs) of the gastrointestinal tract belong to neuroendocrine tumours (1). They are rare lesions, in the colon and rectum comprising approximately 0.2% of all malignancies of this location. They are associated with adenomas and ulcerative colitis, and were described in immunodeficient patients (2). SCCs are characterised by aggressive behaviour and dismal prognosis (2, 4). In most cases they are diagnosed at advanced stage (IV and III according to UICC) with regional lymph nodes involvement and distant metastases mainly to the liver, peritoneum, distant lymph nodes, bone marrow and lungs (1, 2). The prognosis is especially poor for untreated patients, with the average survival measured in weeks and no long-term survivors. In patients receiving chemotherapy initial response followed by rapid progression is common. Their average survival is in the range of 6–12 months, with occasional long-term survivors (2).

A rare case of rectal small cell carcinoma with typical clinico-pathological features is presented here.

CASE DESCRIPTION

A 66-year-old man presented with a three-month history of diarrhea, bloody stool, and spontaneous rectal bleeding. The patient also suffered from arterial hypertension and underwent myocardial infarction ten years ago. He mentioned occurrence of malignancies in both parents. Rectosigmoidoscopic examination revealed a partly obstructing tumour located 4 cm from the anal verge. Biopsy samples taken from the lesion contained only necrotic masses with sparse atypical cells. The abdominoperineal resection of the rectosigmoid was performed. At the operation a few small whitish nodules on the diaphragmatic surface of right and left liver lobes were found. The postoperative course was uneventful, but the patient died of disease five months later.

Gross pathological examination displayed a 4.0 cm x 6.5 cm x 1.0 cm superficially ulcerated circular whitish tumour. Microscopically, it was an undifferentiated malignant neoplasm infiltrating through muscularis propria into the perirectal adipose tissue with massive lymphatics and venous invasion (Fig. 1A). Metastases were present in all nine examined lymph nodes (perirectal and located along with superior rectal artery), as well as in the liver (stage IV according to UICC). All resection margins were free of tumour. The tumour was mostly composed of small, oval to spindle cells with hyperchromatic nuclei with coarse chromatin, inconspicuous nucleoli and scanty cytoplasm forming broad sheets and solid nests separated by abundant fibro-vascular stroma (Fig. 1B). Furthermore, larger, round to polygonal cells with abundant cytoplasm and irregular vesicular nuclei with distinct nucleoli, frequently arranged in small "morulas" were observed. They were regarded as a manifestation of squamous differentiation. The "crush" effect and areas of necrosis were also noted. Mitotic figures and apoptotic cells/bodies were numerous. The regular adenocarcinomatous component was not found. The histochemical reactions for the mucus, i.e., mucicarmine, alcian blue/periodic acid Schiff, and high-iron diamine, were negative.

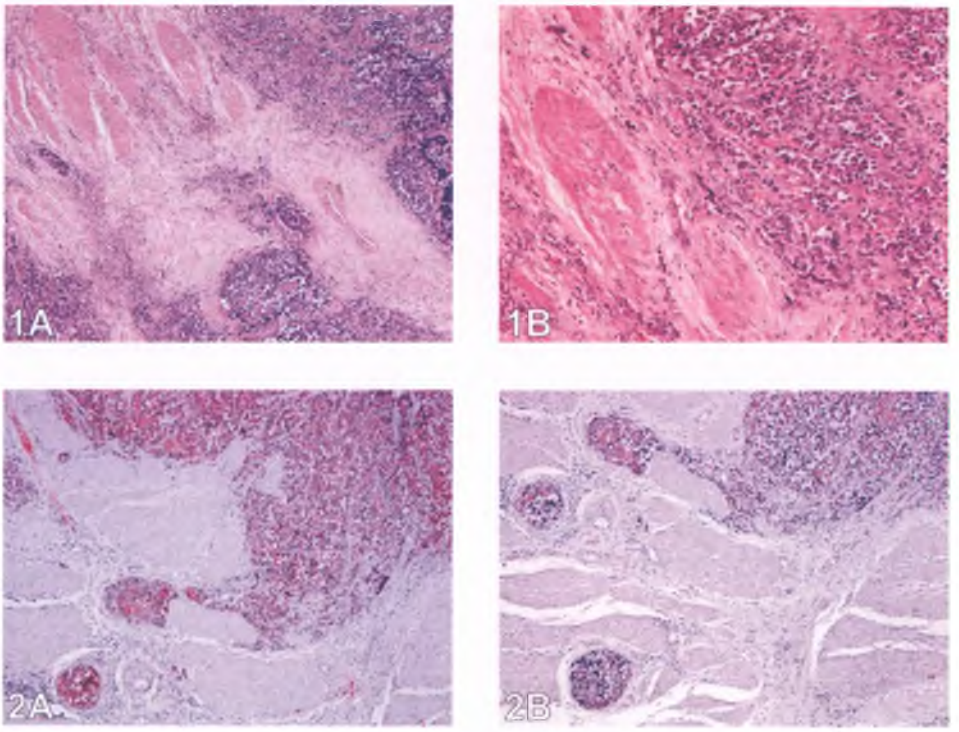

Fig.1. Small cell carcinoma of the rectum A: infiltration of muscularis propria, B: population of small cells with scanty cytoplasm and hyperchromatic nuclei (H&E, magn. A – x50; B – x200)
Fig. 2. Positive immunohistochemical reaction for A: synaptophysin, B: cytokeratin in small cell carcinoma of the rectum (DakoEnvision^{+TM}/HRP, clones SY38 & MNF-116 respectively, magn. x50)

