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The Importance of Eosinophilic Cytoplasmic Inclusion Bodies in Melanocytes as a Clue to Distinguish between Benign and Malignant Melanocytic Lesions

Azita Nikoo[1], Maryam Abdollahi[2], Zahra Hallaji[3]

[1]Associate professor, Department of Dermatopathology, Tehran University of Medical Sciences, Tehran, Iran, [2]Medical graduate, Department of Dermatopathology, Tehran University of Medical Sciences, Tehran, Iran, [3]Professor, Department of Dermatology, Tehran University of Medical Sciences, Tehran, Iran

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Maryam Abdollahi

ABSTRACT

Aim: Since early diagnosis and treatment of melanoma can significantly improve patients' prognosis, discovering new criteria to help differentiate between benign and malignant melanocytic lesions is of significance. In this study we aim to clarify the relationship between the presence of intracytoplasmic eosinophilic inclusion bodies inside melanocytes and the nature of the melanocytic lesion.

Methods: Medical records and pathology slides pertaining to 187 patients with melanocytic lesions who had undergone biopsy in Razi Hospital between March 2014 and March 2015 were gathered. Slides were re-examined by a dermatopathologist using a light microscope. Clinical and pathological data were analyzed using SPSS.

Results: A total of 196 specimens from 187 patients were studied. The median age of our patients was 42.26 years and 61.5% of them were female while 38.5% were male. The specific eosinophilic intracytoplasmic inclusion bodies were observed in 14 specimens; 8 of which were intradermal nevi and the remaining 6 were from compound nevi. These bodies tended to be present in lesions with congenital features. We found no correlation between age, sex or location of the lesion with the presence of aforementioned bodies.

Conclusion: Eosinophilic inclusion bodies present in the cytoplasm of melanocytes are associated with benign melanocytic lesions and are mostly observed in cells with abundant vacuolated cytoplasm and in lesions with congenital features. Therefore these bodies can be helpful in diagnosing benign and longstanding lesions and differentiating them from malignancies.

INTRODUCTION

The incidence rate of melanoma, the most lethal neoplasm of the skin, has been on the rise for the past few decades. It has been proven that early diagnosis and treatment of melanoma can lower the associated mortality rates in a dramatic fashion.

Up until now, different clinical and histopathological features have been suggested to be helpful in differentiating benign melanocytic lesions from melanoma.[1]

The presence of multinucleated melanocytes has been previously reported in different types of melanocytic lesions such as melanocytic nevi, Spitz nevi, Miescher's and Unna's nevi and melanoma (both in-situ and invasive).[1-14] However, the distinctive eosinophilic intracytoplasmic inclusion bodies that we focused on in this study have only been described recently.

In 2002, Gottlieb first described these distinct eosinophilic inclusion bodies inside the cytoplasm of melanocytes pertaining to congenital and acquired melanocytic nevi.[14] Shon et al. carried out an immunohistochemical and ultrastructural study on 3 melanocytic nevi and 1 Spitz nevus containing these inclusion bodies and

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Corresponding Author:
Maryam Abdollahi, MD, Medical graduate, Department of Dermatopathology, Tehran University of Medical Sciences, Razi Hospital, Vahdate-Eslami Square, 1199663911 Tehran, Iran. Mobile no: 0098-9126161954, E-mail: maryam.abdollahi7@gmail.com

observed that these bodies were more likely to be found inside melanocytes with abundant vacuolated cytoplasm, were non-membrane bound and their diameter was between 4 and 7 micrometers.[9] Finally in 2012, Patino et al. described that in their experience these inclusion bodies tended to be present inside vesicular multinucleated melanocytes and were exclusively found in benign melanocytic nevi of long duration.[10]

In this study we chose a variety of different types of melanocytic lesions and searched for aforementioned inclusion bodies in them. Our goal was to distinguish the association between these inclusion bodies and the nature of the melanocytic lesions containing them. Up until now no study has had such a large number of specimens inspected for these distinct inclusion bodies.

