Case Report

A Huge Pelvic-Abdominal Malignant GIST Tumour in a Patient with Neurofibromatosis Type 1: Case Report and Literature Review

Islam Omar, Hani Alsaati, and Ejaz Waris

1Furness General Hospital, UHMBT, NHS, UK
2Oncology Center, King Hamad University Hospital, Bahrain

Correspondence should be addressed to Islam Omar; islamfawzyomar@hotmail.com

Received 29 May 2019; Revised 25 August 2019; Accepted 23 December 2019; Published 4 January 2020

Academic Editor: Mauro Cives

Copyright © 2020 Islam Omar et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Gastrointestinal stromal tumours are rare tumours of the GIT (see comment above) accounting for 0.1%–3% of all gastrointestinal tumours [1, 2]. The most common location is the stomach (55%) followed by the small bowel (31.8%), colon (6%), other various locations (5.5%), and the oesophagus (0.7%). They may also occur in extraintestinal locations. The signs and symptoms of GIST depend on the tumour's location and size. Gastrointestinal bleeding is one of the most common symptoms. Other signs and symptoms include abdominal discomfort, pain or distention; intestinal obstruction, and weight loss. The association between the development of GISTs and neurofibromatosis 1 (NF1) has been established. NF1-associated GISTs tend to have a distinct phenotype, and the absence of KIT/PDGRFA mutations in turn has implications on further management when they do not respond well to imatinib treatment. Here, we present one of the largest GISTs reported in the literature with a total volume of $25 \times 20 \times 14 \text{ cm} + 27 \times 23 \times 8 \text{ cm}$ and an overall weight of 7.3 kg, which developed in a 43-year-old female patient with NF1 and was resected on an emergency basis due to the rapid deterioration and development of abdominal compartment syndrome. Pathology assessment showed a malignant GIST composed of spindle cells with elongated nuclei with necrosis, marked pleomorphism and numerous giant cell. The mitotic count was $>15/50 \text{ HPF}$, Ki 67 was 80%, and the lymphovascular invasion was clear. Immunohistochemistry investigations showed that Vimentin, CD117, and DOG1 were positive, while BCL-2 and CD99 were focal positives. Pan-CK, S-100, CD34, Desmin, SMA, and HMB-45 were negatives.

1. Introduction

Gastrointestinal stromal tumours are rare tumours of the GIT (see comment above) accounting for 0.1%–3% of all gastrointestinal tumours [1, 2]. The most common location is gastric (55%) followed by the small bowel (31.8%), colon (6%), other various locations (5.5%), and the oesophagus (0.7%) [3]. They may also occur in the extraintestinal locations like the mesentery and omentum and in exceptionally rare sites like the gallbladder, urinary bladder, and prostate [4].

The tumour shows no strong sex predilection and usually occurs in adults [5], with a mean reported age of 50.6 years [6]. GIST is extremely uncommon in children and adolescents [7]. Some instances of GISTs show a pattern of familial incidence suggestive of genetic predisposition, whereas others are associated with neurofibromatosis and Carney’s triad [5].

GISTs are believed to arise from the interstitial cells of Cajal or related stem cells [8]. In most cases of GISTs, there is a mutation of C-KIT oncogene, which is responsible for the formation of a protein called KIT. Accordingly, KIT (CD117) positivity is observed in 95% of cases [2]. Platelet-derived growth factor receptor alpha (PDGFRA) mutations play a role in GIST pathogenesis [9].

Benign GISTs outnumber the malignant ones by a margin of 10:1. Clinical presentation depends on the site and size of the tumour and may include abdominal pain, gastrointestinal bleeding from ulceration of the overlying mucosa, or signs of obstruction. However, small tumours
may be asymptomatic. The major clinical findings are upper abdominal ulcer-like pain, dyspepsia, iron-deficiency anaemia, gastrointestinal bleeding, nausea, vomiting, palpable abdominal mass, and weight loss [10, 11]. Also, GISTs with an intra-abdominal abscess have been reported [12, 13].

Many studies confirmed the association between the development of GISTs and neurofibromatosis 1 (NF1) [14–17]. GISTs associated with NF1 seem however to have a distinct phenotype and the absence of KIT/PDGFRA mutations which has, in turn, an implication on further management where they do not respond well to Imatinib treatment [18–20].

