

## Alpha Fetoprotein Producing Small Cell Neuroendocrine Carcinoma of the Stomach: A Case Report and Review of Literature

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### Abstract

Neuroendocrine carcinoma (NEC) is uncommon in the stomach. A 74-year-old man was referred to our hospital for general physical weariness and abdominal discomfort. He had a higher serum level of alpha fetoprotein (AFP). Upper gastrointestinal endoscopy revealed a Bormann Type II gastric tumor in the lesser curvature of the pylorus. The biopsy specimens from gastric neoplasm were diagnosed as small NEC. Meanwhile, computed tomography scan clarified a mass of the right lobe of the liver. Autopsy after his death, revealed that mass of the liver was metastasis of the gastric NEC, and the NEC was positive for AFP by immunohistochemistry. Coexistence of AFP-producing carcinoma (mostly hepatoid adenocarcinoma) and NEC or carcinoma with neuroendocrine differentiation is known. In such cases, AFP-producing carcinoma and NEC usually occupy different spaces. AFP-producing NEC, particularly, small cell type, of the stomach is quite rare. Presumable origin of AFP-producing cells of the NEC is discussed here with review of literature.

**Keywords:** Neuroendocrine carcinoma; Alpha fetoprotein; Neuroendocrine neoplasms; Case report

### Introduction

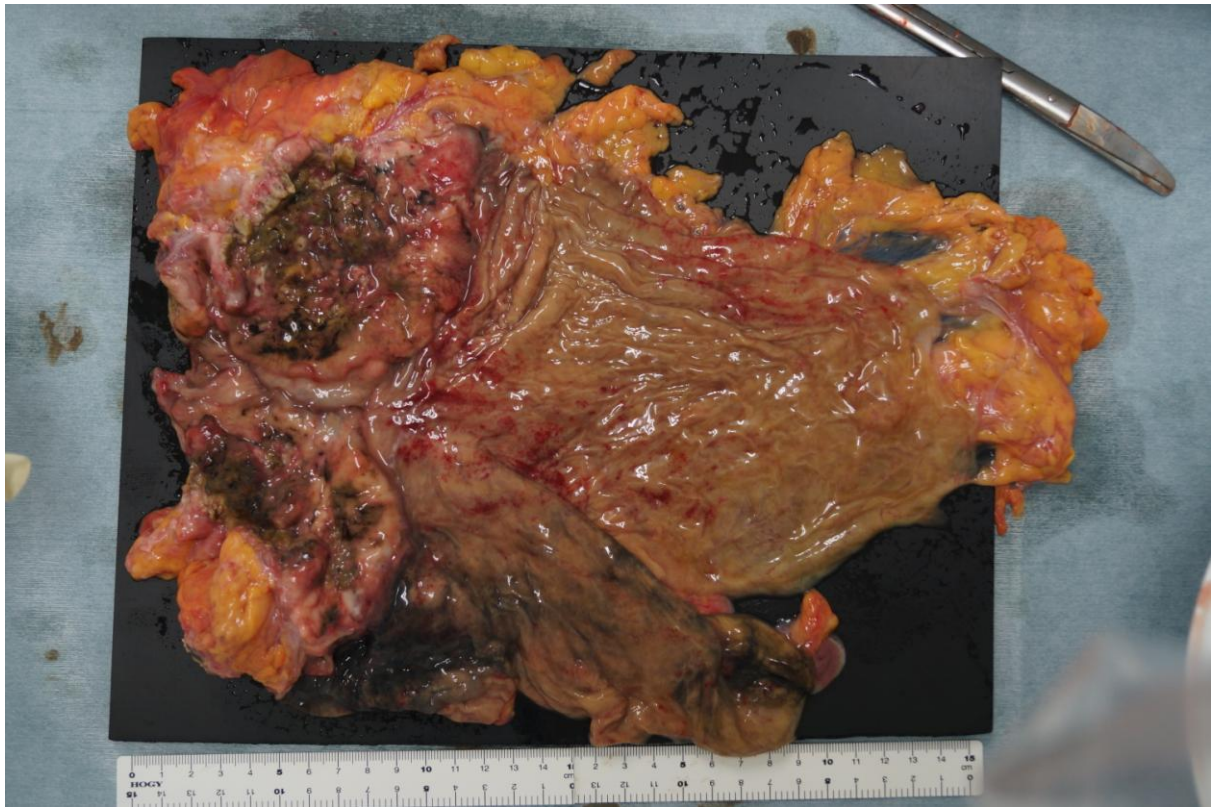
Neuroendocrine Carcinoma (NEC) (large cell type, small cell type) belongs to Neuroendocrine Neoplasms (NET). The incidence of NET of the stomach is higher in Japan where such neoplasms may be attributable to the higher incidence of chronic atrophic gastritis in this country and to intensive screening by endoscopy [1]. However, clinicopathological features of NEC are not fully understood. AFP-producing gastric carcinoma is a rare type of gastric cancer, and most usual AFP-producing gastric carcinoma is hepatoid type. NEC of the stomach has also been regarded as a rare type, and they are single carcinoma or a part of other types carcinomas often as neuroendocrine differentiation. Neuroendocrine component of the gastric mixed adenoneuroendocrine

