

Reviewer's suggestion

the manuscript entitled "NF-1 associated with multiple rectal neuroendocrine tumors: A case report" presents a very interesting and rare case, that would definitely improve reader's knowledge and clinical practice. The paper respects the required structure and content, according to CARE Checklist. The "Title" reflects the main topic of the manuscript. I would, however, suggest "Neurofibromatosis type 1" instead of the abbreviation "NF-1". The "Key words" are appropriately chosen. The "Abstract" summarizes quite well the manuscript, except for the following sentence: "Our aim is to improve clinical understanding, aid diagnosis, and inform treatment decisions for patients with NF-1 who present with multiple diagnoses". The text does not contain detailed data about therapy. Also, please replace "multiple diagnoses" with "associated medical conditions". The "Introduction" presents adequately the status of the present knowledge in neurofibromatosis and in multiple neuroendocrine rectal tumours. Please correct here "The most common symptoms include... similar to those of more common rectal diseases such as hemorrhoids, anal canal rectum,". What "anal canal rectum" disease? The authors wrote: "Our department has received and treated a case of a patient diagnosed with NF-1 in the setting of multiple rectal neuroendocrine tumors, as well as vascular malformations and scoliosis, who was treated in our department." Please delete "who was treated in our department", data is redundant. The "Case Report" is well presented, with all the required data for complete diagnosis and follow-up. Please replace "Ultrasound colonoscopy" with the appropriate name of the technique. The paragraph "Discussion" is well structured and documented, easily to be followed. It presents the paper's relevance to clinical practice, given this rare case. Comments: The authors wrote "Moreover, when compared to Kevin A's case report in 2010", but this report comes in fact from "Ghassemi, K.A., Ou, H. & Roth, B.E. Multiple rectal carcinoids in a patient

with neurofibromatosis. Gastrointestinal endoscopy 71, 216-218 (2010)", therefore this should be changed; it is not Kevin's...but Ghassemi. The authors wrote "Moreover, when compared to Kevin A's case report in 2010" – please insert reference number (and please mention it is "Ghassemi"). The authors wrote "We have summarized the domestic and foreign literature in the past 20 years and found only 14 cases of rectal multiple neuroendocrine tumors of which only one case also held a diagnosis of NF-1(18-26). Please insert here "Table 1". Please explain "domestic and foreign literature". The authors wrote: "A pelvic MRI revealed localized extravasation of the external iliac veins" – please replace "extravasation". The other cases in the literature with multiple neuroendocrine rectal tumours are presented in Table 1, and only one case was associated with neurofibromatosis-1. Please correct reference 26 in Table 1 as well. Name is Ghassemi KA, not Kevin. Please explain abbreviations "SM" AND "M3" IN Table1, for readers. Figures are of good quality and illustrative enough. Some comments: 1. Figure 2B. Please mark the image of the left external iliac vein. 2. Figures 3D-E are mentioned in the text before Figures 3A-B. Figure 3C comes in the end. Please renumber them, to match the exact order in the text. 3. Figure 3 A-B: The nodules appear next to anus. However, the authors mentioned in the text that "they were 10 cm above the anal verge", which does not appear from the figures. I do not see the "star-like distribution". 4. Figure 3C. Please explain NBI. 5. Figure 3. Please delete "F" From "tFumors". 6. Figures 3 E and F: please mark the tumours. Therapy was presented by authors in the only two following sentences: "Surgical resection is generally considered to be the most appropriate treatment option". "Currently, the preferred treatment for patients with NF-1 and vascular malformations includes symptomatic treatment, surgical resection or other surgical intervention." However, they wrote in the end: "In summary: Although surgical and symptomatic treatments are currently preferred for NF-1, patients often require multi-system and multi-disciplinary comprehensive treatment. It is necessary

to formulate the most appropriate intervention based on individual complications, with the comprehensive application of various technologies and inspection methods". How could this be the conclusion, when nothing about interventions and therapies is mentioned in the "Discussions"? Maybe, the techniques described in Table 1 could be inserted and detailed in the text. And also the "multi-system and multi-disciplinary comprehensive treatment" should be briefly addressed. References are not written according to instructions. Minor polishing of English language is required, especially some words require clarification and spaces between words are missing.

Corresponding reply to manuscript question

Reply to the reviewer's questions

First of all, Thank you for your questions and suggestions, I have already replaced or revised the following questions content as you requested.

1. The modification of words and sentences

- (1) Neurofibromatosis type 1" instead of the abbreviation "NF-1".
- (2) The sentence: "Our aim is to improve clinical understanding, aid diagnosis, and inform treatment decisions for patients with NF-1 who present with multiple diagnoses", even though the text does not contain detailed data about therapy ,but the discussion involves the treatment of NF-1-associated complications, so I have replaced "Inform treatment decisions" with "treatment of associated complications" and "Multiple diagnoses" with "associated medical conditions".
- (3) "Anal canal rectum" is not a common disease name, so I have deleted these words.
- (4) I have deleted "who was treated in our department", because the data is redundant.
- (5) Ultrasound colonoscopy instead of Endoscopic ultrasound (EUS)

- (6) “Table 1” have inserted in the sentence “We have summarized the domestic and foreign literature in the past 20 years and found only 14 cases of rectal multiple neuroendocrine tumors of which only one case also held a diagnosis of NF-1” , and “Kevin A's” have been replaced with Ghassemi KA.
- (7) “Domestic and foreign literature” means the related case reports and articles of multiple rectal neuroendocrine, and I have exchanged the “Domestic and foreign literature” into “relevant literatures” .
- (8) The sentence “A pelvic MRI detected segmental thickening of the right external iliac vein, with a thickness of 27.4 mm and sausage-like appearance” instead of “A pelvic MRI revealed localized extravasation of the external iliac veins”
- (9) The name Kevin has been replaced with Ghassemi KA in Table 1.
- (10)The “SM” and “M3” mean “Submucosa” and “Mina muscularismiucosae” in Table 1.
- (11) The “star-like distribution” has been replaced with “patch distribution”.

2. The alterations of Figures

- (1)The image of the left external iliac vein has been marked with red dotted line in Figure 2B.
- (2)Figure 3 has been renumbered to match the exact order in the text.
- (3) there is a mistake in distance of nodules, In Figure 3C-D, we can see the nodules are next to anus, so the correct description is “Colonoscopy revealed multiple yellow-white nodular uplifts under the rectal mucosa at approximately 1 to 10cm from the anal verge”.
- (4)NBI means narrow-band imaging, I gave a more detailed description of NBI in Figure 3E.
- (5)I have deleted “F” From “tFumors” in Figure 3.

3. The modification of discussion

Thanks for you suggstions.

Because nothing about interventions and therapies of NF-1-associated complications is mentioned in the discussion, we have added the descriptions and contents of multi-disciplinary comprehensive treatment and technical choices of rectal multiple

neuroendocrine tumors in discussion as you requested.

Sincerely,

Responder