

Case Report

Clinicopathological features of an ascending colon mixed adenoneuroendocrine carcinoma with clinical serosal invasion

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Abstract: Mixed adenoneuroendocrine carcinoma (MANEC) is exceedingly rare with a poor outcome. In this article, we reported a MANEC in a 68-year-old woman with a symptom of abdominal pain and distension. MANEC derived from the ascending colon with highly aggressive behavior. The diagnosis and distinguish of MANEC must base on histological findings and immunohistochemical findings. In this case, microscopic observation showed tumor cells were arranged in conglobate and nested by fibrous tissue with a visible cell atypia and mitotic. NEC-like and exocrine glandular cells were also been seen in a single neoplasm. MANEC tissues were immunopositive for CK, CK20, P53, CK7, CDX-2, Ki-67 (70%+), E-cad, CD56, CEA, Syn, villin and CgA, and immunonegative for CA125, NSE, ER and PR. Here, the patient was treated by surgical operation and was followed-up near 3 months, no local recurrence and distant metastasis.

Keywords: Mixed adenoneuroendocrine carcinoma, ascending colon, immunohistochemistry

Introduction

Neuroendocrine neoplasms (NENs) arise from endodermal cells, ranging from well-differentiated carcinoids to poorly differentiated neuroendocrine carcinomas (NECs) [1-3]. NEC is a very rare, highly aggressive and poorly prognostic carcinoma and squamous cell carcinoma (SqCC), in which included an additional significant proportion of malignant exocrine glandular cells termed as mixed adenoneuroendocrine carcinoma (MANEC) [2-6]. MANEC is thought to derive from multi-potential stem cells, which have differentiated bidirectionally. According to biclonal transformation of two separate but adjacent neoplasms and multi-directional differentiation of a single neoplasm, MANEC are further classified into collision and composite types [1, 6]. Here, we report a composite MANEC in ascending colon with clinical serosal invasion, and the patient was treated by surgical operation and was followed-up near 3

months, no local recurrence and distant metastasis.

Case report

A 68-year-old woman with a symptom of unexplained abdominal pain and paroxysmal aggravation with nausea and vomiting last for 3 days visited Taiping People's Hospital of Dongguan. Specialist examination showed no chills, no fever, no diarrhea, no jaundice and without frequent micturition, besides a symptoms of decreased appetite. There is no past history of hepatitis, tuberculosis, typhoid fever and other infectious disease, as well as coronary heart disease, hypertension and diabetes. Laboratory tests revealed an obviously rising carcinoembryonic antigen (CEA) level (6.59 ng/ml) and alpha fetoprotein(AFP) level (16.94 IU/ml), but carbohydrate antigen (CA) 15-3 level (6.96 U/ml), CA 125 level (7.90 U/ml), CA 19-9 level (< 0.6 U/ml) and CA 72-4 level (4.68 U/ml) were within normal limits. The patient was diagnosed

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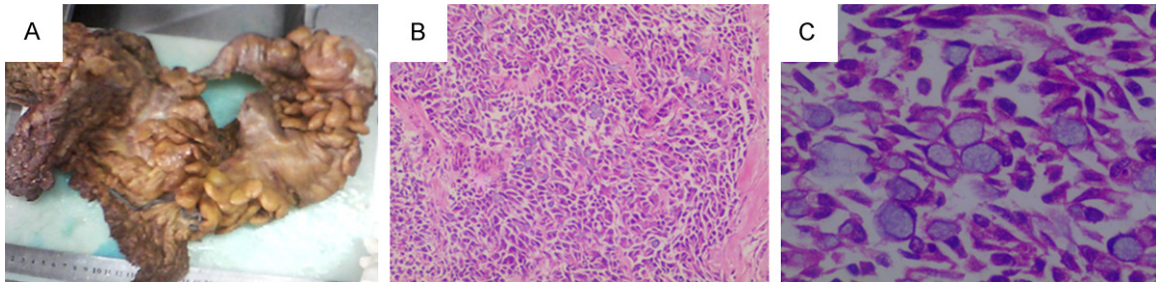


Figure 1. The MANEC tissues were stained with hematoxylin and eosin. A. An intestinal tube and an appendix on ileocecal valve were taken out from patient after surgical operation; B. Tumor cells were arranged in conglobate and nested by fibrous tissue. NEC-like and exocrine glandular cells were also been seen in a single neoplasm (40×); C. A visible cell atypia and mitotic was easy to see on the tumor cells (100×).

