Fig 1. Large, ulcerated squamous cell carcinoma on right forearm.

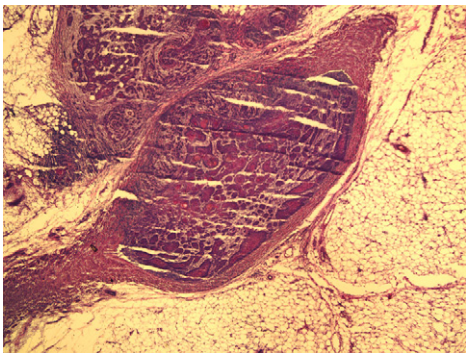

Fig 2. Vessel underlying cutaneous squamous cell carcinoma completely occluded by tumor cells. (Hematoxylin–eosin stain; original magnification: ×2.)

unremarkable. Review of recent computed tomography scans and a chest radiograph revealed no evidence of malignancy. Mohs micrographic surgery was then performed. Histologic examination of the first layer revealed 4 of 6 sections positive for tumor at the deep margin with no evidence of perineural invasion. One of these contained a deep vessel surrounded by fat and completely occluded by tumor (Fig 2). No residual SCC was found in the second layer. After the removal of large standing cones and extensive undermining, the defect was repaired in a side-to-side fashion. After discovering the large tumor thrombus, postoperative radiation therapy was considered. However, because the possible site of metastasis could not be predicted, this intervention was not thought to be indicated. Chemotherapy was not recommended by the oncology department, as there was no evidence of residual tumor and, therefore, therapeutic response could not be evaluated. Despite no adjuvant therapy, however, the patient remained tumor-free 21 months after surgery.

Vascular invasion itself has been seen in cutaneous SCCs and has been loosely associated with a potentially worse prognosis.[2] However, complete vascular occlusion secondary to tumor invasion has not been reported, and this is the first instance encountered in 25 years of practice of the senior author. Even by conventional standards, our patient falls into the high-risk category, given her tumor size and depth of tumor invasion.[1] This alone places her at increased risk for recurrence and possible distant disease. The associated vascular thrombosis leaves many questions unanswered and more studies are necessary to assess the overall significance of this finding. Given the rarity of complete vascular inclusion by SCC, it is difficult to infer its effects on prognosis in our patient and in general.

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Microsatellite stable genome in an epithelioid hemangioendothelioma: An example of a microsatellite stable tumor

To the Editor: Epithelioid hemangioendothelioma (EHE) was originally described by Weiss and Enzinger[1] as a tumor comprised of endothelial cells with an epithelioid phenotype and variable malignant behavior. Of particular concern is the lack of a consistent correlation between the tumor's pathologic features and the patient's clinical course. We describe a patient with an EHE whose evaluation for genomic microsatellite instability was negative, suggesting that these neoplasms represent a microsatellite stable tumor.

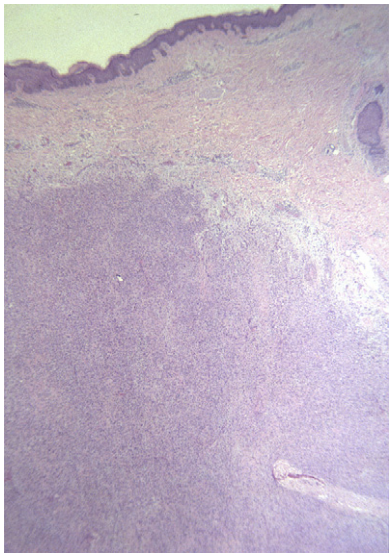

Fig 1. Low-power view demonstrating nodular features of the tumor and epithelioid phenotype. (Hematoxylin-eosin stain; original magnification: ×20.)

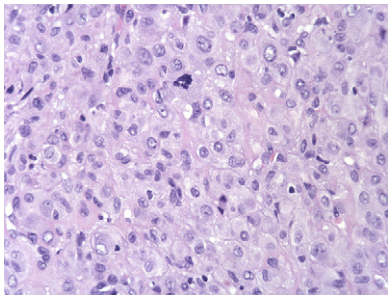

Fig 2. The tumor cells are epithelioid pleomorphic nuclei, atypical mitotic figures, and intracytoplasmic vacuoles containing occasional erythrocytes. (Hematoxylin-eosin stain; original magnification: ×400.)

A 28-year-old male presented to the dermatology clinic at Vanderbilt University with a 1-year history of a slowly growing nodule on the anterior surface of his right forearm. He had been injured in a motor vehicle accident with cuts and abrasions affecting the involved arm 3 years before presentation. The nodule had recently assumed a faint purple color and was mildly tender to palpation. On the patient's forearm was a freely mobile, subcutaneous nodule measuring 1.6 cm in diameter.

Histologically, the neoplasm displayed large aggregates of pleomorphic epithelioid cells with focal areas of spindling (Fig 1). Occasional "hob nail" cells were appreciated. The stroma was intermittently sclerotic with focal areas of mucin deposition. Mitotic activity was sparse. Intracytoplasmic vacuoles, occasionally containing single erythrocytes, were noted (Fig 2). Immunoperoxidase staining for CD31, CD34, and vimentin were positive, but those for pancytokeratin (AE1/AE3), S-100, leukocyte common antigen, neuron specific enolase, CD68, epithelial membrane antigen, and CD30 were negative.

