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Sentinel lymph node biopsy for cutaneous melanoma in a real life setting: analysis of 47 cases treated at a private clinic in Brazil

Biópsia de linfonodo sentinela para melanoma cutâneo na vida real: análise de 47 casos tratados em clínica privada no Brasil

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ABSTRACT

Background: Sentinel Lymph Node (SLN) status has been shown to be the strongest independent prognostic factor of cutaneous melanoma (CM) stage I-II patients. Few papers on CM at private clinics (PC) are available.

Objective: To present clinical and histologic data, complications and frequency of SLN involvement in CM patients diagnosed and followed at a dermatology/cutaneous oncology PC in São Paulo/Brazil, who were submitted to SLNB.

Methods: Retrospective, single-center cohort of patients who attended PC from June 1998 to Jan 2020. Electronic files were selected and analyzed. Minimum period for considering the patient eligible was 1 year.

Results: 215 CM lesions were identified in 184 patients (1.2 melanoma/patient). Forty-seven patients (25.5%) were submitted to SLNB and 59 SLN for histologic examination (1.2 SLN/patient). 10,9% tested positive. SLN identification happened in 95.7%. In 38/47 (80,8%) patients single LBD was found, while multiple-LBD was found in 9/47 (19.1%). Eighteen (72,0%) out of 25 trunk lesions drained to single basin, while in 7 patients multiple LBD was found. Complication rate was 6,0%.

Conclusion: Percentage of CM patients that undergo SLNB, node positivity for metastasis, draining basins and complications in this study were similar to studies in northern hemisphere patients. Clinical and epidemiologic characteristics of CM patients differ markedly between PC and PHS patients.

Keywords: Biopsy; Melanoma; Sentinel lymph node

RESUMO

Introdução: O status do linfonodo sentinela (LNS) tem se mostrado o mais importante fator prognóstico independente no melanoma cutâneo (MC) em estágio I-II. Poucos artigos sobre MC em clínicas privadas (CP) estão disponíveis.

Objetivo: Apresentar dados clínicos e histológicos, complicações e frequência de envolvimento do LS em pacientes com MC acompanhados em CP de dermatologia/oncologia cutânea em São Paulo/Brasil, submetidos a biópsia de LS (BLNS).

Métodos: Coorte retrospectiva e unicêntrica de pacientes atendidos em CP de junho/1998 a janeiro/2020. Prontuários eletrônicos foram analisados. O período mínimo para considerar paciente elegível foi de um ano.

Resultados: Identificamos 215 MC em 184 pacientes (1,2 melanoma/paciente). No total, 47 pacientes (25,5%) foram submetidos à BLNS e 59 LN à exame histológico (1,2 LNS/paciente), sendo que 10,9% foram positivo. A identificação do LNS ocorreu em 95,7%. Dezoito (72,0%) das 25 lesões do tronco drenavam para cadeia única, enquanto em 7 pacientes drenavam para cadeias múltiplas. A taxa de complicação foi de 6,0%.

Conclusão: O percentual de pacientes com MC submetidos a BLNS, positividade de LS, cadeias de drenagem e complicações neste estudo foram semelhantes aos estudos em pacientes do hemisfério norte. As características clínicas e epidemiológicas dos pacientes com MC diferem acentuadamente entre os pacientes de CP e do serviço público de saúde.

Palavras-chave: Biópsia; Linfonodo sentinela; Melanoma.

Original Article

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BACKGROUND

Sentinel Lymph Node (SLN) status is the most decisive independent prognostic factor of cutaneous melanoma (CM) stage I-II patients.¹ Accurate assessment of the regional LN status by SLN biopsy (SLNB) is becoming even more critical in the era of novel effective adjuvant therapies for the microscopic nodal disease.² Some points on SLNB's role and benefit in this setting are still controversial.³

Most published papers on SLNB for CM analyze patients from the northern hemisphere and Australia, large hospitals, or public health system (PHS). Very few articles on CM patients diagnosed and followed at private clinics (PC) are available in the literature.⁴⁻⁸ We have not been able to find papers specifically addressing CM patients from PC who underwent SLNB, which leaves information gaps about what happens in this context.

