

CASE REPORT

Poorly differentiated neuroendocrine cell carcinoma of the rectum : report of a case and literal review

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Abstract : A 56-year-old man was admitted to our hospital because of anal bleeding. Colonoscopy and barium enema revealed type 4 tumor in the rectum. Biopsy revealed poorly differentiated adenocarcinoma. Low anterior resection with total mesorectal excision and lymph node dissection was performed. In immunohistochemical staining, chromogranin A and synaptophysin were positive at major lesion, and CEA were focal positive. The resected tumor was diagnosed pathologically as neuroendocrine cell carcinoma. The Ki-67 labeling index (LI) was 87.8%, so proliferative activity and potential malignancy was very high. Multiple metastatic tumors appeared in pelvis and lung eight months after operation. Treatment for neuroendocrine cell carcinoma of the rectum was controversial. Surgical resection and adjuvant chemotherapy might be one of the methods for gastrointestinal neuroendocrine cell carcinoma. *J. Med. Invest.* 53 : 317-320, August, 2006

Keywords : neuroendocrine cell carcinoma, rectum, Ki-67

INTRODUCTION

Neuroendocrine cell (NEC) carcinomas of the colon and rectum are uncommon, comprising less than 1 percent of colon and rectal cancer. NEC carcinomas typically stain for the immunohistochemical markers synaptophysin, chromogranin, or neuron-specific enolase. It is well known that common colorectal carcinoma has relatively good prognosis, whereas NEC carcinomas of the colon and rectum has very poor prognosis(1-3). A lot of patients had liver and lymph node involvement at the time of diagnosis. Treatments of NEC carcinomas of the colon and rectum are very difficult. We

herein report the malignant potential and the treatment of colorectal NEC carcinoma.

CASE REPORT

A 56-year-old man presented with anal bleeding. Laboratory findings showed no abnormalities on peripheral blood and serum examination. Colonoscopy disclosed type 4 lesion mainly located right side in the lower rectum (Fig.1A). Biopsy from this tumor revealed poorly differentiated adenocarcinoma. Gastrografin enema suggested type 4 tumor in the rectum, 8 cm from anal verge (Fig.1B). Abdominal computed tomography (CT) suggested lymph node metastases in the mesorectum (Fig. 2) and the periarterial lesion along the superior rectal artery. However, there was no liver metastasis. Following a diagnosis as poorly differentiated adenocarcinoma

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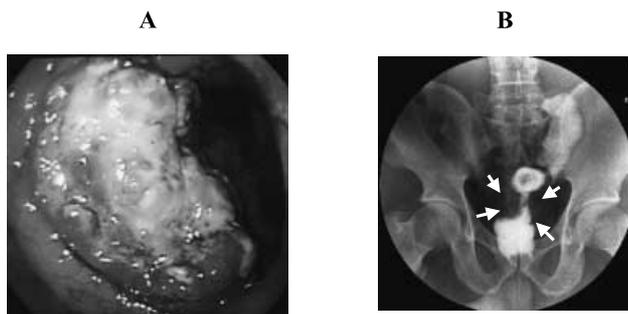


Fig. 1 : (A) Colonoscopy shows type 4 shaped tumor mainly located right side in the lower rectum. (B) Gastrografin enema shows irregular stenosis of the rectum at 8cm from anal verge.



Fig. 2 : Computed tomography shows lymph node enlargement in the mesorectum (arrow) and hypertrophy at right side of the rectum.

of the rectum, low anterior resection with lymph node dissection and total mesorectal excision was performed. The tumor was a 6.0 × 4.0 cm with type 4 shaped (Fig. 3) and the clinical stage was III, T3N2M0 in TNM classification. Histological features were poorly differentiated, nuclei were irregular in size and mitotic figures were frequently identified (Fig. 4A). The tumor was diagnosed pathologically as NEC carcinoma by immunohistochemical study using

Chromogranin A (Chr A) (Fig. 4B) and Synaptophysin (SNP) (Fig. 4C). A part of this tumor was stained with carcinoembryonic antigen (CEA). The proliferation marker, Ki-67, was diffusely stained and Ki-67 LI was 87.8% (Fig. 4D). The post opera-



Fig. 3 : Resected specimen. A type 4 shaped tumor was located in the rectum.

