СРПСКИ АРХИВ
ЗА ЦЕЛОКУПНО ЛЕКАРСТВО
SERBIAN ARCHIVES
OF MEDICINE

Address: 1 Kraljice Natalije Street, Belgrade 11000, Serbia
☏ +381 11 4092 776, Fax: +381 11 3348 653
E-mail: office@srpskiarhiv.rs, Web address: www.srpskiarhiv.rs

Paper Accepted* **ISSN Online 2406-0895**

Case Report / Приказ болесника

Dušan Brkić[1,♣], Zlatibor Lončar[1,2], Dušan Micić[1,2], Zlatko Perišić[1,2], Pavle Gregorić[1,2]

Gastrointestinal stromal tumor of the ileum – case report of life-threatening bleeding

Гастроинтестинални стромални тумор илеума – приказ случаја животно угрожавајућег крварења

[1]University Clinical Center of Serbia, Emergency Surgical Clinic, Belgrade, Serbia;
[2]University of Belgrade, Faculty of Medicine, Belgrade, Serbia

Received: June 6, 2024
Revised: November 27, 2024
Accepted: December 11, 2024
Online First: December 13, 2024
DOI: https://doi.org/10.2298/SARH240606093B

♣**Correspondence to:**
Dušan BRKIĆ
Palmira Toljatija 14, 11080 Belgrade, Serbia
E-mail: brkic.dusan.23@gmail.com

Gastrointestinal stromal tumor of the ileum – case report of life-threatening bleeding

Гастроинтестинални стромални тумор илеума – приказ случаја животно угрожавајућег крварења

SUMMARY

Introduction Gastrointestinal stromal tumor (GIST) is relatively rare neoplasm and according to data in the literature, makes up less than 1% of all tumors of the gastrointestinal tract with the most frequent incidence in the sixth decade of life. The development and discovery of new molecular, biochemical and immunohistochemical methods contributed significantly to the successful identification and better understanding of this type of neoplasm. The most common localization of GIST is stomach, causing merely discomfort and occasional pain in the abdomen as the only complaint.

Case Outline Our patient, a 71-year-old male, came for an outpatient surgical examination due to gastrointestinal bleeding and low hemoglobin values in laboratory findings. We conducted the endoscopic examination of the upper parts of the digestive tract; there were neither active nor old signs of gastrointestinal bleeding. The patient underwent an ultrasound examination and then a computed tomography (CT) of the abdomen. CT scan showed tumor mass in the lower parts of abdominal cavity, highly suspicious for GIST of small intestine (ileum). The patient underwent emergency surgery, with the resection of bleeding tumor and creation of primary anastomosis. The patient recovered well from the surgery and was discharged home in good general condition.

Conclusion The goal of surgery is to achieve an optimal resection line - R0 with an intact pseudocapsule of the tumor. Postoperative adjuvant therapy with Imatinib is indicated in certain cases, in order to ensure the most favorable clinical and oncological outcome.

Keywords: emergency surgery; GIST; ileum; bleeding; Imatinib

САЖЕТАК

Увод Гастроинтестинални стромални тумори (ГИСТ) су релативно ретки и према подацима из литературе чине мање од 1% свих тумора гастроинтестиналног тракта, са најчешћом инциденцијом у шестој деценији живота. Развој и откривање нових молекуларних, биохемијских и имунохистохемијских метода значајно су допринели успешној идентификацији и бољем разумевању ове врсте неоплазми. Најчешћа локализација ГИСТ-а је желудац, док су нелагодност и повремени болови у трбуху, често једине тегобе које болесници наводе.

Приказ случаја Наш пацијент, мушкарац стар 71 годину, дошао је на преглед због сумње на гастроинтестинално крварење са ниским вредностима хемоглобина у лабораторијским анализама. Урадили смо ендоскопски преглед горњих партија дигестивног тракта; није било знакова активног нити старог гастроинтестиналног крварења. Пацијенту су индиковани ултразвучни преглед и потом компјутеризована томографија (ЦТ) абдомена. ЦТ преглед је показао туморску масу у доњим партијама трбушне дупље, са високом сумњом на ГИСТ танког црева (илеума). Пацијент је ургентно оперисан, када је урађена ресекција крварећег тумора са примарном анастомозом. Пацијент се оптимално опоравио од операције и отпуштен је кући у добром општем стању.

