



Case report

Multiple primary gastrointestinal tumors of gastric, pancreatic and rectal origin; a case report

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ABSTRACT

Introduction: The occurrence of multiple primary synchronous or metachronous malignancies is a described phenomenon. Such cases may have genetic predisposition or could be related to environmental risk factors but may also be sporadic. We are reporting a unique combination of triple primary synchronous malignancies in the same patient.

Case presentation: A 71 year old man presented with constipation and per rectal bleeding with a palpable mass 5–6 cm from the anal verge on physical examination. Colonoscopy with biopsy confirmed adenocarcinoma of rectal origin. After multi-disciplinary tumor board meeting, the patient received neoadjuvant chemoradiation therapy followed by single-stage surgery. Re-staging work up showed the presence of pancreatic lesion. Incidental finding of a gastric nodule upon surgical exploration which was confirmed to be a gastrointestinal stromal tumor. The patient had an uneventful postoperative course.

Discussion: Multiple primary malignancies of the gastrointestinal system has previously been reported in the literature; whether in the form of double, triple, quadruple or even quintuple primaries. Furthermore, gastrointestinal malignancies have been reported to be combined with extra-intestinal malignancies. However, this unique combination of pancreatic adenocarcinoma, rectal adenocarcinoma and gastric gastrointestinal stromal tumor has not been previously reported in the literature. Single-stage multiple resections was successful.

Conclusion: We are reporting a unique case of three primary malignancies involving the rectum, pancreas and stomach. For such patients, there is no clear guidelines regarding management or surveillance, but rather should be individualized.

1. Introduction & importance

The occurrence of multiple primary synchronous or metachronous malignancies is not an uncommon phenomenon, with a variable incidence in the literature, ranging from 0.73 to 11.7% [1]. Although it has become more common due to improved life expectancy and advanced diagnostic tools. Such cases may be related to syndromes, genetic predisposition, and environmental risk factors but can also be sporadic. The exact incidence of multiple primary malignancies (MPM) in the absence of known syndromes is uncertain, with the majority of cases reported in the literature being either case reports or case series [2]. MPM may affect any organ in the body, with a common predilection to the

gastrointestinal (GI) system [3]. We are reporting a rare case of three primary GI malignancies in the same patient. This work has been reported in line with the SCARE criteria [4].

2. Case presentation

A 71 year old man, who is known to have diabetes mellitus, presented with constipation and per rectal bleeding for 3–4 months duration. The patient was receiving oral hypoglycemics for his diabetes, and denied any family history of malignancy. Physical examination showed a palpable mass 5–6 cm from the anal verge. He was investigated by colonoscopy which showed a friable mass extending between 3 and 9 cm

Abbreviations: MPM, multiple primary malignancies; GI, gastrointestinal; CEA, carcinoembryonic antigen; CT, computed tomography; MRI, magnetic resonance imaging; CRM, circumferential resection margin; MDT, multi-disciplinary team; RAPIDO, Rectal Cancer and Pre-operative Induction therapy followed by Dedicated Operation; FOLFIRINOX, fluorouracil, leucovorin, irinotecan and oxaliplatin; GIST, gastrointestinal stromal tumor; PET, positron emission tomography.

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from the anal verge. A biopsy was taken from the mass which showed a moderately differentiated adenocarcinoma of rectal origin. Lab works including a complete blood count, renal and liver panel were unremarkable. Carcinoembryonic antigen (CEA) was elevated (5.1 µg/L). Further investigation by staging computed tomography (CT) of the chest, abdomen and pelvis showed thickening of the rectum. However, no distant metastasis was noted at the time of the initial study. Magnetic

resonance imaging (MRI) of the pelvis confirmed the presence of a mid-rectal mass with enlarged regional lymph nodes, giving a clinical staging of T3, N2 (image 1). Circumferential resection margin (CRM) was positive. The case was discussed in a multi-disciplinary team (MDT) tumor board meeting where neoadjuvant chemoradiation therapy was decided. The patient received Rectal Cancer and Pre-operative Induction therapy followed by Dedicated Operation (RAPIDO) chemoradiation therapy