Here, we present a case of a huge pelvic-abdominal GIST in a known patient of NF1 who showed rapid progression over a short time mounting to abdominal compartment syndrome. Consequently, she underwent emergency surgical excision.

2. Case Presentation

A 42-year-old female is a known case of familial NF1. She and her identical twin in addition to her only brother are all affected by NF1. She has no family history of malignancy, has not had previous surgery, and has no other comorbidities. Initially, she presented with fatigue, cough, and shortness of breath. She sought medical advice, and a low haemoglobin of 4 g/dl was discovered. She was resuscitated and received a blood transfusion. She had a history of constipation and change of stool calibre and melena. Clinical examination showed an abdominal mass which was confirmed by the US ultrasound later. An urgent OGD and a colonoscopy were done. OGD revealed normal upper GI study while the colonoscopy showed external compression on the sigmoid and descending colon and neither obstruction nor intraluminal lesion (Figure 1).

After stabilisation, the patient was then referred to our tertiary oncology centre for further evaluation. A CT scan (Figure 2) was done which revealed a huge cystic mass occupying almost the whole pelvic and abdominal cavity, which was lobulated with enhancing peripheral soft tissue components and septations. Moreover, a mild free-flowing peritoneal fluid was noted with diffuse subcutaneous tissue oedema. Of note, there were no signs of metastasis to the liver, lung, or the bones, and the scanned parts of the bowel loops showed no abnormalities.

Tumour markers were done and showed AFP (2.8 μg/L), CA 125 (154.7 U/ml), CA 15-3 (10.5 U/ml), CEA (0.3 μg/L), CA 19-9 (5.4 U/ml), and B-HCG (0.9 mIU/ml). For staging, a whole-body PET CT scan (Figure 3) was done and showed multiple amalgamated, well-defined, oval-to-round soft tissue masses extending from right subhepatic and lumbar regions just behind the anterolateral aspects of the anterior abdominal wall down to the pelvis, compressing the bowel loops. These masses exhibited heterogeneous fluid and soft tissue densities as well as peripheral patchy FDG activity.

They were associated with low-grade FDG, avid areas of peritoneal thickening, and fat stranding with pelvic ascites,
surgery, all the eff.

abdominal distention and the mass eff.

the resected mass exceeded 7.3 kg.

involvement of the sigmoid colon and small bowel. The weight of

occupying most of the pelvic and abdominal cavities with the

8 mm in diameter. Additionally, features of a di

avid small prehepatic node was detected which measured

suggesting peritoneal involvement. Also, a low-grade FDG

avid small prehepatic node was detected which measured

8 mm in diameter. Additionally, features of a diffusely acti-
vated bone marrow were noted, likely proliferative in
response to anaemia.

Given the previous scans, the origin of the mass was not
clear and was thought to be of ovarian origin. The patient
was being optimised and prepared for surgery. At that time,
melena was stopped, but the patient continued to complain
of shortness of breath, constipation, abdominal pain, and
distention.

In an attempt to fully optimize the patient for definitive
surgery, all the efforts were carried out to ameliorate the
abdominal distention and the mass effects through NGT, urin-
ary catheterization, and strict fluid balance management.
Unfortunately, the mass effect was out of control due to the
huge size of the tumour and the patient started to experience
tachycardia and tachypnea. Abdominal pressure measure-
ment showed a pressure approaching 26 mmHg, a value that
met a grade IV ACS [21].

At that stage, the decision was taken to do emergency
surgery to avoid the expected consequences of ACS [22].
Exploratory laparotomy was performed after bilateral ure-
teral stenting. A huge intra-abdominal mucinous mass was
found (Figure 4) coming from the pelvis with no clear origin.
There was involvement of the peritoneum, small bowel, sig-
moid colon, and upper rectum. Moreover, multiple areas of
the small bowel were involved, around 80 cm from the ileocaecal junction. Therefore, excision of the mass was
performed with bilateral salpingo-oophorectomy. Since the
sigmoid colon was found adherent to the tumour, resec-
tion of the sigmoid colon and colostomy creation were done.
Moreover, the involved segments of the small bowel were
resected and primarily anastomosed. The grossly involved
peritoneum was resected.

