

Acroangiokeratitis (Pseudo-Kaposi Sarcoma): Three Case Reports

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SUMMARY Acroangiokeratitis (synonym pseudo-Kaposi sarcoma) is a dermatological condition characterized by purple-colored nodules, plaques or patches, mostly on the extensor surfaces of lower extremities, usually in patients with chronic venous insufficiency and arteriovenous malformations of the legs, but also in hemodialysis patients with iatrogenic arteriovenous shunts, paralyzed limbs and amputation stumps. Acroangiokeratitis in patients with chronic venous insufficiency manifests usually as bilateral skin lesions located on the dorsa of the feet, halux and second toe, or on the medial aspect of lower legs. Acroangiokeratitis may look like Kaposi sarcoma, but in contrast to Kaposi sarcoma, acroangiokeratitis is not characterized by progression of changes, and there is a lack of spindle cells and slit-like vessels on histopathologic analysis. Three cases of acroangiokeratitis encountered in our clinical practice are described. The patients presented with livid-erythematous patches on lower legs and skin changes connected with chronic venous insufficiency, treated at the Department Phlebology Unit. Results of the histopathologic analysis indicated acroangiokeratitis. Thus, in clinical practice it is important to recognize acroangiokeratitis and to exclude Kaposi sarcoma, as sometimes there is similarity with this entity. Topical therapy with neutral and local corticosteroid preparations is often useful, however, the use of compressive bandages and dermatologic follow up are recommended.

KEY WORDS: acroangiokeratitis, pseudo-Kaposi sarcoma, chronic venous insufficiency

INTRODUCTION

Acroangiokeratitis (synonym, pseudo-Kaposi sarcoma) includes skin changes which typically manifest as purple-colored plaques on the extensor surfaces of lower extremities, mostly in patients with chronic venous insufficiency and congenital vascular malformations (1-3). The term acroangiokeratitis was introduced in 1965 by Mali *et al.*,

who described peculiar mauve-colored macules and plaques on the extensor surface of the feet in 18 patients with chronic venous insufficiency (4), whereas in 1967, Stewart (5) and Blefarb and Adams (6) independently described similar lesions on the legs of patients with arteriovenous malformations (AVM). Acroangiokeratitis mostly

belongs to the group of diseases of the blood vessels, considered as a prominent reactive change with vessel proliferation and fibrosis (2). Thus, the term pseudo-Kaposi sarcoma exists due to clinical and histopathologic appearance similar to Kaposi sarcoma. Due to the increasing incidence of the acquired immunodeficiency syndrome (AIDS), recognizing acroangiokeratitis as a separate entity from Kaposi sarcoma, which may be part of the clinical presentation of AIDS, has recently gained in importance.

CASE REPORTS

Case report 1

Eight years before, a 42-year-old male patient noticed erythematous skin changes, at first on the right lower leg, followed by affection of the left lower leg, with appearance of spreading purpuric lesions. One month before presentation, the patient noticed spreading erythematous plaques with inflammatory areas on the right lower leg, which were treated with local antibiotics, epithelialization preparations and heparin. Routine laboratory tests were normal. Despite topical therapy, there was significant deterioration of the local dermatological status, while clinical findings on the right and moderately on the left lower leg indicated vasculitis. Personal history and dermatological status suggested acroangiokeratitis, with Kaposi sarcoma and leukocytoclastic vasculitis as differential diagnosis. The patient complained of intense pain (therefore taking high doses of several analgesics daily), with livid-erythematous areas measuring several centimeters manifesting clinically on the right leg and to a lesser extent on the left lower leg. Hospital management and treatment were indicated. Biopsy of the right lower leg lesion was performed and histopathologic analysis corre-



Figure 1. Lesion on the patient's left lower leg.

sponded to hypostatic dermatitis. Mild corticosteroid and neutral preparations were therefore administered. Insight into the repeat histopathology result in addition to the previous one suggested acroangiokeratitis. Local status remained rather unaltered, with continuous follow up of the patient with the application of compressive bandages (Fig. 1).

