SECTION EDITOR: MICHAEL E. MING, MD

Plaque on the Thigh of a Renal Transplant Recipient

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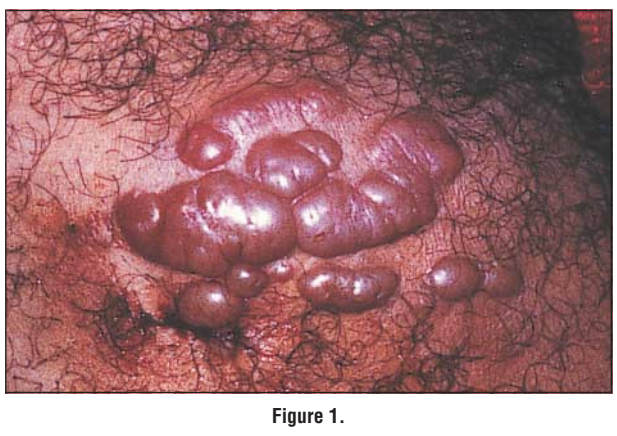
REPORT OF A CASE

A 43-year-old man was referred to our dermatology outpatient clinic from the renal transplantation clinic. His medical history included thalassemia minor, familial polyposis coli, hypertension, and IgA nephropathy that resulted in kidney transplantation. For the last 4 years, he had been treated with the following immunosuppressive therapy: azathioprine (100-150 mg/d), cyclosporine (540-130 mg/d), and prednisone (10-40 mg/d).

Physical examination and routine laboratory tests revealed no abnormalities other than slightly enlarged inguinal lymph nodes bilaterally and a soft, skin-colored plaque on the upper part of the right thigh, with overlying nodules that looked similar to vesicles. The lesion was 10 cm in greatest diameter (**Figure 1**). Computed tomography revealed thickening of the skin and infiltration of the subcutis in the medial aspect of the proximal part of the right thigh. A skin biopsy was performed (**Figure 2** and **Figure 3**).

What is your diagnosis?



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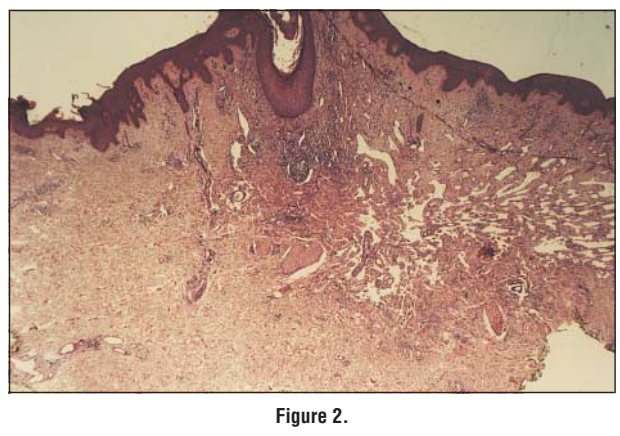

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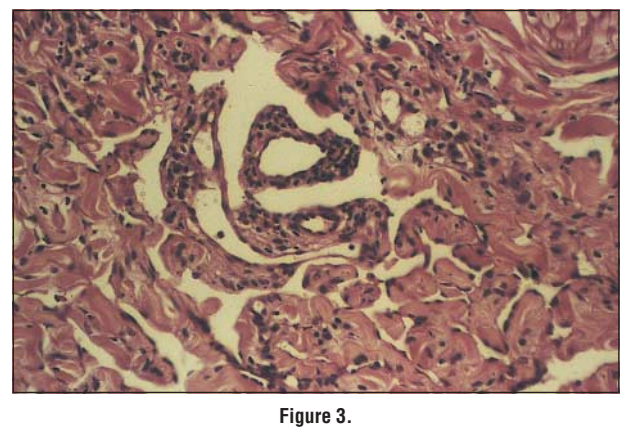

Figure 3.

