Merkel Cell Tumor Presenting as a Painful Patch Lesion on the Right Arm

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Primary small cell cutaneous neuroendocrine carcinoma (Merkel cell carcinoma) is an uncommon, highly malignant, primary cutaneous neuroendocrine carcinoma. Clinically it is seen as a 0.5- to 5.0-cm pinkish purple papule or nodule, usually not ulcerated, on the head, neck, or, less frequently, the roots of the limbs. We present the case of a woman with an atypical clinical presentation of a Merkel cell tumor.

Case Report

A 55-year-old woman presented with a painful subcutaneous nodular lesion on her right arm. It had grown progressively for the previous 9 months, and the patient related it to an insect bite.

The patient's medical history included multivalvular rheumatic heart disease, ischemic cardiopathy, cardiac failure that was treated pharmacologically, and supraventricular tachyarrhythmia that required the implantation of a permanent pacemaker. She was intolerant of vitamin B complex. Her heart disorder was being treated with diuretics and oral anticoagulants.

Results of a skin examination revealed a 1.5-cm purple patch that was indurated, not ulcerated, situated in the infradeltoid region of the right arm (Figure 1). The lesion was slightly painful on palpation. There were no other mucocutaneous lesions. The results of a general physical examination were normal. A biopsy of the skin was performed.

Anatomical and pathological study results showed a tumor localized to the reticular dermis and subcutaneous cellular tissue. It was formed by large anastomosed masses of poorly differentiated cells with small nuclei and scanty cytoplasm. The chromatin was finely granular. There was no nucleolus. A high index of individual tumor necrosis was present with intense peritumoral lymphoplasmocyte inflammatory infiltration (Figure 2). Histochemical study results showed cytokeratin and chromogranin but did not reveal any estrogen or progesterone receptors.

Results of further studies were normal, including a chest x-ray, mammography, thoracic and abdominopelvic computed tomography scans, echography of the thyroid, and bone gammagraphy. The lesion was excised with a wide margin. The patient underwent 4 cycles of chemotherapy with cisplatin and etoposide. Photon radiotherapy was used to treat the surgical scar, as well as the areas of supraclavicular, infraclavicular, and axillary lymph drainage. After 2 years, the patient is still in complete remission with no sign of the disease.

Comment

Merkel cell carcinoma is an uncommon, highly malignant, primary cutaneous neuroendocrine carcinoma. It has many synonyms including primary cutaneous small cell carcinoma, cutaneous apudoma, trabecular carcinoma, and neuroendocrine carcinoma of the skin.[1,2] It usually appears in older adults, although it has been described in young people with congenital ectodermal dysplasias. Clinically it is seen as a 0.5- to 5.0-cm pinkish purple papule or nodule, usually not ulcerated, situated on the head, neck, or, less frequently, the roots of the limbs. Its presentation as a plaque, such as in our patient, is unusual.[1-5]

Histology results show a tumor in the dermis and subcutaneous cellular tissue, formed of basophilic round cells. A grenz zone usually remains unless there is ulceration. Based on the size of the cells and their arrangement in sheets, nests, or trabeculae, 3 histologic patterns may be distinguished: trabecular or classical, formed of small cells; intermediate cell type, with large solid nests of cells that are not small in size; and small cell type, with a pattern of diffuse infiltrating sheets of small cells.

The individual cells of Merkel cell carcinoma are round with an oval nucleus, evenly dispersed chromatin, and ill-defined cytoplasm. A "ball-in-mitt" arrangement of cells is said to be characteristic, with

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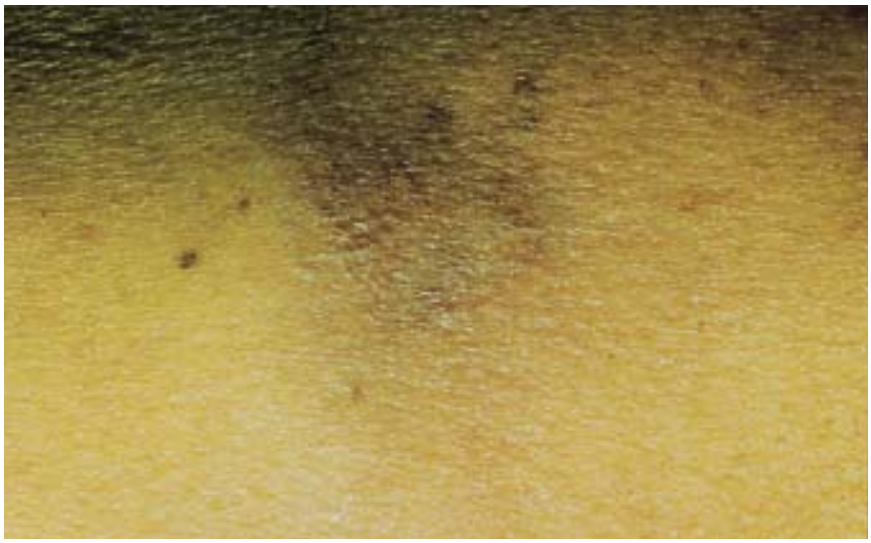

Figure 1. Purple indurated patch located on the infradeltoid region of the right arm.

1 or 2 crescentic tumor cells wrapped around one central round tumor cell. Cell necrosis and apoptosis are common. A high incidence of mitosis and vascular and lymphatic invasion is often found.[1-4]

Ultrastructural analysis shows 2 characteristic features: dense core granules and paranuclear aggregates of intermediate filaments (fibrous bodies). The differential diagnosis includes a cutaneous metastasis of an oat cell tumor, neuroblastoma, and carcinoid tumor. The fibrous bodies establish the diagnosis of Merkel cell tumor.

