Artigo Original

Biópsia de Gânglio Sentinela no Melanoma Maligno Cutâneo da Cabeça e Pescoço

Ana Marta António[1], Cecília Moura[2], Carina Semedo[3], Sandra Bitoque[4], Mariluz Martins[5], Miguel Vilares[6], Manuela Pecegueiro[7], Jorge Rosa Santos[8]

[1]Interna do Internato de Formação Específica em Dermatovenereologia, Serviço de Dermatovenereologia, Hospital Garcia de Orta, Almada, Portugal

[2]Assistente Hospitalar Graduada Sénior de Dermatovenereologia, Serviço de Dermatologia, Instituto Português de Oncologia de Lisboa Francisco Gentil, (IPOLFG), Lisboa, Portugal

[3]Assistente Hospitalar de Cirurgia Maxilo-Facial, Serviço de Cirurgia de Cabeça e Pescoço, IPOLFG, Lisboa, Portugal

[4]Assistente Hospitalar de Cirurgia Maxilo-Facial, Serviço de Cirurgia de Cabeça e Pescoço, IPOLFG, Lisboa, Portugal

[5]Assistente Hospitalar Graduada de Estomatologia, Serviço de Cirurgia de Cabeça e Pescoço, IPOLFG, Lisboa, Portugal

[6]Assistente Hospitalar Graduado de Cirurgia Maxilo-Facial, Serviço de Cirurgia de Cabeça e Pescoço, IPOLFG, Lisboa, Portugal

[7]Assistente Hospitalar Graduada e Diretora de Serviço de Dermatovenereologia, Serviço de Dermatologia, IPOLFG, Lisboa, Portugal

[8]Assistente Hospitalar Graduado Sénior e Diretor de Serviço de Cirurgia Maxilo-Facial, Serviço de Cirurgia de Cabeça e Pescoço, IPOLFG, Lisboa, Portugal

RESUMO – **Introdução**: A biópsia do gânglio sentinela é uma técnica reconhecida no tratamento do melanoma maligno. O objetivo deste estudo foi caracterizar esta técnica num grupo de doentes com melanoma maligno da cabeça e pescoço tratados num centro de referência. **Métodos**: Foi realizado um estudo unicêntrico, retrospetivo dos doentes com melanoma maligno cutâneo da cabeça e pescoço submetidos a biópsia do gânglio sentinela no Serviço de Cirurgia de Cabeça e Pescoço do Instituto Português de Oncologia de Lisboa entre janeiro de 2010 e dezembro de 2017. Foi analisada informação relativa à localização do melanoma, identificação do gânglio sentinela, número e localização dos gânglios excisados e presença de metástases. **Resultados**: 98 doentes foram elegíveis para realização de biópsia do gânglio sentinela durante o período de estudo. As localizações mais frequentes foram o couro cabeludo (24,5%) e a região auricular (23,5%) e as variantes mais frequentes foram o melanoma de extensão superficial (40,8%) e o melanoma nodular (30,6%). Foi identificado gânglio sentinela em 78 doentes. Foram excisados em média 3,8 gânglios/ doente e em 16,7% dos doentes em mais que um nível ganglionar. Os níveis ganglionares envolvidos foram a parótida (39,8%), o nível II (29,5%) e o nível V (18,2%). Foram identificadas metástases no gânglio sentinela em 13 doentes (16,7%). **Conclusão**: A abordagem cirúrgica do melanoma maligno da cabeça e pescoço é complexa. A vascularização linfática redundante pode originar múltiplos gânglios sentinela e em mais que um nível de drenagem e facilitar a ocorrência de falsos-negativos com implicação prognóstica. Independentemente do resultado do gânglio sentinela todos os doentes devem ter um seguimento cuidadoso.

PALAVRAS-CHAVE – Biópsia do Gânglio Sentinela; Melanoma; Neoplasias da Cabeça e do Pescoço; Neoplasias da Pele.

