# A solitary keratotic hemorrhagic nodule on the upper lip

Hussein Hassab El-Naby, MD, Mohamed El-Khalawany, MD

*Department of Dermatology, Al-Azhar University, Cairo, Egypt*

## CLINICAL FINDINGS

A 29-year-old male presented with an asymptomatic skin lesion on the upper lip for one year. The lesion started as a red papule and slowly progressed to form a large nodule. During the last few months, the lesion started to bleed after minor trauma or scratching. There was no history of any other skin disease or systemic illness. On examination, there was a solitary keratotic nodule on the upper lip (Fig. 1) that measured 0.7 x 0.5 cm. The lesion was soft and slightly compressible with central small keratotic horn and minute hemorrhagic crusts on the surface (Fig. 2). The lesion was slightly pedunculated, the borders were well defined and the margin was skin-colored. General examination was irrelevant while routine investigations showed no significant abnormalities.

**Fig. 1** A solitary keratotic nodule on the upper lip

## What is your clinical differential diagnosis?

Pyogenic granuloma, Angiokeratoma, Kaposi sarcoma, Arteriovenous hemangioma, and Intravascular papillary endothelial hyperplasia.

## Pathological findings

An excision biopsy was performed and the lesion was totally excised. Histological examination showed variable-sized blood vessels in the papillary dermis, some showed marked dilatation forming large cavernous channels (Fig. 3). The lumen in most vessels was filled with erythrocytes but few showed clear fluid in association with RBCs (Fig. 4). The epidermis showed epithelial collarette at the margins of the nodule. There was irregular acanthosis with elongated rete ridges and marked hyperkeratosis. The central part of the horny layer showed a large keratotic horn (Fig. 5). The reticular dermis showed sparse inflammatory infiltrate and no vascular collections were observed in the lower dermis or subcutis.

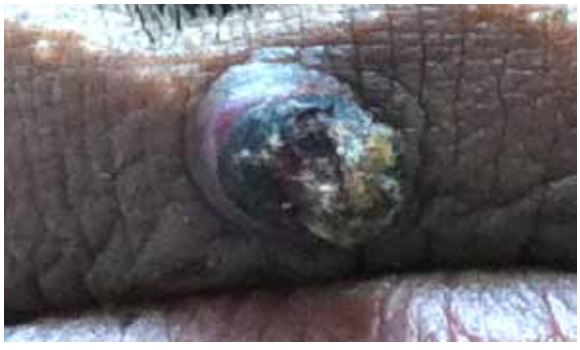

**Fig. 2** The lesion showed central small keratotic horn and minute hemorrhagic crusts on the surface.

***Correspondence:*** *Dr. Hussein Hassab El-Naby, Department of Dermatology, Al-Azhar University, Cairo, Egypt*

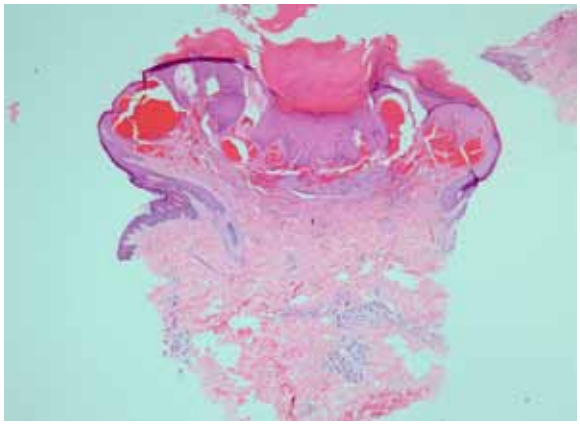

**Fig. 3** Variable-sized blood vessels in the papillary dermis, some showed marked dilatation forming large cavernous channels (H&E x20).

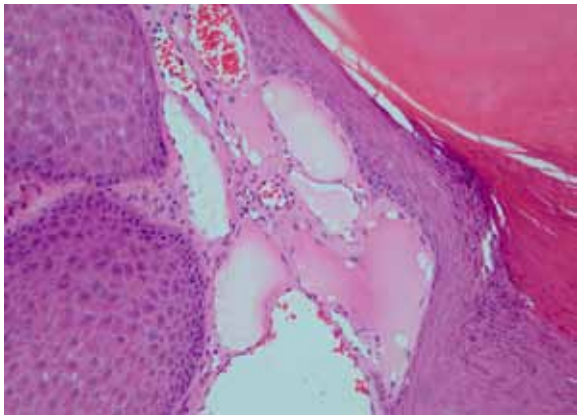

**Fig. 4** The lumen in most vessels was filled with erythrocytes but few showed clear fluid in association with RBCs (H&E x200).