Asymptomatic Nodule on the Upper Lip

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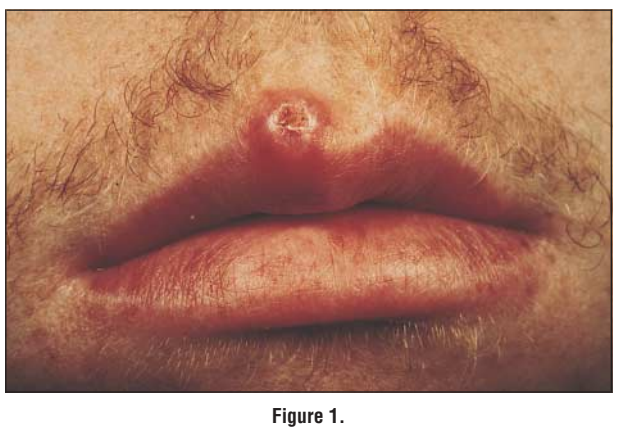
REPORT OF A CASE

A 22-year-old man presented with an 18-month history of a slow-growing, asymptomatic nodular lesion on his upper lip. Physical examination revealed a dark-red, firm, dome-shaped nodule, measuring 8 mm in diameter, with an adherent scale covering the central part of its surface (**Figure 1** and **Figure 2**). The patient appeared to be in good general health, and routine laboratory investigations showed no abnormalities. The lesion was completely excised for light microscopic examination (**Figure 3**).

What is your diagnosis?



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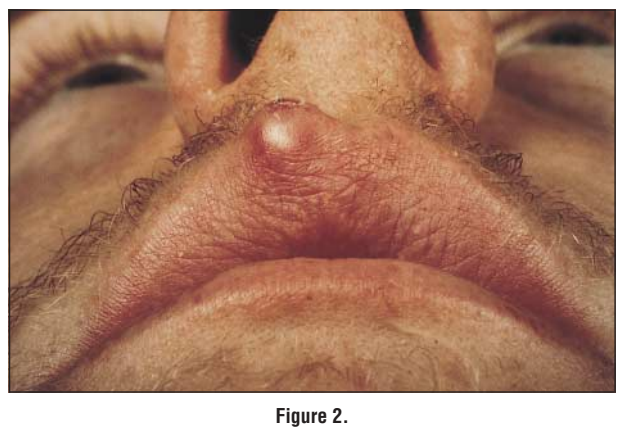

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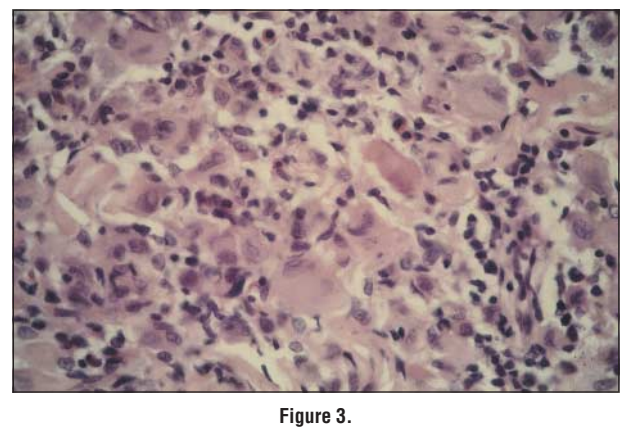

Figure 3.

