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CASE REPORT

Neuroendocrine carcinoma in adenoma of the sigmoid

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Abstract

Background: Neuroendocrine cell tumor in adenoma of the sigmoid is a rare neoplasm coexistence and it is considered as a mixed glandular-neuroendocrine neoplasm.

Description of case: An 84-year-old woman underwent surgical removal of a tumor located in the sigmoid, diagnosed as adenocarcinoma on a previous biopsy. On gross examination, apart from the ulcerated tumor, a polyp measuring 2 cm was observed, which histologically corresponded to a villotubular adenoma. In two sites of the adenoma, solid nests of smaller cells were observed, having small amount of cytoplasm, round nuclei with finely stippled chromatin. Mitoses were abundant. These cells were located in the lamina propria and muscularis mucosa, without disturbing the polyp architecture, and showed immunophenotypic characteristics of neuroendocrine carcinoma (NEC). The histologic findings set the diagnosis of mixed adenoma and NEC. The patient remains free of recurrence or metastasis by NEC, after two years of follow up.

Conclusion: The recognition of NEC in an adenoma will help to avoid potential diagnostic pitfalls. Mixed adenoma and NEC is rare, with uncertain biological behavior. This case reinforces the view that NECs without infiltration of submucosa may have a better prognosis. Hippokratia 2014; 18 (4): 362-363.

Keywords: adenoma, neuroendocrine carcinoma, mixed glandular-neuroendocrine tumor, microsatellite instability, sigmoid

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Introduction

The presence of neuroendocrine cells in intestinal tumors was first described in 1924[1]. Moyana and Murphy[2] introduced the presence of a mixed adenoma-neuroendocrine tumor (NET) of the gastrointestinal tract in 1988. The term mixed glandular-neuroendocrine tumors characterizes an uncommon heterogeneous group of neoplasms. The glandular components range from adenoma to adenoma with adenocarcinoma and to adenocarcinoma. The neuroendocrine components range from well-differentiated neuroendocrine tumor (NET, G1-carcinoid) to well-differentiated neuroendocrine carcinoma (NET, G2) and to poorly differentiated neuroendocrine carcinoma (NEC, G 3, large cell or small cell type). Neuroendocrine cell tumor in adenoma is an extremely rare coexistence in gastrointestinal tract. Herein, a rare case of NEC developing into an adenoma is discussed.

Description of case

An 84-year-old woman underwent surgical removal of a tumor, located in the sigmoid, diagnosed as adenocarcinoma on a previous biopsy. On gross examination, apart from the ulcerated tumor corresponding to adenocarcinoma, a polyp, measuring 2cm in its greatest diameter, was also observed. Unstained sections taken from the polyp, were sent to our department for consultation.

Histologic examination of the polyp revealed the presence of a villotubular adenoma having low grade dysplasia (Figure 1a), in two sites of which, solid nests of smaller neoplastic cells (Figure 1a) with a small amount of cytoplasm and round nuclei, having finely stippled chromatin, were observed. These cells were located in the lamina propria and muscularis mucosa, without disturbing the polyp's architecture.

On immunohistochemical analysis the neoplastic neuroendocrine cells showed the following immunophenotype: cytokeratin (CK) 8/18+, neuron specific enolase (NSE)+, chromogranin++/- (Figure 1b), CK19--/+, CK7--/+, synaptophysin--/+, thyroid transcription factor (TTF1)-, CDX2-, CK20-, suggesting the presence of a primary neuroendocrine neoplasm of the sigmoid. Ki67/MIB1 index was 60% (Figure 1c). The histologic findings set the diagnosis of a mixed adenoma and neuroendocrine carcinoma (NEC, G3) tumor, with a collision architectural pattern. Review of the slides corresponding to adenocarcinoma did not reveal any other site of neuroendocrine tumor. Immunohistochemical evaluation for mismatch repair (MMR) protein expression showed that both adenoma and neuroendocrine carcinoma were

