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Case Report

Rectal Neuroendocrine Tumor (G1) with Liver Metastasis: A Case Report

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Abstract

Background and Objectives: Neuroendocrine carcinoma is a rare tumor and arises from cells dispersed in the neuroendocrine system.

Methods: In this study, we report a 62-year-old man who was presented with a chief complaint of constipation in 2019 at Firoozgar Hospital in Tehran. The patient had no family history of cancer but noted a weight loss of 15 to 20 kg over the past 8 months.

Results: According to the colonoscopy, there was a polypoid lesion about 10 to 15 mm in the rectum, and biopsy was done for histological studies. In the present study, a metastatic rectal neuroendocrine tumor was detected in the liver. Microscopic studies of the mass revealed a well-differentiated neuroendocrine carcinoma. Immunohistochemical (IHC) staining was positive for Chromogranin, Pan-Cytokranine, and Ki-67 and negative for Synaptophysin, Hepar, TTFI, PAX8, and CDX2. After performing diagnostic procedures for excisional rectal biopsy, Transanal Minimally Invasive Surgery (TAMIS) was performed. After a few days, the patient was discharged with a good general condition and stable vital signs.

Conclusions: Although neuroendocrine tumors of the rectum relatively slow growth, they are malignant and can metastasize to other areas. In general, the prognosis of patients with metastatic disease is poor and information about the specific treatment of these patients is limited

Keywords: Neuroendocrine tumor, Rectal neoplasms, Liver metastasis, Liver cancer, Immunohistochemical staining, Case report

Bacground and Objective

The endocrine system is a type of communication system in which hormones, as biochemical messengers, work to regulate the physiological processes of the body[1]. Neuroendocrine carcinoma is a rare tumor and arises from cells scattered in the neuroendocrine system. The tumor was first described in the small intestine and was first called carcinoid[2]. The term neuroendocrine carcinoma is currently used for all neuroendocrine tumors[3].

From the embryological point of view, neuroendocrine cells are derived from the endoderm and belong to one of two functional groups. Amino Precursor Uptake and Decarboxylation (APUD) cells that produce serotonin and catecholamine hormones and cells that can synthesize low molecular weight peptide or protein hormones such as chromogranin, cholecystokinin, and secretin[4].

Neuroendocrine cell-derived tumors (NETs) are found in every organ of the body and have a different prognosis that ranges from slow-growing tumors and low aggressive to rapidly growing tumors and extensive metastatic ability[5].

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In humans, this carcinoma has been reported in the intestines, liver, bile ducts, lungs, gall bladder, esophagus, nasal cavity, and skin[6,7], most of which are highly aggressive[8].

The prevalence of neuroendocrine carcinoma in the gastrointestinal tract is 1% in the esophagus, 2% in the colon, and 0.1% -0.4% in the stomach[9-11]. Neuroendocrine rectal tumors account for 29% of all gastroenteropancreatic tumors (GEP-NET) in the latest report, with the rectum being the most common organ, slightly above the small intestine[12]. These tumors also lead to liver metastasis[8,13]. In this study, we report a patient with rectal neuroendocrine tumor (G1) with liver metastasis who responded well to surgical treatment.

Case presentation

This report is about a 62-year-old man who was referred to Firoozgar Hospital in Tehran with a chief complaint of constipation in 2019. The patient has no family history of cancer and has reported a weight loss of 15 to 20 kg over the past 8 months. On physical examination, abdominal pain was found.

The patient underwent rectal endoscopic ultrasound, which revealed a hypoechoic lesion of about 10 to 15 mm in the submucosal origin of the rectum. Multiple localized lymph nodes were also found. Fortunately, the bladder, prostate, and vesicula seminales were normal.

Subsequently, the patient underwent colonoscopy, the results of which confirmed the presence of a polypoid lesion about 10 to 15 mm in front of the rectum about 10 cm from the anal verge, and biopsy was performed for histological studies. Histological results of this polypoid lesion indicated a well-differentiated neuroendocrine tumor and it was found that a wide surgical margin was removed from the tissues involved. Ki-67 index was about 1% positive. Studies on the mucosal tissue of the rectum also revealed a grade 1 neuroendocrine tumor. The immunohistochemical results of chromogranin and synaptophysin staining were positive and the Ki-67 index was less than 1%.

Due to changes in liver function markers for further investigation, the patient was subjected to nuclear scanning using intravenous injection of technetium 99m. Due to the multiple concentrations of marker material throughout the liver lobes, liver metastasis was determined. Immunohistochemical staining was used for differential diagnosis of neuroendocrine carcinoma and poorly differentiated carcinoma. The results were positive for chromogranin, Pan Cytokeratin, and Ki-67, and for synaptophysin, Hepar, PA CDX2 were negative. The results of histological microscopic studies of the left liver lobe biopsy also confirmed the presence of liver metastasis.

