Dermatology Practical & Conceptual

Junctional Nevus and Early Melanoma on Sun-Damaged Skin of the Head/Neck: a Clinico-Pathologic Challenge

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ABSTRACT

Introduction: Melanoma on the head/neck area can show subtle clinical, dermoscopic and histologic features at early stages, being difficult to differentiate from junctional nevi.

Objectives: This case series aims to raise awareness on the topic of misdiagnosis of early lentigo maligna as junctional nevi.

Methods: From the databases of three pigmented lesion clinics in Italy, Australia, and France, we retrieved all cases of lesions of the head/neck area with an initial histopathologic diagnosis

of junctional nevus (JN) or dysplastic junctional nevus (DJN) which subsequently recurred and were ultimately diagnosed as melanoma. Moreover, we also retrieved those cases with an initial diagnosis of JN/DJN made on a partial biopsy that were diagnosed as melanoma after complete surgical removal.

Results: Here we report 14 cases in which the initial histologic diagnosis was junctional nevus or dysplastic junctional nevus. The lesions recurred over time with a final diagnosis of lentigo maligna.

Conclusions: Clinicians should critically question a given histologic diagnosis of junctional or dysplastic junctional nevus on the head/neck area if the clinical or dermoscopic features are discordant. Clinico-pathologic correlation is the best way to increase diagnostic accuracy and optimize management for the patient.

Introduction

The clinical and histologic diagnosis of early melanoma on sun-damaged skin of the head/neck area may be challenging. Lentigo maligna (LM) is the commonest melanoma subtype occurring on the head and neck region. Clinically, LM usually presents as a macule or patch of variable dimension and coloration, ill-defined borders and slowly grows over time [1-3]. Dermoscopically, atypical pseudo network with asymmetric perifollicular pigmentation, peppering and/or gray circles are found in classical cases.

LM is typically characterized histologically by a lentiginous and sometimes nested proliferation of atypical melanocytes arising in skin typified by sun damaged features of epidermal atrophy and solar elastosis.

Cases of LM lacking the typical clinical and histologic hallmarks can be challenging to diagnose.

From a clinical and dermoscopic point of view, the main differential diagnoses of LM include non-melanocytic benign lesions, such as solar lentigo, pigmented actinic keratoses and lichen planus-like keratoses (LPLK). Nevi are rarely included in the differential diagnosis of LM, since most nevi on the head/neck of adults and elderly are of the compound and dermal subtype. These nevi clinically present as dome shaped to nodular lesions, skin colored or only slightly pigmented [4].

In recent years, it has become increasingly recognized that LM can include a prominent nested component mimicking a junctional or dysplastic nevus. Zalaudek et al first reported one case of a lesion initially diagnosed as junctional nevus on the neck of an adult patient that recurred twice during a 4-year period, after apparent complete surgical excision with clear margins, and was ultimately diagnosed as LM [5]. Histopathologically, the diagnosis of LM can be challenging. In its early phases of development, LM may display subtle features, with only mild cellular atypia and a mixed junctional and lentiginous appearance of proliferating melanocytes with occasional nests [6,7]. In this report, we discuss the challenge of diagnosing facial atypical melanocytic tumors with nested and lentiginous components.

Objectives

With the aim of raising awareness on this clinico-pathologic challenge, we present a series of 14 cases all of which were initially diagnosed as atypical/dysplastic junctional nevi but were ultimately considered to represent melanoma. These include two main scenarios, namely the difficulty of diagnosing melanoma on a partial biopsy of suspicious lesions on the head/neck area, and the diagnosis of melanoma only after several recurrences of completely excised flat junctional lesions.

Methods

From the databases of three pigmented lesion clinics in Italy, Australia, and France, we retrieved all cases of lesions of the head/neck area with an initial histopathologic diagnosis of junctional nevus (JN) or dysplastic junctional nevus (DJN) which subsequently recurred and were ultimately diagnosed as melanoma. Moreover, we also retrieved those cases with an initial diagnosis of JN/DJN made on a partial biopsy that were diagnosed as melanoma after a complete surgical removal.

Information about patient demographic, lesion location, type of biopsy, and first and subsequent histopathologic diagnoses were recorded. In most cases, the initial biopsies were taken outside, and then the patient was referred to one of our specialized centers only after the lesion recurred. Given the difficulty to retrieve the material from the initial biopsies, central histologic review was not performed.