The histogenesis of Merkel cell tumor is not clear. The origin of the cell that proliferates is not known. There is controversy as to whether it is derived from the epidermal Merkel cell or from the neuroendocrine differentiated epithelial cells.

Unlike the Merkel cell, this tumor is not localized to the epidermis, occurring mainly in the head and neck region (palms and soles are the most common sites for Merkel cell). Immunohistochemistry results are positive for neurofilaments.[1-3]

The concept of a "diffuse neuroendocrine system" is not new. Feyster developed this paradigm in 1938 in a philosophical attempt to unify the terms used to identify several locations that had potential secretory functions and similar morphologic characteristics. Other highly malignant neuroendocrine carcinomas are atypical pulmonary carcinoid tumor, small cell lung cancer, anaplastic islet cell carcinomas, and extrapulmonary small cell carcinomas.[6]

Immunohistochemical study results were positive for neuroendocrine markers (chromogranin, synaptophysin, and neurospecific enolase), low molecular weight cytokeratins, VIP, neurofilaments, and membrane epithelial antigen. Tests for S-100 protein occasionally showed faint positivity. However, the leukocyte common antigen, vimentin, desmin, glial fibrillary acidic protein, and the prekeratins were negative. Neurospecific enolase was the most specific marker, though it did not permit differential diagnosis from cutaneous metastases of oat cell carcinoma.[1-4,7,8]

Differential diagnosis is difficult. Other tumors of small basophilic cells that also should be considered include basal cell carcinoma, pyogenic granuloma, malignant melanoma, lymphoma, leukemia cutis, epidermoid anaplastic carcinoma, cutaneous metastasis of pulmonary oat cell tumors, neuroblastoma, retinoblastoma, carcinoid tumor, medullary carcinoma of the thyroid, pancreatic carcinoma, and Ewing's sarcoma.[1,2]

The tumor is aggressive, with a 30% to 50% postsurgical recurrence index, a 50% to 60% recurrence rate of regional metastases, a 30% to 50% recurrence rate of distant metastases, and about a 55% mortality index.[4,9] Distant metastases most frequently involve the liver, bone, brain, lung, and skin. Factors that worsen the prognosis are: tumor size greater than 2 cm, metastasis at the time of diagnosis, location in the head or neck region, vascular and/or lymphatic invasion seen on histological study, histological pattern of small cells, and the finding of more than 10 mitoses per field at high magnification.[1,2]

Treatment depends on the stage of the disease. In localized cases (stage I), either tumor excision with margins of 3 cm or Mohs micrographic surgery is indicated, followed by local and lymphatic gland radiotherapy. If there is ganglion involvement (stage II), removal of the regional lymph glands is indicated.[1,2,10-14]

The use of chemotherapy at stages I and II is controversial; however, because the malignancy potential of this tumor is high, we considered the administration of 4 cycles of adjuvant chemotherapy

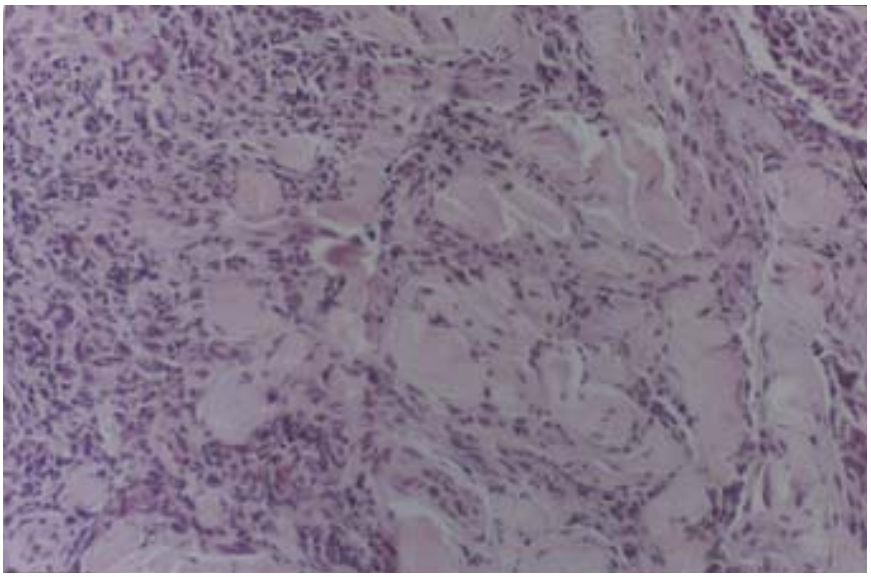

Figure 2. Histologic view of the tumor in which anastomosed masses of poorly differentiated cells can be seen. Individual tumor necrosis and an intense peritumoral lymphoplasmocyte inflammatory infiltrate also are present.

with cisplatin and etoposide to be beneficial. Adjuvant chemotherapy has demonstrated to be of benefit in other neoplasies in localized stages.[15,16] This chemotherapy regimen is also active in metastatic stages of Merkel cell tumor[17] and in other neuroendocrine-originating carcinomas.[18,19]

We consider this aggressive treatment to have been beneficial in our patient; however, this can be confirmed only with prospective studies. In cases with systemic involvement (stage III), polychemotherapy (doxorubicin, methotrexate, etoposide, cisplatin, 5-fluorouracil, vincristine, cytoxan, and streptozocin) is combined with radiotherapy.[11]

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