OBJECTIVE

This study aims to present clinical and histologic data, describing complications and frequency of SLN involvement in CM patients diagnosed and followed at a dermatology/cutaneous oncology PC in São Paulo/Brazil. They were submitted to SLNB, and their data were compared with data from the literature.

METHODS

A retrospective, single-center study selected and analyzed the electronic files of a cohort of patients diagnosed with CM attending a PC from June 1998 to January 2020. Data collected consisted of gender, primary tumor's anatomic location, melanoma clinical type, Breslow thickness, and history of SLNB. Among those submitted to SLNB, we also assessed SLN status, lymph node basins drainage, number of excised SLN, surgical complications associated with SLNB, and eventual local or distant relapses.

The same surgical team, consisting of dermatologic and oncologic surgeons, operated on all but seven patients at different hospitals in São Paulo. Pathologists from the different hospitals where surgeries were performed determined SLN histologic status. After removal, SLN were submitted to serial sectioning and permanent preparations for histological and immunohistochemical examination, according to current recommendations at the time. SLN was identified using Tc-labeled radiopharmaceutical preoperative lymphoscintigraphy and subsequent in-

traoperative detection with gamma probe associated or not with blue-dye.

Follow-up was also based on information contained in the electronic charts. The minimum period for considering the patient eligible was one year.

RESULTS

A total of 215 CM lesions were identified in 184 patients (1,2 melanoma/patient). Forty-seven patients (25,5%) were submitted to SLNB, which harvested 59 SLN for histologic examination (1,2 SLN/patient). In 2/47 (4,2%) patients no SLN was identified. Five/47 patients (10,6%) tested positive.

Primary lesions that led to the indication of SLNB were located on the trunk (26), lower limbs (14), upper limbs (6), and head & neck (2) (Table 1). Pre-operative lymphoscintigraphy allowed identification of lymph node basins drainage (LBD) in all but one patient. In 38/47 (80,8%) patients single LBD was found while multiple-LBD was observed in 9/47 (19,1%).

Eighteen (72,0%) out of 25 lesions drained to single basins, while in 7 patients these lesions drained to multiple basins. Among them, there was a case where CM was located in the interscapular (midline) region and drained to 4 distinct basins (bilateral axilla and bilateral cervical) (Table 3).

Regarding surgical details, SLN identification happened in 95,7% (45/47) of cases. We observed complications four times (3 cases): one patient developed lower limb lymphorrhea and deep venous thrombosis, while two developed lymphorrhea. The complication rate was 6,0% (Table 2).

Thirty-nine patients were eligible for follow-up (at least 12 months). The follow-up period varied from 13 to 177 months. Total follow-up period for the 39 patients was 2410 months, with an average of 61,8 months. False-negatives were identified in 2 cases: 4,0% (per-protocol – PP: 2/47) or 5,1% (intention to treat – ITT: 2/39).

DISCUSSION

Eggermont¹ stated almost two decades ago that SLNB had utterly changed the management of primary CM. Accurate assessment of the regional LN status by SLNB has become even more critical in the present era of novel effective adjuvant

Table 1: Clinical and histologic data of 47 CM patients from PC submitted to SLNB

Gender (n=47)	Anatomical Site (n=47)	Clinical type (n=47)	Sentinel LN status (n=47)	Breslow (mm) (n=47)
M: 24	Trunk - 25	SSM - 29	Positive – 5 (10,6%)	<= 0,8 - 12
	Low limbs - 14	Nodular - 6		>= 0,8/<= 1,0 - 10
F: 23	Up limbs - 6	Acral - 4	Negative – 42 (89,4%)	>1,0 / <= 4,0 - 18
	H&N - 2	LM / LMM - 0		> 4,0 - 6
		Other - 8		ND - 1

Subtitle: H&N – head and neck, SSM – Superficial Spreading Melanoma, LM – Lentigo Maligna LMM – Lentigo Maligna Melanoma, ND – not determined.

