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Coincidental or Connected: Synchronous Giant Gastric GIST and Malignant Colonic Polyp: A Case Report

Tesadüf veya Bağlantılı: Eşzamanlı Dev Gastrik GİST ve Malign Kolon Polipi: Bir Olgu Sunumu

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ABSTRACT

Gastrointestinal stromal tumors (GIST) are rare mesenchymal neoplasms of the gastrointestinal tract, most commonly occurring in the stomach. The concurrence of GIST with another malignancy is an uncommon phenomenon, with few works of literature reported. We report a rare synchronous giant gastric GIST with a malignant colonic polyp. A 70-year-old woman presented with an upper abdominal mass. There were no changes in bowel habits. CEA level was normal. Contrasted computed tomography of the abdomen revealed a huge gastric mass with incidental findings of a suspicious mass in the sigmoid colon. Esophagogastroduodenoscopy revealed extrinsic compression with normal overlying mucosa, suggesting a submucosal mass. Colonoscopy revealed a large polypoidal mass in the sigmoid colon, and initial biopsy revealed tubulovillous adenoma with high-grade dysplasia. Wide local excision of the gastric tumor and table snare polypectomy were performed. The base of the polyp was also taken for biopsy. The patient had an uneventful recovery and was discharged home well. Postoperative histopathological examination showed gastric GIST and adenocarcinoma of the sigmoid polyp. The polyp base showed no malignancy. The patient was started on imatinib 400 mg once a day. GIST and colon malignant polyps are two distinct types of neoplasms that can occur synchronously. GIST tumours arise from the interstitial cells of Cajal and are characterized by mutations in *KIT/PDGFRA* genes. Conversely, malignant polyps are epithelial tumours that arise from the colonic mucosa classically because of alterations in the APC tumour suppressor gene, resulting in overactivation of the Wnt/β-catenin signaling pathway. Synchronous GISTs and malignant colon polyps are rare, and their molecular basis is distinct. However, it is crucial to consider the possibility of genetic predisposition in patients with such tumors. In a case of GIST, the surgeon should recognize the possibility of another tumor with a different histological origin. High clinical analysis needed during laparotomy for GIST to detect a

ÖZ

Gastrointestinal stromal tümörler (GİST), gastrointestinal sistemin nadir görülen mezenkimal neoplazmalarıdır ve en sık midede görülür. GİST'nin başka bir malignite ile birlikteliği nadir görülen bir olgudur ve literatürde çok az çalışma bildirilmiştir. Kötü huylu kolon polipi olan nadir bir senkron dev gastrik GIST bildiriyoruz. Üst karın bölgesinde kitle şikayetiyle 70 yaşında kadın hasta başvurdu. Barsak alışkanlıklarında değişiklik olmadı. CEA düzeyi normaldi. Karın bölgesinin kontrastlı bilgisayarlı tomografisi, sigmoid kolonda şüpheli bir kitleye rastlanan büyük bir gastrik kitleyi ortaya koydu. Özofagogastroduodenoskopide, normal üst mukoza ile birlikte ekstrinsik bası saptandı ve submukozal kitleyi düşündürdü. Kolonoskopide sigmoid kolonda büyük polipoidal kitle saptandı ve ilk biyopside yüksek dereceli displaziye sahip tübülovillöz adenom görüldü. Mide tümörünün geniş lokal eksizyonu ve table snare polipektomisi yapıldı. Polipin tabanından da biyopsi alındı. Hasta sorunsuz bir şekilde iyileşerek taburcu edildi. Ameliyat sonrası histopatolojik incelemede gastrik gist ve sigmoid polibin adenokarsinomu saptandı. Polip tabanında malignite saptanmadı. Hastaya günde bir kez 400 mg imatinib başlandı. GİST ve kolon malign polipleri eş zamanlı olarak ortaya çıkabilen iki ayrı neoplazm türüdür. GİST tümörleri Cajal'ın interstisyel hücrelerinden kaynaklanır ve *KIT/PDGFRA* genlerindeki mutasyonlarla karakterizedir. Buna karşılık, malign polipler, klasik olarak APC tümör baskılayıcı genindeki değişiklikler sonucu Wnt/β-katenin sinyal yolunun aşırı aktivasyonu sonucu kolon mukozasından kaynaklanan epitel tümörlerdir. Eş zamanlı GİST'ler ve malign kolon polipleri nadir görülür ve moleküler temelleri farklıdır. Ancak bu tür tümörlere sahip hastalarda genetik yatkınlık olasılığının da göz önünde bulundurulması önemlidir. GİST olgusunda cerrah, farklı histolojik kökenli başka bir tümörün olasılığını göz önünde bulundurmalıdır. GİST'te senkron tümör tespiti için laparotomi sırasında yüksek klinik analize ihtiyaç vardır. Nadir görülmesi ve literatürün sınırlı olması nedeniyle, cerrahların hasta

