

# Gastrointestinal Stromal Tumor of the Stomach in a Patient with Neurofibromatosis Type 1: Case Report

## Nörofibromatozis Tip 1'li Hastada Mide Gastrointestinal Stromal Tümörü

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**ABSTRACT** Neurofibromatosis Type 1 (NF-1) is a neurocutaneous disease characterized by abnormal skin pigmentations, neurofibromas, skeletal dysplasias and Lisch nodules. Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal tract. Although GISTs occur frequently sporadically, their frequency in NF-1 patients is increasing. A 79-year-old woman with NF-1 presented to emergency room with complaints of abdominal pain and bloody vomiting. Physical examination of the patient was unremarkable except epigastric tenderness. Upper gastrointestinal system endoscopy revealed a submucosal tumoral mass in the fundus of the stomach. Laparoscopic gastric wedge resection was performed. She was discharged on 5<sup>th</sup> day. A GIST arising from gastric fundus in size of 9x6x5 cm and two GISTs in sizes of 0.7 and 0.1 cm in approximately 1 cm neighborhood of the tumor were detected at histopathological examination. Patients with NF-1 have an increased risk of GIST. Laparoscopic surgery can be used for the treatment.

**Key Words:** Neurofibromatosis 1; gastrointestinal stromal tumors; laparoscopy; stomach

**ÖZET** Nörofibromatozis tip 1 (NF-1), anormal cilt pigmentasyonları, nörofibromlar, iskelet displazileri ve lish nodülleri ile karakterize nörokutanöz bir hastalıktır. Gastrointestinal stromal tümörler (GIST) gastrointestinal kanalın en yaygın mezenkimal tümörleridir. GIST'ler genellikle sporadik olarak gözükseler de NF-1'li hastalarda artmış sıklıkta ortaya çıkmaktadırlar. NF-1 tanılı 79 yaşında kadın hasta karın ağrısı ve kanlı kusma şikayeti ile acil servise başvurdu. Fizik muayenesi epigastrik hassasiyet dışında normaldi. Üst gastrointestinal endoskopide mide fundusta submukozaal tümöral kitle tespit edildi. Laparoskopik gastrik vedge rezeksiyon yapıldı. Hasta ameliyat sonrası 5. gün taburcu edildi. Histopatolojik incelemede, mide fundusta 9x6x5 cm büyüklüğünde GIST ve bunun 1 cm komşuluğunda 0,7 ve 0,1 cm büyüklüğünde 2 adet daha GIST tespit edildi. NF-1'li hastalarda GIST görülme riski artmıştır. Tedavide laparoskopik cerrahi kullanılabilircek yöntemdir.

**Anahtar Kelimeler:** Nörofibromatozis 1; gastrointestinal stromal tümörler; laparoskopi; mide

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**N**eurofibromatosis Type 1 (von Recklinghausen's disease) is an autosomal dominant neurocutaneous disease characterized by abnormal skin pigmentations (cafe-au-lait spots and axillary freckling), cutaneous and plexiform neurofibromas, skeletal dysplasias and Lisch nodules (pigmented iris hamartomas). Neurofibromatosis Type 1 results from a defect in neurofibromatosis 1 gene on chromosome 17, which is a tumor suppressor gene. Optic pathway gliomas and neurofibromas are the most commonly encountered neoplasms in the patients with neurofibromatosis.<sup>1</sup> Gastrointestinal stromal tumors are the mesenchymal tumors arising from

Cajal's cells of gastrointestinal system showing c-KIT expression.<sup>2</sup> Although GISTs occur frequently sporadically, their frequency in NF-1 patients is increasing. They arise in NF1 patients 150 times more frequently than in the general population. The incidence of GISTs among NF-1 patients is approximately 3.9-25%.<sup>3</sup> Even though neurofibromas are the most common mesenchymal tumors of gastrointestinal system in NF-1 patients, GISTs, leiomyomas and leiomyosarcomas may also be seen.<sup>4</sup>

Laparoscopic surgery is a minimally invasive method used for the treatment of many intra-abdominal diseases and leading less postoperative pain and surgical trauma. In this article, it was aimed to present a NF-1 case presenting with GIS bleeding due to GIST in the stomach and treated with laparoscopic gastric wedge resection.

