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Neuroendocrine Tumor Developing in the Rectal Mesentery: A Case Who Had Surgery Due to Appendiceal Neuroendocrine Tumor 13 Years Ago

Rektum Mezenterinde Gelişen Nöroendokrin Tümör: 13 Yıl Önce Apendiks Nöroendokrin Tümörü Nedeniyle Ameliyat olan bir Olgu

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ABSTRACT
In the gastrointestinal tract, Neuroendocrine Tumors (NETs) are most observed in the appendix. This study aims to present a 51-year-old male patient diagnosed with NET in rectal mesentery. In 2009, appendiceal NET was diagnosed after appendectomy. Then, a total mesocolonic right hemicolectomy was performed. In the examination conducted in June 2022, a mass lesion was detected on the right side of the pelvis, posterior to the seminal vesicle and anterolateral to the rectum, within the rectal mesentery. Diagnosis of NET was made with a transabdominal biopsy, and then an operation decision was made. The perioperative frozen section confirmed that the mass lesion was a NET with clean surgical margins. In patients with large tumor sizes or high-grade NET, postoperative treatment is continued with chemotherapy or chemoradiotherapy. The patient was administered chemotherapy after surgery and was followed up in the outpatient clinic.
Keywords: Appendix, neuroendocrine tumor, rectal mesentery

ÖZ
Gastrointestinal sistemde Nöroendokrin Tümörler (NET) en sık apendikste görülür. Bu çalışmanın amacı, 51 yaşında rektum mezenterinde NET tanısı koyulan erkek hastayı sunmaktır. 2009 yılında apendektomi sonrası apendiks NET tanısı koyulmuş. Ardından total mezokolonik sağ hemikolektomi uygulanmış. 2022 yılına kadar rutin takiplerinde patolojiye rastlanmayan hastanın 2022 Haziran ayında yapılan tetkiklerinde pelvisin sağ tarafında, seminal vezikülün posteriorunda ve rektumun anterolateralinde, rektum mezenteri içerisinde kitle lezyon tespit edildi. Yapılan transabdominal biyopside NET tanısı koyuldu ve operasyon kararı verildi. Periopreatif frozen section incelemede kitle lezyonun temiz cerrahi sınırlar ile rezeke edilmiş NET olduğu doğrulandı. Büyük tümör boyutuna sahip ya da yüksek dereceli NET'de ameliyat sonrası tedaviye kemoterapi veya kemoradyoterapi ile devam edilmektedir. Hastaya cerrahi sonrası kemoterapi tedavisi verildi ve poliklinik takibine alındı.
Anahtar Kelimeler: Apendiks, nöroendokrin tümör, rektum mezenteri

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INTRODUCTION

According to the 2019 World Health Organization, neuroendocrine neoplasms of the appendix are classified as well-differentiated Neuroendocrine Tumors (NETs), poorly differentiated neuroendocrine carcinomas, and mixed neuroendocrine/non-neuroendocrine neoplasms. Well-differentiated NETs are the most common type, while poorly differentiated NETs are rare.[1]

According to the 2010 WHO classification, the Ki-67 index of NETs is < 20%, and the majority are grade 1 (G1) or grade 2 (G2). 95% are less than 2 cm in diameter, and NETs generally have a good prognosis.[2] However, lymph node involvement at diagnosis was reported to be between 11% and 49%. In addition, up to 10% of cases may present with distant metastases.[3,4]

In the gastrointestinal tract (GIT), NETs are most commonly observed in the appendix. In surgical practice, NET is most commonly encountered in

patients who underwent appendectomy with the preliminary diagnosis of acute appendicitis. NETs that develop in other parts of the GIT are less common. The probability of NETs occurring in appendectomies varies between 1-1.5%.[5]

