



CASE REPORT

REVISED Case Report: The importance of examining colon and rectum in patients with appendiceal cancer [version 2; peer review: 2 approved, 1 approved with reservations]

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Abstract

Appendiceal cancer is rare and is often diagnosed incidentally in patients undergoing appendectomy for acute appendicitis. However, patients with appendiceal cancer are at increased risk of synchronous malignancy. In this case report, we present a 58-year-old man initially diagnosed with acute appendicitis after presenting to the emergency department with abdominal pain. He had an appendectomy and was discharged the following day. Unexpectedly, the postoperative histopathologic examination showed a primary adenocarcinoma in the appendix. A computed tomography scan showed rectal wall thickening and the patient was referred to colonoscopy where an experienced endoscopist found a rectal tumor during the digital rectal examination prior to the colonoscopy. The tumor was initially missed by the newly qualified doctor who examined the patient during his first admittance to hospital. The patient's two primary cancers were treated with a laparoscopic right hemicolectomy for the appendiceal cancer and a low anterior resection for the rectal cancer. This case supports the importance of a full colorectal workup in patients with appendiceal cancer. It also emphasizes the value of a thorough digital rectal examination and the need for improved focus on teaching and practice of the procedure.

Keywords

Appendicitis, appendix cancer, appendiceal cancer, synchronous, rectum cancer, rectal cancer, digital rectal examination, case report

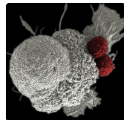
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Approval Status

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version 1 26 Feb 2021	 view	 view	 view

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2. **Cemil Yüksel** , University of Health Science, Ankara Abdurrahman Yurtaslan Oncology Training and Research Hospital, Ankara, Turkey
3. **Wilhelm Graf**, Uppsala University, Uppsala, Sweden

Any reports and responses or comments on the article can be found at the end of the article.



This article is included in the **Oncology** gateway.

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REVISED Amendments from Version 1

- 1) A pTNM classification of the appendiceal adenocarcinoma and rectal carcinoma has been added to the "Case presentation" section.
- 2) The leukocyte count has been added to the "Case presentation" section.
- 3) In the "Case presentation" section, it has been added that a nonperforated appendicitis was found during the laparoscopic appendectomy.
- 4) An elaboration on the decision to give adjuvant chemotherapy has been added to the "Case presentation" section.
- 5) It has been added to the "Case presentation" section that a protective loop ileostomy was also performed when the patient had a combined right hemicolectomy and low anterior resection.
- 6) The text in [Figure 3](#) (timeline of events) has been updated to highlight the decisions taken at the multidisciplinary team conferences. Changes have been made to "DAY 13" and "DAY 27".
- 7) Vital signs have been added to the "Case presentation" section.

Any further responses from the reviewers can be found at the end of the article

Introduction

Primary appendiceal neoplasms are rare and represent 1% of all gastrointestinal cancers, and the incidence is increasing^{1,2}. Typically, symptoms are vague and the patient often presents with acute appendicitis with the tumor being diagnosed incidentally during histopathological examination after appendectomy. In other cases, tumors can present as bowel obstruction or as a palpable pelvic mass³. Several studies have found that appendiceal neoplasms are associated with an increased risk of synchronous colorectal lesions^{1,3-6}. Multiple primary tumors can be divided into synchronous or metachronous tumors. Synchronous tumors are defined as tumors diagnosed less than six months apart while metachronous tumors are diagnosed more than six months apart⁷. It has been suggested, that the association between synchronous tumors in the appendix and the colon and rectum could be due to similar histological pattern and that the appendix derives embryologically from the cecum⁴. Guidelines recommend that patients with appendiceal neoplasms should undergo colonoscopy³. Also, guidelines call for abdominal examination and a digital rectal examination (DRE)³. DRE is a simple, quick, and inexpensive clinical procedure. One retrospective study found a sensitivity of 76% and specificity of 92% of the DRE for finding palpable rectal tumors⁸. Although it is a useful clinical tool for diagnostics and screening, DRE has a learning curve and the sensitivity is highly examiner-dependent⁹.

We present a patient with synchronous tumors in the appendix and rectum. This case underlines the importance of a full colorectal examination in patients diagnosed with primary appendiceal neoplasms and highlights the value of a thorough DRE. The case is presented in accordance with the CARE guideline¹⁰.