Case report 2

An 81-year-old male patient had an ulcer on the right lower leg with hypostatic dermatitis for the past six years, requiring outpatient care. He noticed livid patches measuring several centimeters on the right heel (distally from the ulceration) several years before. *Streptococcus* spp., *Staphylococcus aureus* and *Enterobacter* spp. were isolated from ulcer swabs and oral antibiotic therapy was administered according to antibiotic sensitivity report. On admission, there was extensive ulceration of the right lower leg with irregular margins, almost in the entire circumference, with central granulations, partially covered with yellowish fibrin deposits. The margins and the surrounding skin were slightly erythematous, and the surrounding skin was hypostatically altered. Below the ulceration, posteriorly, there was a livid patch of a palm size, sharply demarcated from the surrounding skin. Skin biopsy was performed and histopathologic analysis indicated acroangiokeratitis with recommended clinical monitoring of the patient and repeat biopsies if necessary. Laboratory tests during hospitalization showed accelerated erythrocyte sedimentation rate and C-reactive protein with a decreased iron level. Repeat ulcer swabs showed bacterial infection (abundance of hemolytic β *Streptococcus* and *Pseudomonas* spp.). The patient was also diagnosed with microcytic anemia, with conclusion of reactive leukocytosis due to inflamed lower leg ulcer based on CBS, with recommended control tests and further follow up. During hospitalization, the ulcer was rinsed with potassium permanganate solution and the patient wore elastic compressive bandages, along with topical corticosteroid and neutral preparations applied to the livid patch on the right heel. He was suggested to monitor laboratory parameters and consult a hematologist and dermatologist at Department Phlebology Unit for further follow up upon discharge from the hospital (Fig. 2).

Case report 3

A 68-year-old female patient was under care of a dermatologist at Department Phlebology Unit for



Figure 2. Extensive ulceration on the right lower leg.

hypostatic dermatitis for several years. She was a diabetic and adipose with a history of cerebrovascular infarction several years before. Clinical examination showed plantar changes interdigitally, with a diagnosis of dermatomycosis (mycologically verified *Trichophyton* spp. infection). There was severe edema with slight erythematous changes manifest on both lower legs. Topical corticosteroids, neutral moisturizers and topical antimycotics were applied locally. As the local status progressed, with visible sporadic induration, skin biopsy of livid-erythematous patches on the lower legs was performed and histopathologic analysis indicated acroangiodermatitis. Topical therapy with neutral and local corticosteroid preparations was continued, with the use of compressive bandages and recommended follow up by a dermatologist at Department Phlebology Unit (Fig. 3).

DISCUSSION

A review by Rashkovsky *et al.* describes acroangiodermatitis as a condition that occurs in 5 different clinical conditions. Namely, besides chronic venous insufficiency and AVM of the legs, it occurs in patients with iatrogenic arteriovenous insufficiency, chronic renal failure treated with dialysis, paralyzed legs and amputation stumps (7).

Acroangiodermatitis is frequently associated with chronic venous insufficiency, where skin changes are often bilateral and usually located on the dorsa of the feet, first and second toe, or on the medial aspect of lower legs (5-7). Skin changes are the result of increased venous pressure, which leads to proliferation and dilation of veins and superficial plexus (2). Chronic pressure changes with vessel proliferation in the upper and mid-dermis and extravasation of red blood cells produce a combination of purplish papules and plaques on the edematous skin (3).

When acroangiodermatitis is associated with AVM, it is usually unilateral, sometimes with palpable thrill. When angiodermatitis is associated with ulceration on the hand, it is virtually diagnostic of a shunt, while acroangiodermatitis on lower leg is often connected with chronic venous insufficiency or paralysis.

Besides skin changes in chronic venous insufficiency, acroangiodermatitis may occur in above-knee amputees who use suction socket prosthesis that exerts negative pressure, or in below-knee amputees, or in patients with arteriovenous shunts (acroangiodermatitis of Mali), when both veins and arteries are involved (3).

Clinically, acroangiodermatitis is characterized by multiple papules, nodules and plaques, sharply defined, usually with central bright red lesions and peripheral more red-brown, sometimes in band-like or bizarre configurations, generally localized on the dorsal aspect of the foot or the base of the hallux and second toes, or rarely the ankle and the lower aspect of the shin, usually associated with edema. Skin lesions may sometimes be ulcerated. In case of chronic venous insufficiency, lesions are often bilateral, while in other disorders there is an underlying clinical defect (signs of vascular or neurologic problem) and the lesions tend to be unilateral (2).

Acroangiodermatitis may also be the result of AVM, which exists at birth but may not manifest until later, mostly localized intracranially, or may be found on the extremities, trunk and viscera (7). The initial presentation of AVM may be a faint or ill-defined area of macular erythema (resembling a port-wine stain), with expansion often in puberty or following trauma or infection, altering to a deeply erythematous to violaceous color, with an underlying subcutaneous mass, with warmth, thrill and



Figure 3. Edema and erythematous lesion on lower legs of the patient.

bruit. End stage lesions of AVM are characterized by ulceration, intractable pain, bleeding and multiple violaceous papules or nodules with a picture of acroangiokeratosis changes (3).