In appendiceal NETs, a tumor size of 2 cm and above is determined as a bad prognostic outcome.[6] Therefore, right hemicolectomy with lymph node dissection is recommended if the tumor size is above 2 cm.[7] After the surgery, the patients must be followed up with laboratory, radiological, and endoscopic examinations. Grade, degree of differentiation, and lymphovascular invasion are other prognostic factors in NETs. 70% of appendiceal NETs are 1 cm or less in size; they are usually located at the distal part of the appendix, and the probability of metastasis is relatively low. The likelihood of metastasis for appendiceal NETs of 2 cm or more is around 20%.[8] While appendectomy is sufficient for NETs less than 1 cm, right hemicolectomy is necessary for NETs 2 cm and above. In appendiceal NETs between 1 and 2 cm, the decision should be made according to the histopathological characteristics of the tumor.[9]

In this study, we aim to present a 51-year-old male patient diagnosed with NET in the rectal mesentery 13 years after appendectomy and right hemicolectomy due to appendiceal NET, with all dedicated laboratory results and radiological findings. Based on the outcome of this case, we would like to highlight the importance of follow-up and medical treatment after surgery.

CASE REPORT

Ethics committee approval is not required. The patient/relatives have signed an informed consent/ consent form, and the study was conducted following the international declaration, guidelines, etc.

In 2009, a 38-year-old male patient underwent an appendectomy due to a preliminary diagnosis of acute appendicitis. After surgery, histopathological examination revealed appendiceal NET with a largest diameter of 2 cm. Then, a total mesocolonic right hemicolectomy was performed. 13 years later, in 2022, the patient was investigated for complaints of dysuria, and a 2.7 cm diameter mass lesion was detected on the right side of the rectal mesentery. There was uptake in the lesion of Gallium-68 PET/ CT (Figure 1).

Serum Chromogranin-A: 62 µg/l, Nse:7.5 µg/L, and urine 5 HIAA:31.6 µmol/24h values were within the normal range. Contrast-enhanced pelvic magnetic resonance examination was performed, and a 27x22x24 mm tumor was observed located in the posterior to the seminal vesicle and anterolateral to the rectum and was close to the surrounding tissues but did not invade any surrounding tissue (Figure 2). The tumor is hypointense on T1-weighted images, hypointense on T2-weighted images, and shows mild diffusion restriction on diffusion-weighted images. The mass shows linear mild contrast enhancement in post-contrast images. Anteriorly, the mass was close to the seminal vesicles. However, no apparent signs of invasion were detected.

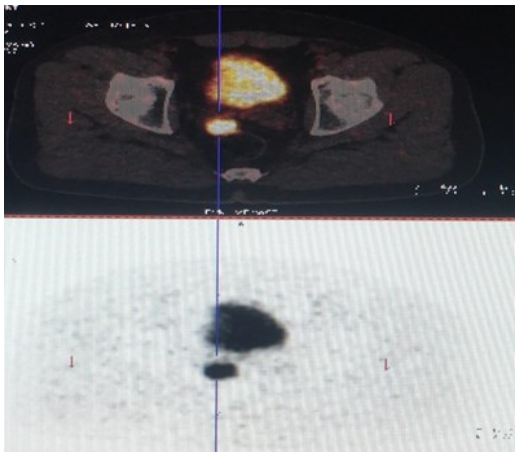

Figure 1. Uptake in the lesion in Gallium-68 PET/CT.

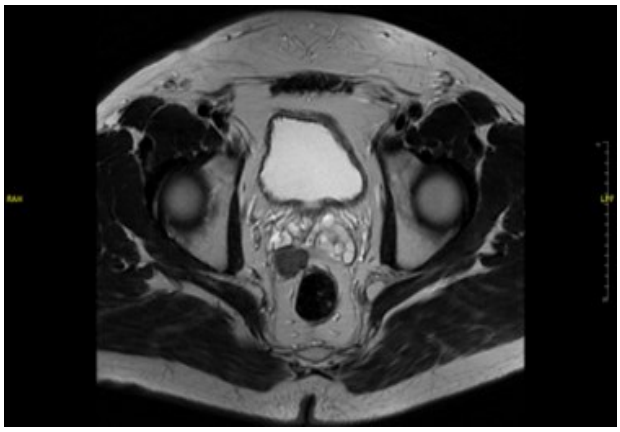

Figure 2. Axial T2-A MRI examination: Hypointense mass with smooth contours in the proper anterolateral aspect of the rectum.

