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Case report

Leucocytoclastic Vasculitis in a Renal Transplant Recipient with Multiple Primary Malignancies – A Case Report

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Abstract

Skin changes are frequent finding in renal transplant recipients. Besides the skin malignancies, many other skin pathologies may be found requiring skin biopsy for establishment of the diagnosis.
We describe a case of renal transplant recipient with history of breast cancer that developed leucocytoclastic vasculitis associated with planocellular and basocellular skin cancer.

Keywords: leucocytoclastic vasculitis; paraneoplastic; renal transplantation; cancer

Introduction

Renal transplant recipients have up to 100 times higher incidence of skin cancer when compared to the general population [1,2]. Nonmelanoma skin cancers make up to 90% of all skin cancers in transplant recipients, most of them being either squamous cell carcinoma (SCC) or basal cell carcinoma (BCC) [3-6].
Leukocytoclastic vasculitis (LCV), also known as hypersensitivity vasculitis, is primarily a histopathologic term commonly used to denote a small-vessel vasculitis [7]. It is characterized by a spectrum of cutaneous lesions, but palpable purpura is most common [9]. While about 50% the cases are idiopathic, LCV may be caused by medications, infections, collagen-vascular disorders or malignancies [8-10]. Infections, drugs, foods, as well as constitutional and local factors may play some part in the initiation or perpetuation of the disease [11-15]. In patients with malignant diseases or cryoglobulinemia, LCV usually presents as a recurrent palpable purpura of the lower extremities [9]. However, determining the true cause may prove to be difficult, particularly if several possible etiologies may be involved. Herein, we present a patient with histologically proven LCV associated with multiple primary malignancies.

Case report

A 77-year-old female with end-stage renal disease of unknown etiology underwent deceased donor kidney transplantation in September 2010. The long-term maintenance therapy consisted of cyclosporine, mycophenolate mofetil (MMF) and prednisone. In March 2014 she was diagnosed with the left-sided breast carcinoma and was treated with mastectomy. According to the pathohistological examination it was an invasive form of breast carcinoma (NOS-G1). Tamoxifen was induced in September 2014 and her immunosuppressive therapy was changed to everolimus, MMF and prednisone. Allograft function remained stable with creatinine levels 55-70 μmol/L, urea 3.8-5.1 mmol/L, glomerular filtration rate 60 ml/min/1.73m^2 and the peak proteinuria of 1.54 g/dU (occurring after everolimus introduction). In October 2016 she presented with painful purpuric-necrotic skin lesions on both legs which were most prominent on her shins. These lesions spontaneously disappeared in June 2017. In October 2017 the necrotic lesions reappeared on both legs in different sizes, starting as an erythematous livid papule and progressing into purpuric infiltrates and ulcerations covered with dry crusts (Figure 1).

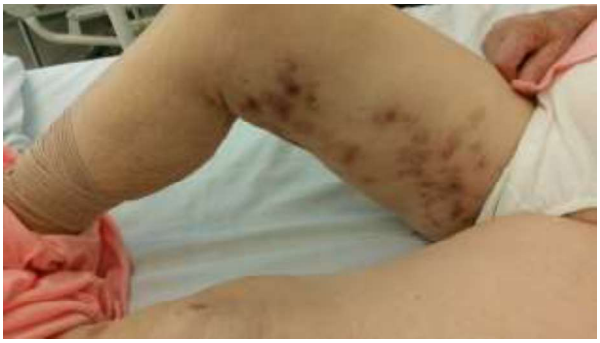

Fig. 1. Necrotic skin lesions on lower extremities.