carcinoma usually comprises NEC, often of large cell type [2]. Furthermore, some gastric carcinomas which are mostly hepatoid adenocarcinoma are known to produce AFP. Coexistence of NEC and AFP-producing carcinoma has been infrequently reported. However, in such cases, component of NEC has been regarded as negative for concerning to AFP production [3-6]. Of gastric NEC, large cell type has been predominant in the literature [2-4]. Thus, more studies for cellular phenotypes, particularly those of comprising small cell NEC are necessary. Presently, we report here a quite rare case of AFP-producing small cell NEC of the stomach. Accordingly, clinicopathological analysis of such neoplasm will be important for understanding of gastric cancers.

### **Case Presentation**

A 74-year-old man was referred to our hospital for general physical weariness and abdominal discomfort. On admission, he had a low value of blood erythrocytes (207x10000  $\mu$ l) and higher serum level of AFP being 470 ng/ml. Abnormal expression of carcinoembryonic antigen was absent. Upper gastrointestinal endoscopy revealed a Borrmann Type II gastric tumor in the lesser curvature of the pylorus. The biopsy specimen from the gastric tumor was diagnosed as small cell NEC. Meanwhile, computed tomography scan clarified a large mass with 70 mm size in S8 area of the liver. He was scheduled to receive a surgical operation for gastrectomy. However, he gradually developed difficulty of food intake, aggressive general condition, and died 2 months later after the hospital admission. His death was followed by an autopsy.

The autopsy revealed a Borrmann Type II gastric tumor on the lesser curvature as shown by the endoscopy, and several swelled tight lymph nodes along the greater as well as lesser curvature were recognized. The size of gastric tumor was 45 x 40 x 15 mm in size (Figure 1). In the liver, a protruded tumor with whitish color at surface in size of 60 x 50x 40 mm was present (Figure 2). The liver tumor had a wide central necrosis and bleeding suggesting rapid growth of the neoplasm, was diagnosed as a metastasis from the stomach tumor since histological characteristics of tumors of the two organs were almost same. In the areas except neoplastic lesion, no clear changes like degeneration, hepatitis and cirrhosis were apparent in the liver. In this case, lymph node metastasis was confirmed in at least three lymph nodes surrounding the stomach.

