Not Just a Cyst: A Case of a Red Nodule

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Background

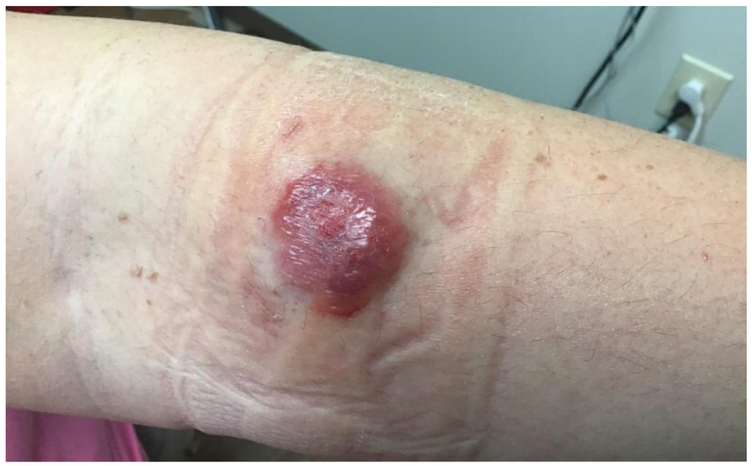
Cutaneous erythematous nodules are a common entity found throughout all medical specialties and practices. This diagnosis can be quite difficult without the appropriate referral and evaluation. The differential diagnosis for erythematous nodules can include benign diseases such as inflamed epidermal inclusion cysts, deep infectious diseases such as leishmaniasis or histoplasmosis, malignant diseases such as basal cell carcinoma and cutaneous metastasis from lymphomas. Our patient case demonstrates the necessity to expand upon this broad differential and use good clinical judgement if lesions fail to improve with treatment.

Methods

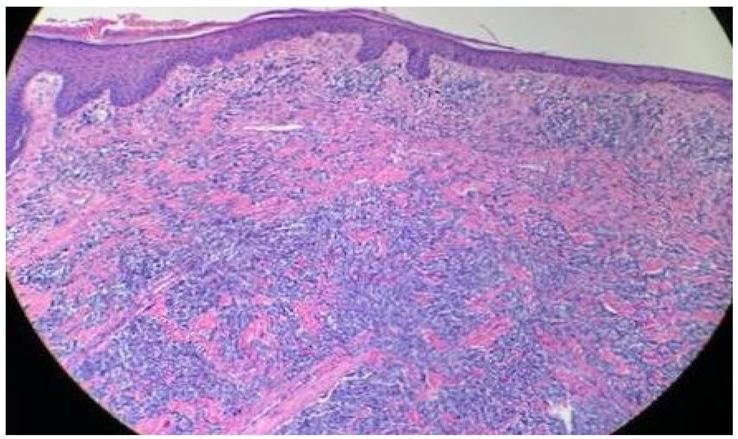
A 47 year old female with a history of diabetes mellitus presented to the dermatologist with an 8 week history of a 2.5 x 2.5 cm erythematous, friable nodule on her left lateral proximal forearm which had previously been treated with a 10 day course of cephalexin and a 14 day course of trimethoprim-sulfamethoxazole without improvement of the lesion. The patient reported the lesion began as a small papule and then had progressively grown into the nodule pictured in top figure. A punch biopsy was taken from the center of the lesion and a bacterial culture was taken of the center of the lesion which was negative except for normal flora. The lesion demonstrated a necrotic, malignant small cell neoplasm in the deep dermis and subcutis. The cells demonstrated prominent nuclear molding, and they had dispersed chromatin with only scantly amphophilic cytoplasm (bottom figure). Immunohistochemical staining demonstrated reactivity for pankeratin, with dot-like paranuclear labeling and positivity for CD56. Staining was negative for S100, CD3, CD5, CD7, CD20, CK20 or TTF-1. The Ki-67 index was 90%. These findings supported a diagnosis of a high-grade neuroendocrine carcinoma, but due to negative specific staining, a definitive diagnosis was not made.