METHODS

In this cross-sectional study, we reviewed the medical records and pathology reports and slides of 187 patients (a total of 196 specimens) with different types of melanocytic lesions who had undergone biopsy between March 2014 and March 2015 in Razi Hospital, Tehran University of Medical Sciences, Tehran, Iran. Our patients were all of Caucasian descent (Fitzpatrick III or IV skin types). Clinical data including age, gender and location of the lesion were collected. Pathological slides were re-examined by a dermatopathologist using a light microscope to determine the presence of eosinophilic intracytoplasmic inclusion bodies inside melanocytes. Presence of congenital pathologic features such as neurotropism, vasculotropism and folliculotropism in the lesions was also recorded.

RESULTS

A total of 196 specimens from 187 patients were examined. One hundred fifteen of our patients were female (61.5%) and 72 were male (38.5%). The mean age of the patients was 42.26 years old (±21.8) and their age range was between 3 and 93 years.

The most frequent type of melanocytic lesion was intradermal nevi that comprised 54 specimens (27.6%). We also had 43 specimens of melanoma and 35 compound nevi. The frequencies of different types of lesions have been summarized in Table 1. Fifty two of the specimens had congenital features. (26.5%)

In total, cytoplasmic eosinophilic inclusion bodies were found in 14 specimens; 8 of them were intradermal nevi while the remaining 6 were compound nevi. Inclusion bodies were not observed in any other type of lesion. (Table 1) We detected these bodies in both mononucleated and multinucleated melanocytes. (Figures 1 and 2) Smaller bodies were basophilic while larger ones tended to be eosinophilic.

Table 1: Frequency of different types of melanocytic lesions and inclusion bodies

	Frequency of lesion	Percentage of lesion	Frequency of inclusion bodies
Intradermal nevus	54	27.6	8
Melanoma	43	21.9	6
Compound nevus	35	17.9	0
Blue nevus	24	12.2	0
Dysplastic nevus	16	8.2	0
Melanoma in-situ	11	5.6	0
Spitz nevus	7	3.6	0
Ota nevus	5	2.6	0
Ito nevus	1	0.5	0
Total	196	100	14

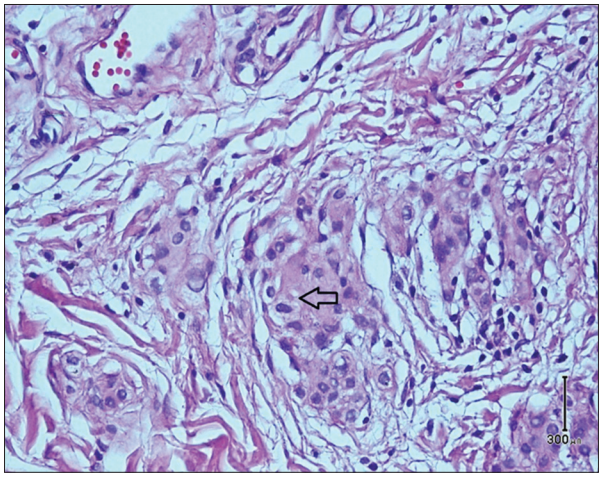

Figure 1: A round to oval eosinophilic cytoplasmic inclusion body is depicted inside a melanocyte pertaining to a melanocytic nevus. (Original magnification ×400)

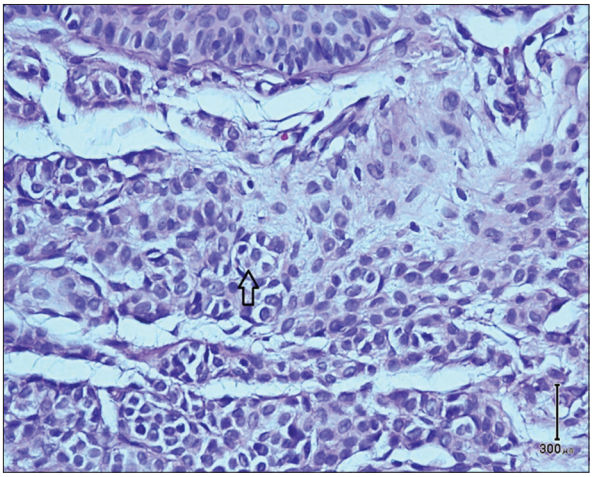

Figure 2: Arrow shows an esosinophilic cytoplasmic inclusion present inside a multinucleated melanocyte from a common melanocytic nevus. (Original magnification ×400)

