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Surgical Management of Head and Neck Cutaneous Melanoma: Regional Staging and Multidisciplinary Treatment of Locally Advanced Cases

PhD Thesis

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1. Introduction

Cutaneous melanoma is a malignant tumor that develops from melanocytes. Its incidence has been continuously increasing worldwide in the last decades. Although melanoma represents only a smaller proportion of all skin cancers, it is responsible for the majority of skin cancer–related deaths. Approximately one-fifth of all cutaneous melanomas develop in the head and neck (H&N) region, which can be considered a distinct anatomical and clinical entity.

Head and neck melanomas are generally associated with worse prognosis compared with melanomas located on the trunk or extremities. Contributing factors include complex lymphatic drainage of the H&N region, advanced patient age, diagnostic delays and technical difficulties of surgical and oncological management. For these reasons, precise staging and careful, individualized multidisciplinary treatment planning are especially important in this region.

The management of H&N melanoma has changed significantly over the past decades. Previously, treatment

was mainly surgical. Wide local excision together with lymph node dissection formed the basis of therapy. The introduction of sentinel lymph node biopsy (SLNB) has changed the treatment algorythm as it enabled accurate pathological staging in clinically node-negative patients. Large randomized trials have demonstrated its value in risk stratisfaction and became the most important independent prognostic factor in melanoma.

Treatment of melanoma has evolved from a predominantly surgical discipline toward a complex, multidisciplinary approach. It incorporates targeted therapies and immune checkpoint inhibitors. In the contemporary era, the role of surgery has shifted from only local disease control toward accurate staging and selection of patients for systemic therapy. Following the results of recent randomized trials, routine completion lymph node dissection (CLND) after a positive sentinel lymph node biopsy is no longer standard of care. Therefore, SLNB now primarily serves prognostic stratification and guides adjuvant treatment decisions.

Despite these therapeutic advances, the management of H&N melanoma still presents several challenges. In this dissertation, we focus on two specific clinical scenarios that represent contrasting aspects of these difficulites.

One of these challenges is represented by large, neglected, locally advanced primary melanomas, where standard guideline-based treatment algorithms may not always be fully feasible. In such cases, treatment decisions often require individualized treatment planning under real-world clinical constraints.

Another important challenge is the clinically node-negative patients with early- or intermediate-stage melanoma. In this group accurate staging by SLNB is essential for reliable risk stratification and guidance towards adjuvant systemic therapy.

These two ends of the clinical spectrum represent different but related surgical problems in H&N melanoma management. Neglected tumors require complex individualized surgical decision-making. On the other hand, technically demanding procedures such as SLNB

should be performed with high accuracy, even outside large tertiary referral centers.

The present dissertation addresses both aspects through two complementary studies carried out at the University of Szeged, which is a medium-volume regional academic center.

2. Aims and Objectives

The overall aim of the doctoral dissertation was to investigate selected challenges in the surgical management of cutaneous melanoma of the head and neck region, with particular focus on accurate staging and individualized surgical strategies.

The specific objectives were:

1. To analyze the management of neglected and locally advanced H&N melanomas
    - To describe clinical characteristics and surgical treatment strategies in late-presenting cases

    - To evaluate oncologic, functional, and aesthetic outcomes
2. To evaluate the role of sentinel lymph node biopsy in H&N melanoma
    - To assess the feasibility, safety, and prognostic relevance of SLNB in a medium-volume regional center
    - To analyze sentinel lymph node identification rates, false-negative outcomes, and long-term oncologic results
3. To evaluate the applicability of current melanoma guidelines in complex clinical scenarios within a regional academic center.
    - To demonstrate that guideline-based melanoma care can be safely implemented in regional centers with appropriate expertise

3. Materials and Methods

3.1 Study I: Neglected, Locally Advanced Head and Neck Melanoma

A retrospective database search was performed at the Department of Dermatology and Allergology, University of Szeged, between 1 January 2008 and 31 December 2019. Inclusion criteria were any surgically treated primary malignant melanoma of the head and neck region larger than 3 cm in diameter.

Patient history, demographic characteristics, histopathological findings, and treatment reports were retrieved from electronic medical records. Surgical treatments were evaluated according to the contemporaneous NCCN guideline recommendations, focusing on resection margins, timing of reconstruction, and the indication of SLNB.

Functional and aesthetic outcomes were assessed clinically during follow-up using a subjective four-grade scale (poor, acceptable, good, excellent), based on surgeon evaluation and patient-reported satisfaction.

3.2 Study II: Sentinel Lymph Node Biopsy in H&N Melanoma

A retrospective single-center study was conducted including patients with primary cutaneous H&N melanoma who underwent SLNB between 2010 and 2022 at the Department of Oral and Maxillofacial Surgery, University of Szeged.

Demographic and clinicopathological data were collected, including age, sex, tumor localization, Breslow thickness, ulceration, and pathological stage. All cases were discussed at a multidisciplinary tumor board, and the indication for SLNB followed the guideline recommendations valid at the time of treatment.