A colonoscopy was performed to eliminate the possibility that the tumor was the second primary tumor originating from the rectum, and no endoluminal pathology was observed. No metastases were detected in other parts of the body, according to Gallium-68 PET/CT. The result of the needle biopsy was grade-2 NET. The patient's first surgery was performed by laparotomy, and the same incision line was used again and open laparotomy was performed. Perioperative frozen sections were performed, NET was confirmed, and the surgical margins were reported with clear margins. The patient was discharged on the 3rd postoperative day with a cisplatin and etoposide chemotherapy protocol planned. No active complaints or residual lesions were observed after chemotherapy in the first year of Follow-Up.

In the microscopic examination, it was observed that the tumor generally formed solid islands. Tumor cells show mild atypia and have round-oval nuclei with small, eccentrically located nucleoli. The nuclear chromatin structure has a fine granular chromatin distribution (Salt and Pepper Pattern) specific to NETs (Figure 3 a, b, and c).

Tumor cells were stained positively with CD56, synaptophysin, and chromogranin. KI-67 index was found to be 18%. With these findings, the case was diagnosed with grade 2/3 NET, showing moderate atypia. (Figure 4a, b, c, and d)

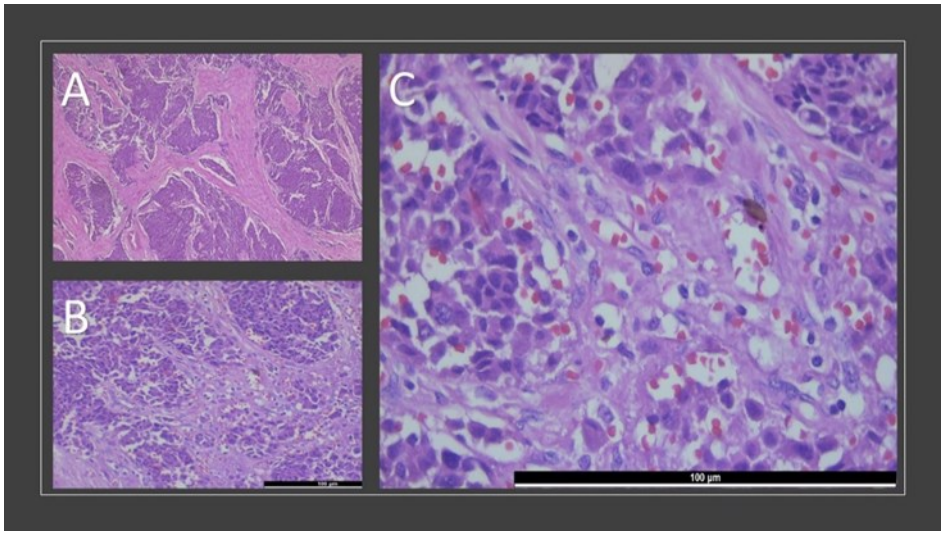

Figure 3. a: Solid tumor islands within desmoplastic stroma (Hematoxylin and Eosin X40); b: The cells forming the tumor show mild atypia and have a fine granular chromatin distribution (Hematoxylin and Eosin X200); c: A closer view of the tumor cells shows round-oval nuclei with small, eccentrically located nucleoli. The nuclear chromatin structure is observed in a Salt and Pepper Pattern (Hematoxylin and Eosin X400).