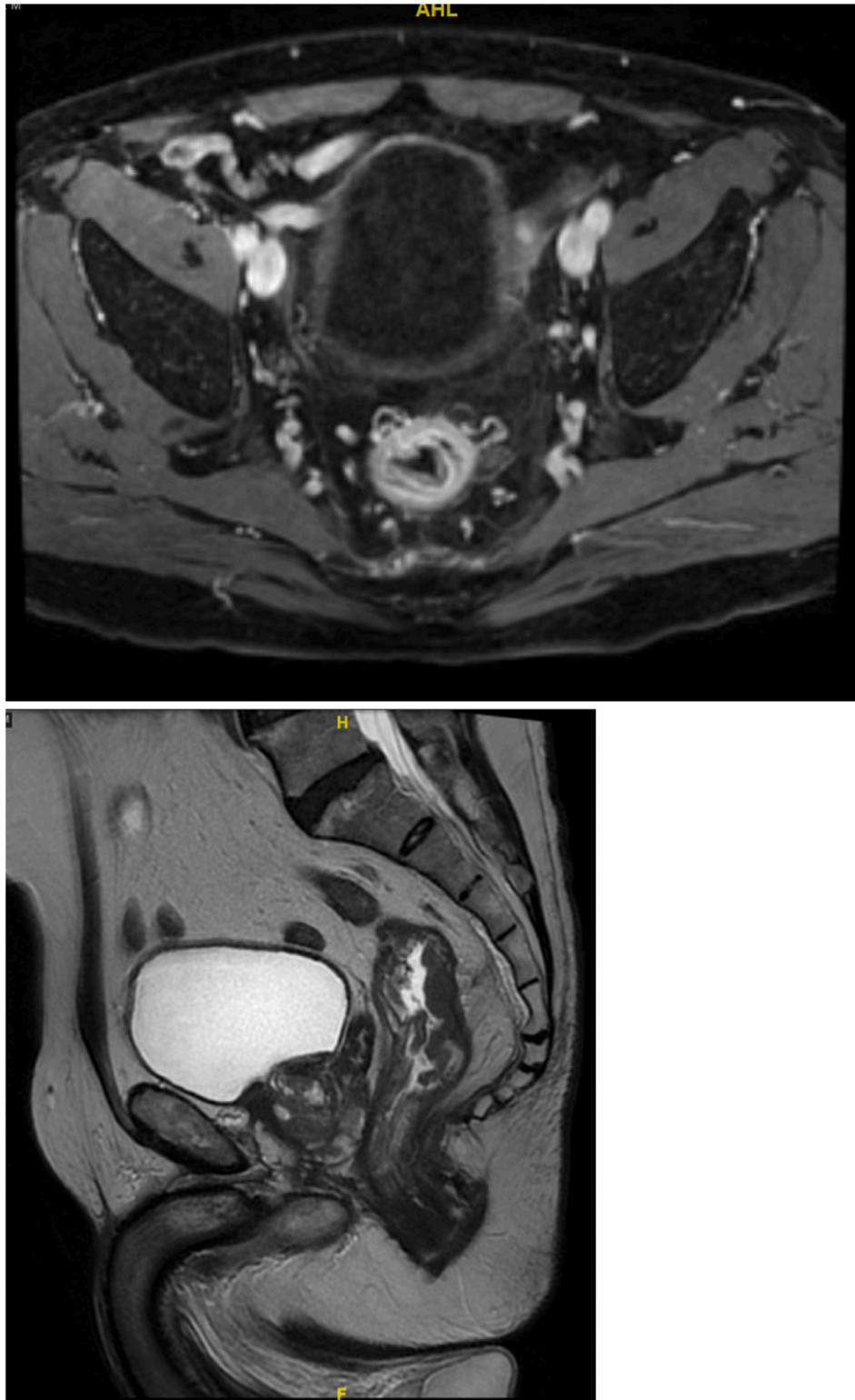


Image 1. MRI of the pelvis showing rectal mass in axial view (a) and sagittal view (b).