## CASE REPORT

A 79-year-old woman with NF-1 having multiple neurofibromas and cafe-au-lait spots greater than 5 mm in diameter presented to emergency room with complaints of abdominal pain and bloody vomiting. Physical examination of the patient was unremarkable except epigastric tenderness. Digital rectal examination of the patient was normal. Laboratory examination revealed the followings: Leukocyte: 6,500/mm<sup>3</sup>, Hb: 10.5 g/dl, Hct: 30.7%, ALT: 19 IU/L AST: 21 IU/L BUN: 37 mg/dL Creatinine: 0.7 mg/dL. Following intravenous fluid resuscitation, upper gastrointestinal system endoscopy was performed. A submucosal tumoral mass was determined in the fundus of the stomach (Figure 1). A well-circumscribed submucosal mass approximately 10 cm in diameter was detected in the gastric fundus by Computed Tomography (Figure 2). An informed consent was received from the patient and laparoscopic gastric wedge resection was performed. The patient had an uneventful postoperative period and she was discharged on 5<sup>th</sup> day. A GIST arising from gastric fundus in size of 9x6x5 cm and two GISTs in sizes of 0.7 and 0.1 cm in approximately 1 cm neighborhood of the tumor were detected at histopathological examination (Figure 3). Surgical margins were intact. Grossly,



FIGURE 1: A submucosal lesion in the stomach shown on endoscopy.



FIGURE 2: Abdominal CT showed well defined round mass in the stomach.

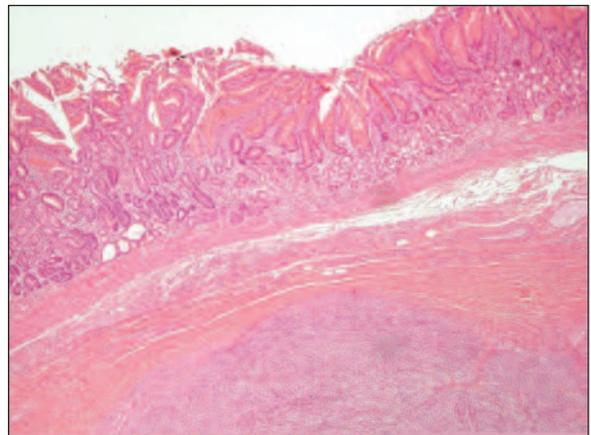


FIGURE 3: GISTs are located in muscularis propria and subserosal layer of the stomach. They are composed of rounded or lobulated lesions with a clearly defined margin (HE, x40).

lesions are located in the pars media of stomach and rounded or lobulated with a clearly defined margin. They primarily involve the muscularis propria

and subserosa and have a smooth, lobulated or whorled-silk appearance on cut section. Microscopically, they are composed of interlacing fascicles and whorls of uniform elongated cells, with cigar shaped vesicular nuclei and eosinophilic cytoplasm. These cells are immunopositive for CD117 (c-kit) and CD34; and are negative for Desmin and S100.

## DISCUSSION

Neurofibromatosis type-1 is a common autosomal dominant hereditary disease with a prevalence of one in 3,000 live births. The syndrome results from germ-line mutations in the NF1 gene located at chromosome 17q11.2, which encodes the tumor suppressor gene, neurofibromin. Although genetic mutations have been described and the responsible gene product-neurofibromin- has been fully characterized, no frequently recurring mutation has been identified, and diagnosis is still based on established clinical criteria. The “classical triad” of symptoms is “café au lait” spots, cutaneous neurofibroma, and neoplasms of nervous system.

Gastrointestinal stromal tumor (GIST) is the nonepithelial tumor that occurs most frequently in the gastrointestinal tract. Although GIST is seen most commonly in the stomach, it is frequently multiple in the patients with NF-1 and affecting the colon more commonly.<sup>5</sup> Stromal tumors may cause obstruction, ulceration, intussusception, bleeding or perforation in these patients.

Clinical symptoms change according to the size and location of the GIST. It has a low malignant potential (3-5%). Malignant potential of the tumor is frequently related to tumor size and its

mitotic index. The liver and the peritoneum are the most common sites of spread in malignant GISTs.<sup>6,7</sup>

Surgical excision is the treatment of choice. Purpose of the surgery is complete resection of the tumor with clear surgical margins. Wedge resection is recommended as the method of choice. Since the tumor does not infiltrate the stomach wall diffusely, surgical margin of 1-2 cm is considered to be sufficient. Lymph node metastasis is very rare and does not require routine lymphadenectomy.<sup>8</sup>

Laparoscopic surgery is a minimally invasive method which can be used in the diseases like cancer, obesity and functional disorders of the gastrointestinal system. Major advantages of the laparoscopic surgery are less post-operative pain, faster return to daily activities, earlier return of intestinal functions and better cosmetic outcomes. Laparoscopic wedge resection has been widely accepted as a treatment for benign gastric tumors. Method was performed for GIST in 1999 by Ohgami et al.<sup>9</sup> Since then, many centers around the world have stated that laparoscopic surgery to be safe and had equal oncological outcomes as open surgery. Due to be difficult to manipulate laparoscopically, the large tumors carry the risk of capsule disruption and peritoneal seeding and they are recommended to be operated with open method but there has been no consensus as to what the cut-off value should be.<sup>10</sup>

In conclusion, patients with NF-1 have an increased risk of GIST. When GIST is detected, it should be resected. Laparoscopic surgery can be used for the treatment. In addition to excision of the tumor with clear surgical margins, a careful dissection should be performed to avoid perforation and intraperitoneal seeding.

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