Brownish Reticulate Maculopapular Eruption on the Flexures

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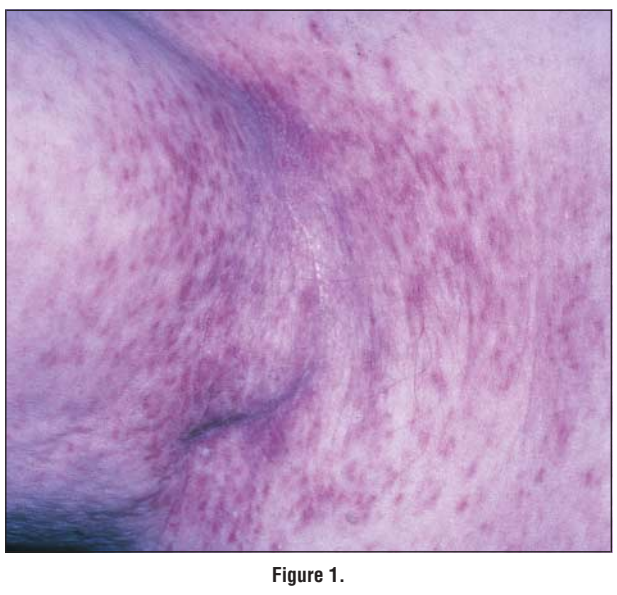
REPORT OF A CASE

A 76-year-old woman presented with an 18-month history of a pruritic eruption on the flexures. She denied episodes of headache, nausea, vomiting, diarrhea, abdominal pain, or palpitations. Her medical history was remarkable for diabetes mellitus and hypertension. Her medications included atenolol and glyburide.

On physical examination, multiple confluent brownish macules and papules that formed a reticulate pattern were present symmetrically on the axillae (**Figure 1**), in the submammary region, and at the inguinal folds. A wheal and flare reaction was noted after the site was rubbed. The results of routine blood tests and urinalysis were within normal limits. Abdominal ultrasonography revealed a fatty liver, and the findings of isotopic scanning of bones with technetium 99m were normal. A biopsy was performed (**Figure 2**).

What is your diagnosis?



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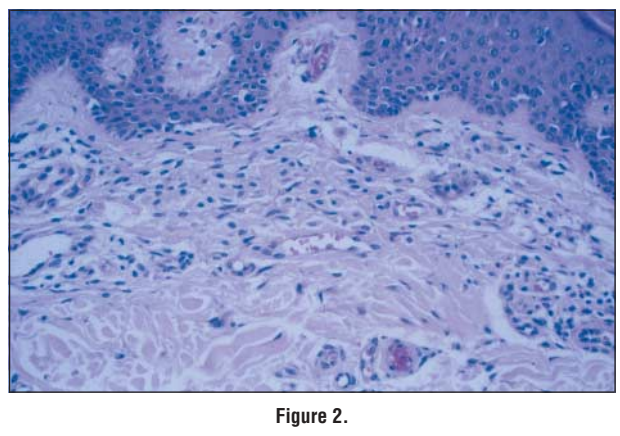

Figure 2.

An Asymptomatic Preauricular Subcutaneous Nodule in a 65-Year-Old Woman

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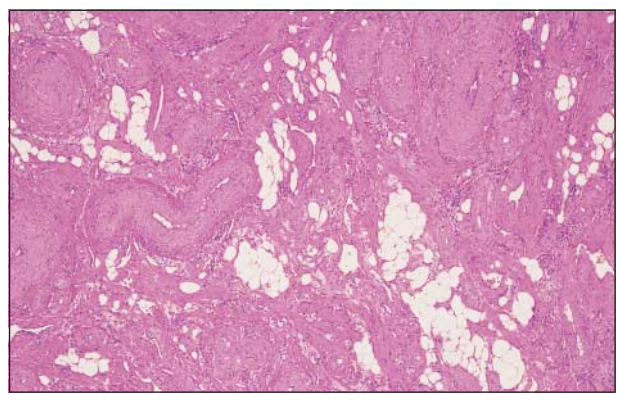
REPORT OF A CASE

A 65-year-old Taiwanese woman presented with a 10-year history of a slow-growing asymptomatic mass in her left preauricular area. Her medical history was unremarkable, and no pertinent family history was reported.

Physical examination revealed a movable, elastic, nontender subcutaneous nodule, measuring approximately 2 cm in diameter, in the left preauricular area (**Figure 1**). The nodule was excised for histologic examination (**Figure 2** and **Figure 3**).

What is your diagnosis?

Figure 1.



