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A second expert pathology review of cutaneous melanoma in multidisciplinary meetings: Impact on treatment decisions

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ABSTRACT

Melanoma causes substantial burden of medical costs and years of life lost. Wide variations in melanoma diagnosis and treatment have been identified at least in the United States, Australia, Germany, Italy and France [1]. The variation especially in the quality of reporting on pathological specimens has been reported. The aim of this retrospective study was to assess the impact of expert pathology review of melanoma on the staging and thus treatment decisions in cutaneous melanoma patients in a multidisciplinary tumor board.

A total of 567 patients were referred to the multidisciplinary meeting with a diagnosis of new invasive or in situ melanoma from 14.10.2014 to 31.5.2018. Among these patients, a second expert histopathologic review resulted in changes in interpretation for 46 out of 567 (8%) patients. Of patients originally diagnosed with melanoma, pathologic review led to a change in diagnosis to benign lesions in 19 cases. The Breslow thickness changed > 0.3 mm in 22 cases leading changes in staging and thus treatment. Minor changes (≤ 0.3 mm) in Breslow thickness was found in 5 cases.

Our data suggest that review of melanoma by an expert dermatopathologist results in frequent, clinically meaningful alterations in diagnosis, staging and surgical treatment. The confirmation of a cancer diagnosis should be the first step in the initiation of multidisciplinary monitoring especially in patients younger than 40 years old and early-stage tumors.

1. Introduction

Wide variations in melanoma diagnosis and treatment have been identified around the world, which has prompted concerns about equitable and timely treatment [1]. Review of histopathologic material by an expert dermatopathologist ensures that appropriate treatment is selected based on the preoperative assessment of pathology results [2]. Especially, review of early-stage melanoma histopathologic material may be of particular benefit to establish correct diagnosis. This information is critical because it defines the recommended surgical management for early-stage melanoma according to guidelines [3].

A trend towards thinner and less invasive melanomas has been observed during recent decades in both central Europe and Australia [4]. Of new cases diagnosed, 70% are thin melanomas (≤ 1 mm) [5]. In a statement of European partnership action against cancer consensus group (EPAAC) (2014), it was recommended that multidisciplinary teams (MDT) should monitor all new and recurrent cancer patients, and every case should be presented at a tumor board [2]. According to European cancer organization essential requirements for quality cancer care (ERQCC) (2018), early-stage melanoma lesions can be managed by a local dermatology unit that does not have the MDT, while all advanced cases should be seen in specialist melanoma centre [6]. Review of histopathologic material by an expert dermatopathologist is commonly performed in MDTs [3].

In our clinic the multidisciplinary melanoma meetings have been performed since 14th October 2014. In this retrospective study the impact of a second expert pathology review on the staging and thus treatment decisions in cutaneous melanoma patients in a Finnish regional university hospital population cohort was evaluated.

2. Materials and methods

A retrospective analysis was carried out reviewing the patient records of cutaneous melanoma cases assessed in the multidisciplinary

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cutaneous melanoma meeting from 14.10.2014 to 31.5.2018 in a Finnish regional university hospital (Tampere university hospital, the region's largest hospital and the tertiary referral centre of Pirkanmaa). The population in the Pirkanmaa region was 509 356 at the end of the study. In this study we sought to determine the impact of a second expert pathology review on the staging and treatment decisions in cutaneous melanoma patients. In addition, we also wanted to find out whether patient's age, gender or tumor Breslow thickness has the connection with changes in pathology review. Patients referred to the multidisciplinary meeting with a diagnosis of new invasive or new in situ melanoma were included in the study. Recurrent melanomas were excluded. In our hospital all invasive cutaneous melanomas in head and neck area are treated at the head and neck clinic with their own MDT and were not included in this study.

All medical records and the initial pathology report are sent from the referral centre (local dermatology clinic) to dermatologists and plastic surgeons at our skin cancer unit. An initial treatment plan is formulated prior to the MDT meeting. The original pathology slides are sent for expert pathology review. Slides are double read independently by two dermatopathologists blinded to the original pathology interpretation and the consensus is recorded. A final treatment plan informed by the expert pathology review is made at the MDT according to international current clinical guideline.

