

Differential diagnosis of leg ulcers

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Abstract

Leg and foot ulcers are symptoms of very different diseases. The aim of this paper is to demonstrate the differential diagnosis of leg ulcers. The majority of leg ulcers occur in the lower leg or foot. In non-venous ulcers the localization in the foot area is more frequent. The most frequent underlying disease is chronic venous disease. In 354 leg ulcers, Koerber found 75.25% venous leg ulcers, 3.66% arterial leg ulcers, 14.66% ulcers of mixed venous and arterial origin and 13.5% vasculitic ulcers. In the Swedish population of Skaraborg, Nelzen found a venous origin in 54% of the ulcer patients. Each leg ulcer needs a clinical and anamnestic evaluation. Duplex ultrasound is the basic diagnostic tool to exclude vascular anomalies especially chronic venous and arterial occlusive disease. Skin biopsies help to find a correct diagnosis in unclear or non-healing cases. In conclusion, chronic venous disease is the most frequent cause of leg ulcerations. Because 25% of the population have varicose veins or other chronic venous disease the coincidence of pathological venous findings and ulceration is very frequent even in non-venous ulcerations. Leg ulcers without the symptoms of chronic venous disease should be considered as non-venous.

Keywords: leg ulcer; venous ulcer; arterial ulcer; non-vascular ulcer; chronic venous insufficiency

Introduction

The term leg ulcer is not a diagnosis but a possible symptom of many different diseases. The majority of leg ulcers occur in the lower leg or foot. In non-venous ulcers, the localization in the foot area is more frequent.¹ The most frequent underlying disease is chronic venous disease. In 354 leg ulcers, Koerber found 75.25% venous leg ulcers, 3.66% arterial leg ulcers, 14.66% ulcers of mixed venous and arterial origin and 13.5% vasculitic ulcers.¹ In the Swedish population of Skaraborg, Nelzen found a venous origin in 54% of the ulcer patients.² In a London population excluding diabetic foot ulceration, Moffat *et al.*³ found a venous

origin in 43% of the ulcers. Koerber found differences in the population between male and female patients. Venous ulcerations were present in 52% of the male 62% of the female population. A mixed venous and arterial origin was present in 18% of the male 12% of the female population and vasculitic ulcers in 12% of the women and in 15% of the men.²

Venous leg ulcers

Venous leg ulcers are defined as ulceration in a region of skin changes due to chronic venous disease.⁴ Venous ulcerations never occur in normal skin but usually in areas with lipodermatosclerosis or white atrophy (Figure 1). In the Bonn Vein Study, we found a prevalence 0.6% healed and 0.1% active venous ulcers in the general population between 18 and 79 years of age.⁵ There was no difference between the male and female population.⁵ In the San Diego Population Study, the advanced chronic venous disease stages including

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Figure 1 Venous leg ulcer with typical signs of chronic venous insufficiency

venous ulcerations (CEAP [clinical, aetiological, anatomical and pathological elements] stages C4–C6) were present in 7.8% of the male 5.3% of the female population.⁶

Other localizations like on the lateral aspect of the lower leg or in the foot region are possible but less frequent.¹ The most frequent localization of venous ulcers is the inner ankle region; the ulcer maybe covered with fibrin or granulating tissue. In venous ulcers and black skin necrosis is an unusual finding. These changes may indicate arterial involvement or an arterial or vasculitic origin of the ulcer. In the surrounding of the ulcer pigmentation, purpura, eczema, white atrophy or dermatoliposclerosis can be found. Venous ulcerations maybe caused by varicose veins or a post-thrombotic syndrome.⁴ A mixed pathology of superficial and deep venous insufficiency may be present. Oedema is also a frequent finding in these patients.

Arterial leg ulcers

Arterial leg ulcers are caused by a deficit of oxygen supply in the tissue due to arterial occlusions. The most frequent pathology is peripheral arterial occlusive disease (PAOD) with arteriosclerotic occlusions of leg arteries. Necrotic ulcers of the toes, foot or leg may occur in the most advanced Fontaines stage IV cases. In Fontaines stage III cases patients suffer resting pain or nocturnal pain without tissue loss. In Fontaines Stage II with intermittent claudication arterial ulcerations may occur after trauma of the lower leg or foot or in combination with chronic venous disease. In this complicated stage II ulcerations resting pain is usually missing.

The typical localization of arterial ulcerations is the foot and toe region in the advanced arterial disease and the malleolar region in the worse stages. The ulcers are typically very painful and show black necrotic areas. Typical signs of chronic venous disease are missing except in cases of mixed ulcers.^{7,8}

Thromboangiitis obliterans is another cause for arterial leg ulcers. In this inflammatory disease of small and medium arteries and veins, thrombotic occlusion of preferably peripheral vessels occurs. Necrotic ulcers mostly of the feet may be the consequence. Arterial venous fistula is another rare cause of chronic ischaemic leg ulcers.⁹

Hafner *et al.*¹⁰ proposed a concept of ischaemic subcutaneous arteriosclerosis. Hypertensive subcutaneous arteriosclerosis may lead to different but similar patterns of ischaemic skin necrosis. This includes distal Martorell's hypertensive ischaemic leg ulcer, proximal non-uremic calciphylaxis in normal renal and parathyroid function, distal calciphylaxis in end-stage renal insufficiency and proximal calciphylaxis in renal disease.^{10,11} In Martorell's ulcer, skin necrosis with livid or black borders localized on the laterodorsal lower leg are typically clinical findings.^{10,12,13} Long lasting arterial hypertension in combination with diabetes mellitus are frequent findings.¹⁰ These ulcers should not be misdiagnosed as pyoderma gangraenosum.^{14,15}

