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Spontaneously Regressing Malignant Melanoma with Unusual Histological Features

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An 85-year-old man with spontaneously regressing primary malignant melanoma is reported. Histological features were considered to be compatible with those of spontaneously regressing malignant melanoma, except that many multinucleated giant cells were observed replacing typical melanoma cells. ***Key words: histological regression; multinucleated giant cell; immune response.***

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Spontaneous regression of malignant melanoma is well recognized among dermatologists. Partial regression is often observed in superficial spreading melanoma and lentigo maligna, which clinically exhibit depigmented macules on the tumors. The complete regression of invasive melanoma has been supported by the presence of metastatic melanoma without any primary lesion (1). Histopathological characteristics of spontaneously regressing primary malignant melanoma are inflammatory cell infiltration, degeneration of melanoma cells, loss of melanocytes and melanin granules in the overlying epidermis (2). We here report a case of primary malignant melanoma of the face with unusual histological features, considered to be in the process of spontaneous regression.

CASE REPORT

An 85-year-old man visited our clinic on June 4, 1990, complaining of a deeply pigmented nodule on a pigmented macule of the face. He had noticed the macule at least 10 years earlier, and it had gradually increased in size and depth of color. In December 1989, a pigmented nodule developed on the macule and grew rapidly for least one month.

Physical examination revealed a deeply pigmented nodule (14 × 17 mm) on a pigmented macule (23 × 33 mm) with an irregular border on the left upper eyelid (Fig. 1). Numerous slightly raised pigmented lesions with keratotic surfaces suggestive of seborrheic keratosis were observed on the face. However, there was no obvious depigmentation, satellite lesion or lymphadenopathy. Chest X-ray, CT-scan of the neck and chest, and ^{67}Ga-scintigraphy of the whole body revealed no abnormalities. As lentigo maligna melanoma was strongly suspected clinically, surgical resection and skin grafting were undertaken on June 27, 1990. He did not accept any further treatment. He has been free from recurrence or metastasis for 3 years.

Histopathological findings

The serial sections of the specimen obtained by surgical resection were examined. In the nodular part, the epidermis was flattened and neither junctional activities nor tumor cells were observed. Masson-Fontana stain revealed the loss of melanin granules in the basal layer of the overlying epidermis and numerous melanin deposits in the dermis. Edema, mild fibrosis and capillary proliferation were seen beneath the epidermis. Numerous lymphocytes and melanophages were infiltrating throughout the nodule. In the center of the nodule, clustered multinucleated giant cells with large atypical nuclei and vacuolated cytoplasm were found mingled with melanophages and lymphocytes (Fig. 2). In some areas, degenerated multinucleated giant cells surrounded by a dense lymphocytic infiltrate were observed. Some multinucleated giant cells possessed fine melanin granules in the cytoplasm.

In the surrounding macular area of hyperpigmentation, the epidermis was flattened with loss or decrease of basal melanin granules and melanocytes. Neither junctional activities nor multinucleated giant cells were observed in any of the sections. Melanophages and lymphocytes were seen scattered in the upper dermis, which is considered to be responsible for hyperpigmentation.

Immunoperoxidase staining for S100 protein as a marker of melanoma cells (3) showed a positive reaction in most multinucleated giant cells and a few mononuclear cells with large atypical nuclei in the nodule (Fig. 3). Melanin-rich mononuclear cells were negative for S100 protein. Immunohistochemical study for lymphocyte markers revealed that inflammatory cells consisted mainly of UCHL1 (CD45R, Pan T) positive cells. Additionally, UCHL1 positive lymphocytes were mostly positive for CD8, while a few CD4 positive lymphocytes were seen.

On the basis of these histological findings and clinical features, we concluded that this tumor was a spontaneously regressing malignant melanoma, in which residual tumor cells mainly took the form of multinucleated giant cells.