Case presentation

A 58-year-old Caucasian man with no prior medical or surgical history was admitted to the emergency department after referral from his general practitioner. The patient complained of constant diffuse abdominal pain for two days with exacerbation upon movement. He had had fever for one day. His stool was normal without blood and there was no nausea or vomiting. The patient had no family history of colorectal cancer. The abdominal examination revealed direct tenderness in both lower quadrants. The DRE that was performed by the newly qualified doctor on call was without palpable tumors. Vital signs were as follows: blood pressure 131/87 mmHg, pulse 78 beats/min, and temperature 37.8 °C. Laboratory blood tests showed elevated C-reactive protein (110 mg/L [normal value less than 3 mg/L]) and a normal leukocyte count ($6.5 \times 10^9/L$ [normal value 4.4 to $10.5 \times 10^9/L$]). All other blood tests were normal. An acute computed tomography (CT) scan of the abdomen showed signs of acute appendicitis. A diagnostic laparoscopy confirmed the diagnosis of nonperforated appendicitis and an uncomplicated laparoscopic appendectomy was performed. The patient was discharged the following day. The postoperative standard histopathologic examination of the appendix showed acute non-perforated appendicitis and, surprisingly, a 13 mm T1 goblet cell adenocarcinoma in the apex of the appendix with tumor-free resection margins. The patient was informed and underwent a new CT scan of the thorax and abdomen. The only new finding on the repeated CT scan was rectal wall thickening. The patient was discussed at a multidisciplinary team conference where it was decided to perform a colonoscopy due to the rectal wall thickening and thereafter a laparoscopic right hemicolectomy due to the tumor in the appendix. Prior to the colonoscopy, the endoscopist, who is an experienced colorectal surgeon, performed a DRE. The endoscopist palpated the distal part of a tumor in the anterior wall of the rectum seven centimeters from the anal opening. The colonoscopy showed a tumor highly suspicious for malignancy with a central depression of 25 mm ([Figure 1](#)). It was classified as National Institute for Clinical Excellence (NICE) type 3. A magnetic resonance imaging

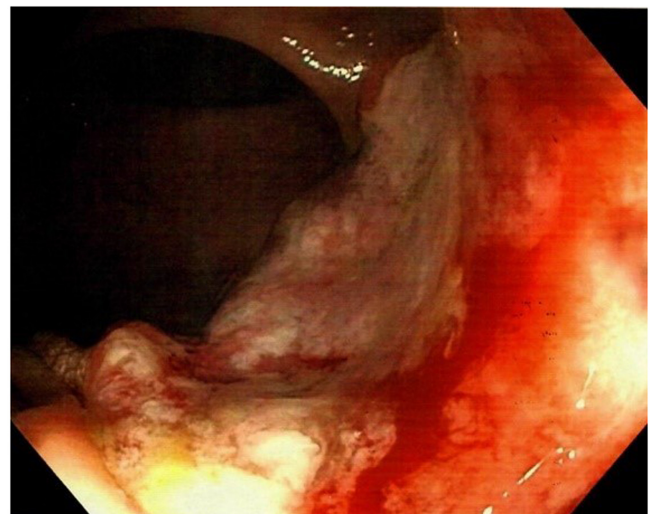


Figure 1. Colonoscopy showing the rectal tumor.

(MRI) scan staged the tumor as a T2 without metastasis to lymph nodes or distant metastasis (Figure 2). The histopathologic examination of the rectal lesion showed a primary signet ring cell carcinoma that was histologically distinct from the appendiceal tumor. Hence, the patient had two primary synchronous tumors. Eventually, the patient was treated with simultaneous laparoscopic right hemicolectomy and low anterior resection. A protective loop ileostomy was also performed.



Figure 2. Magnetic resonance imaging scan showing the rectal tumor.

Figure 3 presents a timeline of the events. Following surgery, the pTNM (pathological tumor-node-metastasis) classification of the appendiceal adenocarcinoma was T1N0M0 and for the rectal carcinoma T2N1M0. The postoperative course was complicated by an anastomotic leakage of the colorectal anastomosis. The leakage was treated with endoscopic vacuum-assisted closure. After the postoperative infection had been successfully managed, the patient received adjuvant chemotherapy for the rectal carcinoma. The decision to treat the patient with adjuvant chemotherapy was multifactorial: N1 staging, presence of tumor satellites, anastomotic leakage, and signet ring cell carcinoma with tumor tissue near the resection margin with a tumor deposit located 1.5 mm from the mesorectal fascia.