Mixed leg ulcers

Mixed leg ulcers of combined venous and arterial origin are present in about 15% of the ulcer population.² In the majority of cases the primary cause of the leg ulcers is the venous origin and the arterial occlusive disease is complicating healing. In many of the older patients the mobility is decreased

because of age and multimorbidity and arterial claudication maybe overseen. The ulcers show the typical signs of chronic venous disease in the surrounding area but may have black necrotic areas in addition. In the majority of cases treatment of venous reflux improves ulcer healing despite of the reduced ankle brachial index.¹⁶ In some cases combined arterial recanalization and superficial venous reflux surgery are indicated.¹⁷

Diabetic leg ulcer

Diabetes mellitus is a risk factor for PAOD. Despite this specific ulcers may occur in diabetic patients.

Diabetic microangiopathy may lead to occlusions of small vessels mainly in the toes and consecutive toe necrosis with a risk of bacterial infection and diabetic gangrene.^{18,19} Independently, diabetes may among other reasons lead to peripheral neuropathy with loss of sensitivity and ulcerations in the pressure areas of the foot. The neuropathy involves the skin regulation, skin physiology, skin sensitivity and also the muscle innervations of the foot.^{20–23} In consequence, pressure distribution of the foot changes. The neuropathic ulcerations are typically located at pressure zones showing hyperkeratosis surrounding the ulcer. Sensory loss is a typical clinical finding identifying neuropathy. A foot ulcer without hyperkeratosis is usually not a neuropathic ulcer and should be differentiated by skin biopsies. Necrobiosis lipoidica is another necrotizing skin disease which usually occurs in patients with diabetes mellitus but may also be present in patients without diabetes. It is a granulomatous inflammation of the skin. Dermal blood vessels are stenosed or occluded. The most frequent location in necrobiosis lipoidica is the anterior lower leg ulcerations in 35% of the cases.²⁴

Vasculitic leg ulcers

A large inhomogeneous group of leg ulcers can be caused by vasculitis. According to the Chapel Hill classification,²⁵ we can distinguish between large vessel, medium vessel and small vessel vasculitis. In the skin, leucocytoclastic small vessel vasculitis with inflammation and palpable purpura maybe present. Multiple small necrotic ulcers may be associated to vasculitis. Vasculitic ulcers maybe also present in patients with cryoglobulinaemia in myeloma or hepatitis C patients²⁶ or in higher autoimmune diseases.²⁷ Cryofibrinogenaemia with vasculitis maybe the cause of rheumatoid arthritis.²⁸

Pyoderma gangraenosum is a specific form of ulceration with non-leucocytoclastic vasculitis caused by an auto inflammatory process.^{29,30} The ulcers with an inflammatory border and skin necrosis are often associated to chronic inflammatory diseases like colitis ulcerosa or rheumatoid arthritis. Pyoderma gangraenosum also occurs after trauma or after operation. As in other vasculitic ulcers they respond well to immunosuppressive treatment.

Leg ulcers of other origin

Leg ulcers may also occur in patients with Klinefelter's syndrome.^{31–33} In these patients with hypogonadism and testosterone-deficit slow healing ulcers may occur with or without chronic venous disease. There is some evidence that abnormal platelet aggregability or fibrinolysis with an elevated activity of plasminogen activator inhibitor-1 may play an important role.³⁴

Ulcers caused by infections may include ectymata caused by bacterial infection of the skin,



Figure 2 Colliquation necrosis after contact with concrete in a do-it-yourself



Figure 3 Squamous cell carcinoma

necrotic cellulitis, cutaneous or subcutaneous leishmaniasis and other infections.

Some drugs may also cause ulcerations. One example is skin ulceration as a side-effect of hydroxyurea treatment in myeloproliferative diseases. Hydroxyurea treatment may cause hyperpigmentation and ulcerations, which can mimic even chronic venous disease.^{35–40}

Artificial ulcers maybe caused by contact of the skin with basic or acid substances. An example is colliquative necrosis of the skin caused by contact with concrete⁴¹ (Figure 2).

The most important differential diagnosis of leg ulcers are ulcerations caused by malignant or semi-malignant diseases. Ulcerating tumours like basal cell carcinoma or melanoma may mimic venous ulcerations.⁴² In long-lasting chronic leg ulcers, squamous cell carcinoma or basal cell carcinoma may also arise as a complication of the chronic ulceration^{43–46} (Figure 3). As a consequence, each leg ulcer with unclear origin or chronic ulcers with no healing tendency or abnormalities in the clinical picture must be investigated by skin biopsies to exclude primary tumour or tumour transformation.

Summary

Leg ulcers and foot ulcers are symptoms of very different diseases. Each ulceration needs a clinical and anamnestic evaluation. Duplex ultrasound is the basic diagnostic tool to exclude vascular anomalies especially chronic venous and arterial occlusive disease. Skin biopsies help to find a correct diagnosis in unclear or non-healing cases. Chronic venous disease is the most frequent cause of leg ulcerations. Because 25% of the population have varicose veins or other chronic venous disease the coincidence of pathological venous findings and ulceration is very frequent even in non-venous ulcerations. Leg ulcers without the symptoms of chronic venous disease should be considered as non-venous.

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Conflict of interest

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