Melanoma With Second Myxoid Stromal Changes After Personally Applied Prolonged Phototherapy

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Abstract: Most malignant melanomas are easily diagnosed; however, melanomas is also one of the lesions most frequently reported to mimic other tumors. One of the most difficult patterns to recognize is characterized by prominent myxoid matrix. A case is presented of primary cutaneous melanoma with abundant myxoid matrix in a patient who underwent prolonged phototherapy. Three years before, after getting sunburns, the patient noticed changes of a congenital nevus located in the area of sunburns. It became darker, started to blanch, and grew, with occasional bleeding. Without consulting a physician, the patient applied phototherapy onto the area for 30 months. He used a Bioptron lamp with polarized, polychromatic, incoherent light, at a wavelength from 480 to 3400 nm, without ultraviolet radiation. Clinically, the lesion was unevenly pigmented, ulcerated, covered with hemorrhagic crust, and measuring 3.5 cm in greatest dimension, with a satellite nodule. Multiple metastatic subcutaneous nodules were also found on the scalp and trunk. Histologically, the primary tumor and metastases were composed of nests and pseudotubular formations of polygonal, spindle, and stellate cells embedded in abundant myxoid stroma that comprised more than 80% of the tumor mass. Focally, in the epidermis and papillary dermis, nests of atypical melanocytes and numerous melanophages were observed. Chemotherapy and immunotherapy were administered as suggested by an oncologist. The patient died from distant metastases 6 months after the diagnosis. Although some authors believe that myxoid changes do not seem to alter the behavior of melanoma, it remains an important differential diagnosis issue.

Key Words: melanoma, myxoid melanoma, myxoid stromal changes, phototherapy


INTRODUCTION

Most malignant melanomas are easily diagnosed. However, they also frequently mimic other tumors.1-3 One of the most difficult patterns to recognize is characterized by prominent myxoid matrix. The presence of myxoid areas in melanocytic lesions is not characteristic of melanomas only. It is also found in common nevi, cellular blue nevi, and Spitz nevi.4-7 Melanomas with myxoid features can be easily mistaken for other benign and malignant lesions, such as focal cutaneous mucinosis, schwannoma, neurofibroma, chordoid syringoma, squamous cell carcinoma, basal cell carcinoma, sweat duct tumor, myxoma, angiomymyxoma, malignant fibrous histiocytoma, mucinous adenocarcinoma, myxoid fibrosarcoma, myxoid liposarcoma, myxoid peripheral nerve sheath tumor, or extraskeletal myoid chondrosarcoma.1,2,4,5 Diagnostic pitfalls may be common in fine-needle aspiration biopsy, particularly if there is no primary cutaneous lesion.8 It is important to consider malignant melanoma on differential diagnosis of myxoid lesions because of differences in therapeutic approach and prognosis.

We present a case of primary cutaneous melanoma with abundant myxoid stromal changes in a patient who underwent prolonged phototherapy.

CASE REPORT

A 43-year-old male white was admitted for pigmented skin lesion on the left pectoral region, clinically suspect of melanoma. Three years before, after getting sunburns, the patient noticed changes on a congenital nevus located in the area of sunburns. It became darker, started to blanch, and grew, with occasional bleeding. Without consulting a physician, the patient applied phototherapy onto the area for 30 months. He used a Bioptron lamp with polarized, polychromatic, incoherent light, at a wavelength from 480 to 3400 nm, without ultraviolet radiation. He finally consulted a physician after having noticed small, dark nodules on the scalp and trunk. Clinically, the lesion was unevenly pigmented, ulcerated, covered with hemorrhagic crust, and measuring 3.5 cm in greatest dimension, with a satellite nodule (Fig. 1A). Multiple metastatic subcutaneous nodules measuring up to 0.7 cm were also found on the scalp and trunk (Fig. 1B). Ultrasound examination revealed enlarged left cervical, supraclavicular, and axillary lymph nodes, suggesting the presence of metastatic disease. Computed tomography showed metastatic nodules in the lungs, liver, spleen, and left adrenal gland. Pectoral lesion, several subcutaneous nodules, and enlarged lymph nodes from the left axilla were surgically removed and referred for pathology.

