# Case series of variants of angiokeratoma

Sachin Somashekhar[a], Heera Ramesh[b], Eshwari Loganathan[c], Varsha Gowda[c]

[a]Department of Dermatology, Gulbarga Institute of Medical Sciences, [b]Department of Dermatology, Karnataka Institute of Medical Sciences, [c]Department of Dermatology, Bangalore Medical College and Research Institute, Karnataka, India

Correspondence to Sachin Somashekhar, MD, 1st Main 1st Cross, Manjunath Nagar, Bangalore 560010, Karnataka, India.
Tel: +91 953 869 0636;
e-mail: Sachinbmcite@gmail.com

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Angiokeratomas are vascular lesions that display an epidermal proliferative reaction with ectatic capillaries in the papillary dermis and are described histologically as one or more dilated blood vessels lying directly subepidermal. Presentation of angiokeratomas varies from a single lesion to generalized involvement. The diagnosis of angiokeratoma is mainly clinical as the histopathology of all variants are identical. In this case series, we discuss the variants of angiokeratoma and their presentations.

**Keywords:**
angiokeratoma, clinical variants, vascular malformation, verrucous hemangioma

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## Introduction

Angiokeratoma is made up of three Greek terms that signify vessels, horn, and tumor [1]. Angiokeratomas are capillary malformations characterized by papillary dermal vascular ectasias and epidermal hyperkeratosis, papillomatosis, and acanthosis [2]. Solitary or multiple angiokeratomas, angiokeratoma of Mibelli, angiokeratoma of Fordyce, Angiokeratoma corporis diffusum, and angiokeratoma circumscriptum are the five clinical manifestations of angiokeratomas [3]. The importance of clinical acumen to diagnose angiokeratoma variants is described in this case series.

## Case Reports

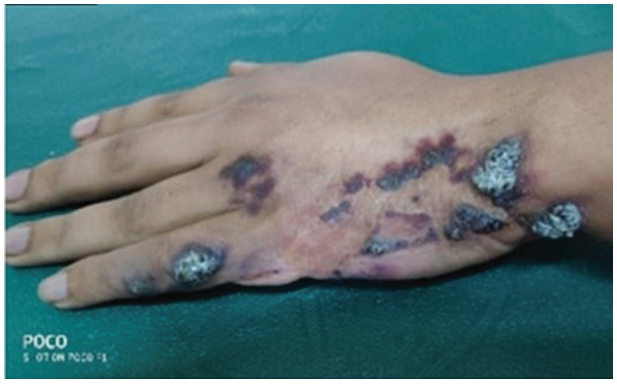
### Case no. 1

A 28-year-old male presented with lesions over the back of the left hand dated since birth. Initially it was pea sized after which it gradually progressed in number and size to involve the inner aspect of the wrist and back of the hand and left little finger. The patient also reported a history of aggravation of symptoms on exposure to cold.

On examination: multiple, discrete, erythematous to hyperkeratotic papules to plaques over the lateral aspect of the dorsum of the left hand with surrounding erythema were present (Fig. 1).

Differential diagnosis: angiokeratoma of Mibelli, verrucous hemangioma.

**Figure 1**




Erythematous to hyperkeratotic papules to plaques present over the lateral aspect of dorsum of the left hand.

### Case no. 2

A 27-year-old male presented with a solitary lesion over the upper back, which he noticed since childhood and it was not associated with pain or bleeding. There was no progression in size of the lesion nor any change in the surface, color, or texture.

On examination – a solitary, well defined, hyperpigmented verrucous plaque measuring 1×1.5 cm in size was present over the upper back (Fig. 2).

Differential diagnosis: solitary angiokeratoma, verrucous hemangioma, melanocytic nevi.

Immunohistochemistry findings – CD 34-positive staining was detected in the blood vessel lining; melan A staining was negative.

**Case no. 3**

A 27-year-old male presented with lesions over his right leg since birth which was initially noted over the medial aspect of the thigh, which later progressed in number and size to involve the legs. No history of pain on exposure to cold. No history of spontaneous bleeding.