Закључак Циљ хирургије је постизање оптималне ресекционе линије – *R*0 са интактном псеудокапсулом тумора. У одређеним случајевима потребна је постоперативна адјувантна терапија Иматинибом, како би се обезбедио што повољнији клинички и онколошки исход.

Кључне речи: ургентна хирургија; ГИСТ; илеум; крварење; Иматиниб

INTRODUCTION

Gastrointestinal stromal tumor (GIST) is relatively rare neoplasm. According to the data in the literature, it makes up less than 1% of all tumors of the gastrointestinal tract, with the most frequent incidence in the sixth decade of life [1, 2]. The development and discovery of new

molecular, biochemical and immunohistochemical methods contributed significantly to the successful identification and better understanding of this type of neoplasms [2, 3]. The paradigm shift related to this type of tumor has occurred in the last two decades, meaning that gastrointestinal stromal tumors are now considered as mesenchymal tumors with predictable behavior and outcome in treatment. The change of name occurred as well, replacing old one such as leiomyoma, schwannoma, and leiomyosarcoma in pathological nomenclature [4]. The name was first coined in 1983 for a special set of mesenchymal tumors of the gastrointestinal tract that do not have ultrastructural and immunohistochemical characteristics of smooth muscle differentiation. In 1998, it was proven that the true precursor of these tumors is a pluripotent mesenchymal stem cell predefined to differentiate into an interstitial Cajal "pacemaker" cell, responsible for initiating and coordinating the motility of the digestive tract. The turning point in the identification of GIST as a unique clinical entity is certainly represented by the discovery of the role of c-kit proto-oncogene mutation in these tumors. Following that discovery, targeted molecular adjuvant and neoadjuvant therapy with thyroxine kinase inhibitors such as Imatinib was established in standard treatment protocols and daily clinical practice [5]. Gastrointestinal stromal tumors may occur along the entire digestive tube, from the esophagus to the rectum, but generally remain undiagnosed, causing discomfort and occasional abdominal pain as the only complaint reported by the patients [6, 7]. The stomach represents the most common localization of GIST described in the literature. The other parts of digestive tube are recorded less, often as sporadic cases and therefore represent a curiosity in clinical practice [7, 8]. According to the previous data in the literature, the crucial moment occurs when the tumor exceeds 4 cm in diameter which could be manifested as an urgent condition in abdominal surgery. That implies abundant gastrointestinal bleeding (due to necrosis of the wall of the hollow organ), intestinal obstruction or perforation (usually in the small intestine as the primary site of tumor localization) [4, 5]. Due to its localization,

especially in the case of small intestine, as well as the possibility of extraluminal growth, this type of neoplasm may be difficult to detect with routine endoscopic examination of the digestive tract [9]. This could be the main reason why it is one of the most difficult causes of gastrointestinal bleeding to detect in emergency setting. Therefore, computed tomography (CT) scan of the abdomen and angiography are sometimes needed in order to verify the tumor and exact site of bleeding [7].

In our case report, we will refer to a gastrointestinal stromal tumor of the small intestine - ileum, which manifested as severe and life-threatening gastrointestinal bleeding.

CASE REPORT

Our patient, a 71-year-old male, came for an outpatient surgical examination, for the first time due to black colored stools and a hemoglobin value of 120 g/L (ref. value 138-175 g/L) in laboratory findings. The patient was examined by the surgeon and referred to a gastroenterologist. There were neither active nor old signs of gastrointestinal bleeding detected on endoscopy of the upper digestive tract. The patient reported that he sporadically took iron supplementation, but did not consume food that would cause pseudomelaena. There was no previous excessive intake of non-steroidal anti-inflammatory drugs, anticoagulant nor antiplatelet therapy. After the examination, he was discharged home with the prescription of proton pump blockers and advice to undergo an elective colonoscopy.

The patient came back later to the Clinic for Emergency Surgery for another outpatient examination due to the persistence of black stools, now with admixtures of fresh blood and with hemoglobin values of 98 g/L in laboratory analyses. We decided to repeat the ultrasound

examination of the abdomen. Radiology reported the exophytic mass of the distal ileum with a diameter of 46b × 32 mm, highly suspicious for a gastrointestinal stromal tumor.

