



# The Role of Intraoperative Frozen Section in Determining the Margin of Excision in Case of Eyelid Nodular Hidradenoma

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## Abstract

**Background:** Nodular hidradenoma is a rare benign skin adnexal tumor originating from sweat glands. It can recurrence and possibly future malignant transformation. An intraoperative frozen section guides the operation and provides margin control.

**Case report:** We reported a case of a 54 year old woman with a lump under the right eyelid who was early diagnosed with suspected basaloma. The lump was initially small as the size of a green bean seed, but grew in these five months to the size of a corn kernel, itchy and sometimes bleeds. A dermoscopic examination showed a nodule with yellowish globules and arborizing vessels. An intraoperative frozen section procedure was performed with a diagnosis of benign lesion and tumor-free incision margins. The patient's final diagnosis of formalin-fixed paraffin-embedded (FFPE) tissue was nodular hidradenoma.

**Conclusion:** Frozen section intraoperative is very useful to prevent recurrence and malignant transformation of nodular hidradenoma. Eyelid tumors, in particular, have shown benefit from frozen section margin assessment for cosmetic or functional purposes.

**Keywords:** Nodular hidradenoma, Frozen section, Eyelid, Margin excision

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## Introduction

Skin tumours develop as a result of proliferation of a single or multiple components of the skin. They range from benign lesions that merely cause cosmetic concern to premalignant lesions and aggressive tumours.<sup>1</sup> Skin tumours are classified based on their primary site of origin. Keratinocytic/epidermal tumours, melanocytic tumours, appendageal tumours, tumours of haematopoietic and lymphoid origin, soft tissue and neural tumors are classification of skin tumours.<sup>2</sup>

Nodular hidradenoma is a rare benign skin adnexal tumor originating from sweat glands.<sup>3,4</sup> Nodular hidradenoma is also known as clear cell myoepithelioma, clear cell hidradenoma, eccrine sweat gland adenoma of the clear cell type, solid cystic hidradenoma, and eccrine acrospiroma.<sup>5,6,7</sup> The incidence is 5 per million cases. Nodular hidradenoma usually occurs in the 4th to 8th decades of life, with a peak in the 6th decade. These tumors are twice as common in women than in men.<sup>8</sup>

Management of nodular hidradenoma is complete excision of the lesion. Complete excision of nodular hidradenoma with wide margins prevents local recurrence. The incidence of recurrence after inadequate excision is 20% of cases.<sup>9</sup>

Nodular hidradenoma is at risk for malignant transformation. The exact frequency of nodular hidradenomas and the risk of their transformation into malignant tumors is not known.<sup>8</sup> Nodular hidradenomas that have undergone malignant transformation have a local recurrence potential of 50% depending on the surgical

margin and can metastasize to lymph nodes, bone, or visceral organs often causing death with a 5-year survival rate of about 30%.<sup>10</sup>

Frozen section intraoperative is very useful to prevent recurrence and malignant transformation of nodular hidradenoma. Nodular hidradenoma occur anywhere on the body such as the axillae, face, arms, thighs, trunk, scalp, and pubic area but the most common locations are the head, neck, and extremities. Frozen section intraoperative also shown benefits for the lesions located in areas where wide-margin excision is not possible or tissue sparing is desirable, such as the eyes, forehead, cheeks, nose, and ears. Eyelid tumors, in particular, have shown benefit from frozen section margin assessment for cosmetic or functional purposes.<sup>11,12,13</sup>

## Case Report

A 54-year-old female with the chief complaint of a lump on the right lower eyelid since 2 years ago. The lump was initially small as the size of a green bean seed, but grew in these five months to the size of a corn kernel, itchy and sometimes bleeds. Blurred vision or double vision were denied. There is no history of previous trauma. The patient has no history of malignancy in other organs.

A dermoscopic examination showed a nodule measuring 0.9 x 0.6 x 0.4 cm with yellowish globules and arborizing vessels (Figure 1). Based on history and physical examination, the patient was diagnosed with suspected basalioma. Tumor excision was performed and a frozen section examination was carried out to determine the type of tumor and incision of margins.