The majority of acroangiokeratosis cases occur in prolonged venous hypertension of lower legs, usually with the appearance similar to Kaposi sarcoma. Acroangiokeratosis is not characterized by progression of changes, and there is a lack of spindle cells and slit-like vessels, which are histologic features seen in Kaposi sarcoma. The pathological differential diagnosis of the disease in the early stages includes a simple angiomatic malformation, and 'venous' dermatitis on lower legs (5-7). The diagnosis of acroangiokeratosis should not be made easily when clinical history of a past injury in the area exists.

There are still AVMs, sometimes known as acroangiokeratosis, which may cause problems. Differential diagnosis includes the possible occurrence of very early stage of Kaposi sarcoma in an HIV-positive patient, but histological characteristics exclude acroangiokeratosis (collagen dissection, large lymphatic-like spaces, angiomatic lesions and spindle-cell proliferation) (5-7).

Acroangiokeratosis may appear in first pregnancy, as pregnant women may have gravity purpura ("dermite ocre of favre") on lower legs (especially over the site of venous varicosities) possibly extending to the dorsa of the feet and toes. The lesions consist of minute purpuric macules, which coalesce to form irregular plaques, or sometimes follicular lesions or edema, sclerosis, ulceration and other signs of venous insufficiency. The disease is chronic, individual lesions persist apparently unchanged for months or years. The treatment is unsuccessful and often unnecessary, but when it is required, treatment of venous insufficiency may show slow improvement (5-7).

The histopathology of acroangiokeratosis includes histologic features similar to those found in stasis dermatitis, including dilated vessels, mild edema, hemosiderin deposition, fibrosis and patchy lymphohistiocytic infiltrates, while vessels are round and lack atypia (2). There is marked vessel proliferation in the papillary and reticular dermis with red blood cell extravasation and abundant hemosiderin deposition and fibrosis, but vessels are round and regular (unlike Kaposi sarcoma), without vascular slits and polymorphic hyperchromatic spindle cells, less obvious dissection of collagen bundles by new vascular channels (5-7).

Differential diagnosis of acroangiokeratosis includes, first of all, Kaposi sarcoma, although clinical findings of these conditions are similar, there are differences in histologic features (2). Generally, the skin changes associated with chronic venous insufficiency, vascular or neurologic insufficiency suggest acroangiokeratosis.

Therapy for acroangiokeratosis includes external compression as the best therapeutic method, in combination with topical antibiotics or topical corticosteroids for early stage lesions (2,3). However, the clue is the treatment of the underlying disease. In patients with chronic venous insufficiency, compression and sclerotherapy usually bring improvement. The edema of the stump may be reduced with short courses of oral diuretics, where medication can be gradually decreased (2,3). In below-knee amputees, the distal part of the stump is edematous, the stump dangles freely in the socket or has no distal support or partial end-bearing (3). The support of the stump end in the socket by temporary cushion or platform leads to compression, which gradually reduces and slowly clears the verrucous condition. The greater compression on the distal stump stimulates more immediate and lasting improvement. The use of compression bandage, shinker socks, other pads and partial end-bearing are important therapeutic measures and can be applied by a prosthetist.

Generally, acroangiokeratosis is considered to be a special form of the 'angiokeratosis' of Favre and Chaix, usually in patients with chronic venous insufficiency, localized mostly on the dorsal areas of the feet and toes (8-10). The occurrence in patients with chronic venous insufficiency with the signs of postthrombotic syndrome was supported by the study of Miura, which has revealed that 60% of women and 38% of men with postthrombotic syndrome showed signs of acroangiokeratosis (8). Acroangiokeratosis may be present in other conditions, for example in AVM; e.g., Lyle *et al.* have reported on acroangiokeratosis in a patient with Klippel-Trenaunay syndrome (1).

While the name "pseudo-Kaposi sarcoma" is based on the close clinical similarity between these two angioproliferative disorders, sometimes there may be histologic similarities as well (1,11). In order to differentiate these two diseases, Kani-takis *et al.* performed immunolabeling with CD34 antigen (a marker of Kaposi sarcoma cells) (11). The immunohistopathologic analysis of 16 biopsies of skin lesions in patients with Kaposi sarcoma and 7 biopsies of skin lesions in patients with acroangiokeratosis showed CD34 on both en-

endothelial cells and characteristic spindle-shaped, perivascular cells in all cases of Kaposi sarcoma, and strong labeling of endothelial cells of hyperplastic vessels of acroangiokeratosis, but without perivascular CD34 expression (in distinction to Kaposi sarcoma). Therefore, the immunolabeling with CD34 antigen appears to be a valuable method to differentiate Kaposi sarcoma and acroangiokeratosis (11).