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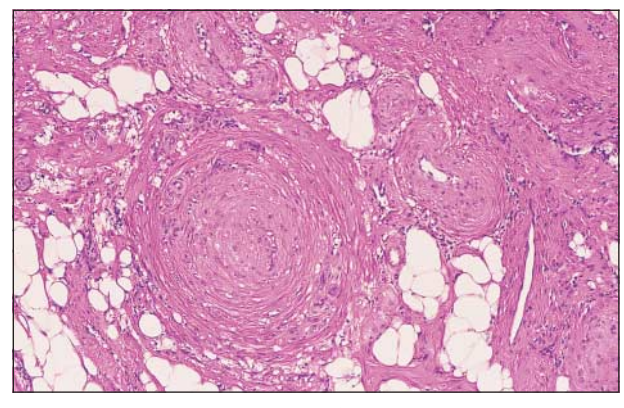

Figure 3.

Plaque on the Thigh of a Renal Transplant Recipient

Diagnosis: Kaposi sarcoma (KS), lymphangiomalike variant.

MICROSCOPIC FINDINGS

The biopsy specimen revealed ectatic, bizarrely shaped vascular spaces that were incompletely lined with endothelial cells. In some areas, normal blood vessels protruded into newly formed vessels (the promontory sign). Erythrocytes were detected inside some of the spaces.

DISCUSSION

Kaposi sarcoma is an endothelial cell tumor that is believed to be caused by infection with human herpesvirus 8.[1] Patients receiving immunomodulatory medication for various indications, such as organ transplantation, autoimmune diseases, or malignancies, are prone to develop KS.[2-4] This phenomenon is seen in as many as 3% to 6% of renal transplant recipients, with a mean period of 20 months of immunosuppressive therapy prior to the development of KS.[5,6] Cyclosporine therapy carries a higher risk for development of KS than azathioprine and prednisone therapy.[6] However, even the use of prednisone alone[2,7] is related to an increased risk for development of KS.[2] It is well documented that this type of KS responds well, and sometimes completely regresses, with reduction of dosage or deletion of 1 component of immunosuppressive therapy.[3]

Kaposi sarcoma classically presents as a reddish bluish macule or patch that may enlarge and coalesce to form nodules or plaques. However, atypical clinical presentations that simulate other dermatoses are also possible.[3] Our patient presented with a clinical picture similar to that of lymphangioma. However, considering his medical history and the enlargement of the lesion over time, a biopsy was performed, and the diagnosis of lymphangiomalike variant of KS was made.

Kaposi sarcoma can mimic lymphangioma both clinically and histologically. This clinical presentation of KS was described by Ronchese and Kern[8] in 1957. In their article, they review 16 anecdotal reports dating back to 1905, mainly from the Italian literature. They describe the appearance of cystic compressible lesions appearing beside typical KS lesions or as a sole manifestation of the neoplastic process. In 1979, Gange and Jones[9] described a microscopic appearance of KS that was similar to that of lymphangioma. Physicians taking care of organ transplant recipients should be aware of the higher incidence of KS in this group of patients, and microscopic evaluation of lesions should be performed if the clinical diagnosis is in doubt.

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Asymptomatic Nodule on the Upper Lip

Diagnosis: Solitary cutaneous reticulohistiocytosis (RH) (reticulohistiocytoma).

MICROSCOPIC FINDINGS

Histopathologic examination revealed a dense dermal infiltrate, predominantly composed of large histiocytes and multinucleated giant cells with a granular eosinophilic cytoplasm, some of which had a ground glass appearance. Neutrophils, lymphocytes, and a few eosinophils were interspersed among the histiocytic cells. Leukophagocytosis and collagenophagocytosis were present in some areas. Immunohistochemically, the mononucleated and multinucleated histiocytes stained positively for KP1 (CD68), but were negative for CD1a and S100 protein.