protocol including 2500 cGy in 5 fractions and 4 cycles of fluorouracil, leucovorin, irinotecan and oxaliplatin (FOLFIRINOX). Re-staging by a CT scan showed a good response of the rectal mass, with findings to suggest the presence of a pancreatic tail lesion (image 2). Tumor

markers were repeated which showed stable levels of CEA (2.2 µg/L), but increased levels of CA19-9 (54.5 kU/L). Following a second MDT tumor board meeting, the decision was to proceed with a combined surgery for both rectal and pancreatic masses. Under the care of a

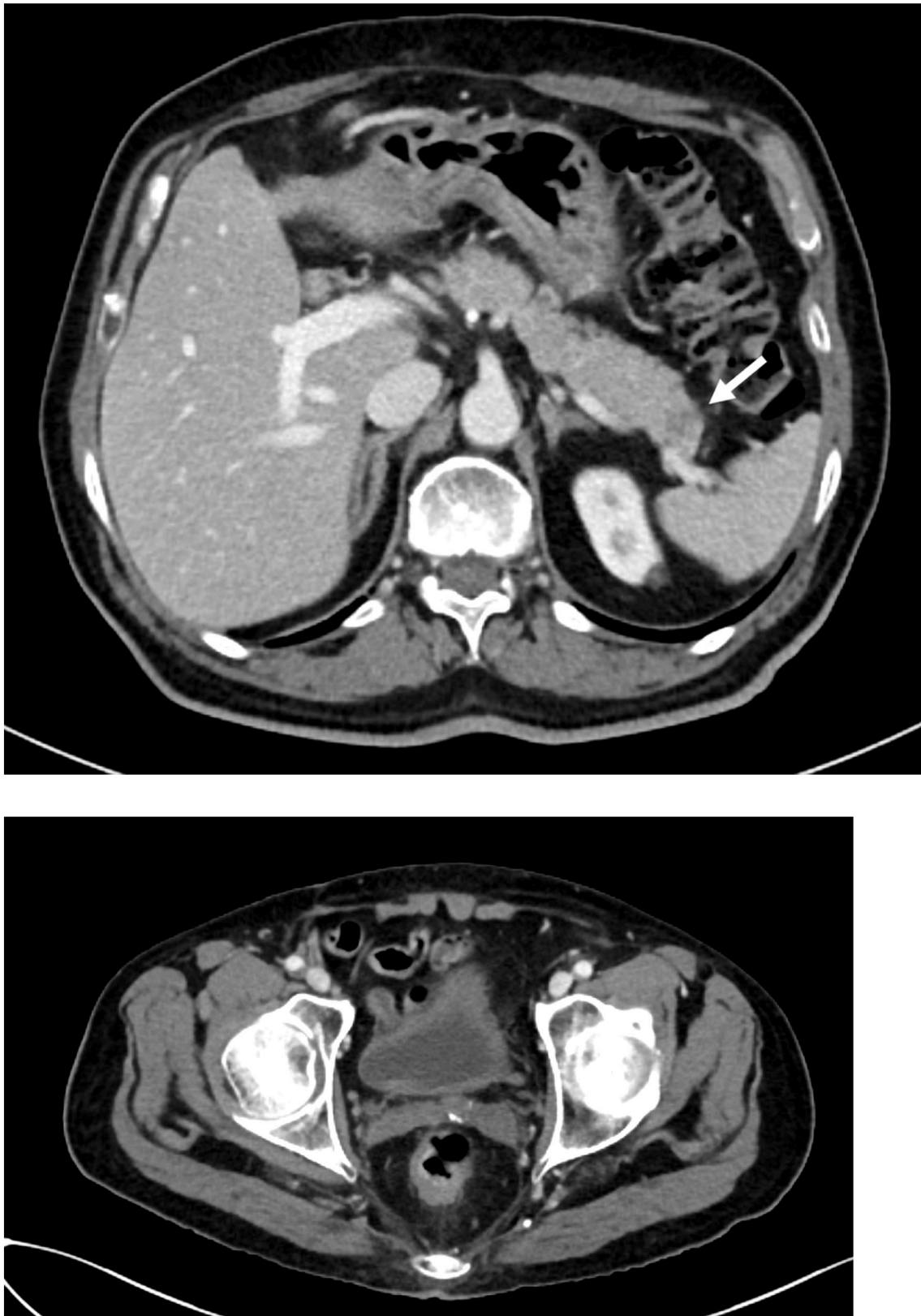


Image 2. Re-staging CT scan showing pancreatic tail lesion (a, arrow) and residual rectal wall thickening (b).