According to the analysis of our results there is a significant correlation between the presence of cytoplasmic eosinophilic inclusion bodies in melanocytic lesions and their pathological diagnosis (P value = 0.023).

Out of the 14 lesions that contained inclusion bodies, 9 of them showed congenital features. There is also a significant correlation between the presence of inclusion bodies and congenital features in a lesion (P value =0.002).

We found no significant associations between the presence of these inclusions and the location of the lesion, age or sex of the patients.

DISCUSSION

We observed distinct eosinophilic cytoplasmic inclusion bodies inside melanocytes pertaining to compound and intradermal melanocytic nevi. These cells mostly had abundant vacuolated cytoplasms. These findings are compatible with those mentioned by Gottlieb in 2002 which was the first time these inclusion bodies were reported in literature. In that study, inclusion bodies were detected inside multinucleated melanocytes of melanocytic nevi.[14] Shon et al. performed an immunohistochemical study on a variety of melanocytic lesions; non-membrane bound inclusion bodies ranging between 4 and 7 micrometers in size were observed inside mostly multinucleated melanocytes of 1 Spitz nevus and 3 common melanocytic nevi.[9] Patino et al. also reported these bodies exclusively in vesicular melanocytes of common nevi.[10]

We did not detect these inclusion bodies in any other type of melanocytic lesions which is in line with finding by Shon et al. who also did not find inclusions in an additional 10 specimens of Spitz nevi, 25 specimens of melanoma and 4 blue nevi. Interestingly we studied 7 specimens of Spitz nevi and none of them contained inclusion bodies while Shon et al. reported them inside 1 out of their 11 Spitz nevi.[9]

We found inclusion bodies in both mononucleated and multinucleated melanocytes while Patino et al. only reported them in multinucleated cells.[10] Shon et al. noted that there is a correlation between multinucleation and the presence of these inclusion bodies.[9]

In this study we found a relationship between the presence of congenital features in the lesion and occurrence of these distinct inclusions. Patino et al. also noted that they had observed these bodies mostly in nevi of long duration with congenital features. Even when melanoma was formed upon a melanocytic nevus, inclusion bodies were confined to areas of the lesion still containing benign cells and nevic nests. They were not detected in parts where malignant melanoma cells were present.[10] All 3 melanocytic nevi containing inclusion bodies studied by Shon et al. had congenital features.[9]

We also tried to elaborate the relationship between the presence of inclusion bodies and patients' age, gender and location of the lesions; an effort that had not been made before this. The results of our analysis showed no significant correlation between aforementioned parameters and the presence of inclusion bodies.

Patino et al. noted that early inclusion bodies were mostly gathered in conjunction with melanosomes which could hint that they originate from degenerated melanosomes.[10] However, Shon et al. reported that inclusion bodies were non-membrane bound, making that theory less likely. Yet Shon et al. reported positive ubiquitin immunoreactivity of inclusions which can direct us toward a degenerative process.[9]

CONCLUSION

In short, eosinophilic cytoplasmic inclusion bodies inside melanocytes have only been observed in benign melanocytic lesions. These bodies tend to be found in congenital nevi with cells containing abundant vacuolated cytoplasms.

Based on this study and previous articles it can be concluded that the presence of these inclusion bodies can be used to distinguish benign melanocytic lesions from malignant ones.

Further investigations are suggested in order to determine the source of these inclusion bodies and to elucidate the processes that result in their formation.

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