Permission to access the clinical records of the melanoma patients for the study was obtained from the scientific centre of Tampere university hospital. Using the patients' social security number, the clinical records of all patients were reviewed. The age and gender of the patient were recorded as well as location and Breslow thickness of the tumor. Changes in a second expert histopathologic review were categorized as follows: the diagnosis changed from malignant to benign, Breslow thickness changed > 0.3 mm, Breslow thickness changed ≤ 0.3 mm.

3. Statistical analysis

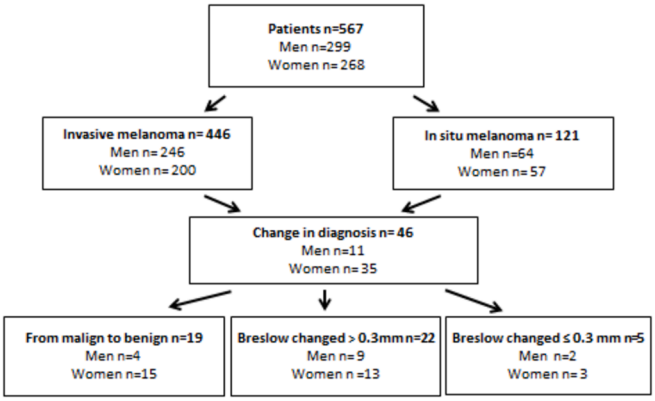
Differences between men and women were described by number of cases with percentages. Median age and median Breslow thickness were calculated.

4. Results

A total of 594 patients (women n = 280, men n = 314) were referred to the multidisciplinary meeting with a diagnosis of invasive, in situ (MIS) or recurrent melanoma from 14.10.2014 to 31.5.2018. Of these melanomas, 27 (women n = 12, men n = 15) were recurrent melanomas and were excluded, leaving 567 (women n = 268, men n = 299) patients in the study. Of these melanomas, 20% (121/567) were in situ melanomas and 80% (446/567) were invasive melanomas. The biopsy type was excisional in 88% (n = 501) of cases and punch biopsy in 12% (n = 66) of cases. The median age of patients was 67 years (IQR 54–75) and the median Breslow thickness of melanomas was 0.8 mm (min 0, max 17 mm). Among these patients, a second expert histopathologic review resulted in changes in interpretation for 8% (46/567) of patients (women n = 35, men n = 11). The flow diagram for the full sample is presented in Table 1. A change in diagnosis occurred in 11% (13/121) of those with in situ melanoma diagnoses at baseline, and in 7% (33/446) of those diagnosed with invasive melanoma at baseline. Furthermore, change in tumor stage occurred in 3% (16/567) of all patients. The median age of patients with misclassification was 57 years (IQR 38–71). The median Breslow thickness of melanomas with misclassification (initial diagnosis) was 0.96 mm (min 0, max 6 mm).

Of patients originally diagnosed with melanoma, pathologic review led to a change in diagnosis to benign lesions in 3% (19/567) cases. In these cases, the median age was younger; 36 years (IQR 27–43). Changes from malignant to benign was more common in women (6%,15/268) than in men (1%, 4/299). The changed diagnosis was most commonly Spitz nevus (n = 11), compound nevus (n = 6) and blue nevus (n = 2). The median Breslow thickness in these tumors (initial diagnosis) was 1.1 mm (min 0, max 3). Misclassification was not associated with location of the tumor. To nine of these 19 patients a sentinel node biopsy (SNB) would have been performed combined to re-excision according to first diagnosis. The detailed data is presented in Table 2.

Table 1
Flow diagram for the full sample.