Different authors report on the association of acroangiokeratosis with various conditions: acroangiokeratosis associated with vascular disease (described by Mali, with chronic venous insufficiency), AVM with angiokeratosis (described by Stewart and Bluefarb) and angiokeratosis occurring after placement of arteriovenous shunt for hemodialysis (5,6,12). In this article, we present our experience with acroangiokeratosis, demonstrated in patients with chronic venous insufficiency. The patients had livid-erythematous patches on lower legs, with chronic venous insufficiency, and were treated by a dermatologist at Phlebology Unit of our University Department. Histopathology indicated acroangiokeratosis, which was important to exclude Kaposi sarcoma, as they may have similar clinical picture.

In the last decades, the recognition of acroangiokeratosis has become ever more important because the incidence of HIV-positive individuals is on a constant rise and classic Kaposi sarcoma may be part of the clinical picture of AIDS (12). Schulze-Osthoff *et al.* analyzed the expression of basic fibroblast growth factor (bFGF) in Kaposi sarcoma patients with AIDS, classic Kaposi sarcoma, and acroangiokeratosis (13). The analysis of antigen expression (immunoperoxidase staining of cryostat sections with affinity-purified anti-bFGF antibodies) demonstrated strong expression of bFGF in basal and suprabasal keratinocytes, which were also intensively stained in normal skin biopsies. The results indicated the generally absent growth factor from the endothelial cells and spindle cells of the neoplasms, which exhibited a very faint staining in a small number of lesions (13).

Acroangiokeratosis presents a similar clinical and histologic picture as developmental foot AVM (acral hyperostoma, Malan's syndrome), where the prognosis is poor, resulting in amputation in some instances. It has been shown that determination of shunt volume by means of radiolabeled macroalbumin or microspheres helps differentiate the two conditions (which both may present similar-

ties with Kaposi sarcoma). The terminal vascular characteristic underlying both conditions (acral hyperostoma and acroangiokeratosis) is the insufficiency of the calf muscle pump, resulting in elevated capillary pressure (anatomical insufficiency in acroangiokeratosis, functional insufficiency in acral hyperostoma) (8). Landthaler *et al.* report on two patients with acroangiokeratosis in paralyzed legs, with the lack of muscle pump and possibly disturbed innervation of vessels (14).

According to clinical, angiologic and histopathologic findings, it is possible to differentiate between so-called "kaposiform" acroangiokeratosis and Kaposi sarcoma (15). The etiopathogenesis, prognosis and therapy of "kaposiform" acroangiokeratosis and Kaposi sarcoma are primarily derived from clinical and histologic criteria. Thus, the clinical and histopathologic picture of acroangiokeratosis usually shows stasis dermatitis in contrast to Kaposi sarcoma (15).

Electron microscopy of skin biopsies is sometimes crucial. Secher *et al.* report on a case of acroangiokeratosis of the feet, in which clinical and light microscopy signs indicated Kaposi sarcoma, but electron microscopy of skin biopsies defined signs of degeneration of vascular walls and infiltrating cells (16). Therefore, when conventional histology is inconclusive or fits poorly to history data and/or clinical picture of the lesions, electron microscopy should be employed (16).

It should also be noted that acroangiokeratosis may occur in above-knee amputees who use suction socket prosthesis that exerts negative pressure. The increasing use of suction-socket lower limb prostheses sometimes produces skin changes, mostly because the skin of the amputation stump must adapt to an entirely new environment, which may manifest as verrucous hyperplasia and sometimes lead to acroangiokeratosis (17). Sbrana *et al.* report a case of amputation stump dermatitis in a patient with suction-socket lower limb prosthesis, clinically resembling verrucous hyperplasia, but histology confirmed acroangiokeratosis (17).

There have also been attempts to establish new diagnostic methods. Rosen *et al.* tried to use sodium pertechnetate Tc 99m radionuclide scanning as a sensitive indicator to detect lesions of Kaposi sarcoma, including occult infiltrations (18). The patients with acroangiokeratosis obtained "false-positive" scan, and the technique was not found to help in differentiation of these two diseases. However, technetium scan may be helpful

in deciding on the course of therapy for acroangiokeratosis by demonstrating the nature of the underlying vascular anomalies (18).

CONCLUSION

In clinical practice, based on different experiences, we conclude that it is important to recognize acroangiokeratosis, especially due to its appearance similar to some other diseases, first of all Kaposi sarcoma, the prognosis of which is often rather poor. Appropriate recognition of acroangiokeratosis is important for the disease prognosis in individual patients.

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