DISCUSSION

The clinical appearance of regressing malignant melanoma often reflects pigmentary disturbances of the tumor. Depigmented lesions are associated with the absence of epidermal melanin granules and a few melanophages in the dermis, and pigmented lesions are related to the presence of a large number of melanophages in the dermis. Histological characteristics of spontaneously regressing primary malignant melanoma are as follows: no melanoma cells at the epidermal-dermal junction (4–12), disappearance of melanin granules and melanocytes from the overlying epidermis (6–8, 11), flattening of the epidermal rete

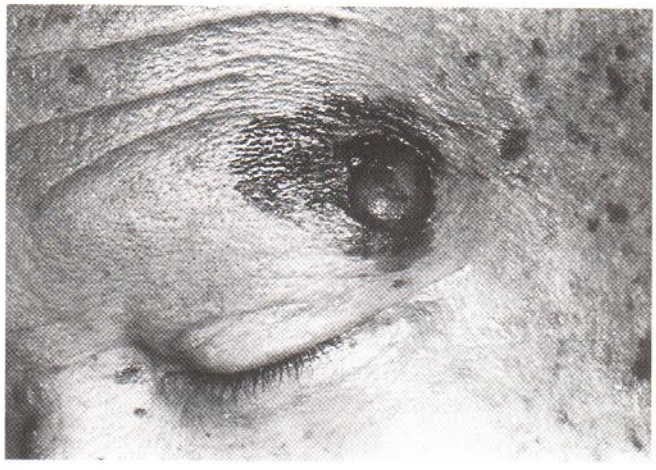

Fig. 1. A deeply pigmented nodule on a pigmented macule of the face.

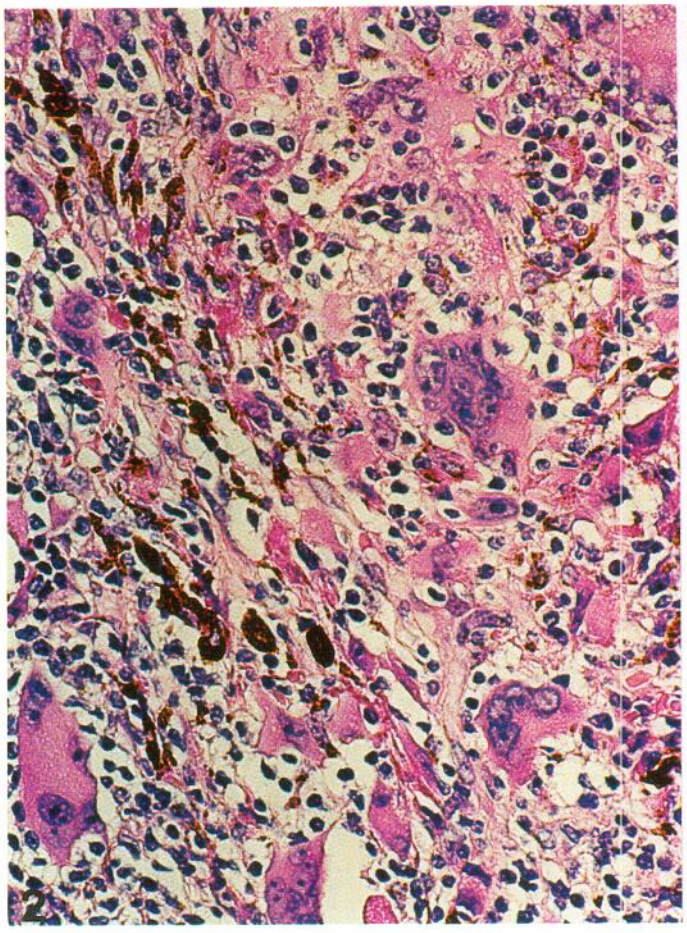

Fig. 2. Photomicrograph near the center of nodule, showing clustered multinucleated giant cells mingled with lymphocytes and melanophages (HE stain; ×200).