The patient was admitted to the hospital and CT scan of the abdomen was performed. Radiology reported an exophytic, hyperdense tumor mass in the distal ileum, measuring about 43 × 49 × 52 mm in diameter, which could correspond to GIST (Figure 1). The mass was described as being in close relation to the caecum and the right external iliac artery, without radiological signs of infiltration. A smaller amount of free fluid (up to 25 mm thick) was also verified in the rectovesical pouch (Figure 2).

The patient underwent emergency surgery, due to the bleeding exophytic tumor mass of the distal ileum (with hemoglobin value of 63 g/L on admission) (Figure 3). We performed medial laparotomy with the exploration of abdominal cavity. In the further course of the operation, we made resection of small bowel with the tumor in the length of 10cm. The procedure was followed by creation of hand-sewn end-to-end ileo-ileal anastomosis, in conventional two layers. The part of resected ileum with the tumor was sent to further histopathological analysis (Figure 4).

The patient recovered well from the surgery and was discharged home in good general condition, five days after the surgery. The histopathological findings showed mesenchymal tumor of the ileum. Additional immunohistochemical analysis revealed that it was a "low risk" GIST of the ileum, with moderate metastatic potential and a 24% risk of progression. According to the TNM classification, the tumor was classified as pTNM 8: G-1; T3 Nx Mx.

Further clinical follow-up of the patient was conducted. The patient was referred to the Oncology Council, whose decision was to continue with regular checkups. The reason for that kind of decision was the absence of rest/recurrence of the disease or signs of secondary

dissemination on postoperative CT scan. Laboratory findings (including conventional tumor markers for the of digestive tract) were also within the reference values.

We obtained verbal and signed consent of the patients to publish the case report. All procedures performed were in accordance with the 1964 Helsinki declaration and its later amendments.

DISCUSSION

In the case of GIST which clinically presents as acute and massive gastrointestinal bleeding, emergency surgery represents the most adequate form of treatment. The goal of surgery is to achieve the R0 line of resection with an intact pseudocapsule of the tumor. This scenario, if implemented on time, ensures the best oncological outcome for the patient. [8]. According to available data from the literature, these tumors do not show a potential to give metastases to regional lymph nodes and therefore do not make lymphadenectomy necessary [7].

Data available from the literature show that tumors of the small intestine make up only 5% of all tumors of the gastrointestinal tract [10]. The small intestine and ileum in this particular case, stands for the rarest location of GIST [11]. Gastrointestinal stromal tumors occur in a slightly higher percentage in males, usually in their sixth decade of life. Those patients could be referred to emergency department due to hematochezia with melena, accompanied by extremely low hemoglobin values in laboratory analyses. Therefore, the above mentioned classifies GIST of the small intestine as extremely rare cause of gastrointestinal bleeding [12].

Discussion goes in the direction of whether the greater benefit for the patient is creation of primary anastomosis or performing a stoma. If the surgeon decides for primary anastomosis, there is always a risk of dehiscence in the presence of peritonitis and the poor vitality of intestine. On the other hand, there are metabolic disorders if it is a high or proximal

jejunostomy/ileostomy [13, 14]. In our case, in absence of peritonitis and due to potential losses from the ileostomy in initially hemodynamically unstable patient, we decided for creation of primary anastomosis. Anastomotic leak after the surgery still remains the major concern among surgeons despite surgical progress and technological advances. The awareness of risk factors should influence treatment and procedure-related decisions [15, 16].

Further discussion is being conducted in the terms of intraoperative abdominal lavage, i.e., whether, what type and amount of solution should be used [14]. Lavage with physiological solution can have a physical/mechanical effect in terms of dilution of tumor cells and bacteria. Utilization of antibacterial and antiseptic agents may act in terms of lysis of the bacterial or cell wall [17, 18]. In the literature, there is still not enough evidence regarding the optimal margin of resection of a tumor mass towards macroscopically healthy tissue. In any case, a negative line resection is necessary to prevent local recurrence [19, 20].

When it comes to a gastrointestinal tumor that exceeds 10 mm in diameter, the previously mentioned Imatinib is recommended as adjuvant postoperative therapy. Furthermore, it is mandatory in pathologically classified "high risk" cases. Previous studies have shown that Imatinib provides an absolute reduction in the recurrence rate of 14%, achieving a 97% recurrence-free survival [20, 21].