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ABSTRACT

synchronous tumor. Due to its rare occurrence and limited literature further GIST with another synchronous tumor must be conducted to help surgeons optimize patient management.

Keywords: Gastrointestinal stromal tumor, malignant colonic polyp, synchronous tumor

ÖZ

yönetimini optimize etmesine yardımcı olmak için başka bir senkron tümörle birlikte daha fazla GİST yapılmalıdır.

Anahtar Sözcükler: Gastrointestinal stromal tümör, kötü huylu kolon polip, senkron tümör

INTRODUCTION

Gastrointestinal stromal tumor (GIST) is the most common mesenchymal-derived neoplasm arising from the gastrointestinal (GI) tract (1). It accounts for only 0.1-3% of all GI neoplasms (1). The incidence is 1.5 per 100,000 per year (1). This indicates the rarity of the tumor. It is peak incidence in the sixth and seventh decades (2). It originates from the interstitial call of Cajal, which is responsible for gut motility and can present anywhere along the GI tract. The most common site of origin is the stomach (60%), followed by the small intestine (30%) (1). Historically GIST is classified as leiomyomas or leiomyosarcoma as it represents similar histological appearance with smooth muscle neoplasm. However, recent studies now consider them as separate entities based on the identification of C-kit receptor or the PDGFR receptor mutation in GIST. GISTs have malignant potential, and their nature is difficult to predict (3). The coexistence of GIST with other primary GI malignancy with different histology origin has rarely been reported in the literature (3).

Malignant colonic polyp is defined as macroscopically benign appearing adenoma that harbors a focus of adenocarcinoma that invades beyond muscularis mucosae into submucosa (4,5). It accounts about 2-5% of all removed polyps (4). Large colon polyps (defined >2 cm) and polyps with high-grade dysplasia (HGD) carry a higher risk of carcinoma (4,6). It is accepted that most malignant neoplasms of the colon arise from the precursor adenomatous polyp. This adenoma-carcinoma sequence is a stepwise progression from normal epithelium to carcinoma, often with intervening dysplasia, that occurs as a result of multiple sequential genetic mutations. Colorectal adenocarcinoma is a significant clinical problem and the third most common neoplasm worldwide (5,7).

CASE REPORT

70-year-old women presented with abdominal discomfort for a year. Patients denied a history of abdominal pain, altered bowel habits, or any constitutional symptom. She had no family history associated with malignancy. On clinical examination noted upper abdominal mass. Her CEA level was normal. She is subjected to radiological and endoscopic workup to identify the origin of the mass.

Contrasted computed tomography (CT) of the abdomen revealed a large, enhancing and fungating homogenous mass gastric mass with an the sigmoid colon. The sigmoid mass could represent a metastasis or synchronous tumor (Figure 1a, b). Esophagogastroduodenoscopy revealed extrinsic compression with normal overlying mucosa, suggesting a submucosal mass. Colonoscopy revealed a large polypoidal mass in the sigmoid colon (>2 cm) (Figure 2), from which an initial biopsy revealed tubulovillous adenoma with HGD.