On gross pathological examination, the overall weight of
the specimen was 7.3 kg. The first specimen (Figure 5(a)) was
a huge mass with dimensions of 25.3 × 20 × 14 cm. The mass
was firm, greyish white with nodular surface, and partially
capsulated. There were multiple foci of haemorrhage, con-
gestion, and necrosis. The cut surface of the mass showed a
variegated appearance with focal greyish white areas. There
were also focal areas of mucinous cystic degeneration, haem-
orrhage, and necrosis. A small bowel segment 8.5 cm in
length by 3.2 cm in circumference was found adherent to
the mass. On opening the bowel segment, its mucosa was
unremarkable. However, the serosal surface adhered to the
mass. The second specimen (Figure 5(b)) came with dimen-
sions of 27.9 × 23 × 8 cm. The external surface of the mass
was nodular, partially capsulated, and showed foci of conges-
tion, haemorrhage, and necrosis. Along with that, an exuda-
tive membrane was found on the surface. The cut surface was
glistening, shiny, and having a variegated appearance with
focal areas of haemorrhage and necrosis in addition to
marked cystic degeneration.

Histopathology examination (Figure 6) of the two huge
masses showed features of a malignant neoplasm. It was
composed of spindle cells with elongated nuclei arranged
in fascicles. Moreover, there was marked pleomorphism
and numerous tumour giant cells. The mitotic count was
>15/50 HPF. Additionally, there were poorly differentiated
areas with 20% necrosis. The tumour was of the high-
grade type.

Risk assessment according to Fletcher et al.’s criteria [23]
showed that the tumour was of high risk. Margins of the
resected small and large bowel loops were free from tumour
invasion. However, evidence of lymphovascular invasion
was clear. Immunohistochemistry investigations (Figure 7)
showed that Vimentin, CD117, and DOG1 were positives,
BCL-2 and CD99 were focal positives, Pan-CK, S-100,
CD34, Desmin, SMA, and HMB-45 were negative, and
Ki-67 was 80%.

Two segments of the small bowel were resected weighing
675 g. The first segment measured 26 cm in length by 4.8 cm
in circumference. A polypoid, soft-to-firm, and tan-to-grey
in colour mass was found adherent to its serosal surface mea-
suring 8 × 5.2 × 1.3 cm. It was 10.1 cm away from the closest
margin, and 17.7 cm away from the distant margin. On open-
ing the small bowel segment, the entire length of mucosa was
gangrenous with an area of perforation identified, measuring
7.6 mm, it was 8.5 cm away from the closest margin.

The second segment of the small bowel measuring
27.9 cm in length and a 5.3 cm circumference, with a polyp-
oid grey soft-to-firm mass, was found adherent to the serosal
surface, measuring 36.5 × 6.7 × 3.4 cm. The mass was 9.5 cm
away from the closest margin and 9.6 cm away from the dis-
tant margin. Grossly, it did not appear to involve the mucosa.
On opening the lumen, the mucosal surface, at the level of

Figure 4: Intraoperative findings showing a huge lobulated mass,
occupying most of the pelvic and abdominal cavities with the
involvement of the sigmoid colon and small bowel. The weight of
the resected mass exceeded 7.3 kg.
mass attached to the serosa, was flattened and the remaining mucosa showed an area of stricture measuring 2.5 × 1 cm, 4.3 cm away from the closest margin with no perforation. Histopathology examination of the bowel loops showed thinning out of the wall with tumour infiltration into the mesenteric fat, reaching up to the muscular layer but the resection margins were negative.

One segment of the sigmoid colon was included and measured 27.9 cm in length by 8 cm in circumference. The specimen was received with an attached mesentery and weighed 299 g. A polypoid grey tan firm mass was found adherent to the mesenteric fat, measuring 10.5 × 3.6 × 2.1 cm, and it was 2.1 cm away from the closest margin. Upon opening the lumen, the mucosal surface along the entire segment was normal with no strictures, perforation, or diverticulosis. Histopathology examination of the sigmoid colonic wall showed tumour infiltration into the mesenteric fat reaching up to the muscular layer with four reactive lymph nodes. The resection margins were clear.