Republic Fund for Health Insurance of our country has registered Imatinib as an adjuvant therapy for pathohistologically confirmed gastrointestinal stromal tumor. Taking into account we achieved R0 resection line, with the GIST being marked as "low risk", in the absence of rest/recurrence and secondary dissemination of the disease on follow-up examinations, the decision of Oncology Council was to continue with clinical, laboratory and radiological follow-up of the patient every six months, up to two years after surgery, then every year regularly.

Conflict of interest: None declared.

REFERENCES

1. Hirota S, Tateishi U, Nakamoto Y, Yamamoto H, Sakurai S, Kikuchi H et al. Members of the Systematic Review Team of the Present Guidelines. English version of Japanese Clinical Practice Guidelines 2022 for gastrointestinal stromal tumor (GIST) issued by the Japan Society of Clinical Oncology. Int J Clin Oncol. 2024;29(6):647–80. [DOI: 10.1007/s10147-024-02488-1] [PMID: 38609732]
2. Gupta A, Ma S, Che K, Pobbati AV, Rubin BP. Inhibition of PI3K and MAPK pathways along with KIT inhibitors as a strategy to overcome drug resistance in gastrointestinal stromal tumors. PLoS One. 2021;16(7):e0252689. [DOI: 10.1371/journal.pone.0252689] [PMID: 34324512]
3. Huang WK, Gao J, Chen Z, Shi H, Yuan J, Cui HL et al. Heterogeneity of Metabolic Vulnerability in Imatinib -Resistant Gastrointestinal Stromal Tumor. Cells. 2020;9(6):1333. [DOI: 10.3390/cells9061333] [PMID: 32466502]
4. Khuri S, Gilshtein H, Darawshy AA, Bahouth H, Kluger Y. Primary Small Bowel GIST Presenting as a Life-Threatening Emergency: A Report of Two Cases. Case Rep Surg. 2017;2017:1814254. [DOI: 10.1155/2017/1814254] [PMID: 31193951]
5. Nagaraj SS, Deivasigamani S, Aruni A, Kumar H, Sachan A, Samanta J et al. Diagnostic and Therapeutic Challenges in the Management of Acute Massive Overt Bleeding of Jejunal Gastrointestinal Stromal Tumours: Case Series. J Gastrointest Cancer. 2023;54(1):316–22. [DOI: 10.1007/s12029-021-00650-w] [PMID: 35199299]
6. Serrano C, Martín-Broto J, Asencio-Pascual JM, López-Guerrero JA, Rubió-Casadevall J, Bagué S et al. 2023 GEIS Guidelines for gastrointestinal stromal tumors. Ther Adv Med Oncol. 2023;15:17588359231192388. [DOI: 10.1177/17588359231192388] [PMID: 37655207]
7. Jabłońska B, Szmigiel P, Wosiewicz P, Baron J, Szczęsny-Karczewska W, Mrowiec S. A jejunal gastrointestinal stromal tumor with massive gastrointestinal hemorrhage treated by emergency surgery: A case report. Medicine (Baltimore). 2022;101(35):e30098. [DOI: 10.1097/MD.0000000000030098] [PMID: 36107510]
8. Saad MK, El Hajj I, Saikaly E. Jejunal gastrointestinal stromal tumor (GIST): a case report presenting as life threatening emergency. Gastrointestinal Stromal Tumor 2020;3:3. [DOI: 10.21037/gist-20-3]
9. Liu H, Santanello A, Jimenez M, Kumthekar N. Jejunal Gastrointestinal Stromal Tumor (GIST) as a Rare Cause of GI Bleed: A Case Report. Cureus. 2022;14(4):e24272. [DOI: 10.7759/cureus.24272] [PMID: 35607565]
10. Martins D, Costa P, Guidi G, Pinheiro P, Pinto-de-Sousa JA. Jejunal Gastrointestinal Stromal Tumor: A Strange Cause of Massive Gastrointestinal Bleeding. Cureus. 2023;15(8):e43229. [DOI: 10.7759/cureus.43229] [PMID: 37692736]
11. Waidhauser J, Bornemann A, Trepel M, Märkl B. Frequency, localization, and types of gastrointestinal stromal tumor-associated neoplasia. World J Gastroenterol. 2019;25(30):4261–77. [DOI: 10.3748/wjg.v25.i30.4261] [PMID: 31435178]
12. Kim MS, Woo IT, Jo YM, Lee JH, Park BS. Life-threatening bleeding with intussusception due to gastrointestinal stromal tumor: a case report. Surg Case Rep. 2019;5(1):154. [DOI: 10.1186/s40792-019-0703-9]
13. Alessiani M, Gianola M, Rossi S, Perfetti V, Serra P, Zelaschi D et al. Peritonitis secondary to spontaneous perforation of a primary gastrointestinal stromal tumour of the small intestine: A case report and a literature review. Int J Surg Case Rep. 2015;6C:58–62. [DOI: 10.1016/j.ijscr.2014.12.012] [PMID: 25524303]
14. Jayant D, Goyal M, Thakur V, Sahu S, Babu B, Subbiah Nagaraj S, Tandup C, Behera A. Advanced and Metastatic Gastrointestinal Stromal Tumors Presenting With Surgical Emergencies Managed With Surgical Resection: A Case Series. Cureus. 2024;16(2):e53851. [DOI: 10.7759/cureus.53851] [PMID: 38465042]
15. Zarnescu EC, Zarnescu NO, Costea R. Updates of Risk Factors for Anastomotic Leakage after Colorectal Surgery. Diagnostics (Basel). 2021;11(12):2382. [DOI: 10.3390/diagnostics11122382] [PMID: 34943616]
16. Ma H, Li X, Yang H, Qiu Y, Xiao W. The Pathology and Physiology of Ileostomy. Front Nutr. 2022;9:842198. [DOI: 10.3389/fnut.2022.842198] [PMID: 35529469]
17. Agha RA, Borrelli MR, Farwana R, Koshy K, Fowler AJ, Orgill DP. SCARE Group. The SCARE 2018 statement: Updating consensus Surgical CAse REport (SCARE) guidelines. Int J Surg. 2018;60:132–6. [DOI: 10.1016/j.ijsu.2018.10.028] [PMID: 30342279]
18. Sato K, Tazawa H, Fujisaki S, Fukuhara S, Imaoka K, Hirata Y et al. Acute diffuse peritonitis due to spontaneous rupture of a primary gastrointestinal stromal tumor of the jejunum: A case report. Int J Surg Case Rep. 2017;39:288–92. [DOI: 10.1016/j.ijscr.2017.08.041]
19. Azimi B, Shahrbaf MA, Iranshahi M, Parsaeian F. A case of jejunal GIST revealed by hematemesis: Unusual situation. Int J Surg Case Rep. 2022;94:107146. [DOI: 10.1016/j.ijscr.2022.107146] [PMID: 35658308]
20. Al-Swaiti GT, Al-Qudah MH, Al-Doud MA, Al-Bdour AR, Al-Nizami W. Spontaneous perforation of jejunal gastrointestinal stromal tumor: A case report. Int J Surg Case Rep. 2020;73:31–4. [DOI: 10.1016/j.ijscr.2020.06.088] [PMID: 32629218]