The patient is scheduled for surgery. The operative findings revealed a large tumor (15x20 cm) originating from the stomach (Figures 3, 4). There were no ascites, peritoneal, or liver nodules. Wide local excision of the gastric tumor and table snare polypectomy of the sigmoid polyp were performed (Figure 5). The base of the polyp was taken for biopsy. The patient had an uneventful recovery and was discharged home well. Histopathological examination of the resected specimens revealed gastric GIST and adenocarcinoma of the sigmoid polyp. The base of the polyp has no dysplasia or malignancy seen. The patient was started on imatinib.

DISCUSSION

GIST is the most common mesenchymal neoplasia of the GI tract, but one-third of cases are detected incidentally during investigations or therapeutic procedures for unrelated diseases (8,9). The incidence of GIST is generally small in size (8,10). GIST predominantly involves the stomach (60%), small intestine (30%), colon (7%), and rectum (7%) and it originates from the interstitial pacemaker cells of Cajal (2). The percentage of GIST with other neoplasm reported between

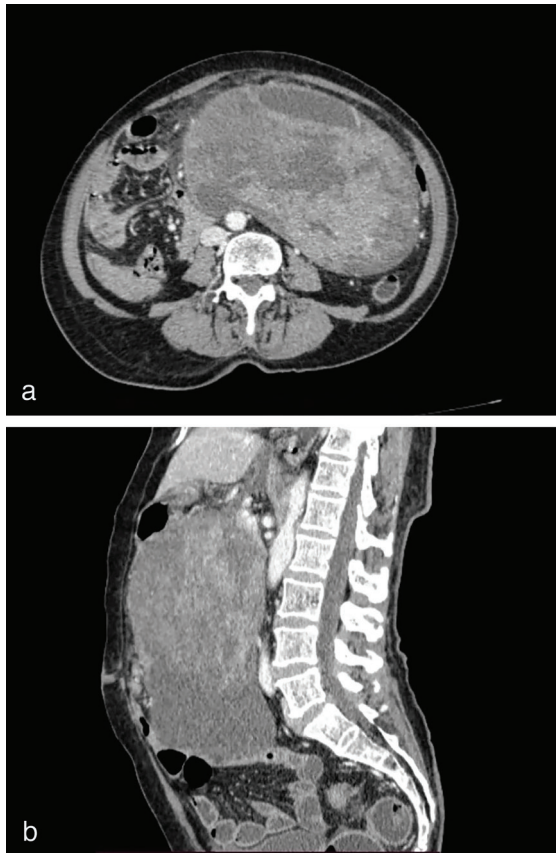

Figure 1. (a, b) CT features of a large heterogenously enhancing and hypervascularised intraperitoneal mass that appears to arise from the stomach (greater curvature) with a cystic component.

CT: Computed tomography.

3-33% (2). The most important markers of GIST are CD 117 (C-kit protein) and CD 34 (hematopoietic cell progenitor antigen). The vast majority of GIST cases are positive for CD 117 (95%), CD 34 (70-80%), smooth muscle actin (40%) PS 100 (5%) and desmin (2%) (9). CD117 immunoreceptors represent the gold standard for diagnosing GIST and the criteria required to initiate imatinib masylate therapy (9). Few syndromes have been reported in literature which associated GIST with other neoplasia such as the Von Recklinghausen's disease, the Carney triad (gastric GIST, lung chondoma and paraganglioma), and familial GIST (11). Outside this scope, it has not been confirmed whether the co-existence is incidental or a result of a related pathophysiological process. The most common secondary neoplasm in GIST cases is GI malignancy (2).

