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Plasma Cell Infiltrate in Common Acquired Melanocytic Nevus

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SUMMARY The presence of plasma cells in melanocytic lesions has been considered in literature as a sign of concern, when evaluated in the appropriate context. Plasma cells have been evaluated in halo nevus, but they are not frequently reported in non-halo common acquired nevus. Our claim was to study how common and frequent plasma cells are in the latter type of nevi. Therefore, we examined 280 of these nevi and selected the cases with an inflammatory infiltrate, even if mild. We then looked for plasma cells in the inflammatory infiltrate in the hematoxylin-eosin routine sections and selected 17 cases in which plasma cells (even if only occasional) could be found in the hematoxylin-eosin staining. Out of these 17, plasma cells were easily found in four cases, which were then further studied with immunohistochemistry for epithelial membrane antigen. The percentage of plasma cells varied in these four cases from 0.5% to 7%. No relation between the amount of plasma cells and either the location of the nevus or the location of the inflammatory infiltrate could be established. We conclude that the main point of this study is not to trust the presence of plasma cells as a solid criterion on its own, when evaluating a melanocytic lesion.

KEY WORDS: plasma cell, melanocytic nevus, epithelial membrane antigen

INTRODUCTION

The presence of plasma cells in the inflammatory infiltrate of a melanocytic lesion is not a trivial finding and, depending on the context, can be quite meaningful. When found in a melanoma, for instance, plasma cells have been demonstrated to have a prognostic value (1-5): an infiltrate rich in plasma cells correlates adversely with the possibility of metastasis.

Moreover, plasma cells have also been suggested as a diagnostic clue in the differential diagnosis between benign and malignant melanocytic lesions: halo nevus usually shows only a discrete number of plasma cells (6,7). Thus, a melanocytic lesion which looks like a halo-nevus but in which plasma cells are numerous should raise concern for melanoma. On the contrary, a low amount of plasma cells does not necessarily exclude melanoma: the inflammatory infiltrate that is evidenced in melanoma regression usually has a few plasma cells (8).

Plasma cells can also be of diagnostic value in the differential diagnosis between desmoplastic Spitz nevus and desmoplastic melanoma; the former nearly always lacks plasma cells (9).

We wanted to study something which is hardly ever mentioned in the literature: how abundant plasma cells are in the inflammatory infiltrate of innocent-looking acquired non-halo nevi. We also wanted to investigate if plasma cells were distributed according to any preferential pattern (band, perifollicular, etc.).

MATERIAL AND METHODS

We examined 280 melanocytic nevi of patients who did not have a clinical halo phenomenon. The nevi were classified according to the eponymic designation that had been previously proposed in the literature (10-12).

From these, we selected those with an inflammatory infiltrate, even if mild. We then looked for plasma cells in the inflammatory infiltrate in the hematoxylin-eosin routine sections and selected those cases in which plasma cells (even if only occasional) could be found in the hematoxylin-eosin staining. The cases in which plasma cells were more easily found, were also studied by immunohistochemistry with epithelial membrane antibody (DakoCytomation, monoclonal mouse antihuman, isotype Ig2a, kappa, immunogen: fat globule membranes from human milk; clone E29, code N1504) in order to quantify better the amount of plasma cells. The percentage of plasma cells in relation to the rest of the inflammatory cells was evaluated in all cases in which immunostaining was performed.

RESULTS

From the 280 nevi examined, we found some inflammatory infiltrate (even if mild) in 41 (14.64%) cases. Of these, plasma cells were occasional in 17 cases in the hematoxylin-eosin slides. Table 1 shows clinical details of these 17 cases, with the location and histologic type of the nevi. In these 17 cases, the distribution of the infiltrate was mainly perivascular superficial in 11 cases, perivascular superficial and deep in 1 case, perifollicular in 3 cases, peri-infundibular in 1 case, and peri-infundibular plus perifollicular in 1 case.

In four cases (cases 1, 2, 3 and 5), plasma cells were found more easily with the hematoxylin-eosin staining (Fig. 2). In these latter four cases, the immunohistochemical study was useful in standing out the plasma cells (Fig. 2). In the total amount of inflammatory cells, plasma cells accounted for a percentage that varied between 0.5% (case 3) and 7% (case 5) (Table 1, Fig. 3).