The patient underwent a wide excision of the biopsy site. No remaining tumor tissue was noted. Radiographs of the chest and right forearm were unremarkable. To date he has had no recurrence of his tumor.

DNA was extracted from paraffin-embedded specimens using the PUREGENE kit (Gentra Systems, Minneapolis, Minn). Genotypes for ten di or tetranucleotide repeat markers representing 5 chromosomes were determined by polymerase chain reaction amplification using fluorescent primers tagged with either HEX, FAM, or TET (Applied Biosystems, Foster City, Calif). Markers analyzed included *TP53*, D17S520 (17p); *APOC2*, D19S601 (19q); *FGR*, D1S253 (1p); D10S215 (10q); and D2S143, D2S116, and D2S334 (2q). Amplicons were subjected to 5% polyacrylamide denaturing gel electrophoresis on an ABI-377 DNA sequencer and analyzed using GeneScan software 3.1 b3 (Applied Biosystems). Identical alleles from both normal and diagnostic tissue specimens were observed for all markers with no evidence of microsatellite instability (MSI) or loss of heterozygosity.

EHEs are vascular tumors typically arising in the lung and liver and are associated with a high rate of metastasis and death.[2] Primary involvement in the skin is uncommon. Lesions typically occur on the extremities as a slightly raised, erythematous, and occasionally tender nodule. No predisposing factors have been discerned. Single lesions are the norm, but cases of eruptive EHE have been reported, usually in association with underlying involvement of bone.[3] CD31 is expressed in most tumors. CD34, factor VIII, and *Ulex europaeus* are variably positive. Some EHEs express cytokeratins, but most do not. S-100, lysozyme, CD68, and epithelial membrane antigen are routinely negative.[2]

The prognosis of EHE is relatively poor for those tumors involving the viscera and deep soft tissues, but is often quite good for the solely cutaneous variant.[4] Weiss et al[5] described 46 patients with cutaneous lesions; 6 patients (13%) experienced a local recurrence and 14 (31%) displayed distant metastases. A small percentage of patients whose lesions demonstrated banal pathologic features experienced metastatic spread. There appears to be no clear association between a patient's prognosis and the pathologic features of their tumors.

Recently, the concept of microsatellite instability (MSI) has arisen as a means of predicting the biologic potential of certain tumor cells, particularly human

non-polyposis colorectal cancer. Microsatellites are repetitive DNA sequences less than 6 bases in length found throughout the human genome. Tumors with variations in the number of repeats at these loci as compared to DNA from normal tissue are said to possess "microsatellite instability."[6] These repeated sequences are unique for a given individual and are usually present in non-coding regions of DNA.[7] Tumors are segregated into 3 groups: those with a low frequency of MSI (MSI-L), those with a high frequency of MSI (MSI-H) and those with stable microsatellites (MSS). In tumor tissue where both alleles of an mismatch repair gene have been inactivated, uncorrected somatic replication errors occur in microsatellite repeats sequences both within noncoding and insignificant locations throughout the genome as well as in coding regions of genes involved in cell growth, DNA repair, and signaling.

The presence of MSI has been reported in a number of cutaneous neoplasms, including basal cell carcinomas[8] and melanomas.[9] Interestingly, neither sporadically arising actinic keratoses nor squamous cell carcinomas have demonstrated MSI.[10] The negative MSI analysis in our patient was prescient in two respects. First, although other studies have employed MSI analysis in the evaluation of benign vascular proliferations, this is the seminal report of its use in a malignant or borderline malignant neoplasm of the skin. Second, internal malignancies with MSI have demonstrated an unfavorable prognosis.[11] Evaluation of vascular tumors for MSI might provide clinicians with additional prognostic information.

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Fixed drug eruption caused by itraconazole: Reactivity and cross reactivity

To the Editor: Fixed drug eruption (FDE) characteristically occurs at the same site every time an offending drug is administered. Cross-reactions may occur with structurally similar drugs. Different immunologic mechanisms incriminated in the pathogenesis of FDE are based on the concept of the circulating drug acting as a hapten and its consequent binding to cellular proteins or receptors, thereby releasing lymphokines and antibodies damaging basal cell layer. Although a single drug is usually responsible in most patients, in rare instances multiple drugs may lead to a FDE. When drugs of totally different chemical structures precipitate exacerbations, it is termed polysensitivity.

A 52-year-old female was administered a single 400 mg dose of fluconazole for extensive pityriasis versicolor. Within 12 hours, she noticed 3 oval, painful, eroded, pigmented patches over her trunk with diameters of 3 cm to 4 cm and erythematous halos. A clinical diagnosis of FDE caused by fluconazole was made. An oral graded challenge with fluconazole, itraconazole, and ketoconazole was performed at 4 weeks.[1] Initially, the dose used was one fourth of the minimum therapeutic dose. If no reactivation of the lesions was observed in next