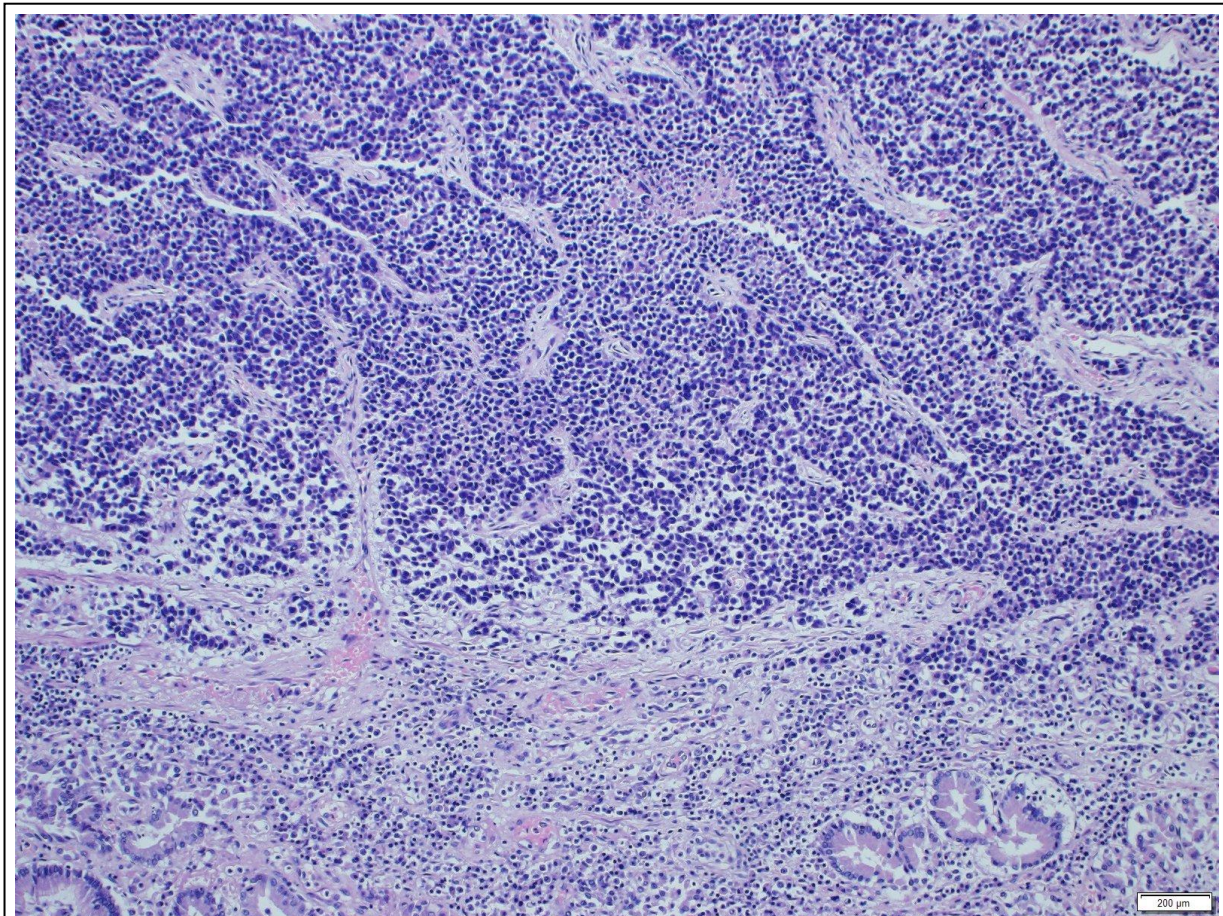


**Figure 1:** Macroscopic appearance of the stomach carcinoma. Bormann Type II tumor mass is located in the lesser curvature of the pylorus.