To determine the origin of the tumour, immunohistochemical reactions with panel of antibodies using DakoEnvision^{+TM}/HRP kit were performed. Almost all neoplastic cells were strongly positive for synaptophysin (clone SY38) (Fig. 2A). Immunoreactivity for chromogranin A (clone DAK-A3) was found in about 50% of cells. Nearly 60% of cells exhibited positive reactions for cytokeratins (clones MNF-116, AE1/AE3) (Fig. 2B). The immunoreaction was strongest in the area of squamous differentiation. The Ki-67 index (clone MIB-1) was 60%. Immunohistochemical reactions for vimentin (clone V9), CD45 (LCA; clones 2B11, PD7/26), melanosome (clone HMB45) and serotonin (clone 5HT-H209) were negative. All applied reagents were from DakoCytomation, Denmark. On the basis of histological and immunohistochemical examinations the diagnosis of rectal small cell carcinoma was established.

DISCUSSION

Neuroendocrine tumours of gastrointestinal tract are heterogenous group of neoplasms all exhibiting features of neuroendocrine differentiation. It comprises well differentiated neuroendocrine tumors, well differentiated neuroendocrine carinomas, as well as highly malignant lesions collectively called poorly differentiated neuroendocrine carcinomas. The last group can be subdivided into small cell carcinomas and large cell neuroendocrine carcinomas (3). SCCs found in gastrointestinal tract are histologically identical to that seen in the lung. Large cell carcinomas of this location are less frequent than small cell ones and their morphological criteria are neither precisely

described, nor commonly approved (1, 3). It should be also mentioned that, otherwise typical gastrointestinal adenomas and adenocarcinomas frequently contain a variety of dispersed endocrine cells (5, 6).

According to some authors poorly differentiated (high grade) neuroendocrine carcinomas are probably unrelated to well differentiated neuroendocrine tumours and low grade neuroendocrine carcinomas, despite their common neuroendocrine differentiation (2). It is also believed that the former are of pluripotent stem cell origin, whereas the latter arise from orthotopic neuroendocrine cells after damage has occurred in partially differentiated precursor cells (4).

The suspicion of poorly differentiated neuroendocrine carcinomas is based on their characteristic cytologic and architectural pattern, but correct diagnosis usually requires confirmation of neuroendocrine nature of the tumour, especially in large cell carcinomas (1). A few special techniques are used for this purpose. Nowadays, identification of neuroendocrine markers by immunohistochemical reactions is a routine method in histopathological diagnosis. The most frequently detected ones are synaptophysin, an integral glycoprotein of the secretory vesicles membrane, chromogranin A, a matrix glycoprotein of secretory granules and a cytosol component – neuron-specific enolase (NSE). Some other substances forming highly conserved protein complex known as SNARE associated with synaptic vesicle docking and/or fusion, i.e., NSF (*N*-ethylmaleimide-sensitive factor), α/β-SNAP (soluble NSF-associated protein), VAMP2 (vesicle-associated membrane protein), syntaxin 1 and SNAP25 (synaptosomal-associated protein), as well as active products of endocrine cells, e.g., serotonin or calcitonin can be also immunohistochemically revealed (2, 4). The other method of endocrine cells identification is transmission electron microscopy that allows visualisation of two types of membrane-bound secretory granules or vesicles. It was found that large, dense-core granules contained chromogranin A, but small synaptic vesicles contained synaptophysin (4). In the past, argyrophil Grimelius reaction that visualized cytoplasmic granules was applied, but the results varied greatly among large intestine poorly differentiated neuroendocrine carcinomas (5).

The differential diagnosis of SCCs of the rectum should include: primary, poorly differentiated adenocarcinoma, lymphoma and leukaemia deposits, as well as malignancies typically invading the anal canal with secondary infiltration of proximal part of rectum, e.g., poorly differentiated squamous cell (cloacogenic) carcinoma and malignant melanoma. First of all however, lung SCC, which is a much more common lesion should be excluded. In opposition to lung lesions, the immunohistochemical reaction for thyroid transcription factor-1 (TTF-1) seems to be usually negative in primary rectal tumours and can be helpful in establishing ultimate diagnosis (2).

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SUMMARY

Small cell carcinomas of the colon and rectum are rare lesions comprising about 0.2% of all malignancies of this part of the gastrointestinal tract. We present a case of a 66-year-old man with advanced tumor of the rectum that infiltrated across the muscularis propria and metastasized to the regional lymph nodes and the liver. Microscopically, the majority of the tumour bulk was composed of undifferentiated small cells displaying positive immunohistochemical reactions for typical neuroendocrine markers, i.e., synaptophysin and chromogranin A, as well as for some cytokeratins, that confirmed the initial diagnosis of small cell carcinoma.

Rak drobnokomórkowy odbytnicy

Raki drobnokomórkowe okrężnicy i odbytnicy są rzadko występującymi nowotworami i stanowią około 0,2% wszystkich złośliwych nowotworów tej części przewodu pokarmowego. Przedstawiamy przypadek 66-letniego mężczyzny z zaawansowanym nowotworem odbytnicy, naciekającym poza błonę mięśniową jelita, z przerzutami do okolicznych węzłów chłonnych i wątroby. Mikroskopowo większa część utkania guza składała się z niezróżnicowanych, drobnych komórek wykazujących dodatnie odczyny immunohistochemiczne na typowe markery neuroendokrynne – synaptofizynę i chromograninę A, jak również cytokeratyny, co potwierdziło wstępne rozpoznanie raka drobnokomórkowego.