Sentinel Lymph Node Biopsy in Head and Neck Cutaneous Malignant Melanoma

ABSTRACT – ***Introduction****: Sentinel lymph node biopsy is the standard of care for cutaneous melanoma, including head and neck melanoma. The aim of this study was to analyse and characterize sentinel lymph node biopsy in a population of head and neck melanoma patients.* ***Methods:*** *A unicentric, retrospective study on patients with cutaneous head and neck melanoma who underwent sentinel lymph node biopsy in the Department of Head and Neck Surgery at the Portuguese Institute of Oncology (IPO) Lisbon between January 2010 and December 2017 was performed. The location of primary melanoma, the identification of sentinel lymph node, the number of the excised lymph node biopsy, its lymphatic basin origin and the presence of infraclinic metastasis*

Correspondência: Ana Marta António
Serviço de Dermatovenereologia - Hospital Garcia de Orta
Av. Torrado da Silva
2801-951 Almada, Portugal
E-mail: anamartaantonio@gmail.com
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were analysed. ***Results:*** *Ninety-eight patients were eligible to undergo sentinel lymph node biopsy during the observation period. The most frequent locations of primary melanoma were the scalp (24.5%) and the auricular and periauricular region (23.5%) and the most frequent variants were the superficial spreading melanoma (40.8%) and nodular melanoma (30.6%). Sentinel lymph node biopsy was successfully executed in 78 patients (79.6%). A mean of 3.8 lymph-nodes per patient were excised and in 16.7% sentinel lymph node were excised in more than one lymphatic basin. The sentinel lymph nodes were identified in parotid region (39.8%), level II (29.5%) and level V (18.2%). Sentinel lymph node biopsy metastases were detected in 13 patients (16.7%).* ***Conclusion:*** *Surgical approach of head and neck cutaneous melanoma is particularly complex. The redundancy of lymphatic system, the multiple sentinel lymph node and sentinel lymph node basins influence the sentinel lymph node biopsy success and may contribute to high rates of false-negatives with its prognostic implications. All patients should be carefully monitored.*
KEYWORDS *– Head and Neck Neoplasms; Melanoma; Sentinel Lymph Node Biopsy; Skin Neoplasms.*

INTRODUCTION

The incidence of cutaneous melanoma is increasing more than other cancers.[1] Regional metastases are the most important prognostic factor for melanoma recurrence and survival.[2,3]

Sentinel lymph node biopsy (SLNB) is considered an efficient and minimally invasive method of staging and is nowadays accepted as the gold standard for the diagnosis of infraclinic lymph node metastasis.[2,4,5] SLNB is recommended for cutaneous melanoma with Breslow thickness higher than 0.8 mm or below 0.8 mm if ulceration is present.[2]

About twenty percent of all melanomas occur in the head and neck region and the poor prognosis linked with this tumor site is well known. The 10 years overall survival of cutaneous melanoma located at scalp and cervical region is about 60%.[6,7] The treatment of malignant tumours of the head and neck region is a surgical challenge due to the difficulty to obtain safe surgical margins in this complex anatomic area, and to a laboured diagnosis and surgical treatment of regional metastatic disease with the presence of vital structures and redundant arborizing lymphatic and vascular structures. The lesion of facial nerve during SLNB of parotid region is the most important complication of this procedure and, therefore, many surgeons perform preferably a superficial parotidectomy concomitant with SLNB rather than isolated intraparotid adenectomy.[8] The high density of lymph nodes in the head and neck and the proximity to the primary tumor may difficult the identification of the sentinel lymph node (SLN) by lymphoscintigraphy. Related with this rich lymphatic network, lymph node drainage is frequently discordant from predicted patterns and drainage to multiple sentinel lymph nodes and to multiple lymphatic basins occurs in most patients.[9,10]

All these facts may contribute to higher false-negatives sentinel lymph node rates in the head and neck region. The global rate of false negatives in the sentinel node is around 8 to 20%[11] and values above 20% are reported in head and neck melanomas.[12] According to some authors false-negatives are associated with a higher risk of recurrence and metastasis contributing to the worse prognosis of melanoma in this location.[12]

The aim of this study was to analyze SLNB in the population of head and neck melanoma patients according to success of the surgical technique, the number of the excised SLN, its location and the presence of infraclinic metastasis.