Discussion

This case illustrates the importance of a full colorectal workup in patients with a primary tumor in the appendix. This is supported by current clinical guidelines. The American Society of Colon and Rectal Surgeons' clinical guideline strongly recommends that a colonoscopy should be performed to exclude synchronous colorectal lesions in patients with appendiceal neoplasms, and also strongly recommends a complete physical examination including a DRE³.

In this case, the patient's rectal tumor was missed during the DRE performed by a newly qualified doctor in the emergency department. Studies have shown that newly qualified doctors lack confidence in performing a DRE, and the DRE is rarely repeated or supervised by a senior doctor^{11,12}. Also,

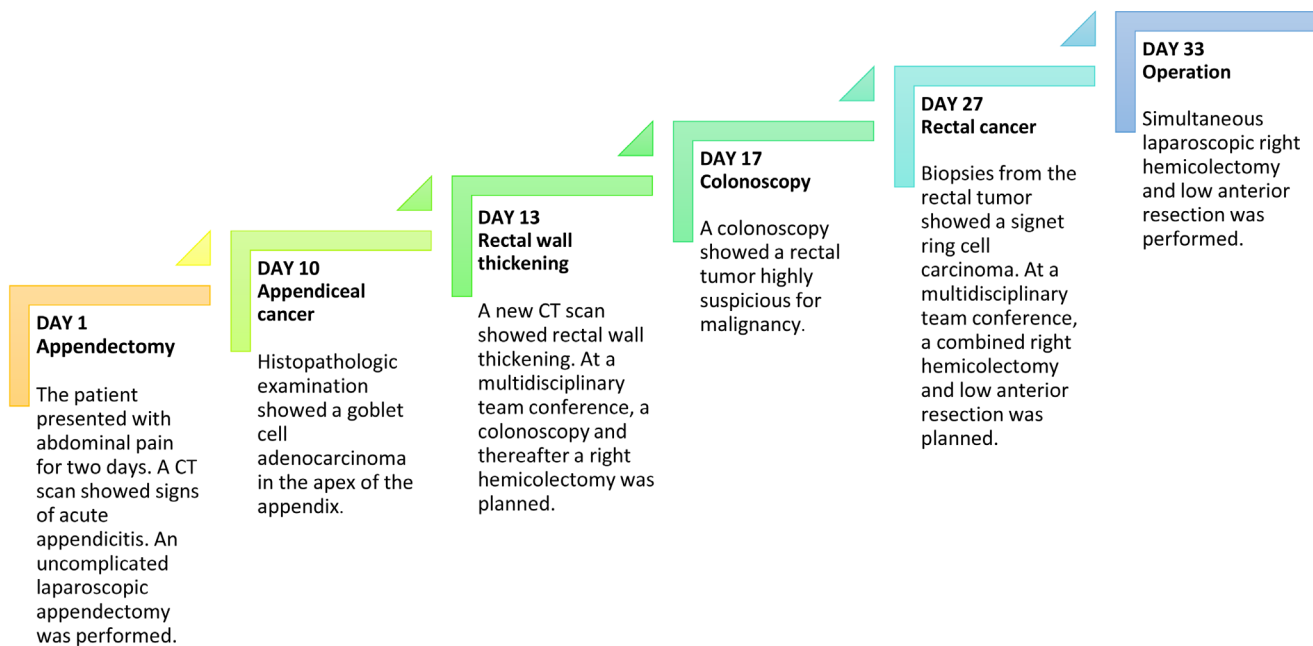


Figure 3. Timeline of events. CT; computed tomography.

clinicians often avoid performing a DRE^{12,13}. The DRE is a cost-efficient and quick procedure to assess and identify numerous conditions in both sexes, e.g. anal fissures, skin tags, pilonidal sinuses, anal fistulas, rectal prolapse, anal warts, skin diseases (e.g. dermatitis), anorectal tumors, gastrointestinal tract bleeding, abscesses, hemorrhoids, sphincter function, constipation, fecal impaction, prostatic hypertrophy, prostate tumors, prostatitis, pelvic inflammatory disease, pelvic floor prolapse (e.g. rectocele), and pelvic floor dyssynergia^{12,14–16}. Hence, the importance of a sufficient DRE should not be underestimated.