The Breslow thickness changed > 0.3 mm in 5% (22/446) of cases (women n = 13, men n = 9) leading changes in staging and thus treatment in 9 cases. The median age of these patients was 65 years (IQR 52–74) and the median Breslow thickness (initial diagnosis) was 0.92 mm (min 0, max 6). Minor change (≤ 0.3 mm) in Breslow thickness was found in 5 cases (women n = 3, men n = 2). The median age of these patients was 83 years (IQR 63–85) and the median Breslow thickness was 0.3 mm (min 0, max 0.3). Changes in Breslow thickness are presented in Table 3.

Staging did not change in 2% (11/567) of cases. Fifteen out of 27 patients (56%) were upstaged; reasons for upstaging included findings of higher Breslow thickness or ulceration. The most of changes were seen in MIS, as nine cases with an outside diagnosis of MIS were upstaged to invasive melanoma. The detailed data of changes is staging are presented in Table 4a and b.

Table 2
Change from malignant to benign.

1st diagnosis/Breslow thickness (mm)	Diagnosis after 2nd review	Age (years)	Location
Women (n = 15, 5%)			
1.0	Spitz nevus	39	thigh
in situ	Spitz nevus	16	thigh
1.5	Compound nevus	37	foot
3.0	Spitz nevus	40	leg
in situ	Compound nevus	39	shoulder
0.9	Spitz nevus	37	arm
0.4	Compound nevus	47	arm
2.0	Blue nevus	30	buttock
1.4	Spitz nevus	29	back
0.5	Spitz nevus	36	back
1.2	Spitz nevus	22	foot
in situ	Spitz nevus	56	back
0.7	Spitz nevus	20	knee
in situ	Compound nevus	28	abdomen
1.4	Blue nevus	29	back
Men (n = 4, 1%)			
1.8	Compound nevus	35	toe
0.5	Spitz nevus	42	arm
0.6	Spitz nevus	43	chest wall
0.5	Compound nevus	30	chest wall

Table 3
Changes in Breslow thickness (> 0.3 mm and ≤0.3 mm).

	1st diagnosis/ Breslow thickness (mm)	Breslow thickness after 2nd review	Age/ years	Location
Women (n = 13, 5%)	0.9	1.5	74	shoulder
	1.0	1.9	54	leg
	in situ	3.0	60	foot
	1.0	0.6	48	back
	1.2	3.5	67	toe
	1.1	1.5	82	back
	in situ	0.4	76	back
	0.3	0.9	65	arm
	0.4	1.0	76	thigh
	0.4	0.9	45	arm
	in situ	0.5	22	abdomen
	in situ	0.7	71	back
	0.6	1.1	77	knee
Men (n = 9, 3%)	1.5	2.1	69	abdomen
	in situ	0.9	78	shoulder
	0.9	1.3	63	chest wall
	0.5	0.9	48	abdomen
	in situ	1.1	66	back
	0.5	0.9	59	chest wall
	6.0	10.5	50	leg
	2.0	3.2	52	finger
	0.5	0.1	57	back
Women (n = 3, 1%)	0.9	1.1	32	back
	0.5	0.7	72	back
	in situ	0.3	91	arm
Men (n = 2, 1%)	in situ	0.3	27	back
	in situ	0.2	71	abdomen

Table 4a
Change in AJCC tumor staging after a second expert pathology review of 27 cases with changes in Breslow thickness.

Tumor Stage	Referral pathology tumor stage		Tumor board pathology tumor stage	
	n	(%)	n	(%)
Tis (MIS)	9	(33)	1	(4)
T1A (< 0.8 mm, no ulceration)	12	(45)	14	(52)
T1B (< 0.8 mm, ulceration)	1	(4)	0	(0)
T2A (> 1.0–2.0 mm, no ulceration)	3	(11)	7	(26)
T2B (> 1.0–2.0 mm, ulceration)	0	(0)	1	(4)
T3A (> 2.0–4.0 mm, no ulceration)	2	(7)	4	(14)

Abbreviations: AJCC, American Joint Committee on Cancer; MIS, melanoma in situ.

Table 4b
Changes in staging groups after a second expert pathology review of 27 cases with changes in Breslow thickness.