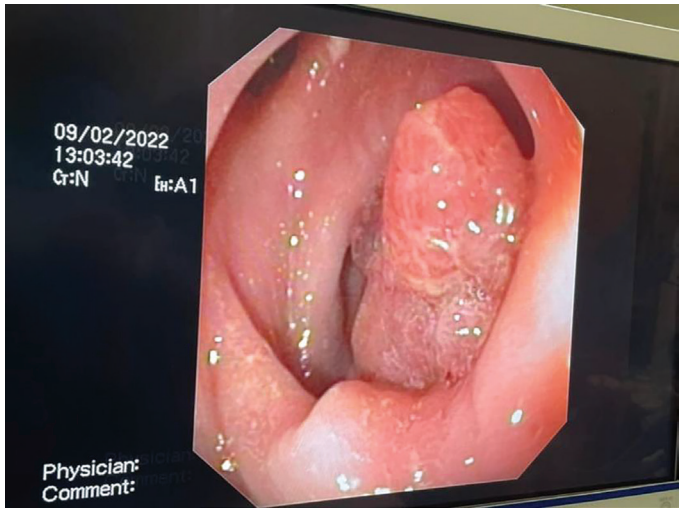

Figure 2. Endoscopic image of the sigmoid polyp.

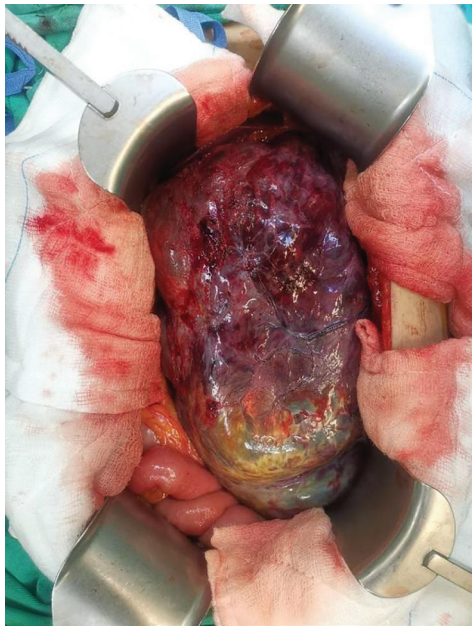

Figure 3. Intraoperative view of stomach GIST.
GIST: Gastrointestinal stromal tumors.

A study conducted by Kaur et al. (2) identified 101 patients with GIST and 14 (13.8%) of them had non-GIST-associated tumors. Nine of the 14 cases were female, median age 68 (10-79 years), and the stomach was the site of presentation of GIST for 8 cases (57.1%). Non-GIST tumor is more frequent in the stomach (adenocarcinoma) and colon/rectum (adenocarcinoma) each 4 cases. The other sites were breast (ductal carcinoma), kidney (clear cell carcinoma), prostate (adenocarcinoma), endometrium (adenocarcinoma), ovary (adenocarcinoma), and adrenal (neuroblastoma), with one case each. The tumors were synchronous in 7 cases. Agaimy et al. (11) analyzed 14 studies that mentioned the presence of GIST with other neoplasia and also their own records and found 444 patients with second tumors in a total of 4,777 patients with GIST (9.3%). The major type of other primary tumors are GI carcinomas (228-47%), with colorectal tumors being the most frequent site (109-22%), followed by stomach (95-19%). The other primaries reported by Agaimy et al. (11) were lymphoma/leukemia (7%), prostate carcinoma (9%), breast (7%), kidney (6%), lung (5%), female genital tract (5%) and carcinoid tumor (3%).

In a study by Liu et al. (12) in China, discovered 54 cases of incidental GIST occurred during surgery for 311 GI epithelial malignant tumors, accounting for 17.4%. Matli et al. (13) reported ileal GIST with ampulla adenocarcinoma. Ding et al. (8) reported a case of dual pathology in stomach: Synchronous poorly differentiated neuroendocrine carcinoma and GIST of the stomach.