Another specimen was retrieved and included two pieces of the peritoneum. The first from the right side measured 13 × 5.3 × 2.2 cm along with a nodule measuring 2.8 × 2 × 1.5 cm and both weighed 47 g. The second piece came from the left peritoneal layer which measured 18 × 5.5 × 0.8 cm and weighed 25 g. The right peritoneum specimen was positive for tumour infiltration where sections revealed tumour infiltration of the fibrofatty tissue. The left peritoneal layer showed small ectopic adrenal tissue and was positive for tumour infiltration.

Specimens of the ovaries and fallopian tubes revealed a left ovary measuring 3.5 × 2.4 × 1.2 cm with the left fallopian tube measuring 5 × 1.2. The overall weight of the left ovary and fallopian tube was 12 g. The right ovary and the attached fallopian tube with surrounding fibrofatty tissue weighed 9 g. The right ovary measured 3.2 × 1.8 × 1.4 cm. The attached right fallopian tube measured 4.2 × 1.2 cm. The attached fibrofatty tissue showed marked areas of congestion. Histopathology examination of the left ovarian mass revealed a normal ovary and fallopian tube with tumour infiltration into the paratubal tissue. The right ovarian mass was free of invasion.

The conclusion of the pathology assessment came as high-risk GIST (pT4, pN0, pMx) with tumour invasion into the left paratubal tissue, small and large bowel, in addition
to the right and left peritoneal tissues. The patient had an uneventful postoperative course and was discharged home. Her case was discussed in the national tumour board—MDT, which recommended starting Imatinib therapy and genetic analysis. Unfortunately, genetic analysis was not available in any local centre. Every effort was made to send the tissue

**Figure 6:** Histopathology of the tumor. (a, b) The tumor composed of spindle cells with elongation. (c) Areas with necrosis. (d) High mitotic figures.

**Figure 7:** Immunohistochemistry staining. (a) Positive CD117. (b) Positive DOG1. (c) Desmin negative. (d) S100 negative.
blocks abroad for genetic analysis; however, logistical obstacles aborted these endeavours.

Although the patient received the first dose of Imatinib, her condition started to deteriorate over the next 2 months after surgery with persistent vomiting and gradual abdominal distention. However, her stoma was functioning and a barium follow-through study confirmed the patency of her bowel. Because of the multiple admissions due to persistent vomiting and abdominal distention, a CT scan was done which confirmed an aggressive recurrence. Because of the severe distention and again abdominal compartment syndrome, the patient was taken to the theatre where an aggressive inoperable tumour was encountered. Laparostomy was performed. The abdomen was left open and covered with a Bogota bag. A few days after the second surgery, the patient passed away.

3. Discussion

The signs and symptoms of GIST depend on the tumour’s location and size, with highly malignant GISTs typically being large and symptomatic at the time of diagnosis. Gastrointestinal bleeding is one of the most common symptoms. Other signs and symptoms include abdominal discomfort, pain or distention, intestinal obstruction, and weight loss [24].

In this case, there was a typical presentation with anaemia, melena, and gradual abdominal distention. Although there was no complete obstruction, the patient gave a history of change of stool calibre and constipation, manifestations that go with the external compression exerted by the huge tumour on the bowel.

GISTs arise in the muscularis propria layer of the stomach or intestinal wall. Small GISTs form intramural or serosal nodules and, as they grow and expand, may develop intraluminal, intramural, and extraluminal components to varying degrees. The extraluminal component of a malignant GIST may be so large that it is difficult to determine the site of origin [24, 25].

On the radiological basis, the tumour in our patient was first thought to have originated from the ovaries due to its pelvic-abdominal position and close proximity to the gonads. However, on histopathology assessment, it was proved to invade the left paratubal tissue planes only. Given its huge size and invasion of both the sigmoid colon and constipation, manifestations that go with the external compression exerted by the huge tumour on the bowel.