On examination: a linear streak of hyperkeratotic plaque with a verrucous surface extending from the medial aspect of the right thigh to the shin was present; the surrounding skin appeared to be normal (Fig. 3).

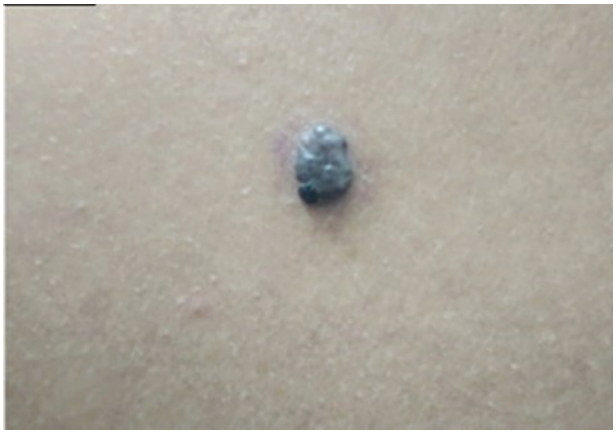
Differential diagnosis: angiokeratoma circumscriptum, verrucous hemangioma.

**Case no. 4**

A 30-year-old male presented with asymptomatic multiple lesions over the abdomen and thigh since 5–6 years that was gradually increasing in size and number.

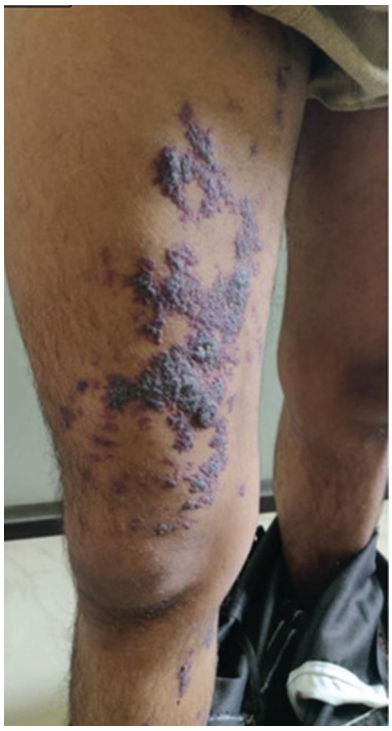
On examination the patient had moderate mental retardation, mild corneal opacity, and typical facies in fabrys disease is described as ″pseudoacromegalic facial appearance,the features of the same which where found in our patient have been described in the highlighted text. (which has been described as 'pseudoacromegalic' facial appearance) in our patient

**Figure 2**



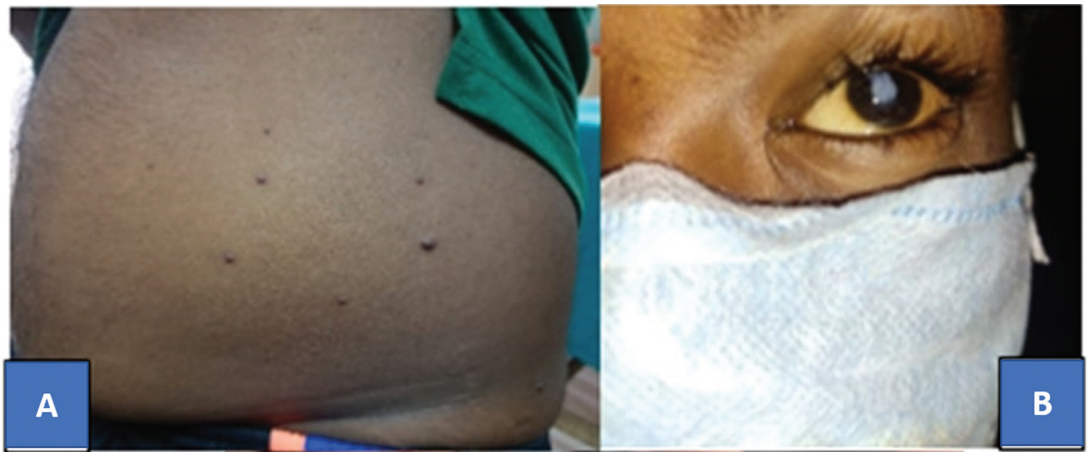
Well-defined, discrete, hyperpigmented verrucous plaque present over the upper back.