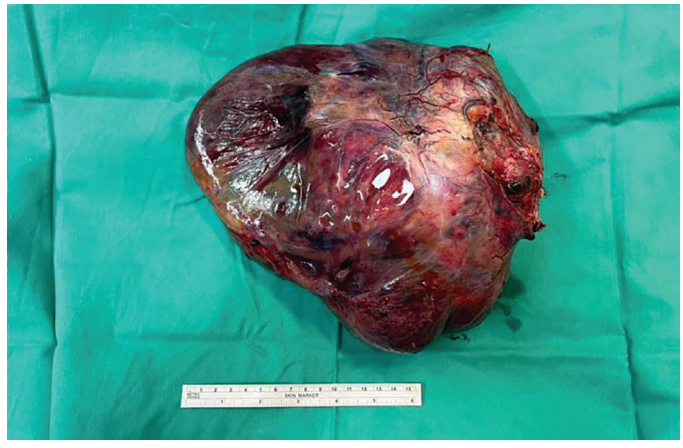

Figure 4. Wide local gastric tumor excision.

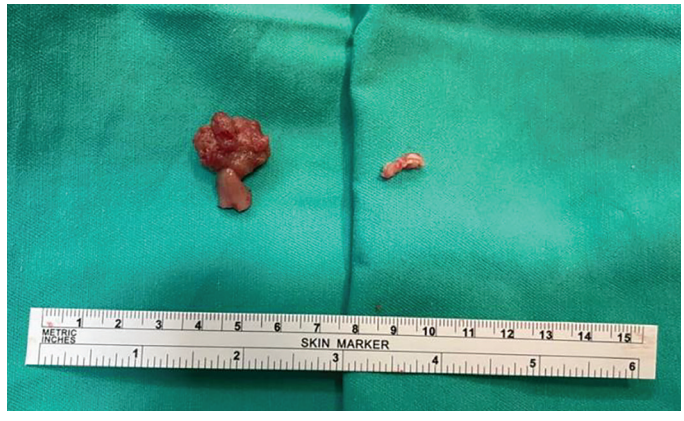

Figure 5. Snare polypectomy specimen.

Synchronous or metachronous occurrence of GIST with other neoplasia must always be considered during patient management. Here, we discuss a case of GIST, and colon malignant polyps are two distinct types of neoplasms that can occur synchronously. GIST tumors arise from the interstitial cells of Cajal and are characterized by mutations in *KIT/PDGFRA* genes. Conversely, malignant polyps are epithelial tumors that arise from the colonic mucosa classically because of alterations in the APC tumor suppressor gene, resulting in overactivation of the Wnt/β-catenin signaling pathway.

Some authors have postulated that they may share common carcinogenic pathways or genetic mutations with the proliferation of different cell lines (14). Further studies are required to analyze the molecular and genetic mechanisms of carcinogenesis.

An interesting matter in our write up here is the synchronous presentation of GIST in the stomach with a malignant colonic polyp. The coexistence of GIST with another histological tumor is uncommon (10,15). To our knowledge, there is no evidence to suggest a common factor in the tumorogenesis of these two pathologically distinct tumors.

CONCLUSION

The managing clinician and histopathologist should be aware of the occurrence of GIST combined with another neoplasm. Dual pathology may be misinterpreted as metastatic nodule or recurrence, which would change the management and patient outcomes. In cases of diagnostic dilemma, histopathological assessment is suggested. It may not always be possible to diagnose a coexisting tumor preoperatively. Surgeons should be aware of cases of GIST to recognize for coexisting pathology during intraoperative assessment and be prepared to modify the surgical plan accordingly. Due to its rarity and limited literature to date, further research on GIST with another synchronous tumor is required. A multidisciplinary approach to GIST management is suggested.

Ethics

Informed Consent: It was obtained.

Authorship Contributions

Concept: T.C., L.L.Y., J.J.M., R.K.S., Design: T.C., L.L.Y., J.J.M., R.K.S., N.A.S., Data Collection or Processing: T.C., L.L.Y., J.J.M., R.K.S., N.A.S., Analysis or Interpretation: T.C., L.L.Y., J.J.M., R.K.S., N.A.S., Literature Search: T.C., L.L.Y., J.J.M., R.K.S., N.A.S., Writing: T.C., L.L.Y., J.J.M., R.K.S., N.A.S.

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

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