A nonhealing ulceration on the nasal apex occurred. Meticulous medical examination was performed. La-

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boratory results were as follows: SE 25, hemoglobin 125 g/L, leucocytes 9, CRP 1.2, AFP 3.3 ug/L, CEA 2.4 ug/L, CA 125 73.1 kIU/L, CA 19-9 49.5 kIU/L, CA 15-3 33.0 kIU/L, NSE 15.75 ug/L, serum proteins 66 g/L, A/G ratio 1.14 with polyclonal peak of immunoglobulin A. Viral infections were excluded as potential cause (HBV, HCV, HIV, CMV, EBV, HSV 1 and 2 and Parvovirus were all negative), as was tuberculosis. Immunological tests were all negative (C3 1.66 g/L, C4 0.24 g/L, ANA negative, ANCA negative) and no cryoprecipitate was found. Breast ultrasound found no recurrence of the breast carcinoma. Multislice computerized tomography scan of the thorax, abdomen and pelvis showed no signs of metastatic carcinoma. Skeletal scintigraphy reflected no alterations of in the metabolic activity of the bone. Peripheral pulses were palpable and limb pletismography revealed normal ankle-brachial index (ABI; 1.03 on the right side and 1.05 on the left), color Doppler of veins was normal and without signs of deep vein thrombosis. Parathyroid hormone (PTH) level was within normal range, as were serum calcium and phospate levels (Ca 2.35 mmol/L, P 1.01 mmol/L). A neck ultrasound showed diffuse changes in the echo structure of the thyroid gland (clinical presentation of chronic thyreoiditis with euthyreosis) with several colloid cysts in the lobes. There was neither enlargement of parathyroid glands nor suspicious lymph nodes. The skin biopsy was taken from the both shins and revealed partly necrotic epidermis covered by crust with cellular debris of neutrophils. Upper dermis was partially necrotic containing large amounts of extravasated erythrocytes, neutrophils, eozinophils and mononuclear cells. Capillaries were filled with fibrin. These features were consistent with a diagnosis of leukocytoclastic vasculitis. Calcyphylaxis was excluded. According to the oncologist, tamoxifen was an unlikely cause of these changes. Biopsy of the nasal apex was also performed and revealed a combined basal cell and planocellular skin carcinoma. In January 2018 surgical excision along with lobe reconstruction was performed. Her last follow up was in April 2018 with normal kidney function and apparent withdrawal of the previously present vasculitic skin changes.

Discussion

LCV is defined histologically as a predominantly neutrophilic perivascular infiltrate affecting cutaneous postcapillary venules with fibrinoid deposits in and around the vessel wall, endothelial swelling, and extravasation of red blood cells [16]. The incidence of LCV is 4.5 per 100 000 per year, rising with age of diagnosis and does not differ between male and female patients [17]. It is characterized by a spectrum of cutaneous lesions, but palpable purpura is the most common [9]. While about half of the causes are idiopathic, LCV may be caused by medications, infections, collagen-vascular disorders or malignancies [8-10]. In patients with cryoglobulinemia and malignant disease, LCV usually presents as recurrent palpable purpura of the lower extremities [9]. Initial therapy for LCV can be conservative. Bed rest, warming, and elevation of the lower extremities, nonsteroidal anti- inflammatory drugs (NSAIDs), analgesics, and antihistamines are used to treat symptomatic complaints such as pruritus and/or burning. The diagnosis of LCV is set primarily by exclusion of other underlying systemic disease so it is crucial to regularly monitor patients' clinical status and laboratory findings. Patients with long term immunosuppressive therapy may have another underlying chronic disease covered by the therapy [16]. Many possible causes of the skin lesions were to be found in our patients' medical history since she has cardiovascular disease, basocellular and planocellular skin cancer, surgically removed breast cancer treated with tamoxifen, transplanted kidney and chronic immunosuppression. Since there were no findings of recurrent breast cancer or metastases on CT scans and scintigraphy that was excluded as a possible cause. Immunological illnesses were excluded by negative ANCA, ANA and normal serum complement concentrations. Caciphylaxisis was another possible cause excluded by pathohistological examination and normal serum calcium and PTH levels. Vascular examinations were without significant pathology. From the medications that she was taking, everolimus was found to be associated with LCV [18,19]. However, appearance and disappearance of the lesions was not in connection with its use.

Three months after the surgical removal of skin carcinomas, follow-up examination showed significant improvement regarding the lower extremities skin lesions that finally disappeared. Since other causes of the skin lesions were excluded, we have concluded that PCC and BCC were the most likely causes. Regarding the fact that other possible causes of LCV are present in this patient, regular follow-up must be performed.

Conclusions

Skin changes in renal transplant recipients require pathohistological examination for the proper diagnosis.

Conflict of interest statement. None declared.

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