21. Nishida T, Blay JY, Hirota S, Kitagawa Y, Kang YK. The standard diagnosis, treatment, and follow-up of gastrointestinal stromal tumors based on guidelines. Gastric Cancer. 2016;19(1):3–14. [DOI: 10.1007/s10120-015-0526-8] [PMID: 26276366]

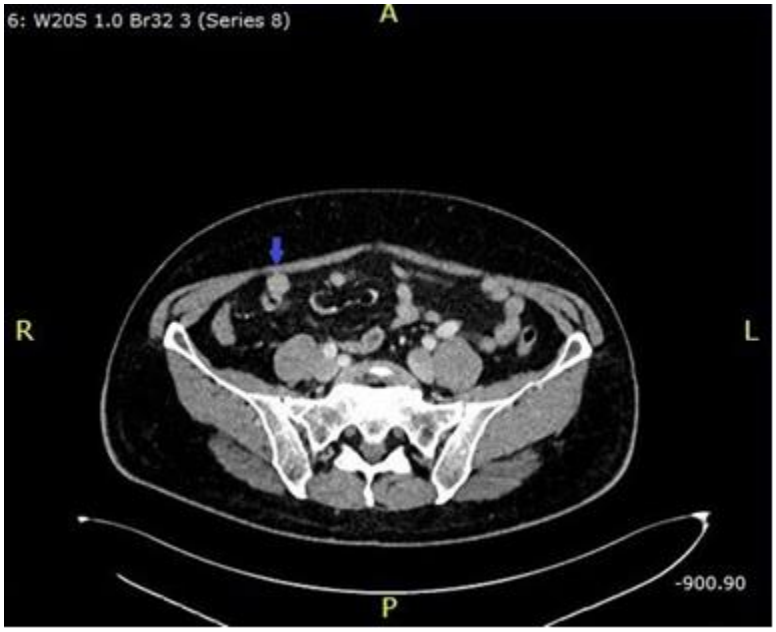

Figure 1. The blue arrow indicates hyperdense neoplasm close to the abdominal wall