Table 2: Data from 47 CM patients from PC who underwent SLNB and world literature

Author - Year	Country	Patients studied (n)	SLN identification (%)	Positive SLN (%)	Complications (%)
Present study 2020	Brazil	47	95,7	10,6	6,4
Nelson <i>et al.</i> 2017 ⁹	Multicenter	2483	Nm	17,4	nm
Duprat <i>et al.</i> 2016 ¹⁰	Brazil	633	Nm	16,1	nm
Rovere <i>et al.</i> 2016 ¹¹	Brazil	62	Nm	12,9	nm
Morton <i>et al.</i> 2014 ¹²	Multicenter	1165	Nm	18,9	nm
Bañuelos <i>et al.</i> 2015 ¹³	Spain	69	98,5	33,8	4,4
Beger <i>et al.</i> 2013 ¹⁴	Germany	201	94,4	16,4	5,5*
Kunte <i>et al.</i> 2010 ¹⁵	Germany	1049	97,2	24,9	nm
Debarbieux <i>et al.</i> 2009 ¹⁶	England	455	Nm	21,5	nm
Koskivuo <i>et al.</i> 2007 ¹⁷	Finland	305	Nm	16,4	nm
Cecchi <i>et al.</i> 2006 ¹⁸	Italy	111	100	15,3	nm
De Vries <i>et al.</i> 2005 ¹⁹	Netherlands	300	99	28,3	7,0
Arens <i>et al.</i> 2003 ²⁰	Germany	381	95,8	25	nm

Subtittle: nm – not mentioned, * head & neck and Breslow > 4,0 mm patients excluded.

Table 3: Draining lymph node basins in 25 CM PC patients with truncal lesions

Single Basin (n=17)	Multiple basins (n=7)	Basin not identified (n=1)
Axilla - 16	Axilla + cervical - 2	
	Axilla bilateral - 2	
	Axilla + chest wall - 1	
Inguinal - 1	Inguinal bilateral - 1	
	Bilateral axilla and bilateral cervical -1	
Total: 17(68,0%)	Total: 7 (28,0%)	Total: 1 (4,0%)

immuno and targeted therapies for the microscopic nodal disease.²

The present study performed the histologic processing of the SLNs harvested at different hospitals, by different pathologists, for over 20 years. In each case, samples were processed according to current international recommendations at the time. Technical details varied over the period. This lack of standardization in the SLN assessment could be understood as a negative point – which might be so if the objective was to conduct a controlled study. This non-standardized methodology used in the study for 22 years by different pathologists in various hospitals reflects the “real-life” situation, which was the paper’s objective.

The percentage of identified and excised SLN among the 47 patients reached 95,7% with an averaged of 1,2 SLN/patient, a number in concordance with international literature (Table 2).

The number of papers reporting on CM patients followed at PC is extremely small.^{5-8,19} As early as 1997, Castro *et al.*⁸ demonstrated that in Brazil, the proportion of Caucasians in dermatology PC and Public Health System (PHS) patients differs markedly. Other Brazilian authors corroborated this finding. It is probably justified by historical aspects and the immense racial diversity in the country, where miscegenation makes its popu-

lation unique, including Caucasians, Africans, Asians, and indigenous Brazilians.^{21,22} Thin CM (Breslow $\leq 1,0$ mm) is diagnosed in a much higher proportion among PC population.^{8,19,21} CM patients studied in the present study tend to have characteristics that resemble northern hemisphere CM patients. In contrast, there is a higher proportion of non-Caucasian patients with acral located, thick and ulcerated lesions among PHS population. Similar findings are also observed in Chile and Mexico.^{5,23}

Murali *et al.*²⁴ found 6.7% positivity for metastatic melanoma cells in SLN when analyzing 432 patients with thin (≤ 1 mm) CM. Although there is a low but significant rate of SLN positivity in patients with primary CM of 0.51 to 1.0 mm in thickness, no SLN positivity was detected in the present study’s patients with primary tumor thickness of $\leq 0,48$ mm.

