Definitive histology control after Mohs micrographic surgery: pleonastic or not?

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Dear Editor,

Histologic control on permanent sections of residual specimens after Mohs micrographic surgery (MMS) is not routinely performed. In our hospital, additional horizontal formalin-fixed sections are regularly produced after MMS as required by the intraoperative protocol of the Pathology Department.

One of our first MMS cases was a 70-years-old woman with an infiltrative basal cell carcinoma (BCC) of the nasal tip. Intraoperative histologic analysis was performed, as usual, by the dermatologic surgeon and dermatopathologist together and all the sections were considered as free of tumor after the first stage. A small rotation flap was immediately executed. The analysis on permanent sections revealed the presence of infiltrative BCC in the deep dermis in two ("upper" and "lateral") of the total three margin sections (Figure 1). Frozen sections review confirmed residual tumor only in the "upper". Thanks to the intraoperative photographs of the patient and to the not complex reconstructive solution, we were able to localize the scar area corresponding to the "upper" margin and to take only a limited additional layer (Figure 2). Resulting formalin-fixed specimen was histologically tumor free. In the "lateral" frozen section we decided not to take an additional layer because specific literature is lacking and the prognostic significance is uncertain.

Among our first 50 cases, the definitive diagnosis did not match the intraoperative report in 14. We observed neoplastic areas not found at intraoperative examination in 23 out of 213 definitive sections (11%). The review of the slides revealed holes in 11 frozen sections and poor quality of hematoxylin and eosin staining in 16. Six frozen sections were 15-60% smaller than permanents, probably for an insufficient flattening before freezing. Epidermis was folded for 20-50% of the total length of 10 frozen sections, whereas it was for 20-50% missing in seven. Dense inflammatory infiltrate in the corresponding peritumoral area was found in five frozen sections, whereas a tumor in situ, not reported during MMS, was detected in two. Finally, seven frozen sections were 20-60% bigger than permanents, probably for excessive trimming after paraffin-embedding (Table 1).

Laboratory errors and low-quality frozen sections are known to reduce the validity of the intraoperative histological examination and increase the risk of recurrence. Moreover, frozen sections should be carefully examined for residual tumor and taking additional layers should be considered in areas of dense inflammation, which may obscure a residual tumor.[1,2,3]

In addition to the case already described, the reoperation was performed for only another patient with an invasive subungual squamous cell carcinoma (SCC) of the second toe, in which the

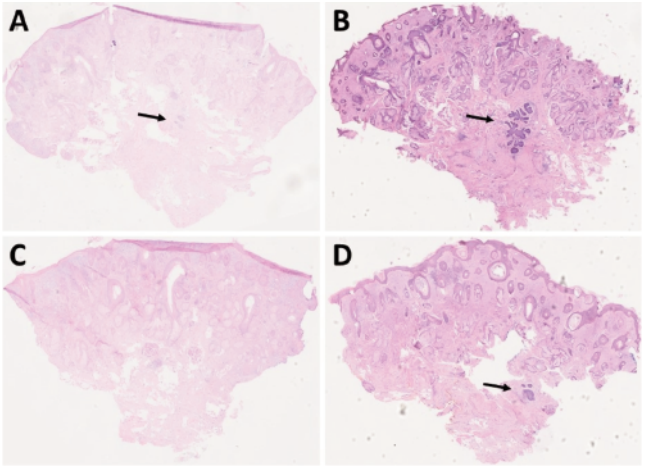

Figure 1. Intraoperative (A; C) and definitive sections (B; D) of the BCC upper (A; B) and lateral (C; D) margins. Revision of intraoperative sections shows an unrecognized BCC area (A; B, arrow). Intraoperative section free from BCC (C), showing technical artifacts (folded epidermis, holes, weak staining); the definitive section instead shows a tumor remnant (D, arrow) (Haematoxylin and Eosin, original magnification, x5).

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Table 1. Data of 14 cases showing residual unrecognized tumor during the intraoperative examination.