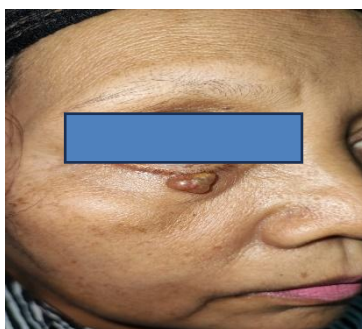


Figure 1. Photograph of the lesion. A tumor with yellowish globules and arborizing vessels measuring 0.9 x 0.6 x 0.4 cm was seen.

The macroscopic appearance is a piece of hairy skin, and brownish tissue measuring 2 cm x 1.5 cm x 1 cm. On the cut surface, a nodule with a diameter of 1 cm is seen (Figure 2). In a cross-section, a cavity filled with yellow pulp appears. The tissue from the superior border labeled I, medial border labeled II, inferior labeled III, lateral border labeled IV, and labeled V from the tumor to the base.

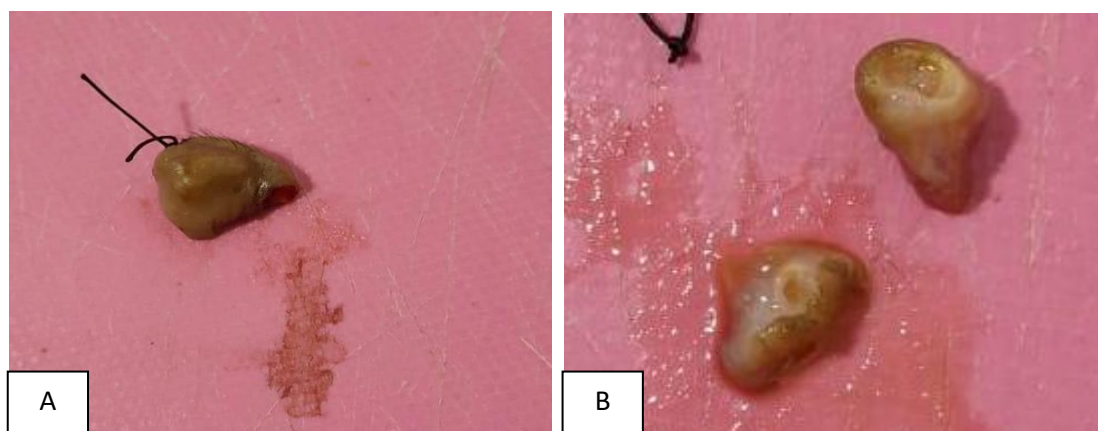


Figure 2 Macroscopic of tumor. A. A piece of hairy skin, and brownish tissue measuring 2 cm x 1.5 cm x 1 cm, on the surface, a nodule with a diameter of 1 cm. B. The cross-section shows one cavity filled with yellow pulp.

Microscopically, there were no malignant cells in the margin excision. Tissue labeled V, which originates from a microscopic tumor mass, it showed pieces of tissue with a surface covered with stratified squamous epithelium. In the dermis, a well-defined cavity is seen, covered by thin connective tissue, without a clear capsule. There is a proliferation of epithelial cells in the cavity forming solid and cystic structures. The cystic mass is lined by one to several layers of the cuboidal epithelium with a lumen filled with an amorphous eosinophilic mass. The solid mass is composed of trabeculae and nests with small, round to polygonal cells, some with a large nucleus, clear - eosinophilic cytoplasm. Cells that are arranged to form a tubular arrangement were seen (Figure 3). The microscopic examination, concluded that the lesion was benign with tumor-free excision margin.