All cases had clinical and dermoscopic images taken before the final excision that led to the diagnosis of melanoma. Dermoscopic evaluation was conducted by consensus by two experienced dermoscopists (GB, CS). Follow up information was recorded when available.

Ethic committee approval was not required, this was analysis of datasets, where the data are properly anonymized.

Results

We collected 14 cases of pigmented lesions of the head and neck with an initial diagnosis of JN/DJN that were ultimately

Table 1. Demographic information of patients and history of lesions, including number of recurrences and type of initial biopsy.

Patient Id	Age at first excision	Sex	Lesion location	Type of biopsy (incisional=0; excisional=1)	First histologic diagnosis	Total number of recurrences	Final histologic diagnosis	Years from first biopsy
1	45	M	Scalp	1	DJN	1	LM	3
2	71	M	Right temple	1	DJN	1	LM	1
3	48	F	Chin	1	DJN	1	LM	2
4	37	M	Left cheek	1	JN	4	LM	12
5	60	F	Right eyelid	1	DJN	1	LM	1
6	51	F	Neck	1	JN	2	LM	3
7	53	F	Right cheek	1	JN	1	LMM 0.5 mm Breslow	9
8	45	M	Frontal	1	JN	1	LM	1
9	55	F	Right temple	1	DJN	1	LM	3
10	62	F	Right eyelid	0	DJN	2	LM	7
11	71	F	Left cheek	0	DJN	2	LM	7
12	53	M	Frontal	0	DJN	-	LM	1
13	89	F	Right cheek	0	DJN	-	LMM 0.2 mm Breslow	-
14	78	F	Scalp	0	DJN	-	LMM 0.2 mm Breslow	-

DJN = dysplastic junctional nevus; JN = junctional nevus; LM = lentigo maligna; LMM = lentigo maligna melanoma.

considered melanoma. We can recognize two main scenarios. Eleven cases had an initial diagnosis of JN/DJN and the final diagnosis of melanoma was made only after several recurrences (cases 1 to 11 in Table 1). The majority of lesions recurred ones after a complete surgical excision (N = 7; 63.6 %), in 3 (27.3%) cases there were 2 recurrences over time, in 1 case the lesion initially diagnosed as JN recurred 4 times after complete surgical excision, with a final diagnosis of LM 12 years after the first biopsy. Mean time from first biopsy to the latest recurrence for the 11 cases was 4.5 years (range 1-12 years).

The second scenario comprises three other cases in which the diagnosis of DJN was made on partial biopsy; however, because of suspicious clinical and dermoscopic features the lesions were excised, and the final diagnosis on the whole specimen was LM (case 12, table 1) and early invasive melanoma (cases 13-14, table 1). Clinical and demographic information of the cases are summarized in Table 1, as well as data on the type of biopsy and the total number of recurrences.

All lesions were flat pigmented macules. Dermoscopically most lesions had ill-defined borders (84.6%). Structureless brown pigmentation was present in six lesions (42.9%), while a black pigmented blotch was seen in 2 (14.3%) lesions. Gray globules were detected in six cases (42.9%). An atypical pseudo network was identified in five cases (35.7%), background erythema was seen in four lesions (28.6%), a regular pseudo-network was seen in three lesions (21.4%). In two lesions, moth-eaten borders were observed (14.3%). Gray circles were seen in one lesion (7.1%). None of them showed prevalent non-melanoma features [8].

Conclusions

The diagnosis of early melanoma involving the head/neck can be very difficult for both clinicians and pathologists. (9) Our series highlights this challenge that encompasses two main scenarios, namely, (i) the diagnostic underestimation following a partial (incisional) biopsy, and (ii) the problem of histopathologically inconspicuous features of very early melanomas that were completely excised.

Flat pigmented lesions of the head and neck are often large in diameter, or even if small in size, given their location, they are frequently biopsied with punch or partial shave biopsies to obtain a histologic diagnosis before performing larger excisions. In three cases in our series (cases 12-14, Table 1), the clinician decided to remove the lesion completely after an initial diagnosis of DJN was made on