Case	Tumor site	Tumor type	Site of residual tumor in permanent sections	Causes of intraoperative misdiagnoses and tumors found at frozen sections review	Closure Type	Follow up/ Reoperation
1	Nasal tip	Infiltrative BCC	BCC papillary dermis	Dense inflammatory infiltrate, low quality staining	Skin flap	Follow up
2	Nasal tip	Infiltrative BCC	BCC reticular dermis	Missing epidermis, holes	Skin flap	Follow up
2	Nasal tip	Infiltrative BCC	BCC reticular dermis	Dense inflammatory infiltrate, intraoperative section smaller than definitive	Skin flap	Follow up
3	Nasal ala	Infiltrative BCC	BCC subcutis	Low quality staining, intraoperative section smaller than definitive	Skin flap	Follow up
3	Nasal ala	Infiltrative BCC	BCC papillary dermis	Low quality staining, intraoperative section smaller than definitive	Skin flap	Follow up
4	Nasal sidewall, nasal ala	Infiltrative BCC	BCC papillary dermis	Holes, low quality staining, intraoperative section smaller than definitive	Skin flap	Follow up
5	Nasal ala	Infiltrative BCC	BCC in situ	Low quality staining , intraoperative section smaller than definitive	Cartilage graft	Follow up
5	Nasal ala	Infiltrative BCC	BCC reticular dermis, subcutis	Missing epidermis, folded epidermis, dense inflammatory infiltrate	Cartilage graft	Follow up
6	Forehead	Infiltrative BCC	BCC papillary dermis	Dense inflammatory infiltrate, intraoperative section bigger than definitive, BCC in situ	Skin flap, skin graft	Follow up
7	Nasal dorsum, nasal tip	Superficial BCC	BCC in situ	Holes, low quality staining	Skin flap, skin graft	Follow up
7	Nasal dorsum, nasal tip	Superficial BCC	BCC in situ	Folded epidermis, low quality staining, BCC in situ	Skin flap, skin graft	Follow up
7	Nasal dorsum, nasal tip	Superficial BCC	BCC in situ	Low quality staining	Skin flap, skin graft	Follow up
7	Nasal dorsum, nasal tip	Superficial BCC	BCC in situ	Missing epidermis, holes	Skin flap, skin graft	Follow up
8	Medial canthus	Superficial BCC	BCC epidermis and papillary dermis	Missing epidermis, folded epidermis, low quality staining, intraoperative section bigger than definitive	Skin flap	Follow up
8	Medial canthus	Superficial BCC	BCC epidermis and papillary dermis	Missing epidermis, folded epidermis, low quality staining, intraoperative section bigger than definitive	Skin flap	Follow up
9	Second toe	Bowenoid SCC	SCC papillary dermis, reticular dermis	Missing epidermids, holes, intraoperative section smaller than definitive	Skin graft	Reoperation
10	Nasal tip	Infiltrative BCC	BCC reticular dermis	Folded epidermis, holes, low quality staining, BCC reticular dermis	Skin flap	Reoperation
10	Nasal tip	Infiltrative BCC	BCC reticular dermis	Folded epidermis, holes, low quality staining	Skin flap	Follow up
11	Nasal ala	Infiltrative BCC	BCC subcutis, muscle	Folded epidermis, holes, low quality staining, intraoperative section bigger than definitive	Skin flap	Follow up
12	Medial canthus	Infiltrative BCC	BCC epidermis, dermis, subcutis	Folded epidermis, dense inflammatory infiltrate, intraoperative section bigger than definitive	Skin flap	Follow up
13	Ear	SCC	SCC subcutis	Folded epidermis, holes, low quality staining, intraoperative section bigger than definitive	Skin graft	Follow up
13	Ear	SCC	SCC epidermis, dermis, subcutis	Holes, folded epidemis, missing epidermis, low quality staining	Skin graft	Follow up
14	Nasal tip	Infiltrative BCC	BCC subcutis	Holes, low quality staining, intraoperative section bigger than definitive	Skin flap	Follow up

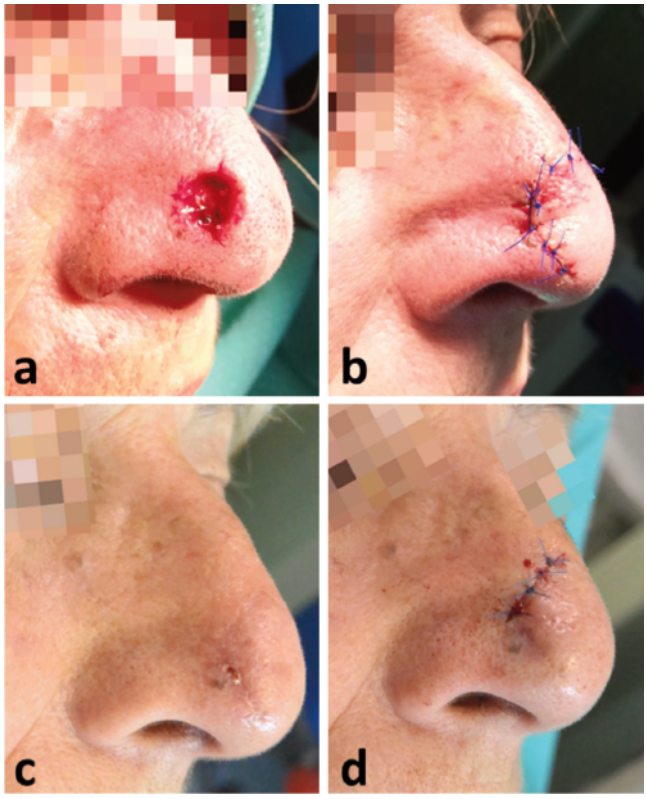

Figure 2. Postoperative defect of the nasal tip after BCC excision (**a**) and after a rotation flap repair (**b**). Scar after ten days (**c**). Suture after taking an additional layer corresponding to the "upper" margin (**d**).

frozen section resulted smaller than the relative permanent and completely missing from the corresponding tumor area. In the remaining cases we opted for follow-up. This decision was mainly influenced by the conspicuous amount of mobilized tissues during the complex reconstructions performed, making the reoperation inconvenient and probably not effective for tumor radicalisation. Recurrence was observed in only one patient (case 7) after 3 years of follow-up.

MMS needs technical equipment as well as technical expertise and trained histopathologists and/or dermatologists for interpretation. Italy is lacking in specific MMS learning courses and training and, even today, MMS is scarcely employed due to high costs, organizational problems and the lack of skilled operators.[4]

Histologic control on permanent sections after MMS is not routinely performed because it is considered as pleonastic; however, we think that in some cases it could instead improve the MMS quality, especially in working environments like ours.[5]

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