Lymph Node Biopsy Results for Desmoplastic Malignant Melanoma

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Desmoplastic malignant melanoma (DMM) is a rare variant of melanoma with distinct histopathologic and clinical features. Compared with other melanomas, the desmoplastic variant demonstrates a greater frequency of local recurrence and a proclivity for tracking along nerves, but it poses a lower risk of distant metastases. Elective lymph node dissection and sentinel lymph node biopsy (SLNB) are commonly used tools for determining prognosis in thick melanomas. The role of these procedures for DMM remains unclear. This study was designed to characterize DMM and determine the frequency of histologically positive lymph nodes in patients with DMM. This retrospective chart review included patients with DMM treated by Johns Hopkins Hospital (JHH) physicians between 1998 and 2003. Among the 28 patients included in the study, 18 patients had biopsies performed on lymph nodes (15 SLNBs and 3 radical neck dissections). One patient had a sentinel lymph node with histology positive for DMM. All others had negative results from histology and S100 stains. This study suggests that the frequency of positive SLNBs in DMM may be substantially lower than that of other melanomas.

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Desmoplastic malignant melanoma (DMM), first described in 1971,[1] is a rare variant of melanoma that is histologically characterized by fascicles of atypical spindle-shaped cells, bands of fibrosis, and poorly defined margins.[2] Clinically, the lesions commonly have a benign appearance. Firm and scarlike, the lesions often are amelanotic.[3] The bland clinical appearance and difficult histology oftentimes delay the correct diagnosis. At the time of diagnosis, the lesions generally are quite deep, with reports of median tumor thickness ranging from 2.5 to 6.5 mm deep.[4,5] Most DMM cases are Clark level IV or V.[6]

The natural history and pattern of spread of DMM differs somewhat from other melanomas. Local recurrence and extension to adjoining areas is common. The tumor also has a particular affinity for invading nerves.[7] In contrast, distant spread is less common than in other melanomas in spite of the greater thickness of DMMs at diagnosis. Consequently, the 5-year survival rate for patients with DMM lesions greater than 4-mm deep has been reported as 61%, compared with only 40% for other melanomas.[6]

General guidelines for melanoma treatment recommend that a sentinel lymph node biopsy (SLNB) be considered for patients with melanomas at least 1-mm thick, as well as thinner lesions that are ulcerated or are at least Clark level IV.[8,9] This procedure provides important prognostic information for patients with melanoma. If lymph node metastases are present (stage III disease), distant metastases will develop in approximately 65% of patients and the 5-year survival rate decreases to between 24% and 65% (depending on the extent of regional nodal disease).[8]

The role of lymph node biopsies (LNBs) for staging DMM is not well-established. The frequency and pattern of metastatic spread differs from other melanomas. In the largest DMM study to date (280 patients), only 4% of patients with DMM had lymph node disease at presentation, whereas 20% of all patients with cutaneous melanoma had lymph node disease at presentation.[5] Other studies specifically addressing the use of SLNBs for DMM

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Table 1.

Demographics

Characteristic	Patients (N=28)
Age, y	
Range	36–90
Median	64
Sex, n	
Men	14
Women	14
Ethnicity, n	
Caucasian	27
Latino	1

have had variable results.[3,4,10-12] Findings from a systematic review provide rates of regional metastases for DMM between 0% and 18.8%.[13] In our study, 14 of 15 patients who received SLNBs and all 3 patients who received radical neck dissection had histologically negative results, suggesting that LNBs may have limited prognostic value for DMM.

Methods

For this retrospective study, the Johns Hopkins Hospital (JHH) dermatopathology database was searched for all reports with the term *desmoplastic malignant melanoma*. All patients with unclear diagnoses or alternative diagnoses were immediately excluded. Additionally, only patients who were treated at JHH were included. Because JHH is a tertiary care center, many of the patients were initially diagnosed elsewhere. Whenever possible, the original biopsy was reviewed at JHH, or diagnosis was confirmed based on tissue from surgical excision. The histologic diagnosis of DMM was based on the presence of atypical spindle cells, desmoplasia, and S100 positivity, as well as other characteristic features.

The JHH electronic record was searched for relevant data including demographics, clinical characteristics, melanoma risk factors, follow-up period, and outcomes.