Given the weight and volume of our tumour (overall weight of 7.3 kg—25.3 × 20 × 14 cm for the first mass and 27.9 × 23 × 8 cm for the second mass), it is one of the largest GISTs reported in the literature. Koyuncuer et al. [26] reported a huge GIST originating from the stomach in a 43-year-old male, which was 6.109 kg in weight and measured 39 × 27 × 14 cm. Also, Cappellani et al. [27] reported a gastric GIST in a 67-year-old male, weighing 8.5 kg and measuring 37 × 24 × 13 cm. Moreover, Cruz et al. described a gastric GIST in a 37-year-old male, which was 32 × 25 × 21 in size and 3.75 kg in weight. Accordingly, to the best of our knowledge, our patient had the largest reported GIST in the literature with a volume of 25.3 × 20 × 14 + 27.9 × 23 × 8 cm and the second heaviest tumour weighing 7.3 kg.

GISTs are potentially aggressive forms of cancer that may develop anywhere in the GI tract [28]. They most frequently metastasize within the abdominal cavity, especially the liver and peritoneum. Bone and lung metastases are far less common [28, 29]. Very rare metastases to the skeletal muscles, adrenal gland, brain, testicles, and heart have also been reported [30–33]. Sizes larger than 10 cm cystic changes, high cellularity, mitotic figures >10/50 HPF, and coagulative necrosis are all more likely to be associated with metastasis [34].

In our patient, the histopathology assessment classified the tumour as a high-risk malignant tumour. Although distant spread to the liver or bones is excluded based on radiological staging, the tumour is proved to be locally aggressive spreading to the peritoneum, bowels, and paratubal tissues. This is expected given the huge nature of the tumour, a mitotic count of >15/50 HPF, and Ki-67 >80%.

Association between GIST and NF1 is established since an old autopsy study had documented a GIST in one-third of the NF1 patients [35]. NF1-associated GISTs are typically reported as multiple, generally low-grade tumours that affect the jejunum, ileum, duodenum, and stomach [15, 36]. Salvi PF et al. [19] in a systematic review of 252 patients with NF1-associated GISTs reported that patients affected by NF1-associated GISTs were younger and tumours were significantly smaller. Moreover, tumours were located mainly in the jejunum and ileum in the NF1 subgroup, whereas the main localization in the sporadic group was the stomach. They also reported a prevalence of low-risk criteria in the NF1 subgroup compared with the sporadic GISTs.

In our case, the patient was young (43 years old), with the tumour most probably originating from the small bowel—criteria that go with the previous literature. However, the tumour was huge and of the high-risk category, which were both striking features.

The genetic basis for the association between NF1 and GISTs is being elucidated. The genetic defect of NF1 disease is a mutation in the NF1 gene which encodes neurofibromin, a tumour suppressor protein that regulates the cellular proliferation via inactivation of RAS through GTPase activity. RAS is known to stimulate signal transduction through the MAP kinase pathway when activated. The resultant loss of the function of neurofibromin predisposes to the development of benign and malignant tumours [37–39]. NF1-related GI disease has been described to occur in three principal forms: neurogenic tumours, stromal tumours, and neuroendocrine tumours [40–42]. The most common of these GI manifestations in NF1 is GIST with one study indicating an incidence of 7% in the NF1 population and another reporting a 150-fold increased risk as compared to the general population [35, 38].

GISTs in adults are typically sporadically occurring and are associated with somatic mutations in the KIT or PDGFRA gene. However, 10%–15% of GISTs lack KIT or PDGFRA mutations. These GISTs can be associated with NF1 or can represent succinate dehydrogenase (SDH)-deficient tumors. The principal forms of GISTs are:

- Neurogenic tumours
- Stromal tumours
- Neuroendocrine tumours
GISTs that include GIST in the Carney triad and the Carney-Stratakis syndrome [43, 44]. GISTs associated with Carney Triad, Carney Stratakis syndrome, along with young and paediatric GISTs have been documented to have a loss of succinate dehydrogenase subunit B (SDHB) expression [20, 45, 46]. Based on the SDHB expression, it has been recently proposed that GISTs could be differentiated into two characteristic subgroups: type 1 SDHB-positive and type 2 SDHB-negative [45]. SDHB-positive GISTs usually occur in adults with no predilection of the tumour’s locations, show homogeneous male-to-female ratio, present KIT or PDGFRα mutations, and, generally, may benefit from the Imatinib treatment. SDHB-negative GISTs occur usually in paediatric and young female patients, locate almost exclusively in the stomach and present an epithelioid morphology. These tumours are usually c-kit and PDGFRα wild-type and do not respond to the molecular treatment with Imatinib [47, 48].

