Case Report

Successful treatment of nephrogenic fibrosing dermopathy in a kidney transplant recipient with photodynamic therapy

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Introduction

Nephrogenic fibrosing dermopathy (NFD) was first described by Cowper et al. [1] as a cutaneous fibrosing disorder associated with renal dysfunction. In the last 3 years there has been a growing body of literature regarding NFD. Clinically, skin is thickened or oedematous with indurated papules and plaques. The pathogenesis of NFD is largely unknown. Several authors have discussed a reaction against the PVC materials used in dialysis, but NFD has also occurred in patients without dialysis [2–4]. Spontaneous healing of NFD has not been documented previously; however restitutio ad integrum after improvement of the renal situation has been reported [2]. The therapy of NFD has to be regarded as difficult and, to date, only experimental therapies have been published. We report the first case of successful treatment of NFD following kidney transplantation.

Case

A 28-year-old patient had undergone successful renal transplantation from a 59-year-old female cadaveric donor. He had been on haemodialysis for 8 years due to reflux nephropathy and chronic interstitial nephritis. The initial immunosuppression consisted of steroids, cyclosporin A, mycophenolate-sodium (1.44 g/day) and basiliximab (20 mg intravenously pre-transplant and on day 4). Seven months after transplantation the patient noticed a painful oedema and the beginning of indurated skin in the area of the medial ankles. Two weeks later, at the patient’s first visit to the dermatological department, large reddish atrophic macules on sclerotic hairless skin on both lower legs were observed (Figure 1a). At this time, the patient was receiving immunosuppressive treatment with cyclosporin A (180 mg/day; trough level: 99 ng/ml), methyl-prednisolone (4 mg/day) and mycophenolate-sodium (1080 mg/day).

The patient had no other diseases, such as diabetes or haematological diseases. Blood pressure was well controlled with antihypertensive medication. The only dermatological diseases he had suffered in the past were

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Fig. 1. (a) Left lower leg (dorsal view) with NFD in a kidney graft recipient. NFD occurred 7 months after kidney transplantation. (b) NFD after successful MAL–PDT.
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verrucae vulgares on both hands 3 years before transplantation. Additionally, the patient had slight acne papulopustulosa on the face since transplantation. Xeroderma that occurred 4 months after the commencement of haemodialysis was also seen.

A skin biopsy of the left lower leg was consistent with the diagnosis of NFD. Histologically, thickened collagen bundles and surrounding clefts in the reticular dermis, plump bipolar spindle cells and longish fibroblasts were seen. The alcian blue staining was positive for mucin. Magnetic resonance tomography only showed a thicker dermis (≤3 mm), but excluded an involvement of deeper layers and soft parts. Other investigations, such as abdominal ultrasound and blood analysis (including electrolytes, blood count and also antibody profile), were inconspicuous.

As therapy we administered photodynamic therapy (PDT) with the lipophilic agent methyl aminolaevulinate (MAL) on the skin of the left lower leg. Following 3 h under occlusion, illumination was performed with red light emitted from high-brightness light-emitting diodes (LEDs) at a distance of 8–10 cm. During the treatment the patient mentioned slight stinging and pain in the illuminated area. No other side effects were observed. After 2 weeks we repeated the MAL–PDT on the same lesion and after a further 4 weeks, normal soft skin with distinct hair growth was observed clearly (Figure 1b). The right lower leg was also successfully treated with MAL–PDT. The immunosuppressive therapy remained unchanged. The patient was content and free of pain and has shown no relapse for 13 months after the first PDT. Thus, MAL–PDT seems to be effective and well tolerated in NFD.

Discussion

Transplantation of solid organs has benefited more than one million patients worldwide. The vast majority of organ transplant recipients still require lifelong immunosuppressive treatment, which is associated with an increased risk of developing infections as well as neoplasms, especially non-melanoma skin cancer [5]. Some transplant recipients develop collagenous disorders, e.g. calciphylaxis or NFD. Calciphylaxis is a very aggressive metabolic disease with rapidly extending ischaemic skin necrosis or acral gangrene, but affects also internal organs [6].

Another rarer collagenous disease is NFD, which shows a thickened or oedematous skin with induration on papules and plaques, often located on extremities and on the trunk. NFD should be distinguished from other fibrotic disorders, such as localized scleroderma, scleromyxoedema, toxic-oil syndrome, sclerodema adultorum, systemic sclerosis, calciphylaxis and eosinophilic fasciitis. All these differential diagnoses have thickened and indurated skin. The correct diagnosis can be established with clinical findings, histological examination and an investigation of internal organs. Until now, no definitive therapy for NFD has been available. Experimental therapies contain chemotoxic and immunosuppressive agents, such as prednisone, thalidomide, mycophenolate mofetil, calcineurin inhibitors and plasmapheresis [7] [www.pathmax.com/dermweb/]. These treatments are costly, cause side effects for the patients and a positive outcome is not guaranteed.

PDT is said to be effective in localized scleroderma, which has, like NFD, an increase and a bundling of collagen in the skin [8]. Therefore, PDT was applied with the haem-prodrug aminolaevulinic acid (ALA). The PDT induces matrix metalloproteinases in fibroblasts and a reduction of collagen synthesis in the dermis [9]. The described elastic effect of PDT in other collagenous diseases was the rationale of our application of PDT in NFD. The mode of action of PDT in NFD is unclear; a supposable functionality beside the induction of matrix metalloproteinases may be the production of oxygen species that make the tissue more elastic due to destruction of collagen [9]. The patient benefited definitely from the treatment that shows very good efficacy and safety.

Usually, PDT is a treatment for some types of cancer. Therefore, the photosensitizing agent is typically applied (cream, instillation) or injected into the bloodstream. The agent penetrates and remains in cells with an increased metabolism, mainly cancer cells, in a higher concentration than in normal cells. Under light exposition, the photosensitizing agent absorbs the light and produces an active form of oxygen that destroys the treated cancer cells (photodynamic effect). PDT causes minimal damage to healthy tissue. For the treatment of internal tumours, a laser light can be directed through a fibre-optic cable, i.e. for lung, oesophageal or bladder cancer [10]. On the skin, topical agents such as ALA or MAL may be used and are indicated for use in PDT. In vivo, these agents stimulate the production of porphyrins, which act as powerful photosensitizers. Porphyrins produced by the action of ALA or MAL can be activated using red light, which is also capable of deeply penetrating the skin (≤5 mm). For PDT light sources, convenient non-laser sources, such as non-coherent filtered lamps, and, more recently, sources containing arrays of LEDs, can be used. The LED lamp in the presented case had an emission spectrum of 634 ± 3 nm and a light dose of 37 J/cm(2).

This survey should be the basis for further investigations in the efficacy and mode of action of PDT in NFD.

Conflict of interest statement. None declared.

References


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