Results

The patient population consisted of 14 men and 14 women, with a median age of 64 years (range, 36–90 years)(Table 1). Most lesions were located on sun-exposed skin, with 57% (16/28) on the head and neck. Several patients had risk factors for melanoma, including history of tobacco use (n=5) or a first-degree relative with melanoma (n=3), colorectal cancer (n=4),or breast cancer (n=2). One patient had a previous history of melanoma, 7 patients had had at least one basal cell carcinoma, and 7 patients had had other cancers. The median time from onset of symptoms to correct diagnosis was 2.5 years. Seven patients presented to JHH with local recurrences (at least 2 of which had been previously misdiagnosed). Biopsy results showed that 15 of 28 tumors extended to the deep margin. The median depth was greater than or equal to 2.3 mm (range, 0.54 to >11 mm). Nearly all were Clark level IV or V. Melanoma lesion characteristics are detailed in Table 2. The demographics (race, age, melanoma site) of patients in this study were similar to those of previous studies, though we report a slightly lower male-female ratio.[3,5] As found in most previous studies, we observed common local recurrence and direct extension but rare distant metastasis.[3,6]

Table 2.

Lesion Characteristics

Characteristic	Patients (N=28)
Location, n	
Head and neck	16
Upper extremity	7
Trunk	3
Lower extremity	2
Pigmentation, n	11*
Time from onset of symptoms to diagnosis, n	
<6 mo	4
6–11 mo	2
1–2 y	4
>2 y	11
Unknown	7
Tumors extending to deep margin of biopsy, n	15
Thickness, mm	
Range	0.54–11
Median	>2.3
Tumors with ulceration, n	2

*Number of melanomas noted to be pigmented.

Table 3.

Sentinel Lymph Node Biopsy (SLNB) Data

SLNBs attempted, n	17 (2 aborted)
Successful SLNBs, n	15
Radical neck dissections, n	3
Patients with ≥1 histologically positive lymph node, n	1

Of the 28 patients included in this study, 15 patients had an SLNB performed and 3 patients had radical neck dissections. Twelve of the patients receiving successful lymph node procedures had positive deep margins of biopsies with depth of invasion ranging from 0.54 to more than 11 mm.

In 17 of 18 patients, lymph nodes analyzed via histology and S100 staining results were negative. One patient had a positive sentinel lymph node by these measures, and notably this patient had a primary melanoma that was greater than 9.8-mm deep. One patient had had an SLNB performed at an outside institution that resulted in negative histology and S100 staining results but polymerase chain reaction positivity. The SLNB data are shown in Table 3.

Patient follow-up ranged from a single visit to a 5-year follow-up visit (median, 21 months) and is detailed in Table 4. At least one patient from this study is now deceased as a result of her melanoma. This patient had an original melanoma depth of 3.1 mm and regional subcutaneous lymph nodes with negative results; she ultimately developed metastasis to the lung and her disease was refractory to chemotherapy.

At the time of the most recent follow-up, 4 other patients were known to have extracutaneous disease. Two of these patients, both with a history of negative lymph node studies, developed brain involvement. One patient had extension from the orbit to the brain and cavernous sinus that was treated with aggressive surgical treatment including enucleation of the eye, as well as stereotactic radiosurgery and radiation treatments, and was without signs of recurrence one year posttreatment. The other patient with brain disease was likewise treated with stereotactic radiosurgery and radiation treatments, but outcome after treatment is unknown.

Two patients had evidence of local spread; one case involved the clavicle and local lymph nodes, and the other case had extensive soft tissue disease with possible involvement of underlying bone. The 23 remaining patients did not have evidence of extracutaneous disease at last follow-up visit (Table 4).

Comment

SLNB is becoming an increasingly accepted procedure for staging of melanoma and high-risk nonmelanoma cutaneous malignancies.[14-16] However, because the natural history of DMM markedly differs from other melanomas, the use of SLNB for this variant remains unclear. A study of 280 patients with DMM showed that, as compared with other melanomas, DMM has a lower rate of regional lymph node metastasis overall, despite much greater depth at initial presentation. In addition, patients with DMM have a lower rate of lymph node involvement at first recurrence.[5] Likewise, in a study of 45 patients with DMM, none of the patients developed lymph node metastases.[7] The pattern of spread and recurrence has been likened to that of a sarcoma, based on the tumor's local aggressiveness but low affinity for lymphatic spread.[4]