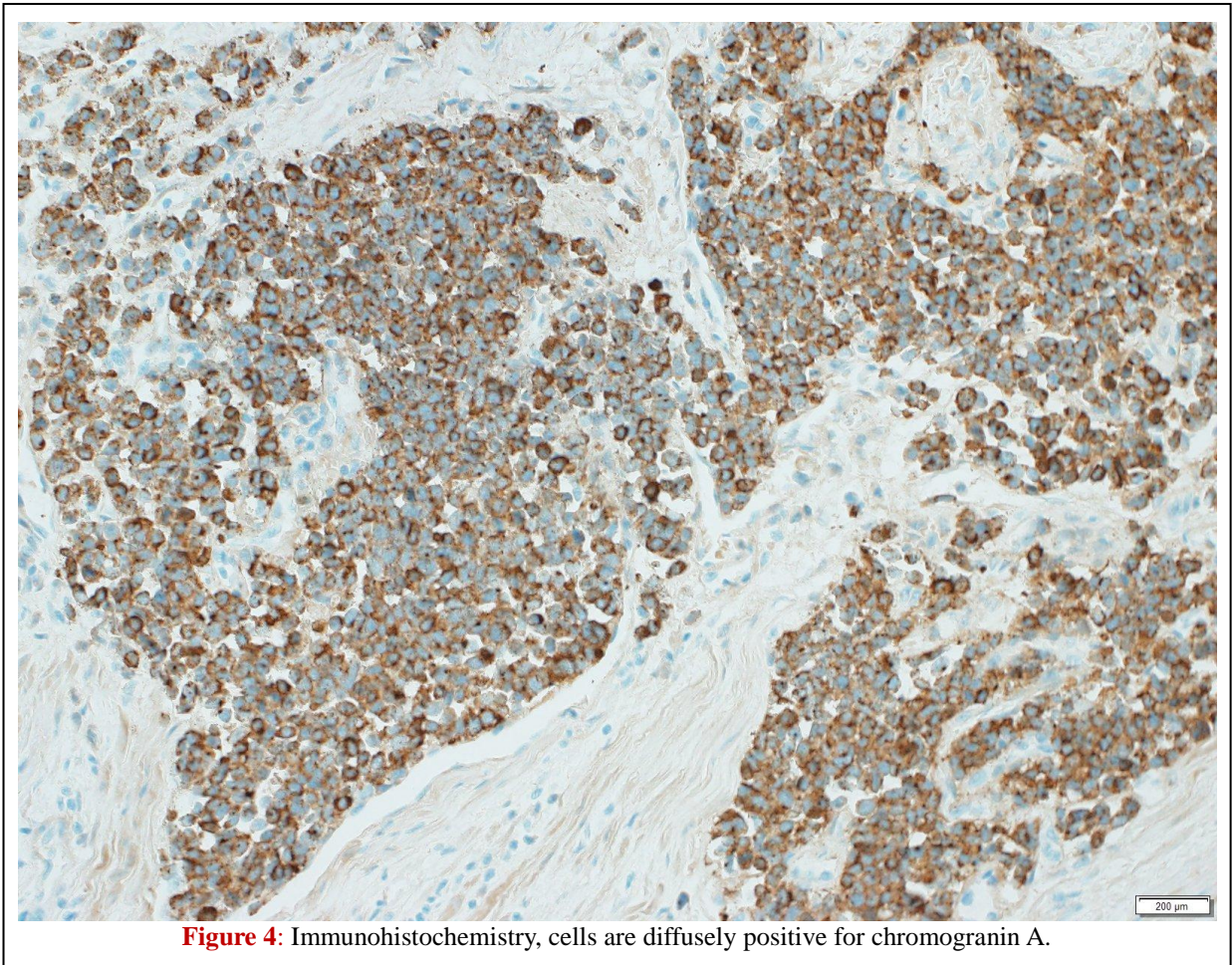


**Figure 2:** Macroscopic appearance of the liver. A big nodule is located in the right lobe.

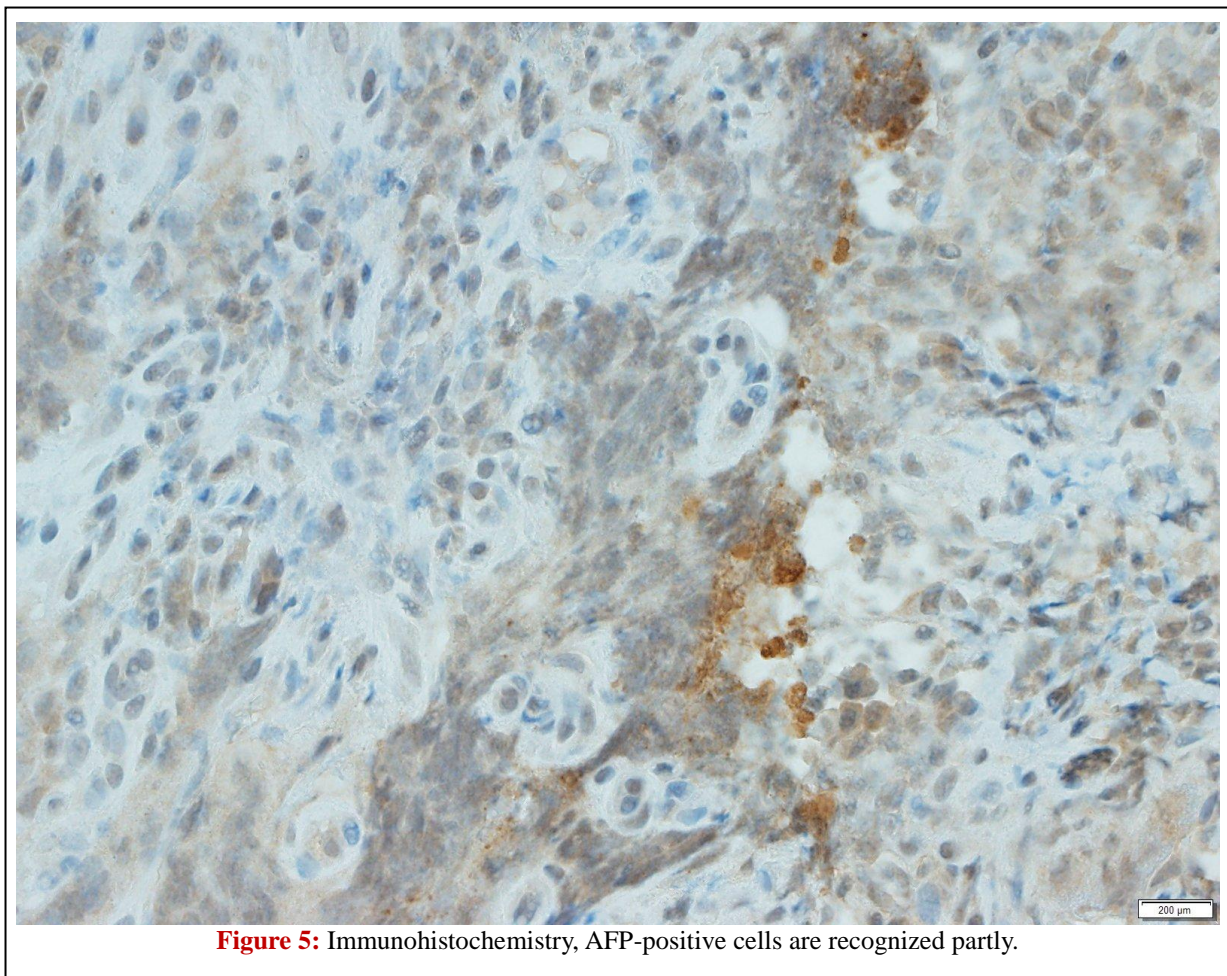
The cells of the tumors of two organs were composed of the nests of round, polyhedral to spindle cells small in size showing high nuclear-cytoplasmic ratio (**Figure 3**). Neuroendocrine markers of synaptophysin and chromogranin A were positive (**Figure 4**). KI 67 labelling index of the tumor cells was quite high (> 70%). Interestingly, AFP positive cells were identified partly or sporadically in the tumors of both organs (**Figure 5**). Other neuroendocrine markers like gastrin or serotonin were negative.