**Figure 3**



Linear streak of hyperkeratotic plaque with verrucous surface extending from the lateral aspect of the right thigh to the shin.

**Figure 4**




(a) Multiple, well-defined, erythematous papules present discretely over the abdomen and (b) mild corneal opacity over the left eye.

features such as. Multiple, well-defined, erythematous papules were present discretely over the abdomen, scrotum and the thighs. No abnormalities were detected on cardiac examination; on urine examination proteinuria was present (24-h urine protein was >1.5 g) (Fig. 4a,b).

Differential diagnosis: capillary hemangioma, multiple angiokeratomas in Fabry's disease.

**Case no. 5**

A 33-year-old male presented with lesions over the scrotum for 15 years, gradually increasing in size and number, which was associated with occasional bleeding. There was a history of prior treatment by electrocautery, but the lesions recurred within 2–3 months of therapy.

On examination multiple, well-defined, erythematous to purplish papules and plaques with few excoriations over the scrotum were detected with surrounding telangiectasia. No bruit or tenderness was observed (Fig. 5).

Differential diagnosis: angiokeratoma of Fordyce, verrucous hemangioma, and lymphangioma.

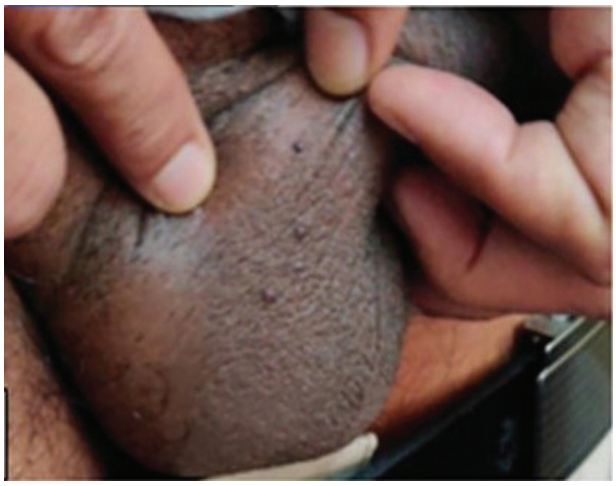
In all cases, a punch biopsy of the lesional skin was performed and sent for histopathological analysis to confirm the diagnosis.

All cases showed a similar picture; the epidermis was hyperplastic with hyperkeratosis, acanthosis, and elongated rete ridges. Vascular ectasia of the papillary dermis was noted with extension into the epidermis. There was no vascular vacuolization or arrector pili muscle changes noted. No vascular ectasia was appreciable in the reticular dermis nor in the subcutis, confirming the diagnosis of angiokeratoma (Fig. 6a,b).

On the basis of age of onset, site of lesion, morphology, and associated clinical features, the following diagnoses were made:

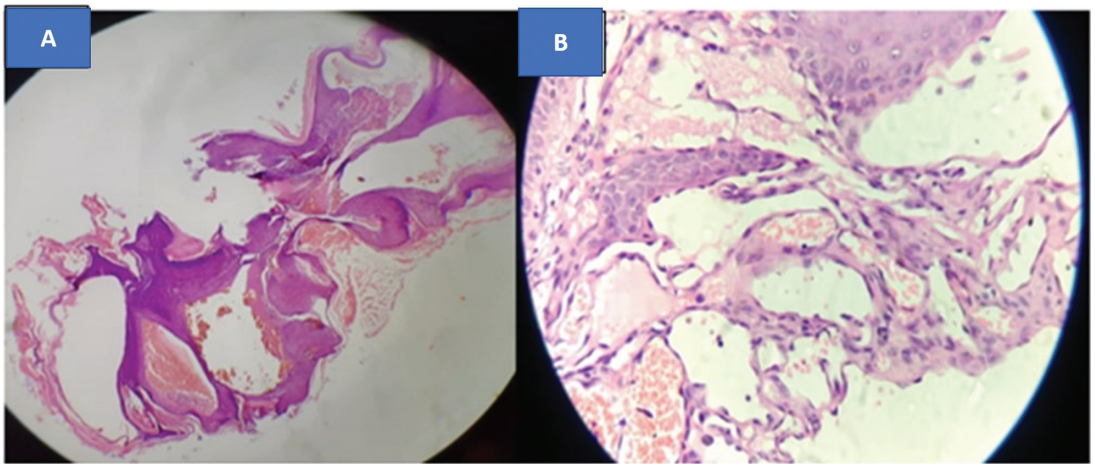
Case no. 1: angiokeratoma of Mibelli.
Case no. 2: solitary angiokeratoma.
Case no. 3: angiokeratoma circumscriptum.
Case no. 4: multiple angiokeratomas in Fabry's disease.
Case no. 5: angiokeratoma of Fordyce.