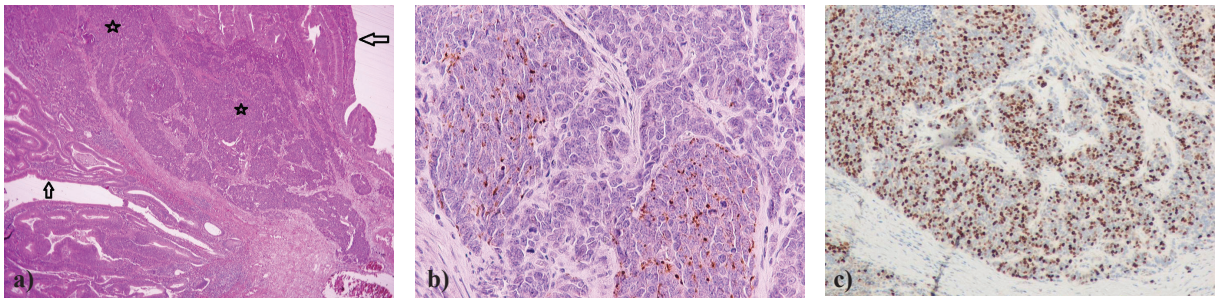

Figure 1: a) Sigmoidal adenoma with low grade dysplasia (arrows) having nests of neoplastic cells with neuroendocrine features (asterisks) (Hematoxylin & Eosin, x 40). **b)** Neoplastic cells positive to chromogranin [Immunohistochemistry (IHC), x 400]. **c)** MIB1 proliferative index: >30% (IHC, x 100).

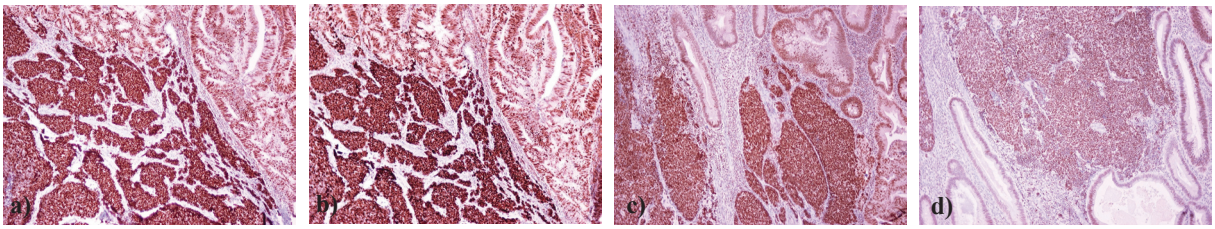

Figure 2: Both adenoma and neuroendocrine tumor cells are positive to MSH2 (**a**), MSH6 (**b**), MLH1 (**c**) and PMS2 (**d**) (Immunohistochemistry, x 100).

MSH2, MSH6, MLH1 and PMS2 positive (Figure 2a-d).

The adenocarcinoma was moderately differentiated (grade II) and the stage was B2 according to Astler Coller staging and T3N0M0, stage IIA, according to TNM staging system. The patient did not receive any further treatment and remains free of recurrence or metastasis for two years in follow up.

Discussion

Mixed benign adenoma-NEC is a rare neoplasm coexistence with uncertain histogenesis and biological behavior. The recognition of NEC in an adenoma will help us avoid potential diagnostic pitfalls. Hence, pathologists should be aware of this coexistence, which has been rarely described in small intestine[3,4] and colorectal tumors[5]. In most of the mixed glandular-neuroendocrine tumors that were reported up to date, the neuroendocrine component was nonfunctional, despite the observed immunohistochemical positivity for a variety of hormones.

The association of colorectal adenomas/adenocarcinomas with NECs may suggest some common molecular features or a common origin. Microsattelite instabillity pathway does not seem to play an important role in most NECs[5,6], as observed in our case.

The prognosis of a benign mixed adenoma-NET cannot be specifically determined, due to the rarity of cases. It seems that similar cases have been completely treated by polypectomy or endoscopic resection technique without recurrence or metastasis. In case of submucosal layer involvement by NET a close follow-up is recommended, because of the relatively higher metastatic rate[6]. Undoubtedly, the presence of NEC causes concern even if it is restricted in the mucosa of an adenoma, since NEC has a highly aggressive behaviour. In this reported case, no recurrence or metastasis was evident during the two years of follow up. However, it is not possible to draw safe conclusions about prognosis due to the small number of similar cases.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgement

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