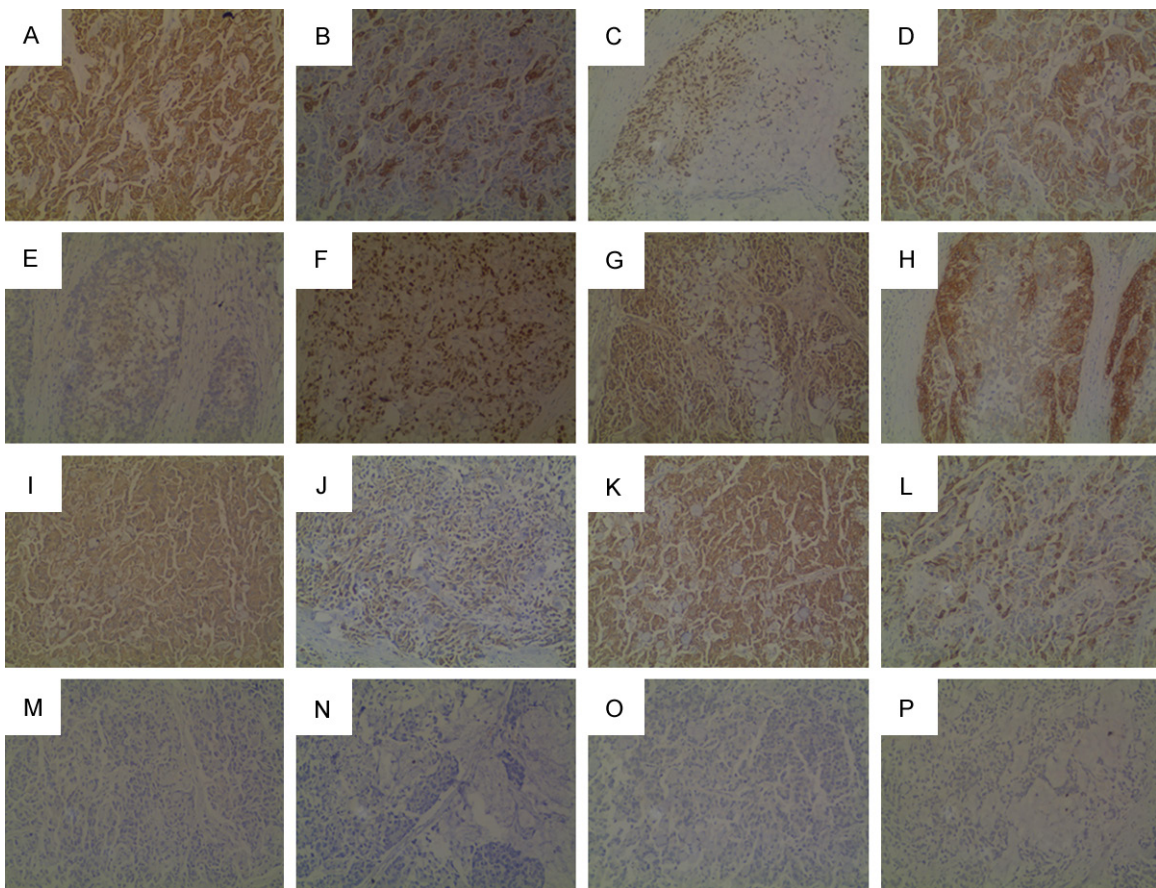


Figure 2. MANEC tissues were stained with immunohistochemistry. The tissues were immunopositive for CK (A), CK20 (B), P53 (C), CK7 (D), CDX-2 (E), Ki-67 (F), E-cad (G), CD56 (H), CEA (I), Syn (J), villin (K), CgA (L) and immunonegative for CA125 (M), NSE (N), ER (O), PR (P) in MANEC tissues (100×).

as ascending colon tumor. An intestinal tube measured 30 cm×13 cm×4.5 cm in diameter, and an appendix measured 7.5 cm×0.8 cm×0.5 cm in diameter on ileocecal valve were taken out (**Figure 1A**). And a hump shaped mass measured 6 cm×6 cm×6 cm in volume on the ascending colon with clinical serosal invasion

was obvious, 7.5 cm in distance away from ileocecal valve. The tumor tissues were stained with hematoxylin and eosin (**Figure 1B** and **1C**). Microscopic observation showed tumor cells were arranged in conglobate and nested by fibrous tissue. A visible cell atypia and mitotic was easy to see on the tumor cells. NEC-like