MATERIAL AND METHODS

The authors performed a unicentric, retrospective study on patients with cutaneous head and neck melanoma treated in the Department of Head and Neck Surgery at the Portuguese Institute of Oncology (IPO) Lisbon between January 2010 and December 2017. The inclusion criteria comprised pathologically confirmed melanoma of Breslow thichness $\geq$ 1 mm or $<$ 1 mm with ulceration and high mitotic rate. Patients with clinical or radiological evidence of regional or distant metastatic disease were excluded. Epidemiological, clinical and surgical data were collected from electronic and paper health records. The authors studied the location of primary melanoma, the identification of SLN by lymphoscintigraphy, the number of the SLN excised and its lymphatic basin origin, the presence of infraclinic metastasis and the recurrence. Data evaluation was performed using descriptive statistics coefficients and chi-square test.

RESULTS

Data from 166 patients with head and neck cutaneous melanoma was analysed. Twenty-seven patients did no fulfil melanoma's thickness criteria for SLNB, 27 patients received a primary complete lymph-node dissection due to clinical cervical metastasis observed during preoperative staging, four patients received systemic treatment due to distant metastasis at the moment of the diagnosis and 10 patients were excluded for other reasons (refusal of SLNB, no clinical conditions).

Ninety eight patients (mean age of 65.5 ± 17.7 years; 50% males) were eligible to undergo SLNB during the observation period.

Location of the primary melanoma

The most frequent locations of primary melanoma were the scalp (24.5%; n=24), the auricular and periauricular region (23.5%; n=23) and the malar area (17.3%; n=17) (Fig. 1). The most frequent variants of melanoma were the superficial spreading melanoma (40.8%; n=40) followed by nodular melanoma (30.6%; n=30) and lentigo maligna melanoma (23.5%; n=23) (Fig. 2). The median Breslow

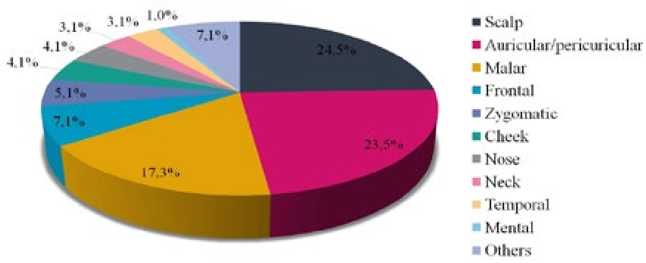

Figure 1 - Location of the primary melanoma.

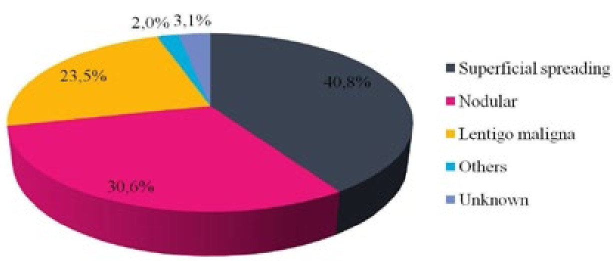

Figure 2 - Variant of primary melanoma.

thickness was 3.7 ± 3.7 mm and ulceration was present in 45.9%.

SLNB procedure

The SLNB procedure involved the marking of SLN using an injection of Technetium[99] in the primary melanoma location the day before the surgery. A lymphoscintigraphy was performed to identify SLN localization. Intraoperative identification of the SLN was then performed using a surgical gamma probe. In 20 patients it was not possible to identify SLN – in 17 patients it was not identified by lymphoscintigraphy and in three patients it was not identified during the surgery. The SLNB was successfully executed in 78 patients.

SLNs overview: number, location, presence of metastases

A total of 286 lymph-nodes were excised, including true SLNs and other non-sentinel lymph-nodes excised in close proximity to the first. A mean of 3.8 ± 3.0 lymph-nodes per patients were excised. In 13 patients (16.7%) SLN were identified and excised in more than one lymphatic basin. According to Robbins Classification, most of the SLN were identified in the parotid region (39.8%; n=35), level II (29.5%; n=26) and level V (18.2%; n=16) (Fig. 3).

Metastases were detected in 13 out of the 78 patients who underwent successful SLNB (16.7%) and in two of these patients metastatic SLN were identified in two or more lymphatic basins.

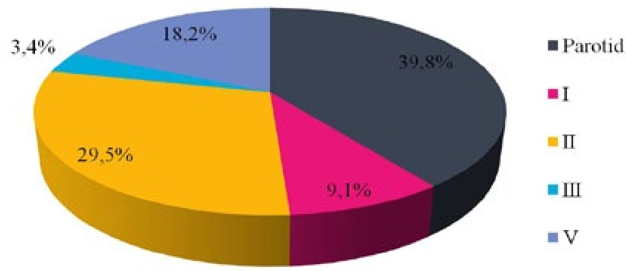

Figure 3 - Sentinel lymph node location.