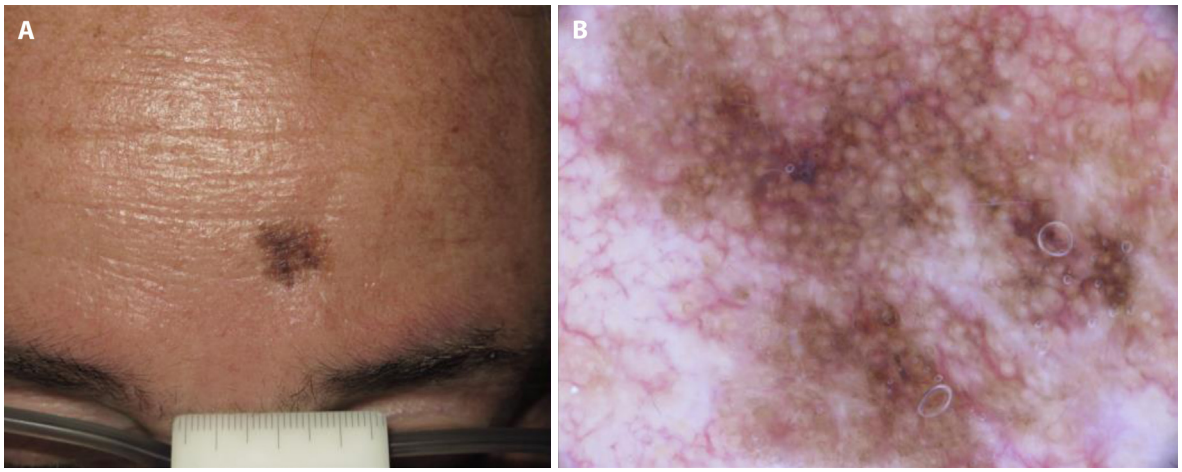

Figure 1. (A) A flat pigmented macule on the frontal region of a 53-year-old man. On an initial punch biopsy, the lesion was diagnosed as atypical junctional nevus. The lesion was left untreated for 1 year. The patient sought consultation because the lesion was enlarging in size. (B) In dermoscopy, pseudo-network and asymmetrically pigmented follicular openings are seen. Histologic diagnosis after a complete surgical removal revealed a lentigo maligna (case #12 from Table 1).

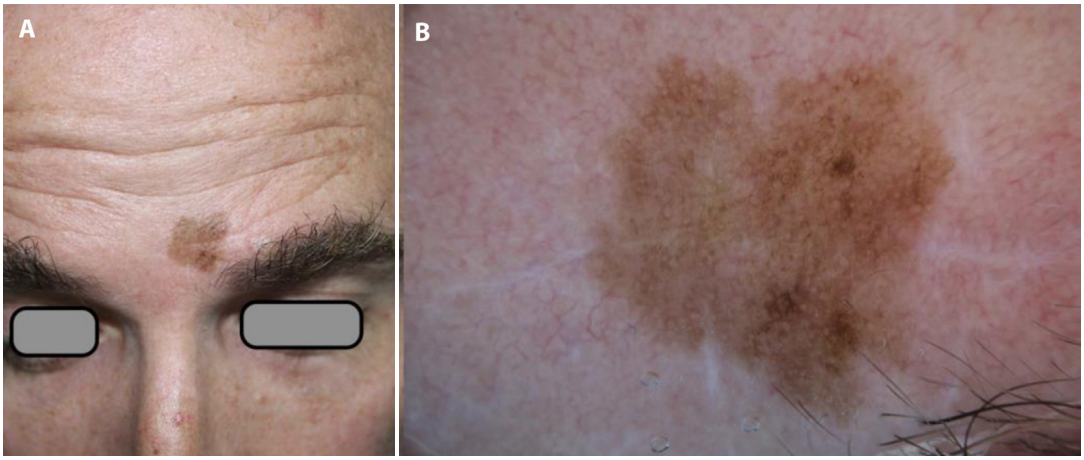

Figure 2. (A) A flat pigmented lesion on the frontal area in a 45-year-old man. The pigmented lesion was recurring one year after acomplete surgical excision, a scar is visible, the initial diagnosis was JN. (B) On dermoscopy brown pseudo network and gray circles were visible at the time of the recurrence. The lesion was excised with a final diagnosis of lentigo maligna (case #8 from Table 1).

partial biopsy. The lesions displayed features of melanoma at clinical and dermoscopic examination. In these 3 cases, the final histologic evaluation revealed LM and early invasive melanomas of the LM subtype (LMM) (Figure 1). These cases underline the need for clinicians to always critically evaluate a histologic diagnosis performed on partial biopsies in the clinical and dermoscopic context of the lesion. The final decision on patient management is in the hands of the clinician, who should be aware of the possibility of a diagnostic underestimation on a small biopsy sample of the given lesion either due to non-representative sampling or simply insufficient tissue to enable full evaluation of the lesion [5-9]. The histologic similarities between LM, LMM and DJN are well-known and can be difficult or impossible to distinguish on small biopsies and represent a recognized pitfall for pathologists [6,7]. Moreover, from an epidemiological point of view, junctional nevi are extremely rare in the adult/elderly population, the majority facial naevi in the adult are intradermal naevi of the Miescher type, clinically presenting as dome-shaped, hypopigmented or skin-colored nodules [10]. Clinicians should be aware of the possibility of diagnostic errors and should promote the best possible clinico-pathologic correlation for these cases. Of note, two of the partially biopsied lesions in our series were finally diagnosed as early invasive melanomas, which would have progressed, even if slowly, if left untreated.

