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A. Rodríguez García, D. Silva Seco
Fuerteventura General Hospital.
Fuerteventura, Spain.
Correspondence:
Alejandra Rodríguez García
Hospital General de Fuerteventura.
Fuerteventura.
jairarodriguez@hotmail.com

C) BRIEF CASE REPORTS

Proximal calciphylaxis in a liver and kidney transplant patient

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Dear Editor,

Studies suggest that incidence of calciphylaxis is 1% per year, with a prevalence of 4% among dialysis patients,[1] however it is rarely present in kidney transplant patients or in those with stage 3 or 4 chronic kidney disease.[2]

The proximal distribution of lesions and the presence of ulceration are associated with a very poor prognosis, mainly because of wound infection and the subsequent death of the patient.[3] In the cases of calciphylaxis described in kidney transplant patients, the prognosis may be even worse[4,5] and the possible role of corticosteroids as a precipitant of the disease has also been discussed. However, although the pathogenesis of this condition is not well known, there are risk factors that could possibly contribute to proximal calciphylaxis and distal calciphylaxis in different ways. Therefore, no specific treatment has been established and in some cases a multidisciplinary and even empirical approach is needed. In any case, it is important to focus on normalising the phosphocalcic product and PTHi levels if they are elevated, since these are potential precipitants.[6]

We would like to present the case of a 66-year-old female patient who underwent her first liver transplant 11 years ago because of chronic alcohol-induced liver disease. She underwent a second kidney transplant three years before this admission because of mesangial glomerulonephritis caused by IgA deposits, which presented hardened lesions with central dermal necrosis that were symmetrical and very painful, located on the inner thigh on both legs and that indicated calciphylaxis (figure 1). A cutaneous punch biopsy was carried out and the diagnosis was confirmed. However, a bone scan showed no extraskeletal uptake. Her usual treatment consisted of furosemide, bisoprolol, prednisone, tacrolimus, mycophenolate mofetil, omeprazole and acenocoumarol (since she presented chronic atrial fibrillation) and subcutaneous darbopoetin. In the tests carried out, the following results stood out: CRP 51mg/l, Hb 10g/dl and creatinine 2.9mg/dl, because of chronic nephropathy of the graft, with proteinuria 2.6g/day, cholestatic pattern with GGT 230U/l and alkaline phosphatase 177U/l, corrected calcium concentration 8.6mg/dl, phosphorous 6.6mg/dl and initial PTHi 653pg/ml. Treatment with cinacalcet 30mg/day and aluminium hydroxide used as a phosphorus binder was administered. Phospocalcic products were normalised and PTHi values were stabilised at 150pg/ml. Despite this, large ulcers developed and enzymatic ointment (Iruxol Mono®), and moist gauzes were applied locally on a daily basis. Opiate derivatives were administered orally for pain relief, as well as 50g intravenous sodium thiosulphate three times a week. Her clinical progress was not satisfactory and haemodialysis was necessary 38 days after diagnosis via a catheter in the right internal jugular vein because of deteriorated kidney function. At the same time, it was also necessary to maintain the correct plasma levels of tacrolimus and avoid any accompanying septic symptoms. A few hours later she suffered non-recoverable cardiac arrest. No autopsy was carried out.

Despite our patient's fatal outcome, we would like to highlight the potential therapeutic benefits of cinacalcet in the treatment of proximal calciphylaxis with secondary hyperparathyroidism.[7] Its usefulness in transplant patients with calciphylaxis is yet to be demonstrated, although its effectiveness in controlling hyperparathyroidism has already been described.[8] Nor have we found any descriptions of other kidney transplant patients who were administered sodium thiosulphate, although its effectiveness has been demonstrated in several published studies involving dialysis patients. It has been observed that this drug is highly soluble in calcium

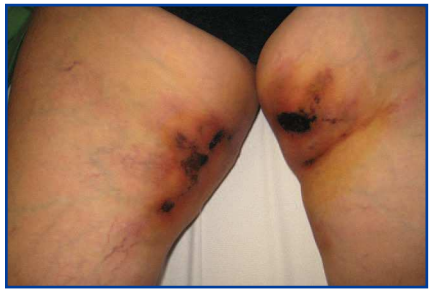

Figure 1.