Medical school is the foundation where students learn the necessary basic skills enabling them to practice medicine when becoming qualified doctors. Worryingly, senior medical students lack training in performing a DRE and up to 44% have never performed the examination on a human subject when graduating^{17,18}. A randomized controlled study found that medical students that had practiced DRE on phantoms and human volunteers had an increased confidence in performing and trusting the results of the examination compared with students who only practiced on phantoms¹⁹. Like many other practical clinical skills, the DRE has a learning curve. A questionnaire survey concluded that the more adequate the training in performing a DRE, the more confident the examiner was in making a diagnosis using the DRE¹². One study comparing novice to more experienced examiners on specially designed simulators found that the latter had a significantly higher detection rate for both prostate and rectal anomalies⁹. This highlights the importance of sufficient training and experience in DRE. When assessing a patient with abdominal or urogenital complaints, the abdominal examination is a core clinical skill. Many clinicians will experience that the abdominal examination is frequently repeated by a fellow and more experienced clinician, but this is not the case with the DRE^{11,18,20}. As both the abdominal examination and the DRE are standard and important

clinical tools of screening in patients admitted to the emergency department, one could question why the abdominal examination is often supervised or repeated while the DRE is not. Nonetheless, the case presented here highlights the need for improved focus on the DRE in medical training.

A strength of this case is that we have a very detailed report of the patient's history from his first contact to his general practitioner to several months after surgery. Also, we have full and detailed reports of the histopathologic examinations as well as both images and detailed reports of the CT scans, the MRI scan, and the colonoscopy. A limitation to this case is that we do not have information on the approximate total number of DREs performed by the newly qualified doctor initially admitting the patient to the hospital making it difficult to evaluate the doctor's experience in performing the procedure.

Conclusion

In this case report, we present a patient with primary synchronous cancers in the appendix and rectum. The case underlines the importance of the DRE as a quick, inexpensive, and useful skill in the everyday clinic. Patients with primary appendiceal neoplasms should have a full colorectal workup and there should be an improved focus on teaching and training the DRE as it improves confidence and diagnostic accuracy of the procedure.

Data availability

All data underlying the results are available as part of the article and no additional source data are available.

Consent

Written informed consent for publication of clinical details and clinical images was obtained from the patient.

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Version 2

Reviewer Report 17 March 2022

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Cemil Yüksel 

Department of Surgical Oncology, University of Health Science, Ankara Abdurrahman Yurtaslan Oncology Training and Research Hospital, Ankara, Turkey

Accept.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 04 March 2022

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Susanne Merkel 

Department of Surgery, Friedrich-Alexander-University Erlangen, Erlangen, Germany

I am completely satisfied with the improvements.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Surgical oncology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 09 September 2021

<https://doi.org/10.5256/f1000research.54002.r91612>

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**Wilhelm Graf**

Department of Surgical Sciences, Uppsala University, Uppsala, Sweden

Thanks for letting me review this case report. My comments are as follows:

1. In the introduction it is stated that these tumors might present as bowel obstruction but in reality this is not true since the appendix is not in the GI passage.
2. The MTD conference should be added to the timeline figure.
3. Please state the body temperature, pulse and blood pressure.
4. Give more details of the MRI exam.
5. The listing of possible findings on DRE in the discussion could be shortened and focused just on malignant findings.

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Partly

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.**Reviewer Expertise:** Surgery**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have**

significant reservations, as outlined above.

Author Response 17 Feb 2022

Hugin Reistrup, Department of Surgery, Herlev and Gentofte Hospitals, University of Copenhagen, Borgmester Ib Juuls Vej 1, Herlev, Denmark

Dear Wilhelm Graf,

Thank you for your valuable comments, which we have read with great interest. We have answered your comments in a point-to-point format.

1) In the introduction it is stated that these tumors might present as bowel obstruction but in reality this is not true since the appendix is not in the GI passage.

Reply: We agree that this is an unlikely event, but although rare, bowel obstruction due to appendiceal neoplasm has been well described in the literature. We have also referred to a reference in the manuscript to back up this statement.