**Figure 3:** Histology of the small cell neuroendocrine carcinoma of the stomach (H & E).



**Figure 4:** Immunohistochemistry, cells are diffusely positive for chromogranin A.



**Figure 5:** Immunohistochemistry, AFP-positive cells are recognized partly.

## Discussion

Usually, NEC is not concerned to produce of AFP. Matsui et al. [7] had a clinicopathologic study on 17 cases of NEC. However, no cases exerted AFP production. According to study by Suzuki et al. [5] who analyzed 11 cases of immunohistochemical features of AFP-producing carcinoma and NEC of the stomach, AFP production was not confirmed in all 6 cases of NEC. In cases of coexistence of AFP-producing gastric carcinoma and NEC or carcinoma with neuroendocrine differentiation, NEC component and AFP-producing carcinoma are reported to occupy different areas in the tumor [3,5]. Nevertheless, rare cases are known to suggest overlapping expression of chromogranin A and AFP [8]. Existence of small number of carcinoma cells with dual differentiation toward neuroendocrine and AFP-producing features is reported in hepatoid adenocarcinoma of the stomach [9]. It is also suggested that origin of NEC and AFP-producing carcinoma of the stomach is the ordinary adenocarcinoma [8], although no adenocarcinomatous component was found in this case. Furthermore, Akiyama et al. [10] reported that gastric AFP-producing hepatoid adenocarcinoma and coexisted tubular adenocarcinoma has an identical origin by analyzing chromosome X in activation, p53 mutation patterns and LOH microsatellite analysis. Furthermore, Nishikura et al. [11] suggested the occurrence of gastric NEC in the preceding adenocarcinoma components by analyzing p53 mutation status. Present case is similar to the case by Takahashi et al. [4] who reported a NEC of the stomach with increased serum AFP. So far as we concerned, such cases of gastric AFP-producing NEC without other components are quite rare. Accordingly, it is suggested that gastric NEC contains stem cells like cells being capable to differentiate to the cells producing AFP. In our case as well

as in Takahashi et al. [4], AFP-positive cells in the cells of NEC are detected partly or sporadically. Similar pathological feature is also described in another study. This may be one of properties of AFP-producing gastric NEC.

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