Author's response to reviews

Title: Radiofrequency-induced thermotherapy of nasopharyngeal angiofibroma - immunohistochemical analysis of vessel proliferation: a case report

Authors:

Mira Krstulja (mirak@medri.hr)
Milodar Kujundzic (milodar.kujundzic@ri.t-com.hr)
Tamara Braut (tamara_braut@hotmail.com)
Niko Cvjetkovic (niko.cvjetkovic@ri.t-com.hr)

Version: 4 Date: 23 May 2008

Author's response to reviews: see over
Dear Sir,

We found the suggestions of our reviewers of great importance and we respected them all.

I got the angiography yesterday and I hope it is not too late. What concerns me is that the angiography figures are not given as high quality, which is not a problem to do if you decide so.

With kind regards,

M. Krstulja

Revision:

1. Will the case report make a difference to clinical practice?

We respect the protocol of preoperative embolization and surgery of nasopharyngeal angiofibroma. This embolization procedure is not performed at our institution. One year after RFITT (17.05-31.05.2006) the patient moved to another institution where embolization-surgery is the protocol and where on repeated angiography no tortuous feeding vessels were found, so the residual tumor was successfully operated. We believe that in this patient RFITT had the effect of tumor embolization, reducing tumor vessels and bleeding. This may make a difference to the clinical practice in small clinics devoid of embolization procedure and make time for patient's preparation for operation in another institution if necessary.

2. ..age sex and ethnic background

Page 3 line 1 added: ...white,...

3. .. the waiting time for surgery of this lesion

Page 3 line 2 added: Clinical staging and tumour embolization reduce surgical morbidity. The therapy protocol is influenced by hospital related factors.

4. Introduction: the authors should clearly state, what they wanted to find out when they decided to treat the patient different to the common concept of embolization followed by surgery; be concise in rewording the goal of this study

Page 3 line 10 added: We looked for a change in angiofibroma cell proliferation through biopsies obtained before and after RFITT when the patient was free of bleeding episodes.

5. page 4 line 7 added: Digital subtraction angiography showed the pathological vascularization of the tumor (08 Mar 2005, Fig.2 a). A CT of the viscerocranium with intravenous contrast revealed a 56 × 48 mm large soft tissue growth that filled the nasopharynx and extended to the left nasal cavity (24 Feb 2005, Fig.2 b). Multiple
slice CT carotidography (10 May 2005) showed the blood supply of the tumor from the external carotid vessels (Fig.2 c).

6. page5 line 7 added: (no hypertrophic feeding arteries were found at repeated angiography before operation).

7. How was the evaluation by immunochemistry planned?

Page 5 line 9 added: The primary intention was to reduce the tumor and alleviate the symptoms using RFITT before operation. Double immunostaining was planned later because of increased Ki67 staining observed in the control biopsy after RFITT. Ki67 is a proliferation marker providing nuclear staining when the cell is in S phase preparing to enter mitosis. To find out which cell type is proliferating in a tissue a second, differentiation marker is added, CD34 for the endothelial cells and SMA for the pericytes.

8. Page 5 line 19 added: This was different from routine less expensive single Ki67 immunostaining where the proliferation index took into consideration all the cells in the tissue without distinguishing vessel cells from stromal cells.

9. The differential diagnosis of JNA and angiocentric lesion of turbinates

Page 7 line 7 added: ..(different pathologies) prone to epistaxis, such as angiofibroma, the angiectatic nasal polyp (5) and the necrotizing angiocentric lesion. The stroma is different in these lesions and quite typical in angiofibroma.

10. the waiting time for surgery

Page 7 line 16 added: Nasopharyngeal angiofibroma is rare event and biopsy is not advised. The first biopsy of our patient resulted from atypical extension of the tumour into the nasal cavity. The dates for the second and third biopsy were chosen regarding the recovery period after RFITT.

Page 7 line 20 added: This includes thermocoagulation as a possible preoperative protocol when embolization is not available.

Page 8 line 21: „and angiofibromas are not considered neoplastic events” instead of „and are not considered neoplastic events”

11. biopsies were taken in February, September and December; were dates chosen by chance or by clinical features (which?)

Page 5 line 4 added: The second and third biopsies respected the recovery time from RFITT and were not complicated by haemorrhage.

12. conclusions

Page 9 line 7 added: Analysis of vessel cell proliferation in tissues treated with thermal ablation might have broader clinical impact across medicine.