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Title: Intestinal metastasis from breast cancer: presentation, treatment and survival from a systematic literature review.

Dear Editor,

We are very grateful to You and the Reviewers, for giving us the opportunity to send the revised improved version of our manuscript.

In this revised version, the corrections have been made to comply with all points raised by the referee and highlighted in the text of the manuscript.

Thank you again

Kind regards

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Reviewer #1

Comments to the Author

The authors present a review of the literature regarding presentation, diagnosis, treatment and survival of patients with intestinal metastasis from breast cancer. This is a rare condition but important to be aware of especially in cases of emergency settings. Surgery of metastatic lesions is usually not routine practice in case of metastatic breast cancer as opposed to for instance metastatic cancer of the colon or the rectum. Therefore, these patients will probably not have planned surgery, but in case of emergency situations like bowel obstruction, bleeding or perforation, this type of surgery may be indicated. This will not be curative treatment from what we know from the literature today, but it will relieve the patient from pain and suffering and probably extend time to death.

Reply to the reviewer

-Abstract Results: we found 96 cases of intestinal metastasis of breast cancer Do they mean 96 individual cases or 96 publications?

We found 96 cases (86 articles).

-Metastatization involved large bowel (cecum, colon, sigmoid, rectum) (49/96; 51%), small bowel (duodenum, jejunum, ileum) (47/96; 49%), and anum (4/96, <1%).

This is correct (see table 1).

I specify in the main text that 4 cases presented with concomitant metastasis of large and small bowel.

The numbers and percentage are correct but I understand your comment. So, I corrected the abstract leaving only the percentage, so that is easier to understand.

-Metastatization – misspelled;

We corrected with metastasization

-Introduction :First reference is cancer statistics from 1996. It would be better to have more updated statistics. The same goes for reference numer two, SEER cancer statistics from 1995. This actually goes for the first five references. Even in case of early diagnosis and application of new therapies, approximately 50% of patients are still at risk of developing distant metastasis. The most common metastatic sites of breast cancer are lymph nodes, bone, lungs, liver, and brain. 50% must be a too big number of patients with metastatic disease of breast cancer. Metastasis to the regional lymph nodes is still considered a loco-regional disease with treatment in a curative intention. This should therefore not be considered metastasis in the same extent as distant metastasis. Again with a more recent cancer statistic reference this number would be much smaller.

We provided more recent references (1-4) and modified the introduction. We maintained reference 5 because it is included in the analysis.

-Method: Well described Results Table 1 is nice It is very interesting that lobular carcinoma more often metastasize to the GI. Lobular carcinomas usually accounts for 15% of the invasive carcinomas and therefore it is interesting that they account for 58% of the metastatic cases. In many cases the diagnosis was made in emergency, for bowel obstruction (39),

bleeding (10) and perforation (2). Other patients complained symptoms such as pain, changes in bowel habits, and in few patients the diagnosis was incidental. I think it would be better to put in the actual number of patients in the different categories, in addition to the percentage.

The number: 39,10 and 2 are the exact number of patients (see table 1). We corrected the manuscript and specified the percentage in the main text.

-Diagnosis was achieved through endoscopy (esophagogastroduodenoscopy, colonoscopy or video capsule enteroscopy), radiological examination (computed tomography, MRI, barium enema or PET) or both endoscopy and radiological imaging. How many was diagnosed with the different modalities?

We specified it in table 1.

Specifically, endoscopy: 54 (56.2%); radiological examination: 82 (85,4%), both endoscopy and radiological imaging in 44/96 cases (45%).

-The other patients started or continued medical therapy (18) such as hormone therapy and chemotherapy. How many had hormonal therapy and how many had chemotherapy, and also what type of chemo was given?

Specifically, 40 patients received hormone therapy (one patient hormone therapy plus palbociclib), 38 patients received chemotherapy and 9 patients received both. Chemotherapy prescribed (included monotherapy agents such as taxane based chemotherapy (paclitaxel, docetaxel) and capecitabine. To note, in most of the reports regimens were not specified.

I added this information in the main text.

-Median overall survival of patients included in this review was available for 46/96 pts (<50%); median survival estimated from the available data was around 12 months. Why was survival data only available for less than 50%. This is a limitation to the study and is nicely described and discussed in the discussion section .

Median overall survival was available for less than 50%.

In the full text of the articles included in this review this information was not specified. We also tried to contact the corresponding author, but in most of the cases we didn't get the missing information. We specified it the main text.

-Discussion Symtoms Symptoms – spelling! There are some more small spelling mistakes in this section It is very good that the author discuss how they differentiate between metastasis

from breast cancer and other site of origin. The treatment is as they discuss totally different and it is mandatory for the clinicians to be aware of these differences

We corrected spelling mistakes.

-Conclusion Good and informative conclusion demonstrating the importance of the manuscript.

Thank you very much for this kind comment.

We hope that all issues have been satisfactorily addressed.

On behalf of all authors

Best regards,

Elena Bolzacchini