Six studies have reported the outcomes of LNBs with some conflicting results. The first 4 studies (published in 2001 and 2003) include a total of 90 patients receiving SLNB or elective LNB.[3,4,10,12] Of those patients, only 2 patients had lymph node involvement detectable on histologic examination. Livestro et al[17] reported 2 patients with positive lymph nodes among 25 patients with SLNB. In contrast, Su et al[11] reported that 4 of 33 patients without clinical evidence of metastasis had positive SLNBs. According to the latter report, the 12% positive rate of SLNB would warrant the procedure.[11] Our finding of only one patient with histologically positive lymph nodes among 15 patients who received SLNB and 3 patients who received radical neck dissection is consistent with the preceding 5 reports. Among the 7 studies, 166 patients in total received LNB, and only 9 patients (5%) had positive lymph nodes by histologic examination. This figure probably does not warrant the morbidity associated with LNB, even if the less aggressive SLNB is selected. Moreover, a substantial percentage of patients with positive lymph nodes have quite deep DMM, which warrants aggressive therapy, regardless of LNB results. Thus, the information from the LNB in these cases is of limited value. For example, the only patient with positive histology results in our study had a DMM depth exceeding 9.8 mm. One of the 2 patients in the earlier studies had a depth of 6.8 mm.[12] Moreover, although Su et al[11] reported no statistical difference, patients with positive lymph nodes did have deeper lesions on average (4.33 vs 3.98 mm).

Table 4.

Tumor Characteristics and Patient Follow-Up*

Patient No.	Tumor Site	Tumor Thickness, mm	SLNB or Radical Neck Dissection Performed?	Follow-up Duration, mo	Local Extension or Metastatic Disease?
1	Arm	2.2	Y (SLNB)	7	N
2	Forehead	3.1	N	55	Y, pulmonary metastases (deceased)
3	Arm	1.1	SLNB attempt aborted	0†	N
4	Forehead	>9.8†‡	Y (SLNB)§	2	N
5	Cheek	1.1	N	29	N
6	Back	>0.95‡	Y (SLNB)	1	N
7	Neck	>1.05‡	Y (SLNB)	25	N
8	Scalp	>4.5‡	N	1	Y, extension to soft tissue (possibly bone)
9	Cheek	>1.1‡	Y (SLNB)	8	N
10	Neck	>11‡	Y (neck dissection)	61	N
11	Scalp	3.4	Y (neck dissection)	9	Y, metastatic to LNs, clavicle, and skin
12	Eye orbit	9.0	Y (neck dissection)	35	Y, extension to brain
13	Scalp	>5.5‡	SLNB attempt aborted	47	N
14	Leg	>1.1‡	Y (SLNB)	26	N
15	Back	N/A	N	57	N
16	Arm	>1.0	Y (SLNB)	31	N
17	Arm	>3.5‡	N	0¶	N
18	Shoulder	>1.0‡	Y (SLNB)	1	N
19	Cheek	>4.0‡	Y (SLNB)	49	N
20	Cheek	3.3†	Y (SLNB)	27	Y, extension to orbit and brain/cavernous sinus
21	Scalp	>2.25‡	Y (SLNB)	41	N
22	Arm	>2.0‡	Y (SLNB)	42	N
23	Cheek	1.2	N	3	N
24	Forehead	2.65	N	39	N
25	Arm	>5.25‡	Y (SLNB)	4	N
26	Neck	2.0	N	0¶	N
27	Back	0.95	Y (SLNB)	17	N
28	Leg	0.54	Y (SLNB)	4	N

*LN indicates lymph node; SLNB, sentinel lymph node biopsy; Y, yes; N, no; N/A, not applicable.
†Ulceration.
‡Extension to deep margin of biopsy; depth of biopsy is listed.
§SLNB results identified the node as positive for desmoplastic malignant melanoma.
¶Single visit, no follow-up.

In contrast to the low frequency of lymph node spread, local recurrence and direct extension is remarkably high in DMM. Significant morbidity and mortality from DMM may be related to direct invasion of the nerves and particularly to extension to the brain by head and neck tumors. In one study, DMM of the head and neck greater than 4-mm deep had only a 38% survival rate, related in part to neurotropic spread.[6] In another study, despite a complete lack of clinical lymph node metastases in 42 patients, the authors observed local spread in 23 patients (55%) and distant spread to cranial cavity or lungs in 17 patients (40%).[7] In our study, most patient morbidity was related to local spread and direct extension to the brain, but only one patient developed distant spread to the lungs during our follow-up period. Based on these findings, Mohs micrographic surgery may be uniquely suited to the treatment of DMM and may serve as an alternative to SLNB plus standard wide excision. The tumors of DMM tend to extend well beyond the clinically visible borders, and Mohs micrographic surgery is well-suited to approximate the true borders of the tumor. Thus, margins may be taken at the appropriate distance from these borders rather than those seen on the skin's surface. Follow-up studies would be necessary to confirm if Mohs micrographic surgery results in better outcomes than traditional wide excision for DMM.

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