Table 1. Clinical and morphological details of cases presenting plasma cells in inflammatory infiltrate

Case No.	Sex	Age (yrs)	Location	Type of nevus	Inflammatory infiltrate distribution	Percentage of plasma cells in the infiltrate
1	Female	70	Nose	Miescher	Perifollicular & peri-infundibular	1
2	Female	68	Neck	Unna	Perifollicular	5
3	Female	35	Right leg	Clark	Perivascular superficial	0.5
4	Female	46	Back	Clark	Perivascular superficial	NS
5	Female	46	Nose	Miescher	Perivascular superficial	7
6	Female	25	Back	Miescher	Perivascular superficial	NS
7	Male	32	Back	Clark	Perivascular superficial	NS
8	Female	24	Back	Clark	Perivascular superficial	NS
9	Female	48	Neck	Unna	Perifollicular	NS
10	Male	72	Face	Unna	Perifollicular	NS
11	Male	59	Back	Clark	Perivascular superficial	NS
12	Female	29	Abdomen	Clark	Perivascular superficial	NS
13	Female	33	Retroauricular area	Unna	Perivascular superficial	NS
14	Female	51	Face	Unna	Perivascular superficial & deep	NS
15	Female	49	Face	Miescher	Periinfundibular	NS
16	Female	59	Face	Miescher	Perivascular superficial	NS
17	Male	26	Scalp	Miescher	Perivascular superficial	NS

NS=not studied

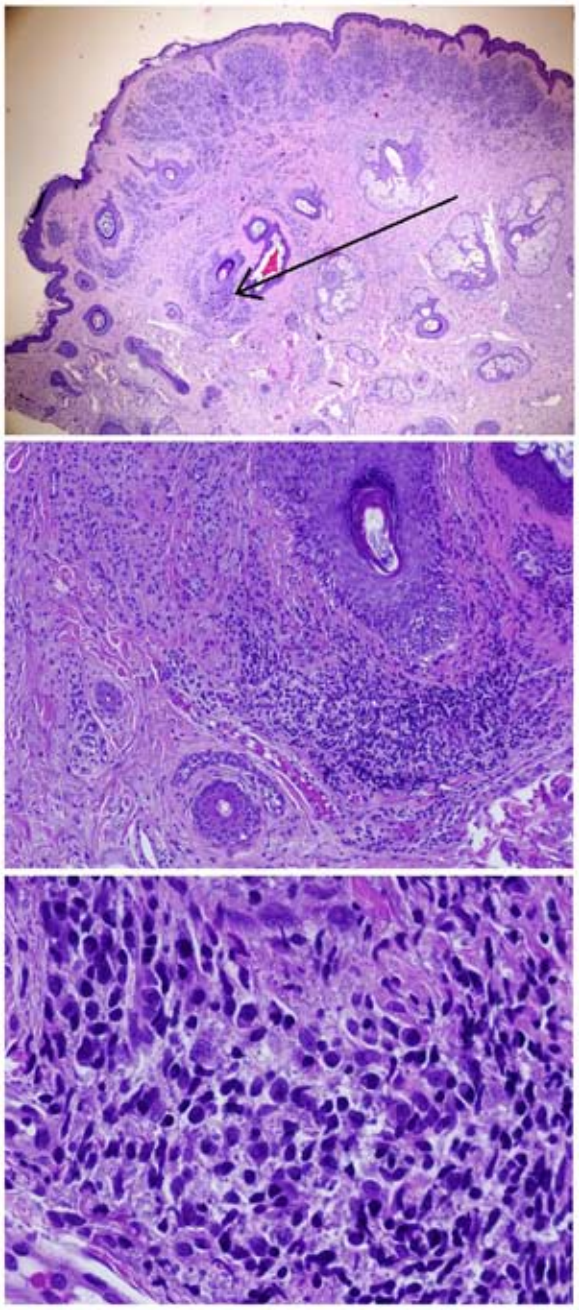

Figure 1. Case 2 in which a mild inflammatory infiltrate was seen in a perifollicular location (top, arrow), but mixed with nevus cells in the deep reticular dermis (middle). When examined at high magnification, plasma cells were easily identified with routine hematoxylin-eosin staining.

DISCUSSION

The presence of plasma cells in melanocytic lesions has been considered as a useful criterion in the differential diagnosis between malignancy and benignancy in the appropriate context. For instance, their presence in what looks like a desmoplastic Spitz nevus should alert the possibility of a desmoplastic melanoma (9).

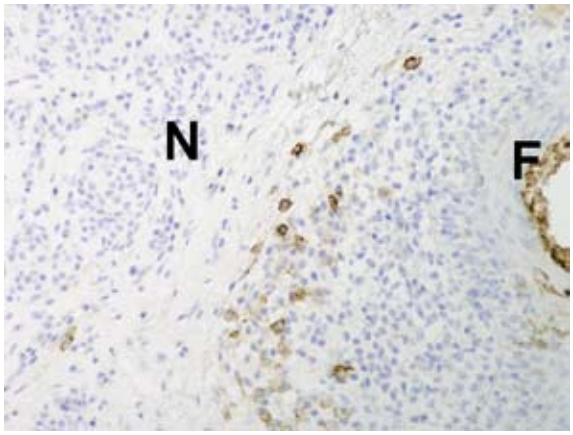

Figure 2. Immunostaining for epithelial membrane antigen in case 2 showing a perifollicular distribution of the inflammatory infiltrate (F, follicle). The technique was useful in standing out numerous plasma cells in the infiltrate, in the proximity of nevus cells (N).