2) The MTD conference should be added to the timeline figure.

Reply: This is a very good point. We have now elaborated the decisions taken at the MDT conferences to the timeline figure.

3) Please state the body temperature, pulse and blood pressure.

Reply: We have now added this information to the "Case presentation" section.

4) Give more details of the MRI exam.

Reply: Unfortunately, there is no further information available on the MRI exam.

5) The listing of possible findings on DRE in the discussion could be shortened and focused just on malignant findings.

Reply: We fully understand your point regarding this. An important message in this study is to highlight the importance of a sufficient DRE. Also, we want to illustrate that the DRE can help diagnose a lot of different conditions, both benign and malign. Hence, we have chosen to make a comprehensive list of these conditions to underline this important point to the reader. As this case also has an educational aim, we are convinced that it is important to show the vast diagnostic benefits of this simple exam.

We hope that you find the comments and additions above to the manuscript sufficient.

Competing Interests: No competing interests were disclosed.

Reviewer Report 24 August 2021

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Cemil Yüksel 

Department of Surgical Oncology, University of Health Science, Ankara Abdurrahman Yurtaslan Oncology Training and Research Hospital, Ankara, Turkey

First of all, I would like to thank the authors for tackling a good topic. One of the most important topics in surgical training is rectal examination and it can sometimes be overlooked.

Some suggestions for the authors:

1. Are the tumor markers of the patient high? I think some blood values can be added to the article, only CRP is given.
2. Was there any peritoneal spread in the surgical findings? It is more likely to be seen in appendiceal tumors.
3. Colonoscopic view could have been better.
4. The tumoral lesion in colonoscopy could have been shown better.
5. Why was neoadjuvant treatment not planned for the patient?
6. Why was a protective ileostomy not planned for the patient? Because ileostomy should be performed for anastomosis safety in lower rectal tumors.
7. Has thoracic tomography been applied?
8. The postoperative condition of the patient has not been mentioned much. When did oral intake start?
9. The patient's family history was not mentioned.
10. Pathology results are not fully mentioned. Surgical margins? Number of lymph nodes removed? Metastasis?

As a result, the article has shortcomings in terms of surgery. However, the subject mentioned is important.

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Partly

Is the case presented with sufficient detail to be useful for other practitioners?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Surgical Oncology, Gastric cancer, Colorectal cancer, Cytoreductive surgery, HIPEC

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 17 Feb 2022

Hugin Reistrup, Department of Surgery, Herlev and Gentofte Hospitals, University of Copenhagen, Borgmester Ib Juuls Vej 1, Herlev, Denmark

Dear Cemil Yüksel,

Thank you for your valuable comments, which we have read with great interest. We have answered your comments in a point-to-point format.

1) Are the tumor markers of the patient high? I think some blood values can be added to the article, only CRP is given.

Reply: Unfortunately, we do not have tumor markers for this patient. In Denmark, tumor markers are not taken routinely when performing an uncomplicated appendectomy, and as soon as the appendiceal adenocarcinoma was diagnosed, a diagnostic colonoscopy was performed shortly afterwards. We agree that further blood samples would add value to the case and we therefore have added the leukocyte count to the "Case presentation" section.

2) Was there any peritoneal spread in the surgical findings? It is more likely to be seen in appendiceal tumors.

Reply: This is an interesting point, but no, there was no peritoneal spread. As stated in the manuscript, the laparoscopic appendectomy was uncomplicated and there were no other abnormalities described during the laparoscopy. To further elaborate the laparoscopic findings, we have now added that the patient had a nonperforated appendicitis in the "Case presentation" section.

3) Colonoscopic view could have been better.

Reply: We completely agree that the photo (figure 1) from the colonoscopy could have been of a better quality. Unfortunately, this was the best colonoscopic view available. Still, we are convinced that it does add value to the case.

4) The tumoral lesion in colonoscopy could have been shown better.

Reply: Here, we presume that you are referring to the same photo as mentioned in comment no. 3. Therefore, we would like to refer to our response to that comment.

5) Why was neoadjuvant treatment not planned for the patient?

Reply: Unfortunately, this information is not supplied in the patient's journal. But according to Danish guidelines on neoadjuvant treatment of resectable rectal cancers, rectal tumors classified as T1 tumors are not treated with preoperative chemotherapy.