In the other group (case 1 to 11, Table 1), we have a series of lesions with an initial diagnosis of nevus that, despite displaying very subtle features histologically, behaved as melanoma, recurring and growing after apparently complete surgical excision (Figure 2). The time to reach a definite diagnosis ranged from 1 to 12 years after the initial biopsy,

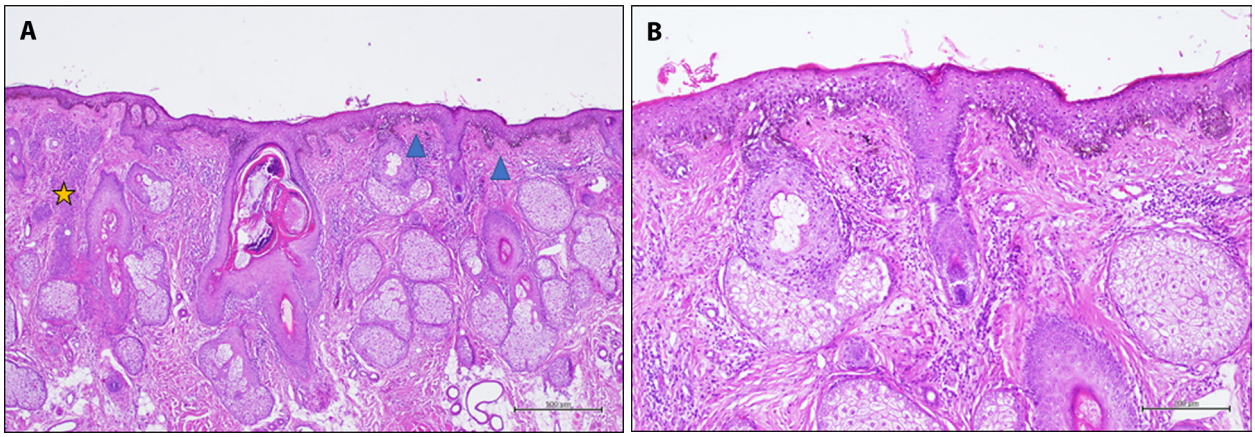

Figure 3. Histologic image of the case in figure 2. (A) Histology showing a lentiginous intraepidermal proliferation of melanocytes (right, blue arrowheads). A benign intradermal nevus is detectable on the left (yellow star) (H$E, original magnification 40x). (B) The melanocytic proliferation is arranged in a continuous lentiginous pattern (H&E, original magnification 100x).

with a mean time of 4.5 years and a number of recurrences after complete excision ranging from 1 to 4.

The scenario of completely excised junctional proliferations recurring over time and finally diagnosed as LM can be interpreted into different ways, namely precursor lesions or early phases of a neoplastic process. Some authors elaborated the concept of atypical junctional nevi being possibly melanoma precursors, acquiring malignant potential over time [11,12]. However, in our estimation a lesion showing the tendency to multiple recurrences after complete excision is most probably a very early phase of a neoplastic proliferation rather than a precursor lesion.

From a clinical point of view, these very initial lesions will probably never affect the patients' life expectancy. However, it is well known that melanoma prognosis depends mainly on Breslow thickness rather than the histologic subtype, and until now we do not have a reliable marker to predict which lesion will evolve to invasive melanoma [13-15].

One limitation of our study is that we did not review the histological slides from the initial biopsies. This was because they were mainly cases from other centers that were referred to us only after recurrence. However, the majority had only slight atypia also at the final histologic evaluation, as highlighted by Figure 3.

From a clinician perspective this case series aims to raise awareness on the topic of misdiagnosis of early LM. Clinicians should revise critically a given histologic diagnosis of JN, DJN on the head/neck area. The best possible clinico-pathologic correlation is the only way to increase diagnostic accuracy and assure the best possible management to the patient.

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