Preoperative dynamic lymphoscintigraphy was performed in all patients to identify sentinel lympahtic drainage basins on the day before surgery. SLNB was carried out using a combined technique using radiotracer and blue dye. Histopathological examination included serial sectioning and immunohistochemical staining with Melan-A and HMB-45 to increase diagnostic sensitivity.

The primary endpoints of the study were sentinel lymph node identification rate, false-omission rate (FOR), recurrence-free survival (RFS), and overall survival (OS).

Survival outcomes were analyzed using Kaplan–Meier methods, and univariate Cox regression analysis was performed.

To contextualize our findings, a structured review of previously published SLNB series in cutaneous H&N melanoma was conducted using PubMed and other biomedical databases, including studies with at least 75 patients that reported follow-up data and nodal outcome metrics.

4. Results

4.1 Neglected, Locally Advanced Melanomas

Among 2793 malignant melanomas diagnosed during the study period, 375 were located in the head and neck region. Five patients fulfilled the inclusion criteria of tumors larger than 3 cm.

The median age of these patients was 76 years. Tumor size ranged from 3 cm to 29 × 15 cm, including one giant melanoma of the scalp. The average tumor thickness was 9.6 mm.

In all cases, wide local excision with 1–2 cm safety margins was performed. Immediate reconstruction was carried out using individualized techniques, including split-thickness skin grafting, cervicofacial flap, transpositional flap and modified Mustardé flaps.

Sentinel lymph node biopsy was not performed in these cases based on multidisciplinary tumor board decisions. Reasons for omission incluided large tumor size, advanced patient age, comorbidities, and the expected influence on further management.

After a median follow-up of 52 months, four of the five patients showed no local recurrence. One patient developed regional nodal metastasis eight months after primary tumor excision and underwent radical neck dissection followed by systemic therapy.

Functional outcomes were excellent in all patients, and esthetic results were rated as good or excellent in most cases.

The reasons for delayed presentation included insufficient knowledge about melanoma, fear of medical treatment, advanced age, comorbid conditions, and in one case, diagnostic error as well.

4.2 Sentinel Lymph Node Biopsy Study

A total of 38 patients underwent SLNB during the study period. The median follow-up time was 6.8 years, and the median Breslow thickness was 3.12 mm.

The sentinel lymph node identification rate was 100%. Positive sentinel lymph nodes were detected in 8 patients (21.1%). Two false-negative cases were observed, resulting in a false-omission rate of 6.7% and a negative predictive value of 93.3%.

Patients with negative SLN status demonstrated longer recurrence-free and overall survival compared with SLN-

positive patients; however, these differences did not reach statistical significance, most likely due to the limited sample size.

In the intermediate-risk subgroup (pT1b–pT3a), 18.5% of patients had positive SLNs, underlining the clinical importance of SLNB in identifying patients who may benefit from adjuvant therapy.

When compared with previously published large H&N melanoma series, both the identification rate and the false-omission rate were within the reported ranges.

5. Discussion

The results of this dissertation highlight two complementary aspects of H&N melanoma management.

The first main finding of this work is that surgical treatment continues to play a central role in melanoma care, even in the era of modern systemic therapies. In patients with neglected or locally advanced H&N melanoma, strict guideline-based algorithms are often

difficult to apply. In these cases, wide local excision combined with immediate reconstruction resulted in satisfactory oncologic control and acceptable functional and aesthetic outcomes. Our results suggest that, in selected patients, immediate reconstruction does not compromise oncologic safety and may represent a reasonable and patient-oriented approach, especially in elderly patients or those with significant comorbidities.

The second study shows that SLNB can be performed safely and with reliable diagnostic accuracy in a medium-volume academic center, provided that adequate multidisciplinary institutional background is available. In our cohort, the sentinel lymph node identification rate and the false-omission rate were comparable to those reported by large international series, despite the long follow-up period of the study. These findings indicate that institutional case volume alone is not the most important factor determining SLNB performance. Standardized surgical technique, appropriate nuclear medicine imaging, and careful histopathological evaluation appear to be equally important.

Taken together, these findings underline the continued importance of surgery in complex H&N melanoma cases and emphasize the crucial role of accurate staging in the era of personalized systemic therapy.

The work presented in this dissertation contributes to the growing evidence supporting the safe implementation of SLNB in medium-volume centers and highlights the importance of surgery in complex H&N melanoma management. The findings support individualized treatment strategies that combine evidence-based principles with real-world clinical considerations to achieve optimal oncologic and patient-centered outcomes.

6. Conclusions

Head and neck melanoma represents a distinct clinical entity that requires precise staging, careful surgical planning, and close multidisciplinary collaboration.

In neglected, locally advanced cases, wide local excision and immediate reconstruction can provide acceptable

oncologic control together with satisfactory functional and esthetic outcomes.

Sentinel lymph node biopsy is a safe and clinically meaningful staging procedure in H&N melanoma and can be reliably performed in medium-volume regional centers when adequate infrastructure and professional expertise are available.

The integration of guideline-based staging with individualized surgical strategies supports optimal oncologic safety and patient-centered care in the management of head and neck melanoma.