Author's response to reviews

Title: Small primary adenocarcinoma in adenomyosis with nodal metastasis: a case report

Authors:

Giacomo DR. Puppa (gpuppa@yahoo.com)
Makio DR. Shozu (shozu@med.kanazawa-u.ac.jp)
Tiziana DR. Perin (tperin@cro.it)
Kazuhito DR. Nomura (nomura@med.kanazawa-u.ac.jp)
Annunziata DR. Gloghini (agloghini@cro.it)
Elio DR. Campagnutta (ecampagnutta@cro.it)
Vincenzo DR. Canzonieri (vcanzonieri@cro.it)

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To the Editor BMC Cancer

We read the attached referees’ reports: once again we agree with all the suggestions, so we adjusted our ms accordingly.
In particular, we made an effort to add the suggested immunohistochemical stainings that were not previously performed.
We believe that in this way the early progression of the neoplasm has been widely investigated: for this reason we are grateful to the reviewers.

Reviewer-2 Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1) Fig 1 C is not adequate to demonstrate the metastasis of endometrial carcinoma into a lymph node. I think that this image could correspond to histological section of neoplasm, at high magnification. It is necessary to show a more convincing images which can reveal at low and high magnification that the figure corresponds to cytological specimen. Moreover, the presence of lymphoid cells is indispensabile to demonstrate metastatic nature of lesion.
We carefully identified a field where the cytological nature of the specimen (namely cell-block) is more evident, because of the presence of blood debris and lymphocytes. (new Figure 1C).

2) To demonstrate limphonodal metastasis I have suggested an immunohistochemical analysis with Ca-125 marker.
We performed immunocytochemistry on the same specimen with Ca-125 and p53, which were both positive in the neoplastic cells (new figure 1D, shown only Ca-125 that was requested), similarly to the primary tumor (new figure 1D).

3) Only few cases of adenomyosis undergo malignant transformation. Why?
The Authors should respond to this question, althought this is not the initial aim of their work.
To respond to this question, I have suggested to evaluate P53 and Cox-2 immunoreactivity.
The immunoreactivity to COX-2 which have been considered is not discussed in terms of carcinogenetic event by authors.
Only adenomyotic foci with p53 mutation subsicono a neoplastic transformation (see previous references indicate in previous referee’s report). Only hyperestrogenic environment is not sufficient to explain the neoplastic transformation
I think that demonstrating this, your work becomes more complete, more interesting and will can be published.
Other author already have demonstrated that leymioma represents hyperestrogenic environment, thus your work do not add other new information to literature.

We expanded in the discussion the carcinogenetic role of COX-2 and introduced the significance of p53 mutation in adenomyosis and in its malignant transformation, by referring to the results of neoplasm and adenomyotic foci immunostaining.

Reviewer-2 Discretionary Revisions (which the author can choose to ignore)
Even though the authors addressed many (most in fact) of the criticisms made by both reviewers, I still think I couple of lines should be inserted under the pathologic findings describing the existence (or lack of) stromal invasion.
We added such features in the pathologic findings section.
Thank you very much for the oppotunity to enrich our ms.

Dott. Giacomo Puppa
Dott. Vincenzo Canzonieri