Verrucous Skin Lesions on the Feet in Diabetic Neuropathy in the Context of Podiatric Practice – Our Pilot Experiences

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ABSTRACT
Skin changes in patients with diabetic foot (DF) are relatively common. The most frequent lesions feature papillae or cilia of various forms. The condition known as “verrucous skin lesions on the feet in diabetic neuropathy” (VSLDN) occurs in patients with distal diabetic sensorimotor neuropathy and is commonly located in places of high mechanical pressure. However, there is a scarcity of published data on the diagnosis and treatment of VSLDN. Our paper describes various types of VSLDN skin pathology, summarizes the diagnostic procedure options available, and documents the experience of our diabetic foot clinic in applying short-term VSLDN therapies as part of routine podiatric practice.

KEY WORDS: diabetic foot, VSLDN, carcinoma

INTRODUCTION
Preventive assessments and regular follow-ups of at-risk patients or patients with diabetic foot (DF) ulcers or Charcot osteoarthropathy are integral elements of standard foot care. As part of daily podiatric practice at our DF clinic, the investigators provide a range of diagnostic procedures and therapies to target peripheral arterial disease, local treatment, management of infection, and adequate foot off-loading (1,2). During examination of patients at risk of DF or with pre-existing DF, skin changes and lesions (both benign and malignant) in the lower extremities are monitored. One of the frequent changes observed in our daily podiatric practice is verrucously modified skin of the lower extremities, a condition first described in 1995 by Gerbing and Hunziker as “verrucous skin lesions on the feet in diabetic neuropathy (VSLDN)” (3). As its name applies, the disease is characterized by the appearance of hyperkeratotic lesions with wart-like surfaces on the feet of diabetic patients affected by diabetic neuropathy (4). They occur in sites with frequent skin traumatization due to increased mechanical stress or long-term friction (5).

Etiopathogenesis and diagnostics
The etiopathogenesis of these lesions is poorly understood, but chronic pressure or friction in the field of distal sensory neuropathy is probably the real cause (6). Predisposing factors generally present as
deformities, scars, or transplant skin grafts (3,7). Similar changes to verrucous skin lesions are also found in other conditions such as lower limb lymphedema (6).

Clinical diagnosis, which consists of visually inspecting wounds and assessing for the presence of predisposing factors, should ideally be followed up by histological examination. Pseudoepitheliomatous hyperplasia, which mimics squamous cell carcinoma of the skin without cell atypia, can be detected histologically (Figure 1, a and b). The hyperplastic squamous epithelium often permeates bacteria and the acute inflammatory cell infiltrates (6). Histopathology aids differential diagnosis and helps to exclude VSLDN-like lesions, especially squamous cell carcinomas (Figure 1, c, d) and verrucous carcinomas (5).

TYPES OF VSLDN

Based on clinical findings of VSLDN and podiatric inspections of other skin changes, we categorize the abnormalities as follows:

(1) **Hard forms of VSLDN** – hyperkeratotic lesions with wart-like surfaces frequently located around the defect, in the scar area, or at sites of increased mechanical stress. We observed several cases of hard-form VSLDN occurring in regions with skin grafts. Lesions should be debrided sharply using a scalpel, usually resulting in bleeding. The poorest findings are typically observed in patients with neglected foot care (Figure 2, a).

(2) **Soft forms of VSLDN** – soft papillae–resembling cilia most frequently located at sites with dehiscent/chronically unhealed surgical wounds or diabetic foot ulcers. Sharp debridement often results in bleeding of soft tissue and papillae. Not only are these forms very difficult to remove, they re-grow rapidly after debridement (Figure 2, b). Based on our clinical experience, soft forms of VSLDN often become colonized or infected with multi-resistant bacterial flora (predominantly Gram-negative microbes) particularly in immunocompromised individuals (8).

(3) **Combined forms of VSLDN** – combined forms, which commonly occur, are characterized by the co-presence of soft ciliary papillae in the wound and verrucous hyperkeratotic lesions (Figure 2, c).

The categorization of VSLDN into different forms should simplify the clinical approach to the therapy, because, based on our experience, individual lesions react in different ways to local therapeutics. It seems that the difference between the various forms of VSLDN will be based on clinical and therapeutic features. So far, we have not detected any discrepancies in the occurrence of distal sensorimotoric neuropathy (all patients suffered from severe diabetic neuropathy diagnosed by Biothesiometer with Vibration Perception Threshold above 50 V) as of histological examinations (9). Patients with peripheral vascular disease were not excluded. Whether the VSLDN differences could be caused by any abnormalities such as structural skin composition, collagen changes, or other microscopic variations has not yet been studied. This hypothesis needs to be verified in a larger study.

THERAPY

Although a standard therapeutic approach aimed at resolving vascular problems and managing infection has yet to be determined, it is generally recommended to properly off-load patients using different types of devices based on lesion site, clinical status, and comorbidities (10-12). In cases where signs of inflammation are only local, oral antibiotics or locally acting antibacterial agents can be used over the short term. However, in cases of moderate infection or where there are systemic signs of infection, antibiotics should be administered as part of the treatment (11).