specialized colorectal surgeon and hepatobiliary surgeon, the patient underwent laparoscopic low anterior resection with creation of primary colorectal anastomosis and a diverting loop ileostomy, as well as distal pancreatectomy, splenectomy and wedge resection of an incidentally found gastric nodule on the posterior wall of the stomach. The procedure was carried out within 420 minutes and estimated blood loss was 50–100 mL. The post-operative course was unremarkable and the patient was discharged home in stable condition on post-operative day 6 after reintroduction of diet and physical mobility. The final histopathology report revealed complete response of the rectal tumor with no residual invasive carcinoma or high-grade dysplasia (ypT0N0), pancreatic tail ductal adenocarcinoma (pT2N0), and low grade gastric spindle cell type gastrointestinal stromal tumor (GIST).

3. Clinical discussion

Multiple primary malignancies of the GI system has previously been reported in the literature; whether in the form of double, triple, quadruple or even quintuple primaries [2,3,5]. Moreover, GI malignancies have been reported to be combined with extra-intestinal malignancies. For example, many previous reports of pancreatic and colorectal malignancies, have been reported in conjunction with prostate cancer, and hematopoietic malignancies such as lymphoma [6]. Furthermore, MPM can develop in a synchronous or metachronous manner, with our case having three synchronous tumors. Upon reviewing the current literature, we report the first case of this unique combination including primary adenocarcinoma of the pancreas and rectum, with gastric GIST.

Similar to our case, GIST is commonly a silent disease and often incidentally found during work up of other causes or during operative exploration. Furthermore, the co-existence of GIST with other malignancies is common, with the most common type being gastrointestinal malignancies, particularly adenocarcinoma of the stomach [7]. However, colonic, rectal, and pancreatic associations have also been reported in the literature. In fact, many authors have reported an increased risk of developing synchronous or metachronous malignancies in patients with GIST and have proposed a closer surveillance. Although there is no clear scientific basis to prove genetic, molecular, or even environmental associations between GIST and other malignancies, the common incidence of this relationship does raise many questions and hypotheses in this regards [8]. GIST in our case was extremely small (<1 cm) and had a low mitotic rate on final pathology which may question the benefit of resection. However, in the presence of other malignancies, surgical resection of even small lesions is recommended. Although the presence of GIST provides no prognostic benefit, it does not appear to affect the overall survival in these patients. Also, resection is important to confirm the diagnosis, exclude metastases and provide treatment if indicated [8,9]. In fact there have been cases of recurrence even among the very low/low risk groups [10].

Few cases have been reported of synchronous gastric GIST combined with pancreatic adenocarcinoma [11,12]. In two previously reported cases, the pancreatic mass was affecting the head, while our case involved the tail. The presence of the mass in the head of pancreas creates an ease in terms of the surgical technique, because the part containing the gastric mass was included in the originally planned pancreatic specimen. Whereas when the mass involves the pancreatic tail, it necessitates additional resection (stomach). While in one case the gastric GIST was large and identified pre-operatively on imaging [12], the other case was small and it was identified intra-operatively [11]. The latter also reported low mitotic figure rate similar to the histopathology of our patient. Both of these cases were T3, while ours was T2.