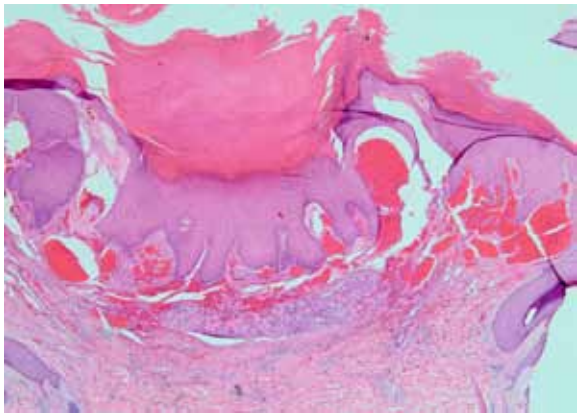

**Fig. 5** The epidermis showed epithelial collarette at the margins of the nodule. The central part of the horny layer showed a large keratotic horn (H&E x400).

## DIAGNOSIS

Solitary Angiokeratoma.

## COMMENT

The term angiokeratoma (AK) is derived from three Greek words meaning vessels, horn, and tumor. These lesions are not true angiomas but are merely telangiectasias of preexisting vessels. Angiokeratomas may arise in isolation or in groups of multiple lesions, as solitary cutaneous forms or generalized systemic forms. They can occur in both healthy individuals and in those with underlying systemic disease due to inherited enzyme deficiency or other acquired predisposing factors.[1]

Five clinical variants have been recognized and all have similar histopathological features. The Mibelli type develops in childhood and adolescence, with warty lesions over the bony prominences of the hands, feet, elbows, and knees.[2] The Fordyce (scrotal) type arises as early as the second and third decades, but is seen most commonly in elderly men.[3] Solitary and multiple types occur on any part of the body, but the lower extremities are most commonly affected.[4] Angiokeratoma circumscriptum is the least common variant which is consists of a unilateral, plaque composed of small discrete papules on the leg, trunk, or arm.[5] The fifth variant is Angiokeratoma corporis diffusum that consists of multiple papules, frequently in clusters, and usually in a bathing-trunk distribution.[6]

The current division of localized angiokeratoma includes the following: (i) Bilateral form occurring on the dorsa of the fingers and toes-angiokeratoma of Mibelli, (ii) localized scrotal form-angiokeratoma of Fordyce, (iii) plaque form-Angiokeratoma circumscriptum, (iv) solitary papular angiokeratoma, and (v) localized vulval form-angiokeratoma of the vulva.[7] Most forms of localized angiokeratoma present during the first

## The clinicopathological challenges of Solitary Angiokeratoma

| Diagnosis | Clinical | Pathological |
|---|---|---|
| **Pyogenic granuloma** | • Common sites include the gingiva, lips, fingers, and face<br>• Predominant in males<br>• Commonly presents as polypoid or pedunculated lesion, but they may be sessile<br>• Mostly red or red-brown in color<br>• Usually with rapid progressive course and the surface is often ulcerated and bleeds easily | • The lesion is classically formed of lobulated proliferation of capillary-sized vessels separated by myxoid or fibrous connective tissue septa<br>• The deep lobules are compact and cellular, with small indistinct lumina<br>• Occasional mitotic figures may be seen within the cellular lobules<br>• Toward the surface, the lobules are larger and less tightly packed<br>• Secondary ulceration, edema, hemorrhage, and inflammatory changes are common |
| **Kaposi sarcoma** | • Commonly in epidemic type, associated with AIDS (HIV)<br>• Commonly located on the trunk, arms, head and neck<br>• Lesions are usually multiple<br>• There is frequent involvement of mucosal surfaces and internal organs<br>• Early lesions are brown to red macules or patches resembling a bruise<br>• Well developed lesion appear as papules, nodules, or plaques with bluish or purple color and may ulcerate | • Well developed lesion shows dermal proliferation of interlacing bundles of spindle cells and intimately related, poorly defined slit-like vessels<br>• There is an associated inflammatory cell infiltrate consisting predominantly of lymphocytes and plasma cells<br>• Dilated thin-walled vessels are found at the periphery of the tumor<br>• The spindle-cell component shows variable nuclear pleomorphism<br>• Mitotic figures are present, but not usually frequent<br>• Clusters of eosinophilic hyaline globules may be seen in an extracellular location |
| **Arteriovenous hemangioma** | • Presents as a solitary, red or purple papule<br>• More predilection for the lips, the perioral skin, the nose, and the eyelids<br>• Common in middle-aged to elderly<br>• Men<br>• It is usually asymptomatic and measure 0.5-1.0 cm in diameter | • A well-circumscribed non-encapsulated collection of large, thick-walled vessels in the upper and mid dermis<br>• These vessels are lined by endothelium and have a fibromuscular wall which contains elastic fibers but no definite elastic laminae<br>• The stroma is often myxoid |
| **Intravascular papillary endothelial hyperplasia** | • Mostly presents as a single lesion, but multiple lesions are described<br>• Present clinically as firm, sometimes painful nodules<br>• May appear blue or purple in color<br>• Most commonly found on the fingers, head and neck, and trunk<br>• There is a female predominance | • A vascular proliferation which is limited to the lumen of an identifiable vein or vessel<br>• Occasionally there is only a fibrous capsule lacking definite features of a vessel wall<br>• The lumen of the vessel shows masses of papillary processes covered by a single layer of plump endothelial cells<br>• Almost always the vessel shows thrombus<br>• Mitotic figures may be present |