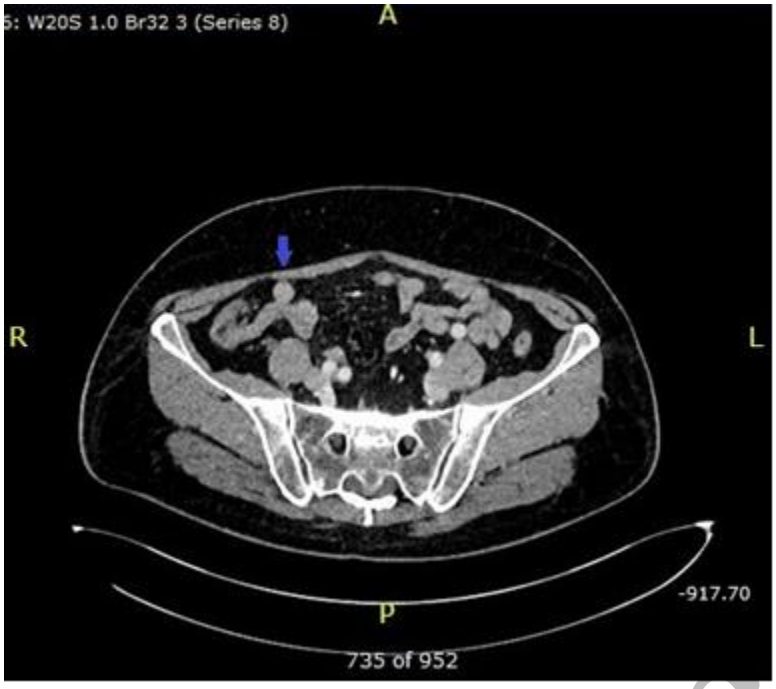

Figure 2. The blue arrow indicates tumor mass in the distal ileum in close relation to the caecum and the right external iliac artery, without radiological signs of infiltration

Figure 3. Specimen obtained after the resection showing the signs of bleeding

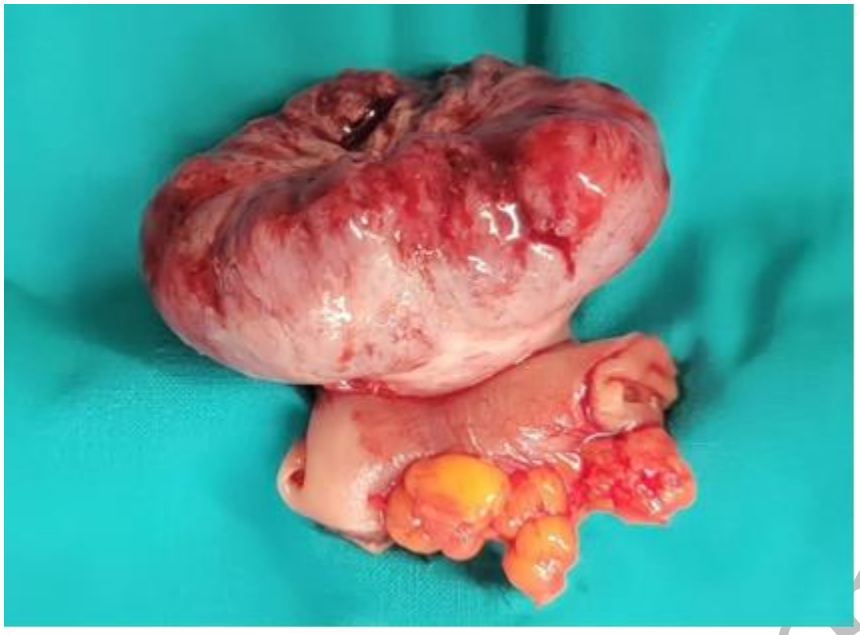

Figure 4. Extraluminal tumor mass of small intestine (ileum)