Pancreatic adenocarcinoma tends to have a late presentation and is associated with poor prognosis, which can impose a challenge during surgical management. Although less common than GIST, pancreatic adenocarcinoma can similarly exist with other primary malignancies whether in a synchronous or metachronous manner. Furthermore, the

second primary site may vary from other GI organs, to genitourinary or hematopoietic systems [13,14]. Reports show that the presence of a second primary malignancy in a patient with pancreatic cancer may have a survival benefit, a finding that maintained its statistical significance in multivariate analysis [15]. In addition, they found that the site of the second primary may influence the median survival with the highest median survival in thyroid followed by stomach [15]. In that report, the stomach was the most common site of a second primary malignancy, although adenocarcinoma was more common, 3 patients had gastric GIST. Colorectal cancer was the second most common second primary in that report [15]. A recent publication reported a patient with inoperable pancreatic adenocarcinoma who started to become symptomatic from his rectal mass four months after initiation of chemotherapy in the form of tenesmus and per rectal bleeding [16]. On the other hand, in our case the rectal cancer was the symptomatic disease. The pancreatic mass was silent and found incidentally on imaging and fortunately was resectable.

For patients with MPM, there are no clear management guidelines. Although, the role of MDT approach is highly valuable [5,17]. In fact, the standard of care for treatment of most cancer cases in our institute is individualized and based on the MDT decision. Each MDT consists of surgeons, oncologists, radiation oncologists, radiologists and pathologists. Advanced diagnostic modalities such as positron emission tomography (PET) scan, as well as genetic testing are also important tools to consider [18,19]. Single-stage multiple resections was successful in our case, particularly due to the early stage of all three tumors. The gastric lesion was unrecognizable during screening and only identified intra-operatively as a small lesion. Additionally, the rectal cancer was not only recognized early but also had complete radiological and pathological response to neoadjuvant chemoradiation therapy. With regards to the management of multiple synchronous lesions, one of the most essential factors to determine the appropriate treatment plan is the stage of each lesion found at the time of presentation [5]. In our case, each tumor was in the early stage amenable to single stage surgery. Finally, no clear guidelines exist regarding surveillance, however studies have recommended more frequent surveillance, particularly since these cases can often develop into more numerous metachronous conditions.

4. Conclusion

Multiple primary malignancies involving the GI system has previously been reported with an uncertain incidence and variable pattern. We are reporting a unique pattern of three primary malignancies involving the rectum, pancreas and stomach with a successful single-stage resection. Single-stage multiple resections can be considered an optimum management given the early recognition of these primary tumors. For such patients, there is no clear guidelines regarding surveillance, but rather should be individualized.

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Ethical approval

Case reports do not require ethical approval by our institution.

Consent

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

written consent is available for review by the Editor-in-Chief of this journal upon request.

This case has not been previously presented in any regional or international conferences.

Author contribution

All authors contributed to the manuscript preparation including data acquisition, literature review and writing.

Research registration

N/A.

Guarantor

Abdullah Aloraini is the guarantor and will accept full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

Declaration of competing interest

The authors have no conflicts of interest to disclose.