The high number of Breslow $< 0,8$ mm patients submitted to SLNB (12/47 – 25,5%) deserves comment: criteria indicative of SLNB varied during the study period. The presence of mitosis and regression would be decisive to indicate SLNB at some point in time and nowadays is no longer so.²⁵ In the present study, different reasons justified SLNB for Breslow $< 0,8$ mm patients: regression was identified in 5 cases, 1 acral lesion, 1 lesion with satellitosis, 2 of mitotic rate > 1 , one incomplete shave

biopsy, where Breslow thickness was determined as “at least”, 2 cases where patients demanded to have the surgery for their own will.

Skip metastases

Skip metastases are one of the most significant drawbacks of the method and can be found at different rates. The present study identified two cases. The first was a truncal CM with Breslow thickness 4,5mm and Clark level IV draining to the left axilla. The SLN tested negative for metastases. Ten years later pulmonary and intestinal metastases were identified and quickly led the patient to death. The second was also a truncal CM with Breslow thickness 5,85 mm and vascular invasion draining to both inguinal basins. The three SLN tested negative for metastases. Two years later, cerebral metastases were identified.

Draining basins

Preoperative lymphoscintigraphy has proved to be a vital planning instrument to guide complete removal of all SLNs, mainly when the primary lesion is located on the trunk, as found in the present paper, where 7 out of 25 (28,0%) patients had more than one drainage basin identified (Table 3). Truncal CM presents multiple-LBD from 17% to 34,6% of cases, especially when the lesion is mid-line. The present study associated double axillary/cervical and bilateral axillary drainage with upper back lesions.

The significance of multiple-LBD in truncal melanoma patients undergoing SLNB has long been debated. Currently, it is widely accepted that multiple-LBD is not an independent risk factor for SLN metastasis and has no independent prognostic significance. Among matched pairs, multiple-LBD did not affect rates of LN metastasis overall survival, overall recurrence, locoregional recurrence, or distant recurrence.²⁶⁻²⁸

Complications

SLNB is an invasive procedure and is not free of risks. Complications and sequelae are far less common when compared to complete LN dissection. Wrightson et al. reported on a total of 2120 patients submitted to SLNB. Overall, 96 (4.6%) of them developed major or minor complications. In contrast, 103 (23.2%) of 444 patients experienced complications when SLNB was followed by complete LN dissection, a number five times higher.²⁹

CM complication rates reported after SLNB are highly variable in the literature, ranging between 1.8% and 29.9%.³⁰⁻³² In a systematic literature review, Moody et al.²⁵ found an overall complication rate of 11.3% among SLNB patients, most temporary. Incidence of infection was 2.9%; seroma, 5.1%; hematoma, 0.5%; lymphedema, 1.3%; and nerve injury, 0.3%.

The frequency of complications observed in the present study (6,0%) fits the interval described in Moody et al. review paper.²⁵ One patient developed lower limb lymphorrhea and deep venous thrombosis, while two developed lymphorrhea.

CONCLUSION

Despite the relatively small number of patients studied, we could observe that data obtained from CM patients at PC submitted to SLNB closely resembled those described in northern hemisphere patients regarding the percentage of individuals that undergo SLNB, node positivity for metastasis, age, draining basins, and complications.

Clinical and epidemiologic characteristics of CM patients in Brazil differ markedly between PC and PHS population. The present study's findings are restricted to CM Brazilian patients from PC and should not be extrapolated to Brazilian patients from the PHS. ●

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