thiosulphate form as it inhibits calcium precipitation and dissolves calcium deposits in tumours and calciphylaxis.[9]

We hope that by describing other cases of calciphylaxis in kidney transplant patients we are able to raise awareness about the use of treatments like cinacalcet, sodium thiosulphate and bisphosphonates, among others. Although, in this case, bone scan was uninformative, it seems that this procedure has a high sensitivity for diagnosing this disease, showing an abnormal isotope uptake on a subcutaneous level in 97% of cases.[10]

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M. Picazo Sánchez, M. Cuxart Pérez, R. Sans Lorman, C. Sardà Borroy
Department of Nephrology. Empordà Health Foundation. Figueres Hospital. Figueres, Spain.
Correspondence:
Montserrat Picazo Sánchez
Servicio de Nefrología. Fundació Salut Empordà. Hospital de Figueres. Figueres.
montserratpicazo@yahoo.es

Pneumonitis caused by sirolimus: improvement after switching to everolimus

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Dear Editor,

Sirolimus is the foremost proliferation signal inhibitor (PSI) used in medicine to prevent acute rejection in solid organ transplants. Among the main advantages of this drug is its very low nephrotoxicity and above all, its antitumour action, especially in transplanted patients that develop Kaposi's sarcoma.[1] However, one of its most serious side effects is interstitial pneumonitis, which in most cases leads to the suspension of treatment with this drug.[2]

We would like to describe the case of a 64-year-old woman who underwent a transplant for the first time in September 1992 and experienced early graft loss because of acute vascular rejection. She received a second kidney transplant in December 2000 and was treated with daclizumab, steroids, mycophenolate and tacrolimus. In the third month following the transplant, mycophenolate treatment was suspended definitively because of leukopenia. In June 2003 she developed Kaposi's sarcoma which did not respond to a reduction in the tacrolimus dose. Therefore, in November 2003 tacrolimus was substituted by sirolimus and excellent progress was made before the patient fully recovered in a short period of time. With regard to the patient's recovery from Kaposi's sarcoma, this is something that had been described previously in a study on a series of patients from different hospitals in Spain.[1]

She remained asymptomatic and with stable kidney function (CRP 1.2-1.3mg/dl) until July 2008. From that moment onwards she made several visits to the Emergency Departments complaining of dyspnoea. The chest x-ray repeatedly showed parenchymatous infiltrates in the middle and lower lobes on both sides of the chest. Although there were no significant findings in the echocardiogram (mild LVH and preserved ejection fraction), a diagnosis of heart failure was made and diuretic treatment was indicated. In September 2008, when she was checked in a transplant clinic and no clinical or radiological improvements were observed, interstitial pneumonitis was suspected and further tests were carried out: 1) full blood count and biochemistry did not indicate any relevant abnormalities; 2) sirolimus levels: 7ng/ml; 3) arterial gases at baseline: pH: 7, 44, pCO_2: 35, pO_2: 73, $SatO_2$: 95%; 4) Chest CAT scan: bilateral peripheral pulmonary infiltrates, with ground glass opacity in some areas and a reticular pattern in others, no adenopathies; 5) respiratory function tests: mild restrictive ventilatory pattern and moderately affected difussion capacity; 6) immunological study (ANA, ANCA, CRP, rheumatoid factor, complement, immunoglobulins): normal; 7) angiotensin-converting enzyme: 32U/L (normal); 8) testing for common and atypical infections, including pneumocystis, using the induced sputum technique: negative. In light of these findings, once we had ruled out infectious and autoimmune causes, we made the diagnosis of interstitial pneumonitis caused by sirolimus. Given the seriousness of the symptoms that prompted the change to sirolimus (Kaposi's sarcoma), we decided to switch to a different PSI, everolimus. The response to the new treatment was fast and very positive, the patient made a full recovery and the chest x-ray and respiratory function tests were normal within a period of a few weeks. The patient remained asymptomatic with everolimus levels at around 7ng/ml.

Interstitial pneumonitis caused by sirolimus is characterised by allergy-like symptoms and its incidence is relatively significant (4-14% according to some series).[2] This has also been observed with