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cells in a typical mass comprised infiltrative nests of small uniform tumor cells, and exocrine glandular cells with NEC-like cells were seen in a single neoplasm. Tumor tissues were immunopositive for CK (+++), CK20 (++), P53 (+++), CK7 (+++), CDX-2 (+), Ki-67 (70%+), E-cad (+++), CD56 (partly+), CEA (++), Syn (partly+), villin (+++) and CgA (partly++), and immunonegative for CA125 (-), NSE (-), ER (-) and PR (-) (**Figure 2**). According to histopathological and immunohistochemical findings, this patient was diagnosed as an ascending colon mixed adenoneuroendocrine carcinoma with clinical serosal invasion.

Discussion

Neuroendocrine carcinomas (NECs) arising in the ascending colon are rare neoplasms with highly aggressive behavior [2-5]. Here, we report a case of NEC mixed with adenocarcinoma, named mixed adenoneuroendocrine carcinoma (MANEC), in the ascending colon. MANEC was first described by the Cardier in 1924. However, until in 2011, a new WHO classification of digestive neuroendocrine tumors classified it as five main digestive neuroendocrine neoplasms categories along with neuroendocrine tumor G1, neuroendocrine tumor G2, small cell type neuroendocrine carcinoma and large cell type neuroendocrine carcinoma [1]. MANEC is exceedingly rare, and the location of MANEC influences the treatment and outcome. Most of them arise in the gastro-intestinal tract like stomach, colon, esophagogastric junction and cecum, also arise in the gallbladder, bile duct, ampulla, appendix and uterine cervix [7-14]. MANEC is thought to derive from multipotential stem cells, which have differentiated bidirectionally. So the diagnosis and distinguish of MANEC must base on histological findings and immunohistochemical findings. In this case, microscopic observation showed tumor cells were arranged in conglobate and nested by fibrous tissue with a visible cell atypia and mitotic. NEC-like and exocrine glandular cells were also been seen in a single neoplasm. MANEC tissues were immunopositive for CK (+++), CK20 (++), P53 (+++), CK7 (+++), CDX-2 (+), Ki-67 (70%+), E-cad (+++), CD56 (partly+), CEA (++), Syn (partly+), villin (+++) and CgA (partly++), and immunonegative for CA125 (-), NSE (-), ER (-) and PR (-). According to histopathological and immunohistochemical findings, this case was diagnosed as an ascending colon

mixed adenoneuroendocrine carcinoma with clinical serosal invasion.

MANEC along with neuroendocrine tumor G1 (G1 NET), G2 NET, small cell type NEC and large cell type NEC are five main digestive neuroendocrine neoplasms categories [1]. So, it is important to distinguish MANEC from them. Neuroendocrine neoplasms (NENs) including NET and NEC arise from endodermal cells. These cells have monomorphous endocrine cells, sharing common features such as looking similar, producing biogenic amines and polypeptide hormones [15]. NENs range from well-differentiated carcinoids to poorly differentiated NECs, which included an additional significant proportion of malignant exocrine glandular cells termed as MANEC. The monomorphous endocrine cells of MANEC have a characteristic of bidirectional differentiation. So, exocrine glandular cells are the key points of MANEC distinguish from other NENs. MANEC are further classified into collision and composite types. Collision tumors have two different histologic patterns from endocrine cells and exocrine cells in close contact, resulting from biclonal transformation of two separate but adjacent neoplasms. However, composite tumors, the endocrine and exocrine cells are intermixed within the same tumor, arising through multidirectional differentiation of a single neoplasm [6]. Our case was a composite tumor.

NCCN clinical practice guideline indicated patients with the neuroendocrine tumor could treat by palliative operation, adjuvant chemotherapy and somatostatin analogue [2]. And, location of the MANEC influences the treatment and outcome. Ito et al. [16] reported a 39-year-old woman with colonic MANEC died on postoperative day 110, even if the combined use of chemotherapy. Marando et al. [17] also reported a 65-year-old male with colonic MANEC died on postoperative 1 month. Ascending colon MANEC is an uncommon tumor with a strong malignant potential and an extremely poor prognosis. Here, the patient was treated by surgical operation and was followed-up near 3 months, no local recurrence and distant metastasis.

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Disclosure of conflict of interest

None.

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