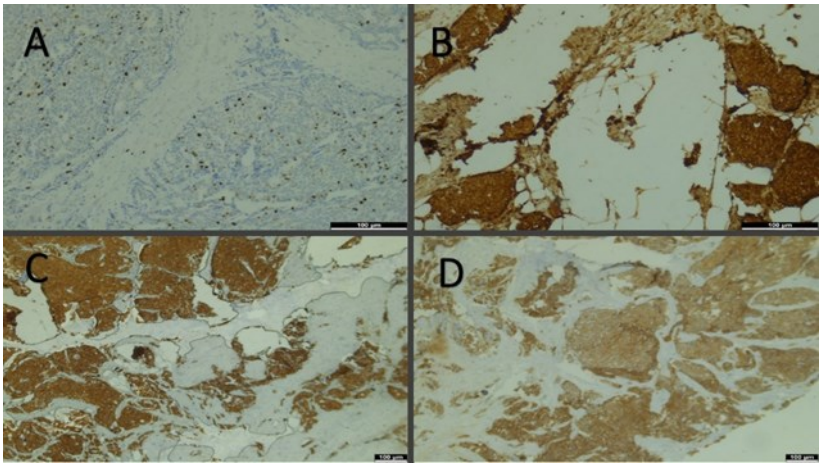

Figure 4. a: Brown positive staining with Ki 67 in 18% cell nuclei (X40); b: Brown positive staining with CD 56 (X40); c: Positive staining with synaptophysin (X100); d: Moderately positive staining with chromogranin (X40).

DISCUSSION AND CONCLUSION

Although appendiceal NETs are unlikely to metastasize, this possibility should always be considered. By a majority, NETs tend to metastasize to the liver. However, there is also the possibility of synchronous and metachronous colon cancer and other primary tumors.[9] Therefore, patients must undergo a colonoscopy and whole-body scanning with Gallium-68 PET/CT. Lymphovascular invasion can be considered a poor prognostic factor. Ki-67 index and grade are crucial and highly related to prognosis. In high-grade NET cases, complete resection and adjuvant chemotherapy can only increase overall survival.[5]

The grading system of NETs often involves assessing the histological appearance of the tumor cells and the Ki-67 proliferation index. There are three grades. Grade 1 (G1): Ki-67 index is usually less than 3%. Tumors with this grade tend to grow slowly and have a lower likelihood of aggressive behavior. Grade 2 (G2): Ki-67 index is between 3% and 20%. Tumors with this grade have an intermediate growth rate and behavior. Grade 3 (G3): Ki-67 index is more than 20%. Tumors with this grade tend to grow rapidly and have a higher potential for aggressive behavior and metastasis. In our case, the tumor was grade 2 due to the Ki 67 proliferation index being 18% and the presence of mild nuclear atypia.

Metastasis is influenced by factors such as tumor grade, size, location, and the presence of specific cellular markers. High-grade tumors, including high-grade appendix neuroendocrine tumors, are generally associated with a higher risk of metastasis due to their aggressive growth behavior.[5,6] It has also been found to be associated with tumor size and high-grade lymph node metastasis.[3,4] Conversely, it was shown that adverse outcome was significantly associated with tumor advanced stage, older age, and the presence of positive resection margins and extramural extension.[2] Particularly for NETs of pancreatic origin, the risk of recurrence is related to the Ki-67 ratio >10% and poorly differentiated pathological findings. Recurrences have been reported mainly in the pancreatic tissue, liver, and abdomen. However, specific recurrence sites for other NETs have not been frequently reported in the literature.[10] In this study, possible metastasis, even after a long time, may be related to the tumor's high grade, a size larger than 2 cm, and high Ki-67 proliferation index. The recurrent anatomical area is also remarkable.

In conclusion, the appearance of metastasis generally indicates that the tumor has progressed to an advanced stage. The treatment approach for metastatic neuroendocrine tumors often involves a combination of therapies, which may include surgery, targeted therapies, chemotherapy, and other interventions to manage symptoms and slow disease progression. A higher Ki-67 index generally indicates a higher rate of cell proliferation, which can suggest a more aggressive tumor behavior. However, each case is unique, and factors such as the tumor's characteristics, the patient's overall health, and other variables can influence the disease progression timeline.

Ethics Committee Approval: Ethics committee approval is not required. The patient/relatives have signed an informed consent/consent form, and the study was conducted following the international declaration, guidelines, etc.

Conflict of Interest: No conflict of interest was declared by the authors.

Author Contributions: Concept-KG; Supervision-KG; Materials-KG, DD; Data Collection and/or Processing-KG, DD; Analysis and/or Interpretation-MU; Writing-KG, DD, MU.

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