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From the Clinic

Angiosarcoma in vascular access after transplantation

Introduction

The most frequent complications that occur after the completion of an internal arteriovenous fistula are thrombotic. Other complications, such as infection, cardiac decompensation, aneurysm/pseudoaneurysm or median nerve injury, are less common. Nonetheless, after transplantation, adjuvant immunosuppression has long-term side effects, such as the development of malignancies. Here, we report the case of a patient subjected to renal transplantation who developed an angiosarcoma located in an internal arteriovenous fistula.

Case report

The patient was a 47-year-old woman with a history of chronic renal failure secondary to right nephrectomy due to a renal cell carcinoma and left kidney hypoplasia. She had been included in a haemodialysis programme from July 1998 to February 2003. At that time, she received a kidney transplant from a deceased donor. She had had an internal arteriovenous fistula for vascular access since August 1998. No significant complications deriving from fistula completion were observed. Renal function after transplantation was stable, with creatinine levels ranging from 70.72 to 79.56 μmol/L (0.8–0.9 mg/dL). Immunosuppressive maintenance therapy included the administration of cyclosporine A and mycophenolic acid.

During a routine checkup in June 2011, she reported nail-bed splinter lesions in the homolateral fistula arm, with no other symptoms. A biopsy of these lesions revealed haematic extravasation with no signs of vasculitis or embolic phenomena.

Some weeks later, she presented complaining of distal pain in the fistula, a lack of functionality and retraction of the hand and of the third, fourth and fifth fingers. In August 2011, she underwent a magnetic resonance imaging of the limb, where periarticular inflammatory changes, periarticular haematic collections and an unidentified ischaemic injury aspect were noted. An electromyographic study showed the involvement of the median and ulnar nerves at the elbow level, probably due to a thrombotic or aneurysmal fistula complication.

In September 2011, she presented complaining of an increase in pain and further digital retraction. She also had asthenia, dyspnoea while performing normal activities and fever. The analytical results revealed severe anaemia [a haemoglobin level of 0.77 mmol/L (5.2 g/dL)] and positive citomegalovirus polymerase chain reaction. There were no significant findings in the chest X-ray. Digestive endoscopy was normal. Accordingly, treatment with valganciclovir was started.

During patient admission, the fistula was removed. Two old thrombosed veins and old thrombi were found in the brachial artery. During pathological examination, an angiosarcoma of uncertain malignancy grade was found (Figures 1 and 2).

Additional computed tomography also revealed images compatible with bone and lung metastases.

The patient was treated with chemotherapy (paclitaxel), but died 2 months after diagnosis due to oncologic complications.

Discussion

Increased cancer risk in patients with a kidney transplant has mainly been attributed to the immunosuppressive therapy applied [1]. The overall incidence of malignancy after renal transplantation has been reported as being 3- to

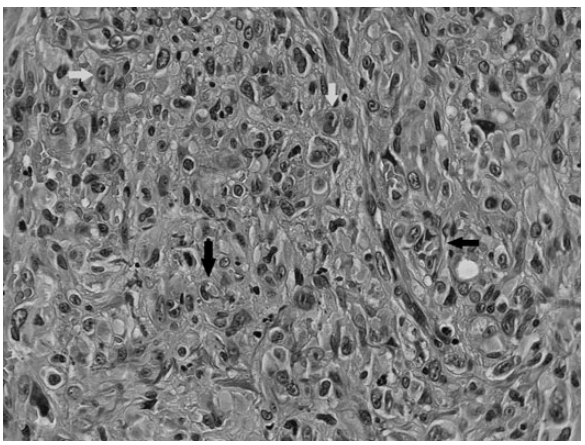

Fig. 1. Angiosarcoma 40× (HE)-Proliferation of atypical cells with large nuclear pleomorphism (and atypical mitosis-white arrows), which form vascular structures, sometimes with a intracytoplasmic erythrocytes (black arrows).

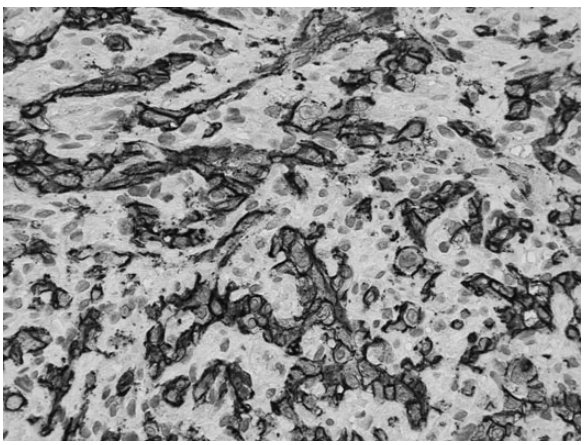

Fig. 2. Angiosarcoma (CD31)-Immunohistochemistry positivity to CD31 in tumoural cells.

5-fold higher than in the general population [2]. Among other factors, the duration and intensity of immunosuppression emerged as a particularly strong risk factor [2].

It has previously been reported that malignancies are more common in patients treated with triple immunosuppressive therapy including anticalcineurin inhibitors—cyclosporine or tacrolimus—azathioprine or mycophenolate mofetil and steroids [3]. In contrast, mTOR inhibitors (e.g. rapamycin) seem to have antineoplasic effects.

Ischaemic, aneurysmatic and thrombotic complications in the vascular access are relatively common findings. However, the development of tumours at this location is infrequent.

In renal transplant recipients, the most frequent types of tumours are skin cancer, due to exposure to ultraviolet radiation and lymphoproliferative disorders [3, 4]. The finding of a non-Kaposi sarcoma is very rare. Angiosarcoma is an extremely rare type of cancer (<1% of all cancers an ∼2% of localized soft tissue level). It has been demonstrated that chronic lymphoedema in a limb can favour this type of tumour [5]. Other authors have reported that alterations in blood flow and intraluminal pressure affect metabolism and endothelial cell proliferation due to exposure to chronic hypoxia [4]. These phenomena could stimulate carcinogenesis at the cellular and tissue levels by activating the hypoxia-inducible factor-1 (HIF-1). HIF-1 plays an important role in cancer progression through activation of multiple genes that regulate microvasculature, glycolysis, oxidative phosphorylation, cell death, cell migration, tissue invasion and metastatic genes [4]. Such phenomena, together with transplant immunosuppression, could have influenced the appearance of this tumour in our patient.

Conflict of interest statement. None declared.

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