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Prominent Transepidermal Melanin Deposition Is a Distinguishing Histopathological Feature of Melasma: A Clinicopathologic Study

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Keywords

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Dear Editor,

Melasma and postinflammatory hyperpigmentation (PIH) are the most common causes of acquired hyperpigmentation. Melasma has been described as having increased melanin in all layers of

the epidermis [1–3], a “cap” of melanin pigment located over keratinocytic nuclei [2, 4], variable changes in melanocyte density, and an increase in dermal melanophages, mast cells, and solar elastosis [2, 4, 5]. PIH has been described as having variable changes in basal layer melanin deposition, variable changes at the dermal-epidermal junction, and an increase in dermal melanophages [3, 4]. Clinical presentation and history are the most important means of distinguishing melasma and PIH; however, these diagnoses are occasionally difficult to distinguish clinically, and validated histopathological criteria to differentiate between melasma and PIH in the literature are lacking. The purpose of this study was to histologically compare cases of melasma and PIH. Of the previously described histological attributes of melasma, we hypothesized that prominent melanin deposition in all layers of the epidermis, i.e., transepidermal melanin deposition, as detected by Fontana-Masson staining, would favor a diagnosis of melasma over PIH.

Cases of melasma and PIH diagnosed between July 4, 2010 and July 23, 2018 were sought from the pathology archives of Aurora Diagnostics Global Pathology (Miami Lakes, FL, USA) and the Brigham and Women's Hospital (Boston, MA, USA). Medical records, the site of biopsy, and/or clinical photographs were evaluated by a dermatologist (F.H.) to ensure the accuracy of the diagnosis. Cases with clinical presentations that were inconsistent with the histological diagnosis were excluded. In total, 30 biopsies (27 patients) of melasma and 37 biopsies (35 patients) of PIH were obtained and compared using the histopathological criteria listed

Fig. 1. Representative photomicrographs of melasma and postinflammatory hyperpigmentation. **a** PIH. H&E. **b** PIH. FM. **c** Melasma. H&E. **d** Melasma. FM. All pictures were taken at 200×. Prominent transepidermal melanin deposition is noted in the melasma sample but is absent in the PIH sample. PIH, postinflammatory hyperpigmentation. H&E, hematoxylin and eosin. FM, Fontana-Masson.

Table 1. Histologic comparison between melasma and postinflammatory hyperpigmentation (PIH)

	Melasma (<i>n</i> = 30)	PIH (<i>n</i> = 37)	<i>p</i> value		Melasma (<i>n</i> = 30)	PIH (<i>n</i> = 37)	<i>p</i> value
Age, years				Solar elastosis			
Mean	51.5	58.5	0.12	0	7	19	0.03
Sex				1	10	6	
Male	7	3	0.06	2	0	1	
Female	11	23		Not specified/undetermined	13	11	
Not specified/undetermined	12	11		Average score (0–2) ± SD	0.6±0.5	0.3±0.5	
Site				Vascular density and size			
Sun-exposed skin	17	24	0.04	0	5	6	0.72
Unexposed skin	1	12		1	7	13	
Not specified/undetermined	12	1		2	4	7	
Basket weave stratum corneum				Not specified/undetermined	14	11	
Present	28	34	1.00	Average score (0–2) ± SD	0.9±0.8	1.0±0.7	
Absent	2	3		Melanocyte density ^b (IHC with SOX10)			
Not specified/undetermined	0	0		0	0	1	0.33
Orthohyperkeratosis				1	7	17	
Present	2	3	1.00	2	0	8	
Absent	28	34		Not specified/undetermined	23	11	
Not specified/undetermined	0	0		Average score (0–2) ± SD	1.0±0	1.3±0.5	
Rete ridge effacement				Mast cells (IHC with CD117)			
Present	4	10	0.36	0	5	25	0.35
Absent	22	27		1	1	1	
Not specified/undetermined	4	0		2	0	0	
Dermal melanophages (FM)				Not specified/undetermined	24	11	
Present	20	31	0.36	Average score (0–2) ± SD	0.2±0.4	0.04±0.2	
Absent	8	6					
Not specified/undetermined	2	0					
Melanin cap (FM)							
Present	21	20	0.28				
Absent	7	14					
Not specified/undetermined	2	3					
Transepidermal melanin deposition ^a (FM)							
0	2	15	3.6×10 ^{−6}				
1	5	14					
2	21	5					
Not specified/undetermined	2	3					
Average score (0–2) ± SD	1.7±0.6	0.7±0.7					

H&E, hematoxylin and eosin. FM, Fontana-Masson. IHC, immunohistochemistry. SD, standard deviation. For the variables categorized as either 0, 1, or 2: 0 = none to minimally increased/normal, 1 = moderately increased, and 2 = markedly increased.

^aFor transepidermal melanin deposition, a score of 0 was given for no epidermal melanin or melanin localized only to basal layer, a score of 1 for melanin deposition present in suprabasal layers but only focally, and a score of 2 for multifocal presence of suprabasal melanin deposition.

^bMelanocyte density was determined using SOX10 immunohistochemistry and reflects the ratio of epidermal melanocytes to basal keratinocytes (MC/KC). 0 = MC/KC <0.05, 1 = 0.05 ≤ MC/KC ≤ 0.15, 2 = MC/KC >0.15.

in Table 1. Differences among variables were assessed using Fisher's exact test. Statistical tests were two-sided and used a significance threshold of $p < 0.05$.

As shown in Table 1, cases of melasma demonstrated a significantly greater degree of transepidermal melanin deposition ($p = 3.6 \times 10^{-6}$) and solar elastosis ($p = 0.03$) compared to cases of PIH on univariate analysis. After simultaneously adjusting for both biopsy site and skin phototype, an increase in transepidermal melanin deposition was still associated with the diagnosis of melasma (rather than PIH) on multivariate logistic regression analysis ($p = 0.02$). However, solar elastosis was no longer associated with melasma (rather than PIH) after controlling for these variables ($p = 0.20$). Representative photomicrographs are shown in Figure 1.

Melasma has been hypothesized to be due to hyperfunctional melanocytes activated by a trigger (e.g., UV irradiation) [1], and prominent transepidermal melanin deposition may represent the histologic correlate of this melanocytic hyperactivity. Other attributes that have been associated with melasma and PIH were not distinguishing features in this study [2–5].

The limitations of this study merit consideration. Given that melasma and PIH are essentially clinical diagnoses that require clinicopathological correlation in challenging circumstances, the final diagnoses were rendered only after reviewing histology as well as all available clinical information, including physical examination, clinical notes, and/or photographs.

Many of the histologic features attributed to diseases of hyperpigmentation reported in the literature are not unique and are shared by many disease entities [3, 4]. However, this study has shown that prominent transepidermal melanin deposition as detected by the Fontana-Masson stain – an accessible and inexpensive stain available in most laboratories – is a specific histologic feature of melasma and can support its diagnosis in the appropriate clinical context.

Key Message

Prominent transepidermal melanin deposition is a distinguishing feature of melasma compared to postinflammatory hyperpigmentation.

Statement of Ethics

This study was approved by the Institutional Review Board of the Brigham and Women's Hospital (Boston, MA).

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Farhaan Hafeez designed and executed the study and was principally responsible for writing the manuscript. Douglas A. Mata conducted the statistical analysis and revised the manuscript for important intellectual content. Christine G. Lian and Evangelos G. Poulos assisted in the design and execution of the study.

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