Even though NF1-associated GISTs have been documented to be type 1 SDHB-positive tumours [20], they could be differentiated by several features including the predilection of localization to the jejunum and small intestines, common tumour multiplicity, the lack of GIST-specific mutations (kit and PDGFRα wild type); and they are KIT-positive with hyperplasia of ICCs. Moreover, and alike the SDHB type 2 tumours, they do not respond well to Imatinib treatment [15, 20, 49–51].

Given the above, the therapeutic challenges for advanced NF1-associated GISTs are evident with expected resistance to Imatinib therapy. However, Sunitinib is the second-line tyrosine kinase inhibitor and has shown activity with clinical benefit in 56% of wild-type patients and can be used for the patients who develop resistance to Imatinib as well [52].

4. Conclusion

NF1-related GISTs represent a unique entity of GISTs relevant to their different molecular basis and presentation. When advanced and unresectable, they pose a great challenge due to resistance to Imatinib therapy. Here, we present one of the largest GISTs reported in the currently available literature with an overall weight of 7.3 kg and volume of 25.3 × 20 × 14 + 27.9 × 23 × 8 cm, which was resected on an emergency basis due to the rapid deterioration and development of abdominal compartment syndrome.

Ethical Approval

This study is approved by the ethical committee.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

[1] S. Phongkitkarun, C. Phaisanphrukkun, J. Jatchavala, and E. Sirachainan, “Assessment of gastrointestinal stromal tumors with computed tomography following treatment with imatinib mesylate,” World Journal of Gastroenterology, vol. 14, no. 6, pp. 892–898, 2008.
[2] I. K. Skandalos, N. F. Hotzoglou, K. C. Matsi, X. A. Pitta, and A. I. Kamas, “Giant extra gastrointestinal stromal tumor of lesser omentum obscuring the diagnosis of a cholecystocele,” International Journal of Surgery Case Reports, vol. 4, no. 10, pp. 818–821, 2013.
[3] K. Søreide, O. M. Sandvik, J. A. Søreide, V. Giljacac, A. Jurecková, and V. R. Bulusue, “Global epidemiology of gastrointestinal stromal tumours (GIST): a systematic review of population-based cohort studies,” Cancer Epidemiology, vol. 40, pp. 39–46, 2016.
[4] A. Mekni, I. Chelly, H. Azzouz et al., “Extragastrointestinal stromal tumor of the urinary wall bladder: case report and review of the literature,” Pathologica, vol. 100, no. 3, pp. 173–175, 2008.
[5] J. R. Goldblum, “Gastrointestinal stromal tumours: Chapter 26 - Mesenchymal Tumors of the GI Tract,” in Surgical Pathology of the GI Tract, Liver Biliary Tract, and Pancreas, R. D. Odze and J. R. Goldblum, Eds., pp. 681–694, Saunders, Philadelphia, PA, USA, 2nd edition, 2009.
[6] M. Vij, V. Agrawal, A. Kumar, and R. Pandey, “Cytomorphology of gastrointestinal stromal tumors and extra-gastrointestinal stromal tumors: a comprehensive morphologic study,” Journal of Cytology, vol. 30, no. 1, pp. 8–12, 2013.
[7] M. Benesch, “Gastrointestinal stromal tumors,” in Rare Tumors in Children and Adolescents, Pediatric Oncology, D. Schneider, I. B. Brecht, and T. A. Olson, Eds., pp. 279–280, Springer, Berlin, Berlin, 2012.
[8] I. Judson, R. Bulusu, B. Seddon, A. Dangoor, N. Wong, and S. Mudan, “UK clinical practice guidelines for the management of gastrointestinal stromal tumours (GIST),” Clinical Sarcoma Research, vol. 7, no. 1, article 6, 2017.
[9] J. Lasota and M. Miettinen, “KIT and PDGFRA mutations in gastrointestinal stromal tumours (GISTs),” Seminars in Diagnostic Pathology, vol. 23, no. 2, pp. 91–102, 2006.
[10] B. P. Rubin, GIST, EGIST, Enzinger and Weiss’s Soft Tissue Tumors, Saunders, Philadelphia, PA, USA, 6th edition, 2013.
[11] A. Ahmad, F. Mahmood, C. Shen, S. Cabezon, and V. Rao, “Malignant gastrointestinal stromal tumour – a case report,” Journal of Case Reports: Clinical & Medical, vol. 12, 2013.
[12] Y. Maeda, T. Shinohara, T. Katayama, A. Nagatsu, N. Futakawa, and T. Hamada, “Gastrointestinal stromal tumour of the stomach with an abscess excised by laparoscopic surgery,” Case Reports in Gastroenterology, vol. 10, no. 2, pp. 399–405, 2016.
[13] S. Yardimci, T. K. Uprak, F. E. Kombak, H. Kaya, and S. C. Yegen, “Ruptured gastric stromal tumour into gastric lumen with an abscess,” ANZ Journal of Surgery, vol. 84, no. 9, pp. 687–689, 2014.
[14] N. De la Fuente, M. Rodríguez Blanco, G. Cerdán, and V. Artigas, “Hemorragia digestiva aguda en paciente con neurofibromatosis tipo 1 afecto de múltiples GIST y ganglioneuromatosis intestinal,” Cirugía Española (English Edition), vol. 97, no. 4, pp. 237–239, 2019.
[44] C. A. Stratakis and J. A. Carney, “The triad of paragangliomas, gastric stromal tumours and pulmonary chondromas (Carney triad), and the dyad of paragangliomas and gastric stromal sarcomas (Carney Stratakis syndrome): molecular genetics and clinical implications,” Journal of Internal Medicine, vol. 266, no. 1, pp. 43–52, 2009.

