DMR DIGESTIVE MEDICINE RESEARCH
A JOURNAL FOCUSING ON BASIC AND CLINICAL RESEARCH ON DIGESTIVE MEDICINE

Peer Review File

Article information: http://dx.doi.org/10.21037/dmr-20-123

Reviewer

Carcinoid tumors are neuroendocrine tumors that originate from enterochromaffin cells and primarily affect the gastrointestinal tract. In the manuscript "Rectal Carcinoid in a 30-year -old Male: A review of current treatment options", authors presented a case report of a 30-year-old male with a carcinoid tumor of the rectum that was treated with endoscopic mucosal resection and provide a review of endoscopic treatment options.

(1) There were many similar reports about rectal carcinoid treated with colonoscopy in PubMed. What is the novel idea in the paper? Please elaborate in the introduction.

Reply 1: This type of cancer is usually found on screening colonoscopy. Therefore, finding this cancer in a 30-year-old is rare, making this case interesting and suggesting that this type of cancer may be seen in patients younger than 50, but is often never found. In this patient, his diverticulitis diagnosis led to the need for coloscopy, which is how we discovered the rectal carcinoid. In addition, the similar reports about rectal carcinoids often compare one or two methods of treatment. This case report compares 8 different treatment options and weighs them against each other in order to inform readers about the risks and benefits of each.

Changes in Text: We have modified our text to convey this at Page 3, line 64.

(2) Rectal carcinoids are commonly asymptomatic and are identified on routine colonoscopy. What are the differences between rectal carcinoid and rectal cancer? Are they identified on routine colonoscopy, without histopathological examination? Under what status, patients went to hospital and performed colonoscopy?

Reply 2: Rectal carcinoid tumors are a type of rectal cancer. They are less common and more benign compared to rectal adenocarcinoma, which is another form of rectal cancer. This is discussed in the paragraph beginning at Page 6, line 110. The

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tumors are often asymptomatic, and are found incidentally on routine screening colonoscopy, and then are analzyed with histology which reveals positive staining for CD56, synaptophysin, or chromogranin, indicating a neuroendocrine origin. A study that analyzed 114 intestinal neuroendocrine neoplasms, majority of which were in the rectum, found that the positive rate of immunohistochemical staining for synaptophysin was 97.4% and 75.4% for CD-56, showing that these glycoproteins are widely accepted neuroendocrine markers.

Changes in text: The fact that these tumors are found on routine screening and the histological staining patterns have been added to the abstract starting at Page 2, line 29 and to the introduction on page 2, line 47.

(3) It is better to provide representative Pathological images of positive for CD-56 and synaptophysin.

Reply 3: We do not have the respresative pathological images in this patient to present. However, synaptophysin and CD-56 are two of the more common markers for neuroendocrine carcinoid tumors. As stated in reply #2 above, among neuroendocrine cancers the positive rate of immunohistochemical staining for synaptophysin was 97.4% and 75.4% for CD-56. This shows that these proteins are widely accepted as neuroendocrine markers.

Changes in text: This has been added to the text on page 2, line 47.

(4) What are the causes leading to fever in the case?

Reply 4: The patient had a fever when he first presented to the ED which was caused by the sigmoid diverticulitis. The carcinoid tumor was found 10 weeks after his discharge on a follow-up colonoscopy to assess the status of the diverticulitis. The carcinoid tumor was not the cause of the original fever, the fever was only mentioned to show the clinical course of his diverticulitis.

Changes in text: n/a

(5) Whether CT scan or ultrasonic test can be used for diagnosis for rectal cancer?

Reply 5: Both CT scan imaging and transrectal ultrasonography can be used to diagnose and stage rectal carcinoids. Transrectal ultrasonography was shown to be more accurate than conventional CT in assessing the depth of invasion of the tumor and regional lymph node metastasis in a study that analyzed 89 patients with rectal

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cancer. Ultrasound depicts the layers of the rectal wall more clearly, and therefore is more accurate when determining the depth of invasion of rectal tumors.
Changes in text: This was added to the text in page 3, line 57.

(6) What are your advisements for treatment for rectal cancer? Please supplement in the discussion.
Reply 6: The advisement for treatment specific to rectal carcinoid tumors was discussed in the Conclusion section. We advised that gastroenterologists strongly consider local endoscopic excision over radical resection (Page 9, line 193). However, when deciding between different endoscopic techniques, the endoscopist must take into consideration their own level of technological skill and the risk of metastasis for the individual tumor before choosing a mucosal or submucosal resection (Page 9, line 195). The treatment of rectal carcinoma, a different, more common rectal cancer, differs in some respects to that of rectal carcinoid, and is not in the scope of this paper.
Changes in text: This discussion occurs in the first paragraph of the conclusion section (page 9, line 192), therefore no changes to the text were made.

(7) How to identify the metastasis of rectal cancer?
Reply 7: Larger carcinoid tumors with an atypical surface that invade either the muscular, perineural, or lymphovascular layers of the rectum are at much greater risk for metastasis (Page 6, line 110). After carcinoid tumors have been identified by biopsy, an analysis for either regional (lymph node) or distant metastasis should be conducted. The most common site for distant metastasis is the liver. Metastasis would be identified by additional imaging, including chest xray, CT scan imaging, and position emission tomography scan imaging. If a carcinoid had metastasized, the treatment options in our case report would be modified to include more systemic treatment regimens.
Changes in text: A discussion of metastasis work-up has been added to page 6, line 116.

(8) What is the meaning of "EMR" without full-name in the manuscript?
Reply 8: The meaning of EMR is endoscopic mucosal resection.

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Changes in text: The full name and abbreviation have been added to the abstract on Page 2, line 39 and to the introduction on page 3, line 63 for further clarity.

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