The patient returned to the clinic for a complete shave removal of the lesion that was also sent to dermatopathology for H&E. The pathology demonstrated a central ulcer from previous punch biopsy, as well as a dermal based malignant neoplasm with distinctive neuroendocrine ctyologic features. Sheets and cords of malignant cells were present. Immunohistochemical staining was again performed to further characterize the lesion. The cells were positive for CK20 in a juxtanuclear-dot pattern and failed to demonstrate positivity for TTF-1. These staining results in the setting of the findings seen on H&E supported a diagnosis of primary cutaneous Merkle Cell carcinoma.

Patient Presentation



The patient underwent a wide local excision with an accompanying sentinel lymph node biopsy (SLNB). A CT showed a large left ovarian cyst, umbilical level hernia, hepatic steatosis and a stable benign RML nodule. The SLNB showed metastasis in 3 of 5 lymph nodes. PET/CT demonstrated no evidence of FDG avid metastasis. Patient was diagnosed with Stage 3 merkel cell carcinoma. Patient underwent 28 radiation treatments to left axilla and arm.



Discussion

Merkel cell carcinoma is a rare, but aggressive cutaneous malignancy that generally affects older adults with light skin types. The annual incidence rate of MCC worldwide is about 0.13-1.7 per 100,000 (4). The average ages of diagnosis are 76 years old for women and 74 years old in men (1,3). Risk factors for the development of MCC include: Merkel cell polyomavirus (MCPyV), ultraviolet (UV) radiation exposure, immunosuppression, and other malignancies such as CLL and multiple myeloma. It typically presents as a rapidly growing, non-tender, flesh-colored to bluish red, nodule in older individuals on sun exposed areas. According to one study, the most frequent anatomic locations for primary tumors were head and neck 43%, upper limbs and shoulder 24%, lower limbs and hip 15%, trunk 11%, and other areas 9%. In this study, patients presented with local disease in 65% of cases, while 26% had regional lymph node involvement and 8% had distant metastasis (4). Our patient is a unique presentation of MCC due to her young age of 47 years old. However, her clinical presentation occurred in a sun exposed area and in a common location of the upper extremity.

Diagnosis of MCC can be a difficult diagnosis to make clinically. It is often confused with benign lesions such as epidermoid inclusion cyst, lipoma, or more malignant lesions, such as basal cell carcinoma and amelanotic melanoma. The acronym AEIOU was developed based on a series of 195 cases to describe MCC, which stands for asymptomatic; expanding rapidly; immunosuppression; older than 50 years old; UV exposed areas in fair-skinned individuals. The presence of at least three of these features increases the suspicion (4). This is a valuable mnemonic to apply to the clinical assessment of a patient with a rapidly growing lesion that has not responded to other treatment options. Our patient was positive for three of these features, including asymptomatic, expanding rapidly, and UV exposed area. However, the best diagnostic test is biopsy for hematoxylin and eosin (H&E) and immunohistochemical stains. A Merkel cell tumor is composed of monotonous, round, and blue cells, containing large basophilic nuclei and minimal cytoplasm (2). Immunochemical staining is an important diagnostic tool to help differentiate MCC from other malignancies. Merkel cells express epithelial markers, such as AE1/AE3, CAM 5.2, pan-cytokeratin, and Ber-EP4. It can also stain for various neuroendocrine markers, such as chromogranin, synaptophysin, calcitonin, vasoactive intestinal peptide, and somatostatin receptor (3). The most specific and sensitive marker for MCC is CK20, with a characteristic paranuclear dot-like positivity (4). Our patient initially was negative for CK20, but due to H&E characteristics and clinical concern, we repeated the biopsy and CK20 marker was positive, confirming the diagnosis of MCC in our patient.

In this case, we present to you a clinical presentation of a young 47-year-old patient with primary MCC with positive sentinel lymph nodes and MCPyV positive. Our patient demonstrates the necessity for having MCC on your differential diagnosis, along with the importance of
clinical examination with physical exam, H&E, and immunohistochemical markers. MCC is expected to continue to increase due to the “baby boomer” generation with a projected increase to 3,284 cases in 2025, which is a substantial increase from approximately 2,000 cases a year (5,6). Therefore, it is important to have MCC on your differential diagnosis for lesions that fail to improve with treatment and/or present at least three of the clinical features of the AEIOU mnemonic.

References

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