DISCUSSION

Reticulohistiocytosis represents a spectrum of rare clinical entities: the solitary cutaneous form,[1-3] originally called *reticulohistiocytoma*; the diffuse cutaneous form without systemic involvement[4]; and multicentric RH with systemic involvement.[5] The skin lesions in all these conditions demonstrate an identical histologic pattern that is characterized by the presence of numerous mononucleated or multinucleated histiocytes with abundant, eosinophilic, homogeneous to finely granular cytoplasm with a ground glass appearance. Immunohistochemically, the histiocytes within the infiltrate stain positively for KP1 (CD68), HAM56, vimentin, factor XIIIa, lysozyme, and α_1-antitrypsin. In contrast, these cells are usually negative for CDla, S100 protein, Leu-M1 (CD15), and Mac387. Ultrastructurally, the histiocytic cells show one or more Golgi apparatus and are rich in mitochondria, lysosomes, dense bodies, phagosomes, and myelin figures. Birbeck granules are absent.

Solitary cutaneous RH was first described by Zak[1] in 1950. It commonly presents as a hard, yellow to brownish red, asymptomatic nodule, characterized by rapid growth. The lesion has a predilection for the upper part of the body but may be found on almost any cutaneous site. Oral and nasal mucosae are rarely involved. Most of the patients described in the literature have been adults, RH being extremely rare in children.[3] The onset may be preceded by trauma. The clinical course is benign, and there is no evidence of systemic involvement, with the lesion rarely recurring after surgical excision.

The etiology of RH remains unknown. Reticulohistiocytosis may represent an abnormal immunologic reaction to various stimuli, with local trauma sometimes playing a role in solitary forms,[2] as mentioned above. However, our patient's history failed to reveal any trauma preceding the appearance of the lesion.

The case reported herein is notable because of the location of the lesion on the upper lip, which, to our knowledge, has never been reported before. Many entities, both common and rare, should be considered in the differential diagnosis, including pyogenic granuloma, Spitz nevus, solitary dermatofibroma, and the solitary variant of self-healing RH of Hashimoto and Pritzker.

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Brownish Reticulate Maculopapular Eruption on the Flexures

Diagnosis: Cutaneous mastocytosis (urticaria pigmentosa [UP]).

MICROSCOPIC FINDINGS AND CLINICAL COURSE

Histologic examination of the biopsy specimen showed a perivascular and interstitial mast cell infiltrate involving the papillary and middle dermis. The mast cells were round and oval, with abundant granular cytoplasm and a central nucleus. The cytoplasmic granules of the mast cells stained metachromatically with Giemsa stain (**Figure 3**). These findings were consistent with the diagnosis of cutaneous mastocytosis.

The patient was treated with oral antihistamines and a medium-potency topical corticosteroid preparation (0.1% betamethasone valerate cream applied twice a day for a few weeks), with only partial improvement. During the next year, there was gradual extension of the eruption toward the flanks and thighs.

DISCUSSION

Mastocytosis was first described by Nettleship and Tay[1] in 1869. Cutaneous mastocytosis, which encompasses a spectrum of disorders resulting from the abnormal proliferation of mast cells, is classified into 4 clinical types: UP, solitary mastocytoma, diffuse erythrodermic form, and telangiectasia macularis eruptiva perstans.[2]

Urticaria pigmentosa, which is the most common form of mastocytosis, is characterized clinically by multiple tan macules and papules that show a wheal and flare reaction in response to rubbing or stroking, a finding known as Darier sign. The lesions occur in a random distribution, most commonly on the trunk, although all skin areas, including the mucous membranes, may be affected. The palms, soles, face, and scalp are usually spared.[2,3] Urticaria pigmentosa may develop at any time from birth to middle age, but it usually affects young children, with 75% of cases occurring during the ages of 2 to 4 years. In one study involving 30 patients with adult-onset UP,[4] the mean age at onset was 31.4 years.

Figure 3.