**Figure 5**



Multiple, well-defined, erythematous to purplish papules and over scrotum.

**Figure 6**




Hematoxylin and eosin stain (a ×10 magnification, b ×40 magnification). Epidermis: hyperplastic with hyperkeratosis, acanthosis, and elongated rete ridges partially enclosing the dilated vascular channels in few areas was noted. Vascular ectasia of the papillary dermis with no involvement of the deeper dermis.

## Discussion

Mibelli coined the word angiokeratoma in 1889, based on the anatomic description of lesions on the dorsum of a 14-year-old girl's hands and feet [4]. Fordyce established the term angiokeratoma of Fordyce after reporting the first instance of atypical angiokeratoma of the scrotum in 1896 [5]. A comparable skin condition associated with cardiorenal involvement was identified by Fabry in Germany in 1898. Fabry initially described the patient's condition as purpura nodularis hemorrhagica, but later altered the diagnosis to angiokeratoma corporis diffusum in 1915 [6].

The prevalence of angiokeratoma is said to be 0.16%, more commonly affecting males than females, can present as solitary papule or a verrucous plaque that gets pigmented during the course [7]. Majority of angiokeratomas are asymptomatic while few of them show profuse bleeding either sporadically or secondary to trauma.

The pathogenesis of angiokeratoma is still obscure; end capillaries of the skin are located in the dermal papillae and are composed of smaller arterial and larger venous limbs that branch off from the respective subpapillary plexus at right angles perpendicular to the skin surface, at the tip of the papillary dermis capillary loops are present. Some authors believe ectasia of the walls with stasis of blood can lead to increased luminal pressure, in turn causing dilation of capillaries and accumulation of blood, which is triggered by factors like recurrent trauma, hypoxia, chillblains, and hemodynamic alterations. Few researches attribute epidermal hyperkeratosis and acanthosis as secondary reactive phenomenon that prevent further expansion of the vascular space [8,9].

Variants of angiokeratoma, their age of onset, and clinical features are described in Table 1 [1].

Histopathology of the variants of angiokeratoma are similar in picture having the following characteristics: marked vascular dilatation of the papillary vessels, forming large lacunae in the papillary area of the dermis, altered appearance of the epidermis, with acanthosis and elongation of the rete ridges, partially or completely encasing the vascular lacunae, intimate vascular and epidermal relationship, and absence of many dilated vessels in the underlying dermis or of lobules of capillaries, suggestive of hemangioma.