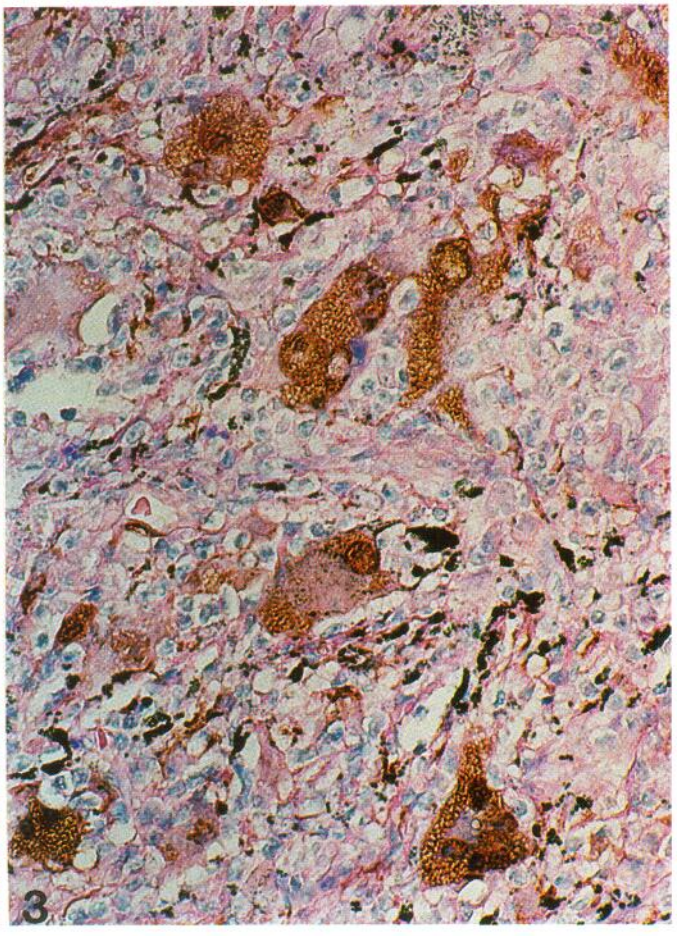

Fig. 3. Antibodies to S100 protein show strong cytoplasmic and nuclear staining of the multinucleated giant cells. Melanin granules are stained dark green by Giemsa counterstain (×200).

ridge (6, 8, 13), presence of melanophages and/or degenerated effete melanoma cells in the dermis (7, 9–12), superficial dermal inflammatory cell infiltration composed mainly of lymphocytes (4–7, 9, 12) and reactive capillary proliferation with interstitial edema and fibrosis (4–6, 10, 13). These histological features may suggest that certain immunological mechanisms attack not only melanoma cells but also normal melanocytes.

The clinical differential diagnosis in our patient may include nothing other than lentigo maligna melanoma. However, the histological examination revealed no abnormal epidermal melanocyte proliferation or melanoma cell infiltration in the dermis, essential for typical lentigo maligna melanoma. Instead, the present case showed all the characteristics of spontaneously regressing primary malignant melanoma, except for the presence of numerous multinucleated giant cells, though we sometimes encounter malignant melanoma with a few multinucleated tumor cells intermingled among numerous mononuclear melanoma cells. The multinucleated giant cells of our case were considered to be derived from residual melanoma cells based on the following findings: 1) the giant cells possessed large atypical nuclei; 2) some giant cells had fine melanin granules in the cytoplasm, different from those in melanophages which had dense and coarse melanin granules; 3) giant cells expressed a strong positive reaction for S100 protein in their nuclei and cytoplasm; and 4) most giant cells possessed vacuolated cytoplasm and some were degenerated.

With respect to the histogenesis of the multinucleated giant cells, it is possible that residual melanoma cells did not complete cytoplasmic mitosis but could finish only nuclear mitosis, progressing towards a degeneration process through some immunological mechanism.

In conclusion, our case is considered to be regressing malignant melanoma with a histologically peculiar appearance, since most of the melanoma cells existed in the form of multinucleated giant cells.

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