6) Why was a protective ileostomy not planned for the patient? Because ileostomy should be performed for anastomosis safety in lower rectal tumors.

Reply: This is a very good point. A protective loop ileostomy was actually performed. We have added this information to the "Case presentation" section.

7) Has thoracic tomography been applied?

Reply: Yes, as mentioned in the "Case presentation" section, a CT thorax and abdomen was performed. *"...The patient was informed and underwent a new CT scan of the thorax and abdomen."*

8) The postoperative condition of the patient has not been mentioned much. When did oral intake start?

Reply: The patient started oral intake the day after surgery, which is standard in Denmark following this type of surgery. We have deliberately chosen to omit details such as these from the manuscript to keep the manuscript short and concise.

9) The patient's family history was not mentioned.

Reply: As mentioned in the "Case presentation" section, there was no family history of colorectal cancer. *"...The patient had no family history of colorectal cancer"*.

10) Pathology results are not fully mentioned. Surgical margins? Number of lymph nodes removed? Metastasis?

Reply: We fully agree that this has not been elaborated sufficiently in the case, hence, we have added the following to the "Case presentation" section.

- "...Following surgery, the pTNM (pathological tumor-node-metastasis) classification for the appendiceal adenocarcinoma was T1N0M0 and for the rectal carcinoma T2N1M0"
- "...After the postoperative infection had been successfully managed, the patient received adjuvant chemotherapy for the rectal carcinoma. The decision to treat the patient with adjuvant chemotherapy was multifactorial: N1 staging, presence of tumor satellites, anastomotic leakage, and signet ring cell carcinoma with tumor tissue near the resection margin with a tumor deposit located 1.5 mm from the mesorectal fascia."

We hope that you find the comments and additions above to the manuscript sufficient.

Competing Interests: No competing interests were disclosed.

Reviewer Report 28 June 2021

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Susanne Merkel 

Department of Surgery, Friedrich-Alexander-University Erlangen, Erlangen, Germany

The authors present an interesting case report of a common condition (acute appendicitis) with an incidental finding of increasing incidence (primary adenocarcinoma of the appendix). They emphasize the importance of rectal digital examination.

The case report is well written according to the CARE guidelines. However, I miss the pTNM classification of appendiceal carcinoma after appendectomy plus hemicolectomy and the pTNM classification of rectal carcinoma. I also miss the rationale for the indication for adjuvant chemotherapy: Synchronous multiple carcinomas? Signet ring cell carcinoma? Anastomotic leak? Lymph node metastases?

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Yes

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Surgical oncology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 17 Feb 2022

Hugin Reistrup, Department of Surgery, Herlev and Gentofte Hospitals, University of Copenhagen, Borgmester Ib Juuls Vej 1, Herlev, Denmark

Dear Susanne Merkel,

Thank you for your valuable comments, which we have read with great interest. We have answered your comments in a point-to-point format.

1) The case report is well written according to the CARE guidelines. However, I miss the pTNM classification of appendiceal carcinoma after appendectomy plus hemicolectomy and the pTNM classification of rectal carcinoma.

Reply: We agree that the pTNM classification would be of value to the present case. Therefore, we have added this to both the description of the appendiceal adenocarcinoma after appendectomy plus hemicolectomy (T1N0M0) and rectal carcinoma (T2N1M0) in the "Case presentation" section.

2) I also miss the rationale for the indication for adjuvant chemotherapy: Synchronous multiple carcinomas? Signet ring cell carcinoma? Anastomotic leak? Lymph node metastases?

Reply: We agree that the reason for choosing to treat the patient with adjuvant chemotherapy should be elaborated. The patient received neoadjuvant chemotherapy for the rectal carcinoma (signet cell ring carcinoma). The appendiceal carcinoma (goblet cell adenocarcinoma) did not require further treatment postoperatively. The oncologists based their decision on adjuvant chemotherapy on the following: N+, tumor satellite, anastomotic leakage, and signet ring cell carcinoma with tumor tissue near the resection margin with a tumor deposit located 1.5 mm from the mesorectal fascia. We have added these details to the "Case presentation" section.

We hope that you find the additions above to the manuscript sufficient.

Competing Interests: No competing interests were disclosed.

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