Recurrence

During the study period locoregional or distant recurrence was detected in 38.5% of patients in the positive SLN group and in 15.4% of patients in the negative SLN group ($p = 0.05$) (Fig. 4). Recurrence was observed in four out of 20 patients (20.0%) in whom the sentinel node was not identified.

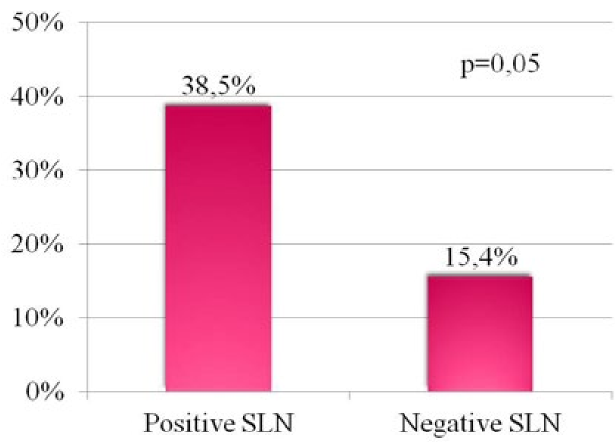

Figure 4 - Recurrence according to sentinel lymph node result.

DISCUSSION

The complexity and redundancy of lymphatic drainage of the cervical region was illustrated by the number of lymph-nodes excided for patient (> 3 lymph-nodes) and the multiple SLN basins (16.7% of patients), as reported by other reports.[9,10,13]

As reported by other work groups[13] a significant rate of patients showed drainage to parotid region and occipital region beyond the level II, which is classically involved. This fact is very important if we consider that for a long period of time the primary lymph-node dissection was the first surgical approach to head and neck cutaneous melanoma and in the majority of patients these areas were not explored. This reinforces the importance of SLNB, its impact on melanoma prognosis, as demonstrated in the MSLT-1 trial,[14] its efficacy and safety in head and neck melanoma[6,15,16] and its potential role in the selection of patients who may benefit from adjuvant therapy.

Lymph-node metastases were identified in 16.7% of the studied patients and in two patients were present in multiple lymph-node basins. These results are consistent with results of other groups: a positive SLN was identified in 19% of patients in the study by Evrard D *et al*[16] and in about 15.08% in the study by de Rosa N *et al*[17](median Breslow thickness 3.01 mm and 2.53 mm respectively).

Some authors report a high detection in SLNB with a successful technique occurring in more than 90% of the patients,[16,17] but in our study SLN identification was not successful in 20 patients (20.4%). This discrepancy can be explained because this study presents the results of a tertiary centre, which collects the most complex cases, and many patients had high actinic damage and underwent several previous surgeries that can alter the lymphatic drainage of the face and complicate SLN identification. Compared to other studies, this series collected an important number of melanomas in the periauricular area, close to the parotid lymph-nodes, which also could compromise SLN identification.

Redundancy of lymphatic system and complexity of SLNB contribute to the relatively high false-negative rate. One important limitation of this study is its retrospective design and also the inability to calculate the number of false negatives since in many cases it was not clear in which lymph node basin the relapse occurred. As mentioned above, the false-negative rate was inversely correlated with prognosis. If we add to these patients those who we were unable to identify SLN we get a group of patients which would benefit from a close surveillance.

The results about recurrence were not surprising, showing a significant difference between patients with positive and negative SLN in terms of locoregional and distant recurrence as expected.

CONCLUSION

The occurrence of lymph-node metastases remains one of the most important prognostic factors in the treatment of malignant melanoma and its diagnosis is absolutely essential. Head and neck cutaneous melanoma patients belong to a distinct group with a particular complexity in respect of SLNB technique. Redundancy of lymphatic system, multiple SLNs and SLN basins and lymphoscintigraphy limitations in SLN identification may contribute to higher rates of false-negatives, with its prognostic implications. From this perspective, all patients with cutaneous head and neck melanoma should be very closely monitored regardless of the presence of SLN metastasis.

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