It has also been mentioned how plasma cells are only occasionally found in the inflammatory infiltrate of a halo nevus (6). This was later confirmed at the ultrastructural level (7). Even when halo nevi are studied in their several evolutional stages, neither plasma cells nor B-cells in general seem to be a main component of the infiltrate (13).

On the other hand, plasma cells can be numerous in the inflammatory infiltrate accompanying melanoma and this fact has been found to have an adverse prognostic value (1-5): whenever a heavy infiltrate of plasma cells is present in a melanoma,

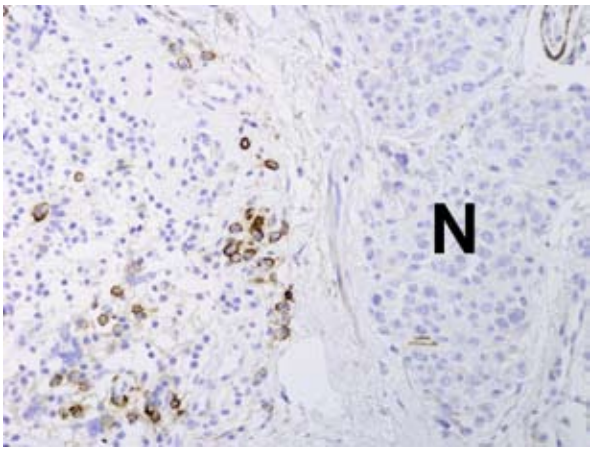

Figure 3. Immunostaining for epithelial membrane antigen in case 5 showing a focus rich in plasma cells close to nevus cells (N).

the possibility of lymph node metastasis should be considered. Therefore, if a large amount of plasma cells are seen in a lesion that looks like a halo nevus, the possibility of melanoma should be considered. This is especially important in cases of halo Spitz nevus, where epitheloid melanocytes can already be a concern for malignancy. Nevertheless, plasma cells are absent in a halo Spitz nevus, unless there is a traumatic epidermal defect (9).

In spite of this diagnostic use of plasma cells, studies investigating them in the inflammatory infiltrate of halo nevus are not so frequent (6,7), and the ones investigating these cells in common acquired nevus are even rarer (14).

Our results indicated that on some occasions plasma cells could be present and easily found in common, innocent-looking nevi. A similar result was reported in conjunctival nevi, although mainly in patients who presented a history of allergic disease (14).

We found no explanation for the conspicuous plasma cells in these four cases, since the features of the four were not peculiar: the location of the lesion, the histological type of nevus or the location of the infiltrate were not different in these four cases from some other examples in the rest of the cases in our series. The location of the lesion could suggest the possibility of trauma in some cases (the neck or nose), but not easily in others (back). Again, among our cases, there were many examples of nevi on the face and nose with only very few and occasional plasma cells.

Therefore, in our opinion, the main point of our findings is that the presence of plasma cells should not necessarily make one think of malignancy, even if the other morphological features of the melanocytic lesion evaluated point towards benignancy.

The reason why plasma cells seem to be more common in melanoma than in nevi has not yet been elucidated. Nevertheless, it might have something to do with the fact that the inflammatory infiltrate, according to some, could be just an epiphenomenon in halo nevus (i.e. not necessarily for the nevus clearance) (15). It would, on the contrary, represent an immune response against melanoma cells. Nevertheless, this interpretation is not a consensus (13). For some, the inflammatory infiltrate plays a crucial role in the regression of the halo nevus (16,17), but it should be noted that such a role is mainly played by T-cells and not by B-cells (13,18,19). In melanoma, on the contrary, it is mostly agreed that the presence of a B-cell infiltrate would be the result of sensitization of the lymphocytes which have travelled to the skin from the lymph nodes, where they had been in contact with the metastatic melanocytes (15). This explains the observations reported in the past on the predictability of nodal metastasis, based on the presence of plasma cells in the inflammatory infiltrate of melanoma (4,5). It would also explain the paradox on how a prominent inflammatory infiltrate in a melanoma is not correlated with a better prognosis (20), opposite to what happens in many other tumors (21,22).

A therapeutic proof of this sensitization has been obtained in patients with metastatic melanoma who were vaccinated with autologous melanoma cells. Although the resected metastatic nodules, previous to vaccination, presented a minimal inflammatory infiltrate, a dense inflammatory infiltrate with plasma cells was found in metastatic lesions resected after the vaccination (23).

This sensitization has nothing to do with the reported presence of “plasmacytoid cells” in some inflammatory infiltrates induced by topical treatments of melanocytic lesions (24): plasmacytoid cells are not related to plasma cells; the former are CD4+ cells (17,24) which are able to produce large amounts of type 1-interferons (25-30).

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Veramon - against pain; year 1936.
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