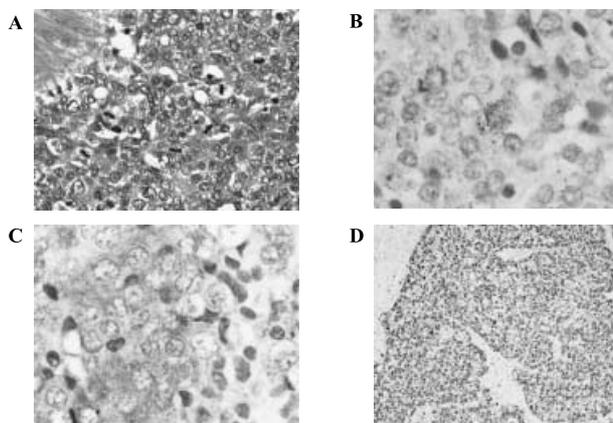


Fig. 4 : Histological features. (A) Nuclei of the NEC carcinoma cells were irregular in size and mitotic figures were frequently identified (×100).

Immunohistochemical features. The NEC carcinoma cells are immunoreactive for (B) Chr A (×200) and (C) SNP (×200). (D) Nuclear labeling index of Ki-67 immunostaining shows 87.8% in the NEC carcinoma (×100).

Table 1. Review of the literature.

Author	Cases (rate)	Treatment	(n)	Survival
Saclarides TJ, <i>et al.</i>	15(1.5%)	unknown		MST 5.0 months
Bernick PE, <i>et al.</i>	38(0.6%)	surgery ± CT or RT	29	MST 10.4 months
		CT ± RT	8	
		best supportive care	1	
Grbowski P, <i>et al.</i>	9(0.4%)	surgery (± CT or RT unknown)	9	2 year survival rate 11%

CT : chemotherapy
RT : radiotherapy
MST : median survival time

tive course was uneventful. However, the multiple recurrent tumors appeared in pelvis and lung, eight months after operation, and he died 1 year after operation.

DISCUSSION

Neuroendocrine cell (NEC) carcinomas of the colon and rectum are uncommon, comprising less than 1 percent of colon and rectal cancer. The first documented series of colonic small cell undifferentiated carcinomas with neuroendocrine features was reported by Gould and Chejfec in 1978(4). In Japan, The first case of a neuroendocrine cell carcinoma of the rectum was reported by Shimoda in 1984 (5). Since that initial description in Japan a total 40 cases of neuroendocrine cell carcinomas of the rectum have been reported (6, 13-14).

To determine NEC carcinoma, the immunohistochemical study by both Chr A, a marker for large dense core vesicles, and SNP, a marker for small synaptic vesicles are needed(7-8). In this case, the tumor was immunohistochemically stained with Chr A and SNP. However, a part of this tumor was stained with CEA. It seems that this tumor had both components of neuroendocrine cell carcinoma and adenocarcinoma. According to the recent report, it was considered that both NEC carcinoma and adenocarcinoma are derived from a same common epithelial cell of the rectum(7-8). Neuroendocrine cell is seen in the colorectal epithelium(7). However, NEC carcinoma, especially poorly differentiated type, is not capable to arise from neuroendocrine cell(8).

NEC carcinomas of the colon and rectum are clinically more aggressive than colorectal adenocarcinoma and they are capable of rapid distant spread, so the prognosis is generally worse(8). Grabowski *et al.*(12) showed that neuroendocrine differentiation was often seen in small cell undifferentiated colorectal cancer. NEC carcinoma would be a part of poorly differentiated adenocarcinoma. However, the underlying mechanism for the aggressiveness of this disease is still not clear. The Ki-67 LI of poorly differentiated NEC carcinoma is very high, demonstrating that the proliferative activity and the potential malignancy are high. In this case, the Ki-67 LI was very high and the prognosis was very poor.

Treatment of the disease has not yet been established. It was reported that combination chemotherapy of etoposide (VP16) plus cisplatin (CDDP)

would be effective in poorly differentiated NEC carcinoma(9). Mitry, *et al.*(10) reported that a response rate was 41.5% and median survival range was 15 months. Bernick, *et al.*(11) reported that a median survival range was 10.4 months.

Adjuvant chemotherapy was not performed in this case and remains controversial. If lymphatic infiltration or nodal involvement is present, radical surgery with lymph node dissection and adjuvant chemotherapy are the treatment of choice.

In conclusion, the prognosis of NEC carcinoma seems to be worse than that of adenocarcinoma. NEC carcinoma would be a part of poorly differentiated adenocarcinoma. Surgical resection and adjuvant chemotherapy would be the main treatment for colorectal NEC carcinoma.

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