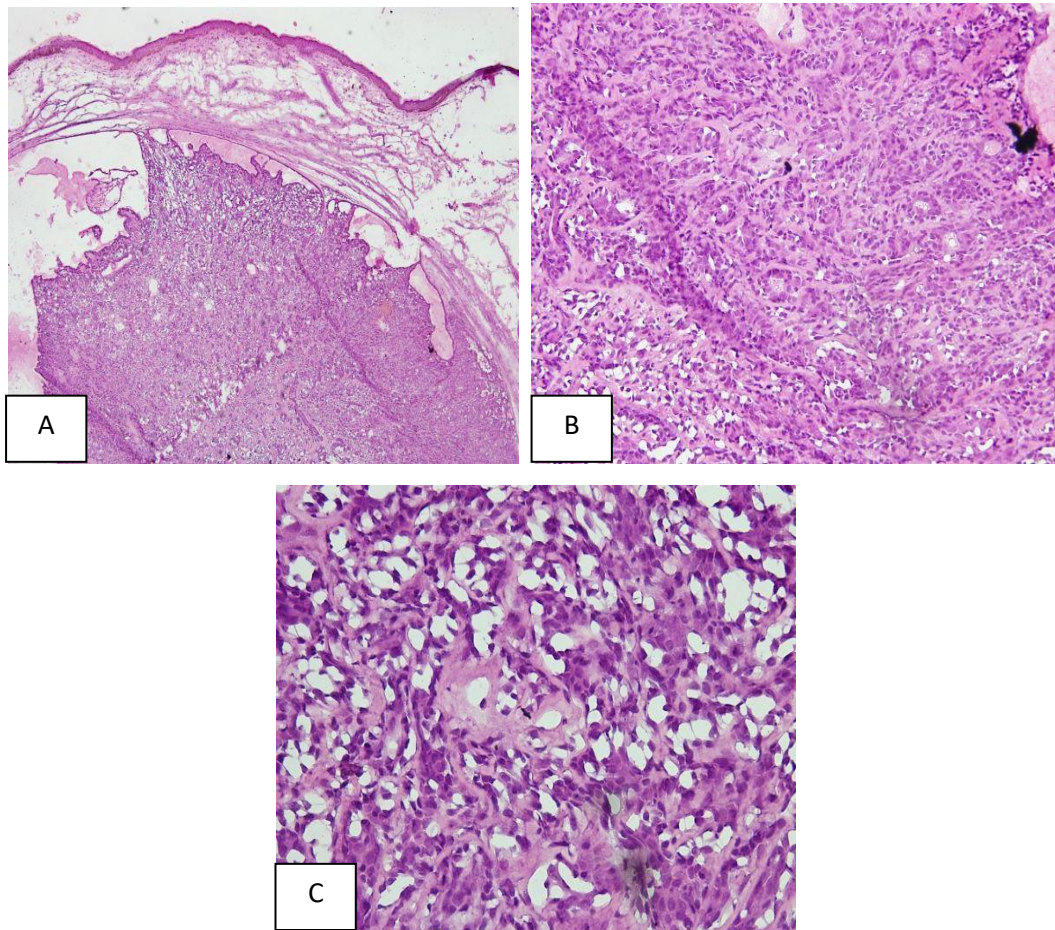


Figure 3. Microscopic features of the base tumor mass in the frozen section. A. In the dermis, a well-defined cavity is seen, covered by thin connective tissue, without a clear capsule. There is a proliferation of epithelial cells in the cavity forming a solid and cystic mass. B. Solid mass composed of the trabecular, nest, and tubular arrangement. The cystic mass is lined by one to several layers of the cuboidal epithelium with a lumen filled with amorphous eosinophilic masses. C. Small, round to polygonal cell appearance, partially with a large nucleus of clear – eosinophilic cytoplasm. (HE, 40x, 100x, 400x magnification).

Tissues were also prepared from Formalin-Fixed Paraffin-Embedded (FFPE) to determine the tumor type diagnosis. Based on histopathology examination of the FFPE tissue, the patient was diagnosed with nodular hidradenoma

## Discussions

In dermatopathology, a frozen section is used when prompt histological assessment improves patient care. The frozen section guides the operation and provides margin control and diagnostic information.<sup>12</sup> Some skin lesions require assessment of the margins and primary diagnosis of the lesion if it is unclear whether the lesion

is benign or malignant or primary or metastatic. Overall, the accuracy of frozen section analysis of skin specimens has been reported to range from 71% to 99%. Several kinds of literature evaluating the use of frozen sections especially for certain skin cancers especially focus on basal cell carcinoma, squamous cell carcinoma, melanoma, and on Mohs micrographic surgery.<sup>11</sup>

The initial diagnosis of this lesion as basal cell carcinoma. Clinically, basalioma, especially the nodular type, often occurs in the head and neck area. It presents as a pearly plaque or nodule, often with telangiectasia. On dermoscopy, a pattern of arborizing vessels is seen. The cystic variant may appear as translucent cystic nodule and mucin filled cystic cavities.<sup>2</sup> This clinical feature resemble with benign lesion such as nodular hidradenoma. Basal cell carcinoma can be ruled out because microscopically there is not proliferation of basaloid cells arranged in palisading at the peripheral and no artefactual retraction was seen.<sup>5</sup>