Despite the absence of concrete recommendations regarding local therapy, the principal treatment would appear to be debridement followed by local therapy. The rare case reports in the literature, nonetheless, describe patients cured by cryotherapy,
bactericidal solutions, hydrocortisone, topical maxacalcitol, 5-fluorouracil, and tacalcitol. But the level of evidence for VSLDN treatment is very weak and based only on some case reports (6).

DISCUSSION

Our pilot experiences with VSLDN and its treatment

As part of our clinical practice, we have begun to implement various promising therapeutic procedures in collaboration with dermatologists (from 6/2017). So far, we have diagnosed 27 patients with VSLDN lesions. More than half (16/27) of them have been selectively treated for VSLDN by various local devices/substances (see below). The rest of patients (41% – 11/27) were without specific treatment in the case of hard-form VSLDN, while in the case of soft or combined form they were treated by modern local devices. Written informed consent was provided by each subject of this case report to publish case details and associated images.

As an integral part of VSLDN, all forms of VSLDN should be properly treated by the effective method of off-loading. Based on our pilot experience, hard forms of VSLDN are more easily curable than soft forms. Hard forms of VSLDN (skin changes) healed in all patients (100% – 4/4) in 9.5 months (4-12 months), while soft forms healed in 1 patient only (25% – 1/4). Other patients with soft forms of VSLDN healed after amputation or resection procedures – during 14 months on average (1-31 months). Combined forms of VSLDN healed only in 3 patients (38% – 3/8) in 24 months (14-30 months).

Based on our experience, for milder instances of hard-form VSLDN (typically at surrounding a foot ulcer or in a healed scar) we typically apply an ointment containing 5% salicylic acid and 10% urea. For more advanced lesions, we use Arievich’s ointment, a keratolytic agent containing 12 g of salicylic acid per 100 g of base. After several days of application, the hyperkeratotic lesions begin to disintegrate and bleach, making them easier to remove using a scalpel, pumice, grinder, or glass file.

When applying this kind of therapy, attention should also be given to the patient tolerability of treatment. The risk of skin damage should never exceed therapeutic benefit, with ointment applied only to hard lesions once a day or every second day. A balance should be struck between inadequate irregular application on the one hand and excessive administration on the other, while minimizing any irritation or destruction of healthy skin.

Figure 2. Types of VSLDN: (a) Hard form of VSLDN its detail in a patient with DF and poor hygiene; (b) Soft form of VSLDN and its detail in a patient with a neuropathic ulcer; (c) Combined form of VSLDN its detail in a patient with DF; (d) Effective treatment of soft-form VSLDN by AgNO3 + off-loading.
We are also currently trialing a soft-form VSLDN therapy (present at the edges or at the bottom of diabetic foot ulcers) for the elimination of ciliary papillae. The treatment involves the local application of AgNO₃ (Figure 2, d) to the wound followed by the placement of a gauze saturated with disinfectant solution containing polyhexanide, superoxide antiseptic liquid, and/or NaCl. If the wound is too wet, a diluted povidone-iodine solution is used. Both forms of treatment can be locally combined as required.

As an integral part of any prospective treatment, all patients should be educated in all aspects of local care, off-loading, and diabetes maintenance on an ongoing basis.

CONCLUSION

Although diagnosis and treatment of VSLDN should largely remain the domain of dermatologists, its occurrence in foot clinics is presumably relatively frequent and therefore clinically relevant. Hyperkeratotic verrucous skin lesions can manifest as pre-ulcerative lesions or develop secondarily as a result of prolonged mechanical pressure around the diabetic ulcer. Irrespective of form, they complicate the treatment of DF and prolong the healing process. The disease is under-researched in the literature, with no clear recommendations in terms of its etiopathogenesis or treatment. We believe that, in the context of daily foot care, as long as the number of patients with DF increase so will the various manifestations of VSLDN (13).

This article is intended to draw attention to a clinically relevant finding in the lower limbs – VSLDN, which may negatively affect wound healing or may be mistaken in several cases for tumor lesions. Unfortunately, data about these structural changes are lacking in the literature and it is necessary to examine this issue more closely. This article offers a clinical perspective and pilot experience with this issue, including pilot data on this diagnosis. The classification is only descriptive and clinical, and has no evidence base yet. Our clinical practice is now guided by the goal of developing new diagnostic and therapeutic approaches in this area. However, it is necessary to always collaborate with dermatologists and histopathologists regarding the appropriate medical approach.

Our preliminary case report has some limitations. Since we assume that the number of these lesions has increased recently, we have started to diagnose the presence of VSLDN more precisely – at this moment we monitor only selected cases. Therefore, we have not yet data available on the real incidence of such skin abnormalities. This paper is only a preliminary notice sharing our experience with diagnostic procedures and our efforts to determine the appropriate therapy. We are preparing a study with the detection of lesion incidence, histological examinations, and follow-up of patient treatment.

Ethics statement

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. The paper is exempt from ethical committee approval since this was a pilot project based on our experiences trying to map the occurrence of VSLDN, specify the clinical types of VSLDN and therapy possibilities.

Conflict of interest:

The authors have no conflicts of interest to disclose.

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JB contributed to the study protocol and designed and reviewed the manuscript. MD, VW, VW, RB, and JH researched the data and reviewed the manuscript. LW performed histological assessment and reviewed the manuscript. DD, EV, and AJ reviewed/edited the manuscript.

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