References

- [1] I. Papaconstantinou, D.S. Mantzos, K. Asimakoula, V. Michalaki, A. Kondi-Pafiti, A 12-year experience at a tertiary hospital on patients with multiple primary malignant neoplasms, *J. BUON* 20 (1) (2015) 332–337.
- [2] Q. Huang, X. He, H. Qin, X. Fan, M. Xie, L. Lian, Triple primary malignancies in a patient with colorectal adenocarcinoma: a case report, *Int. J. Surg. Case Rep.* 42 (2018) 34–37.
- [3] A. Nanashima, T. Tominaga, T. Nonaka, K. Wakata, M. Kunizaki, S. Tobinaga, et al., A case of multiple synchronous quadruple cancers of the stomach, sigmoid colon, rectum, and pancreas, *Int. J. Surg. Case Rep.* 35 (2017) 4–7.
- [4] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, A. Kerwan, The SCARE 2020 guideline: updating consensus surgical Case Report (SCARE) guidelines, *Int. J. Surg.* 84 (2020) 226–230.
- [5] S.H. Kim, B.S. Park, H.S. Kim, J.H. Kim, Synchronous quintuple primary gastrointestinal tract malignancies: case report, *World J. Gastroenterol.* 23 (1) (2017) 173–177.
- [6] B. Bittorf, H. Kessler, S. Merkel, W. Brückl, A. Wein, W.G. Ballhausen, et al., Multiple primary malignancies: an epidemiological and pedigree analysis of 57 patients with at least three tumours, *Eur. J. Surg. Oncol.* 27 (3) (2001) 302–313.
- [7] N. Arnogiannaki, I. Martzoukou, P. Kountourakis, E. Dimitriadis, A. Papathanasaki, E. Nastoulis, et al., Synchronous presentation of GISTs and other primary neoplasms: a single center experience 24 (1) (2010) 109–115.
- [8] A. Diamantis, K. Bouliaris, G. Christodoulidis, D. Vasdeki, K. Perivoliotis, K. Tepetes, Gastrointestinal stromal tumors and synchronous intra-abdominal malignancies: review of the literature, *J. BUON* 23 (6) (2018) 1573–1579.
- [9] R.K. Pandurengan, A.G. Dumont, D.M. Araujo, J.A. Ludwig, V. Ravi, S. Patel, et al., Survival of patients with multiple primary malignancies: a study of 783 patients with gastrointestinal stromal tumor, *Ann. Oncol.* 21 (10) (2010) 2107–2111.
- [10] N. Vassos, A. Agaimy, W. Hohenberger, R.S. Croner, Coexistence of gastrointestinal stromal tumours (GIST) and malignant neoplasms of different origin: prognostic implications, *Int. J. Surg.* 12 (5) (2014) 371–377.
- [11] C.A. Dasanu, T. Mesologites, G. Trikidanathan, Synchronous tumors: adenosquamous carcinoma of pancreas and GIST of stomach, *J. Gastroint. Cancer* 42 (3) (2011) 186–189.
- [12] J.J. He, K.F. Ding, L. Zheng, J.H. Xu, J. Li, Y.L. Wu, et al., Adenosquamous carcinoma of the uncinate process of the pancreas with synchronous gastrointestinal stromal tumor of the stomach: case report and review of the literature, *Oncol. Lett.* 4 (6) (2012) 1191–1194.
- [13] N. Eriguchi, S. Aoyagi, M. Hara, K. Okuda, T. Tamae, S. Fukuda, et al., Synchronous or metachronous double cancers of the pancreas and other organs: report on 12 cases, *Surg. Today* 30 (8) (2000) 718–721.
- [14] S. Mehta, G.I. Tan, C.B. Nahm, T.C. Chua, A. Pearson, A.J. Gill, et al., Pancreatic resection in patients with synchronous extra-pancreatic malignancy: outcomes and complications, *ANZ J. Surg.* 90 (3) (2020) 290–294.
- [15] S.J. Shin, H. Park, Y.N. Sung, C. Yoo, D.W. Hwang, J.H. Park, et al., Prognosis of pancreatic cancer patients with synchronous or metachronous malignancies from other organs is better than those with pancreatic cancer only, *Cancer Res. Treat.* 50 (4) (2018) 1175–1185.
- [16] J.K. Triantafillidis, M. George, V. Costas, Apostolos PEJAoC, M.C. Reports, Synchronous pancreatic and rectal carcinoma in the same patient: case report and review of the literature 4 (1) (2020) 59–64.
- [17] K.H. AlBaqmi, F.A. AlMudaiheem, S. Boghdadly, K.A. AlHussaini, N. Shokor, N. AlOudah, Multiple primary malignancies of the colon, stomach, and kidney in a patient with bowel obstruction requiring emergency surgery: a case report, *Am. J. Case Rep.* 21 (2020), e926472.
- [18] A. Salem, R. Abu-Hijli, F. Abdelrahman, R. Turfa, R. Amarin, N. Farah, et al., Multiple primary malignancies: analysis of 23 patients with at least three tumors, *J. gGastroint. Cancer* 43 (3) (2012) 437–443.
- [19] L. Pang, G. Liu, H. Shi, P. Hu, B. Li, D. Cheng, Nineteen cases with synchronous multiple primary cancers studied by (18)F-FDG PET/CT, *Hell. J. Nucl. Med.* 20 (1) (2017) 36–40.