two decades of life. Among these five types of localized angiokeratoma, solitary angiokeratoma is the most common while angiokeratoma circumscriptum is the least frequent.[8]

Solitary angiokeratoma generally arises during the second to fourth decades or later. However, solitary angiokeratoma consists of a much smaller lesion than angiokeratoma circumscriptum. And is a warty, black papule, rather than plaque, usually on the lower limbs. Angiokeratoma is usually asymptomatic, but with local trauma they may become irritated and can bleed, given their highly vascular nature.[9]

The etiopathogenesis of angiokeratoma is uncertain. The first event is the vascular ectasia within the papillary dermis just beneath the basement membrane. The epidermal hyperplasia is the secondary reaction. Increased venous pressure proximal to the site and raised intra-abdominal pressure can predispose to the formation of angiokeratoma.[10]

Angiokeratoma of Fordyce in the scrotum is associated with varicocele, hernia, prostatitis, lymphogranuloma venereum, carcinoma of the bladder, and thrombophlebitis.[11] Vulvar form is associated with pregnancy, vulvar varicosity, postpartum period, and hysterectomy. These conditions cause increase in the local venous blood pressure. Thus these patients should also be examined both clinically and radiologically for the abdominal masses.[12]

Mucosal involvement, including the oral cavity, has been described both as localized and systemic types, as a component of Fabry's disease, or as a component of fucosidosis. It is more common in females, and the most common site of involvement is the tongue.[13]

Histopathologically angiokeratomas are composed of marked dilatation of papillary dermal vessels, forming large cavernous channels. There is associated irregular acanthosis of the epidermis with elongation of the rete ridges, which partially or completely enclose the vascular channels. A collarette may be formed at the margins of the lesions and there may be thrombosis of the vessels. The surface epidermis may show varying degrees of hyperkeratosis.[14]

The occurrence of a deep dermal hemangioma has been reported in association with angiokeratoma circumscriptum. This combination may represent a verrucous hemangioma. In patients with Anderson Fabry disease, there is vacuolation of smooth muscle in arterioles and arteries and in the arrectores pilorum.[15]

Dermoscopic features of angiokeratoma showed the presence of well-demarcated, round, and dark lacunae. Which, histologically represent dilated vessels with thrombosis is a strong diagnostic sign of angiokeratoma. Red lacunae refer to dilated vascular spaces without thrombosis in the upper dermis, while a whitish veil corresponds to acanthosis or hyperkeratosis.[16] Angiokeratomas are divided into three patterns by dermoscopic view. All patterns include dark lacunae and whitish veil. Pattern 1 (sensitivity 84.4%, specificity 99.1%) consists of no other features, while pattern 2 (sensitivity 43.8%, specificity 100%) consists of peripheral erythema, and pattern 3 (sensitivity 53.1%, specificity 99.6%) consists of hemorrhagic crusts.[17]

The electron microscopy shows vascular channels lined by very thin endothelial wall. There cytoplasm shows microfilaments, pinocytosis vesicles and vacuoles with scarcely electron-opaque content, with a diameter of 2,000 and 4,000 A and scanty cytoplasmic organelles, such

as mitochondria and endoplasmic reticulum.[18] Excision, electrodessication, cryotherapy, or laser ablations are the various modes of therapy.[19] Recurrences have been reported after surgical excision. Malignant transformation has not been reported in angiokeratoma.[20]

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