[45] A. J. Gill, A. Chou, R. Vilain et al., “Immunohistochemistry for SDHB divides gastrointestinal stromal tumors (GISTs) into 2 distinct types,” American Journal of Surgical Pathology, vol. 34, no. 5, pp. 636–644, 2010.

[46] J. Gaal, C. A. Stratakis, J. A. Carney et al., “SDHB immunohistochemistry: a useful tool in the diagnosis of Carney-Stratakis and Carney triad gastrointestinal stromal tumors,” Modern Pathology, vol. 24, no. 1, pp. 147–151, 2011.

[47] B. Pasini, S. R. McWhinney, T. Bei et al., “Clinical and molecular genetics of patients with the Carney-Stratakis syndrome and germline mutations of the genes coding for the succinate dehydrogenase subunits SDHB, SDHC, and SDHD,” European Journal of Human Genetics, vol. 16, no. 1, pp. 79–88, 2008.

[48] P. J. Oppelt, A. C. Hirbe, and B. A. Van Tine, “Gastrointestinal stromal tumors (GISTs): point mutations matter in management, a review,” Journal of Gastrointestinal Oncology, vol. 8, no. 3, pp. 466–473, 2017.

[49] C. Mussi, H. U. Schildhaus, A. Gronchi, E. Wardelmann, and P. Hohenberger, “Therapeutic consequences from molecular biology for gastrointestinal stromal tumor patients affected by neurofibromatosis type 1,” Clinical Cancer Research, vol. 14, no. 14, pp. 4550–4555, 2008.

[50] J.-L. Lee, J. Y. Kim, M.-H. Ryu et al., “Response to imatinib in KIT- and PDGFRA-wild type gastrointestinal stromal associated with neurofibromatosis type 1,” Digestive Diseases and Sciences, vol. 51, no. 6, pp. 1043–1046, 2006.

[51] W. J. Jessen, S. J. Miller, E. Jousma et al., “MEK inhibition exhibits efficacy in human and mouse neurofibromatosis tumors,” The Journal of Clinical Investigation, vol. 123, no. 1, pp. 340–347, 2013.

[52] M. C. Heinrich, R. G. Maki, C. L. Corless et al., “Primary and secondary kinase genotypes correlate with the biological and clinical activity of sunitinib in imatinib resistant gastrointestinal stromal tumor,” Journal of Clinical Oncology, vol. 26, no. 33, pp. 3352–3359, 2008.