A common diagnostic pitfall in frozen section of skin is confusing tangentially sectioned hair follicles for BCC. Basal cell carcinoma can be distinguished from a hair follicle by cleft formation around the tumor nests, as well as mitotic figures and apoptotic cells within the tumor nests. Hair follicles are surrounded by a fibrous sheath, which also serves to separate the follicles from BCC.<sup>14</sup>

In this case, the patient was a 54-year-old female. According to the literature, nodular hidradenoma often occurs in women. These tumors arise in adulthood, more than 40 years and over. Tyminski Zofia et al. 2018 also reported a case of nodular hidradenoma in a 51-year-old woman.<sup>15</sup> As well as Kim Sun Je et al. in 2020, also reported a case of nodular hidradenoma in a 70-year-old woman.<sup>16</sup>

Nodular hidradenoma can appear anywhere on the body but is more common on the head, neck, and extremities. In this case, the patient complained of a lump on the right lower eyelid. The lower right eyelid is the head area and this location is the most common location for nodular hidradenoma. There are several case reports reporting nodular hidradenoma of the eyelids. The first case was reported in 1964 by Boniuk Milton et al.<sup>17</sup> In 1968 Greer CH reported one case of nodular hidradenoma on both lower eyelids, initially diagnosed as basal cell carcinoma.<sup>18</sup> In another study Alkatan et al. reported a case of nodular hidradenoma in a 46-year-old woman who presented with complaints of swelling of the eyelids. The lower right side has not been painful for 18 months.<sup>19</sup> Even in 2015 Turan Meydan et al. also reported a case of nodular hidradenoma on the right lower eyelid.<sup>9</sup>

The patient complained of a lump on the right lower eyelid since two years ago, itching, and sometimes bleeding. From the results of the dermatological status examination, efflorescence was obtained in the form of a tumor measuring 0.9 x 0.6 x 0.4 cm. According to the literature, these tumors are usually solitary, measuring between 0.5-2 cm, although sometimes they can be larger (up to 6 cm in diameter), and grow slowly, over several months or years. Subjective symptoms in most cases are often absent. Sometimes it can be associated with bleeding and itching. Some tumours discharge serous material while others tend to ulcerate.<sup>4,5,8,20</sup>

This diagnosis is also supported by the macroscopic appearance of tumor cells where a cross-section is found to contain a cavity filled with yellow pulp. According to the literature, nodular hidradenoma can be a solid or cystic lesion. Alkan et al. also reported a case of nodular hidradenoma with a yellowish appearance with small cavities.<sup>19</sup>

Nodular hidradenoma show a well-defined tumor consisting of lobule epithelium located in the dermis. Focal cystic changes are seen with the lumen filled with a clear amorphous to eosinophilic mass. The tumor is composed of clear, polygonal cells, some of which appear fusiform, duct-like structures can be identified, as well as the hyalinized stroma that is characteristic of some nodular hidradenoma.<sup>5</sup>

The malignant transformation from nodular hidradenoma to hidradenocarcinoma can also be excluded. Hidradenocarcinoma are usually larger, asymmetric, and show invasion into the surrounding tissue. In addition, there may be angiolymphatic invasion. Mitoses are usually easily detected, and some may be atypical. In this case there is no nuclear atypia, pleomorphism, atypical mitosis, necrosis, and no infiltrative growth.<sup>5</sup>



Even though the patient is diagnosed with nodular hidradenoma, the role of the frozen section is very beneficial for the patient. Tumor-free margins and the absence of malignant transformation can provide a good prognosis for patients. Tumor-free margins prevent recurrence and possibly future malignant transformation. Besides that, the benefits of the frozen section in this case can provide a wide margin of excised tissue, which has functional and cosmetic benefits for the patient particular of eyelid tumor.

## Conclusions

Surgical management of nodular hidradenoma has an important role, namely tumor-free margins that can prevent recurrence and the possibility of malignant transformation in the future. The goal of the intraoperative frozen section of this patient is to determine whether the lesion is benign or malignant and to determine whether the margin is tumor free and the excised tissue margins are not wide which is of functional and cosmetic benefit to the patient.

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## Declarations of competing interest

No potential competing interest was reported by the authors.

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