Histologically, the primary tumor was composed of nests and pseudotubular formations of polygonal, spindle, and stellate cells (Fig. 2A) embedded in abundant myxoid stroma that comprised more than 80% of the tumor mass (Fig. 2B). Focally, small- to medium-sized nests of atypical melanocytes and numerous melanophages were observed in the epidermis and papillary dermis (Fig. 2C). Mitoses were frequent (up to 8 mitoses per 10 high power field [HPF]), and a loose lymphocytic infiltrate was found at the base of the...
tumor and between tumor cells. The tumor deeply infiltrated subcutaneous fat tissue with maximum thickness of 12 mm. Myxoid stroma was alcian blue positive and periodic acid Schiff negative, with no intracytoplasmic mucin. Immunohistochemically, tumor cells were positive for S-100 protein and HMB45 (Fig. 2D) and negative for cytokeratin, epithelial membrane antigen, and carcinoembryonic antigen. Five lymph nodes contained metastases. Lymph node metastases and metastatic subcutaneous nodules had the same histology as the primary tumor. Chemotherapy and immunotherapy were administered as suggested by the oncologist. Six months after the diagnosis, the patient died of distant metastases. Autopsy was not performed.

DISCUSSION

There are several microscopic variants representing the most commonly recognized pathological patterns of primary malignant melanoma: superficial spreading, nodular, lentigo maligna, acral-lentiginous, and “minimal deviation.” There also are some histologic patterns that may be very confounding in the diagnosis of melanoma. Adenoid or pseudopapillary, small-cell, myxoid, hemangiopericytoma-like, signet-ring cell melanomas, desmoplastic, neurotropic, nevoid, Spitz nevus-like, balloon cell, and other variants have been described. Hitchcock et al defined neoplasm with at least 15% of basophilic, myxoid stroma on the examined cross-sections as myxoid malignant melanoma. Macroscopically, they are not different from other melanomas, and most of them appear as a pigmented nodule or tumor. Limbs are the most common site. In primary tumors, there are usually areas that could be recognized as typical melanoma. Multinucleated giant tumor cells can also be found. Necrosis, ulceration, and prominent inflammatory cell infiltrates are infrequent. In myxoid areas, melanocytes tend to appear smaller than in the adjacent non-myxoid stroma, assuming a stellate or spindle shape. Mitoses are variably common. The HMB45 positivity is a rule but may be weak or only focal. Melanoma-associated stromal mucin is usually positive for alcian blue at pH 2.5 and colloidal iron and negative for periodic acid Schiff. Intracytoplasmic mucin was not found within tumor cells. These findings support the observation that myxoid stroma is produced by reactive mesenchymal cells and occurs as a result of accumulation of stromal glycosaminoglycans in the form of hyaluronic acid. Some of the described melanomas with myxoid changes were amelanotic lesions, but they all showed premelanosomes on electron microscopy. Therefore, some authors consider myxoid malignant melanoma as a variant of amelanotic melanoma, whereas others believe that it could be a variant of spindle cell or desmoplastic melanoma.

Nottingham et al and Bhuta et al describe cases of metastatic malignant melanoma with prominent stromal myxoid changes. The interval between primary and metastatic melanoma varied from 2 months to 24 years. In most cases, primary tumors were without myxoid changes.

In our case, primary tumor and metastases had similar histology. Melanoma appeared in the area damaged with sunburns. Levin et al showed accumulation of dermal mucin in patients exposed to prolonged psoralen ultra violet A (PUVA) therapy. The amount of mucin deposition showed correlation with the length of PUVA therapy, and in some patients, mucin disappeared upon PUVA withdrawal, suggesting that the change is reversible.

Some evidence for the increasing amount of glycosaminoglycans to facilitate growth and invasion in stroma has been reported. Various mechanisms are proposed to be involved, for example, cellular migration is easier in a loose surrounding tissue; glycosaminoglycans also are acting as modulators of growth factor activities; and an increased number of mast cells can enhance melanoma cell growth through the release of growth factors. In some cases of myxoid melanoma, an increased number of mast cells and increased expression of transforming growth factor (TGF)-β were
observed. TGF-β regulates the structure and expression of proteoglycans within the cellular matrix and is commonly involved in fibroblast stimulation. Therefore, Patel et al. hypothesize that TGF-β and mast cells may be involved in the mechanism of myxoid melanoma growth.

Despite these opinions, myxoid changes probably do not alter the behavior of melanoma as compared with the more conventional morphological types, and seem to have diagnostic rather than prognostic significance.

Myxomatous changes can occur in many benign and malignant tumors. The lack of awareness of this stromal pattern in malignant melanomas may result in diagnostic and therapeutic errors. Cutaneous neoplasms that may exhibit myxoid stroma include epithelial neoplasms, neoplasms with neural crest differentiation, metastases from primary tumors that may display myxoid features, and soft tissue tumors.

A combination of cytokeratin, vimentin, S-100, and HMB45 immunostains may have a discriminatory value in definitive interpretation; however, HMB45 positivity is not the rule in all melanomas. Therefore, on making the diagnosis of malignant melanoma and especially melanoma with myxoid changes, one should combine clinical data with histologic findings and immunohistochemistry and electron microscopy as necessary.

REFERENCES


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