Change in staging	Number of cases	(%)
Tis to T1a	7	(26)
Tis to T2a	1	(4)
Tis to T3a	1	(4)
T1a to T2a	4	(15)
T1a to Tis	1	(4)
T1b to T2b	1	(4)
T2a toT3a	1	(4)
No change in stage	11	(41)

5. Discussion

This study shows that review of melanoma by an expert dermatopathologist results in frequent and clinically meaningful alterations in diagnosis, staging and surgical treatment in cutaneous melanoma patients. This is in agreement with earlier study by Suzuki et al. (2018), whose findings suggested that second opinion by pathologists trained in melanocytic lesions is likely to show significant differences from the original report [7]. Although the rate of agreement with the referring diagnoses is quite high, misdiagnosing can result in unnecessary psychological distress and over or under treatment to the part of the patients. This possibility of mistreating according to initial diagnosis was also found in this study. Using tumor thickness as criteria for SNB, we identified that using a tumor thickness ≥0.8 mm, a change in recommendation in SNB was observed in 12 out of 27 cases. Furthermore, to nine out of 19 patients whose referral diagnosis of melanoma changed to benign SNB would have been performed combined to re-excision according to the initial diagnosis.

In addition to assess the impact of expert pathology review of melanoma on the staging and treatment decisions, we also wanted to find out whether patient's age, gender or Breslow thickness of the tumor have the connection with changes in pathology review. The importance of a second expert histopathology review especially in difficult pigmented lesions in the group of young patients younger than 20 years of age has been presented earlier [8]. We found that the median age (36 y) in the patients whose diagnosis changed from malignant to benign was lower than in patients with changed diagnosis (57y) or patients with changes in the Breslow thickness of the tumor (> 0.3 mm, 65 y and ≤0.3, 83 y). Change in diagnosis was also more common in women than in men. Of patients originally diagnosed with melanoma, pathologic review led most commonly to a change in diagnosis to Spitz nevus. This could be explained by the fact that some benign melanocytic lesions exhibit a wide spectrum of atypical histologic features simulating melanoma and are more frequent in younger patients [3]. The identification of this subset of patients who are at particular risk of misdiagnosis strongly supports the concept of referral of younger melanoma patients to a multidisciplinary tumor board.

The changes in diagnosis especially in early-stage melanomas have also been seen in earlier studies but the impact of expert pathology review has not been quantified [3]. In this study, the median Breslow thickness in tumors with changed diagnosis showed that most of the tumors were early-stage melanomas. Our data also revealed that the most of changes were seen in in situ melanomas. The review of lesions referred with a diagnosis of MIS resulted in change in diagnosis in 11% of all in situ patients, while change in diagnosis occurred in 7% of invasive melanoma cases. An outside diagnosis of melanoma in situ was most commonly upstaged to invasive melanoma. The change in diagnosis led to alterations in expected prognosis and in the recommended excision margins and SNB indications. A trend towards thinner and less invasive melanomas has been observed [4]. Of new cases diagnosed, 70% are thin melanomas (≤1 mm) [5]. Currently, most multidisciplinary melanoma care focuses on patients with advanced disease while patients with early-stage melanomas may be potentially overlooked [3]. According to our study, referral of MIS and thin melanoma histopathologic material to a second expert histopathology review may also be of particular benefit to establish correct diagnosis and staging.

Our study has several limitations. First, pathologic stage could be affected after expert review of recut slides as Breslow depth may be changed in recut sections. In this study, however, the original slide was requested from the reference laboratory. Second, interobserver variation in the histopathologic reporting of melanoma affects staging. Several studies have shown that despite the existence of well-established criteria for the diagnosis and microscopic staging of melanocytic lesions, there is still considerable disagreement among pathologists when faced with actual histologic specimens [9].

6. Conclusion

Our data demonstrate that review of melanoma by an expert

dermatopathologist results in frequent, clinically meaningful alterations in diagnosis, staging, and surgical treatment. The confirmation of a cancer diagnosis should be the first step in the initiation of treatment especially in patients younger than 40 years old and in early-stage melanomas.

Conflicts of interest

None declared.

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