The diagnosis of UP is confirmed by characteristic histopathologic findings that consist of an interstitial and perivascular mast cell infiltrate in the dermis. Metachromatic stains, such as Giemsa and toluidine blue, highlight the cytoplasmic granules, thereby facilitating identification.[5]

The differential diagnosis of reticulate pigmented eruptions on the flexural surfaces includes acanthosis nigricans, Dowling-Degos disease, and confluent and reticulate papillomatosis of Gougerot and Carteaud.[6,7] We were able to find only a single previously reported case of UP that involved the axillae of a 9-month-old patient.[8] Although UP that primarily involves the flexures is a rare clinical presentation, it should be kept in mind in cases of reticulate pigmented eruptions of the flexures.

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An Asymptomatic Preauricular Subcutaneous Nodule in a 65-Year-Old Woman

Diagnosis: Cutaneous angiomyolipoma.

MICROSCOPIC FINDINGS

Histopathologic examination revealed a well-circumscribed subcutaneous tumor with a loose fibrous pseudocapsule. The tumor was composed of a mixture of smooth muscle, mature adipose tissue, and vascular spaces. The smooth muscle was arranged in fascicles that were intermingled with mature adipocytes or around vascular spaces in a way that resembled tunica muscularis. A stain for smooth muscle actin was positive. The vascular spaces were of various shapes and sizes and lined by endothelial cells. There was no evidence of mitotic figures or nuclear atypia in the tumor.

DISCUSSION

Cutaneous angiomyolipoma was first reported by Hwang[1] as *cutaneous angio(lipo)leiomyoma* in 1985 and was later referred to as *cutaneous angiomyolipoma* by Argenyi et al[2] in 1986. The largest series, which included 8 cases, was reported in 1990 by Fitzpatrick et al,[3] who called the tumor *cutaneous angiolipoleiomyoma.* Approximately 14 cases have been reported in the English-language literature.[2-8]

Angiomyolipoma is a benign tumor, almost exclusively of the kidney, that is often associated with tuberous sclerosis.[9] Cutaneous angiomyolipoma usually presents as a solitary subcutaneous or deep dermal nodule, 1 to 4 cm in diameter, with a dome-shaped surface in acral parts. The age of the patients ranges from 33 to 77 years. All but one of the reported cases have developed in men. There were no signs of tuberous sclerosis in the reported cases.

Microscopically, the tumor shows proliferation of 3 principal components: smooth muscle, adipose tissue, and vessels.[3] Abundance of the 3 components varies in reported cases.[2-8] The smooth muscle, usually bland and mature, can be arranged in fascicles, in groups of cells, or around vascular spaces in a way resembling tunica muscularis. However, pleomophic changes were demonstrated in one case.[6]

Mature adipocytes are dispersed in groups or as single cells in the tumor and are intimately associated with smooth muscle and vascular spaces. The vascular component consists of different types of vessels, including capillaries, venous structures, and muscular arterioles. Partially formed or bizarrely shaped internal elastic laminae can be demonstrated by a stain for elastin in some vessels. The microscopic differential diagnoses include angioleiomyoma, angiolipoma, and arteriovenous hemangioma.

In contrast to angiomyolipoma of the kidney, reactivity for HMB-45 is negative in the smooth muscle component of cutaneous angiomyolipoma.[7,8] In our case, the reactivity for HMB-45 was also negative. In previously reported cases, the tumor was easily shelled out or excised, and no recurrence has been noted. However, massive bleeding occurred when we shelled out this tumor and excised it from the base. A large feeding artery was revealed at the base of the tumor on histologic examination. There was no recurrence after 2 years of follow-up in our patient.

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Submissions

Clinicians, local and regional societies, and residents and fellows in dermatology are invited to submit quiz cases to this section. Cases should follow the established pattern and be submitted double-spaced. Photomicrographs and illustrations must be clear and submitted as 3 positive color transparencies and as 3 color prints. Material should be accompanied by the required copyright transfer statement, as noted in "Instructions for Authors." Material for this section should be submitted to Michael E. Ming, MD, Department of Dermatology, University of Pennsylvania Health System, 2 Maloney Bldg, 3600 Spruce St, Philadelphia, PA 19104-4283. Reprints are not available from the authors.