After performing diagnostic procedures for excisional rectal biopsy, Transanal Minimally Invasive Surgery (TAMIS) was performed. After a few days, the patient was discharged with a good general condition and stable vital signs.

Discussion

Neuroendocrine carcinoma was first described by Lubarsch more than 100 years ago[14]. Gastrointestinal neuroendocrine neoplasms are commonly known as gastroenteropancreatic tumors (GEP-NETs). GEP-NETs are a heterogeneous group of tumors derived from embryonic intestinal neuroendocrine cells that exhibit a common phenotype in staining with chromogranin A and synaptophysin[15]. The former GEP-NET classification divided tumors by embryonic derivation, which included the foregut (respiratory, upper gastrointestinal tract, and pancreas), the midgut (small intestine and ascending colon), and the hindgut (the remaining two-thirds colon and rectum). However, even in this classification, there is heterogeneity and differences in tumor function; therefore, classification based on anatomical location and tumor grading is more appropriate. In 2010, the World Health Organization (WHO) defined a new classification for neuroendocrine neoplasms of the gastrointestinal tract, according to which all tumors with metastatic potential are malignant[16].

Tumor grade based on the count of mitotic forms and cell proliferative activity (Ki-67 index) at the three levels defined in Table 1. This new classification includes neuroendocrine tumor (NET), neuroendocrine carcinoma (NEC), and Adenoneuroendocrine mixed cancer. According to this classification, the patient was in the G1 group and his Ki-67 was 1%[3].

Table 1- Tumor grade according to mitotic count and proliferation.

WHO grade	Mitotic count (10 HPF*)	Ki-67 index
G1	< 2	≤ 2%
G2	2 - 20	3 - 20%
G3	> 20	> 20%

* Per 10 high-power fields.

NETs are well-differentiated neoplasms with low cellular atypia and proliferative activity that are part of Grade 1 or 2. NECs are also poorly differentiated neuroendocrine neoplasms that exhibit distinct cellular atypia and high proliferative activity and are part of Grade 3 [15]. Most of these patients have no symptoms and are diagnosed with lower endoscopy or nonspecific symptoms [2]. In symptomatic patients, the most common symptoms include gastrointestinal bleeding, pain, constipation, and tenesmus. The primary symptom of the patient under study was constipation to pursue treatment. Most rectal NETs are small-sized lesions. In a recent systematic review, 79% of tumors were less than 1 cm and only 5% were more than 2 cm[17].

Kasuga et al reported an average tumor size of 7.1 mm. As suggested by Kim et al, most lesions occur in the mid-rectum, with 74.8% of tumors occurring between 5 and 9.9 cm from the rectum[18,19]. Most rectal NETs (89%) are confined to the submucosal layer and have low grades. Weinstock et al reported that G1 88.1, G2 8.2, and G3 tumors account for 3.5% of rectal neoplasms. Lymph node and distant metastasis were also reported in about 8% and 4% of patients, respectively[16].

Fortunately, rectal NETs have a good overall prognosis with a 5-year survival rate of 88.3% - 75.2%[7]. Risk factors for the metastatic disease include tumor size, muscularis propria invasion, proliferation index, as well as lymphovascular and perineal invasion[20]. Tumor size is the most important predictor of tumor behavior. Lesions smaller than 1 cm have little risk for lymph nodes and distant metastasis. The result of lesions is less pronounced on average (between 1 and 2 cm) but has a greater risk of metastasis and a poorer prognosis than individuals less than 1 cm[21]. However, research has shown that rectal NETs of up to 2 cm with low mitotic rate and without propria muscle invasion or involvement of lymph nodes mainly respond to treatment[1].

Conclusions

Although neuroendocrine tumors of the rectum are rare, their incidence is increasing, and recent updates on classification, diagnosis, and treatment approaches are noteworthy[12]. Unfortunately, despite their relatively slow growth, they are malignant and can metastasize to other areas. In general, the prognosis of patients with metastatic disease is poor and information about the specific treatment of these patients is limited[22].

Most of the risk factors reported for the metastatic disease include tumor size greater than 1 cm, muscularis propria invasion, high proliferation index, and lymphovascular invasion. In general, low-risk tumors can be treated by anal resection via a minimally invasive procedure, and high-risk tumors require surgical excision[23].

Competing Interests

The authors declare no competing interests.

Authors' Contributions

The authors contributed equally to the writing of the article

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