**Table 1 Variants of angiokeratoma, their age of onset, clinical features, and histopathological findings [1]**

| Type | Clinical appearance | Site of predilection | Age at onset | 1. Hereditary<br>2. Sex prediliction | Comments | Histopathology |
|---|---|---|---|---|---|---|
| 1. Angiokeratoma corporis diffusum (Fabrys disease) | Purple, red, dark blue, occurs in crops (1–3 mm) | Particularly between umbilicus and the knee | Adolescence | 1. Yes<br>2. Male>Female | Cardiovascular, renal involvement: in women, usually no skin eruption | Mild hyperkeratosis and acanthosis; papillary lacunae are smaller; vacuolization in arterioles, arteries, and arrector pili muscle |
| 2. Angiokeratoma Mibelli (1889) | Warty, vascular, elevated lesion (2–5 mm) | Bony prominence of hands and feet | Childhood to adolescence | 1. No<br>2. Both sexes, but predominantly young girls | Associated with chilblain; purely cutaneous affection | Marked hyperkeratosis and acanthosis: vascular lacunae are larger |
| 3. Angiokeratoma of Fordyce (1896) | Warty, vascular elevated lesions related to superficial vessels of the scrotum (1–5 mm) | Scrotum can extend to penis upper thighs | 2nd to 3rdtt decade | 1. No<br>2. Male | Half of the cases associated with increased venous pressure such as varicocoele | Moderate to marked hyperkeratosis and acanthosis; papillary lacunae are usually drained by dilated venules |
| 4. Angiokeratoma circumscriptum (1915) | Warty, elevated lesions; occur in bands or streaks (20–70 mm) | Lower Extremities (occasionally upper) usually unilateral | At birth | 1. No<br>2. Both | Purely cutaneous affection; represents a true Telangictasia | Mild hyperkeratosis; dilated dermal papillary capillaries are drained by dilated venules |
| 5. Solitary and multiple angiokeratoma | Lesion similar to Mibelli type: smaller than angiokeratoma circumscriptum (2–5 mm) | Occurs on any part of the body predominantly on lower extremities | 2nd to 4th decade | 1. No<br>2. Both | Frequently mistaken for nevus or melanoma | Similar to mibelli type but not preceded by chilblains |

The histopathologic appearance of the various clinical forms of angiokeratomas are practically the same, without the aid of clinical history. The lesion may be objectively identified solely as angiokeratoma. Although there are a few small differences between the variants, both solitary angiokeratoma and the Fordyce type have larger vascular lacunae and more hyperkeratosis and parakeratosis than angiokeratoma corporis diffusum. Fabry's disease shows vacuolization in the muscles of the arteries, veins, capillaries, and in the arrector pili muscle, but is not seen in other kinds of angiokeratoma [1].

Verrucous hemangioma, cherry angioma, lymphangioma circumscriptum, and pyogenic granuloma are clinically relevant differential diagnoses to consider when suspecting angiokeratoma. Histopathology plays a crucial role in distinguishing them from angiokeratoma.

Verrucous hemangioma includes capillary and cavernous hemangioma where vascular lacunae extends up to the reticular dermis and subcutaneous tissue, while vascular spaces in angiokeratoma are restricted to the upper dermis.

The overlying epidermis in cherry or senile angioma is not hyperkeratotic, but is thin and atrophic, with flattening of the rete ridges.

Angiokeratoma is differentiated from lymphangioma circumscriptum by the presence in the latter of a proteinaceous content of the vascular space, but if erythrocytes have spilled into the spaces the differentiation may be difficult.

Angiokeratoma is easily differentiated from granuloma pyogenicum by the frequent presence in the latter of an ulcerated surface, lobules of capillary-like vessels embedded in myxoid and fibroblastic stroma, and the presence of inflammatory cells [1].

Dermoscopy also helps differentiate angiokeratoma from its differentials, where it shows dark or red lacunae, peripheral erythema, and a whitish veil [10].

Treatment modalities include electrocautery, diathermy, curettage, and cryosurgery for smaller lesions. Larger lesions require deep excision followed by grafting or laser ablation [3].

Our case series aims at demonstrating the usefulness of clinical examination in aiding the diagnosis of variants of angiokeratoma. Histopathology being similar in all variants, age of onset, and characteristic site of lesions helps in coming to a diagnosis: angiokeratoma of Fordyce (located on the genitalia, including the scrotum), angiokeratoma corporis diffusum (associated with Fabry's disease), angiokeratoma of Mibelli (located on acral sites), solitary or multiple angiokeratomas (often located on lower extremities), and angiokeratoma circumscriptum (congenital and occurs on the trunk and extremities in linear streaks or patches).

This case series is being reported because it is one of the few that includes all angiokeratoma variants in a single study, as well as the role of histopathology in confirming the diagnosis of angiokeratoma and distinguishing it from other commonly confused conditions such as verrucous hemangioma, cherry angioma, and lymphangioma circumscriptum.

#### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

#### Conflicts of interest

There are no conflicts of interest.

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