nutrition. Parenteral nutrition was subsequently started, when kidney failure occurred (oligoanuria, creatinine 1mg/dl, urea 90mg/dl), accompanied by anaemia and thrombopenia (haemoglobin 7.7g/l, platelets 21,000/mm³). Therefore, continuous venovenous haemofiltration was started. Although the presence of schistocytes was unknown, we suspected that he suffered from atypical HUS. Cerebral echography showed severe cortical atrophy. 30 days after admission the diagnosis of methylmalonic acidemia with homocystinuria was confirmed. Given the unfavourable prognosis, we decided upon a limitation of therapeutic effort.

The most noteworthy data from the metabolic and genetic study of both patients, required for diagnosis, are shown in Table 1. Our patients were suffering from the most common variant of the disease (cblC), which is caused by homozygous or compound heterozygous mutations in the MMACHC gene [methylmalonic aciduria (cobalamin deficiency) cblC type, with homocystinuria], which is located on the 1p34 chromosome.

A symptom-free period is typical in methylmalonic acidemia with homocystinuria, since for clinical symptoms to appear, protein intake is required, with the consequential accumulation of methylmalonic acid and homocysteine. This explains why, in our patients, deterioration was observed on restarting feeding, whether enteral or parenteral. At times, there was a larvate clinical sign which was precipitated by intercurrent disease, often an infection, as occurred in case 2. Dilated myocardiopathy (case 2) is also described as a complication, of which a case diagnosed prenatally was reported[2], as well as other cardiac disturbances in relation to thromboembolisms.

The pathogenesis of thrombotic microangiopathy is related to the increase of plasma methylmalonic acid and homocysteine levels. The latter modifies the vascular endothelial's antithrombatic properties by interfering in the inhibition of platelet aggregation mediated by nitric oxide, which favours the union of the tissue plasminogen activator with the endothelial. This results in an increase of the endothelial expression of procoagulants. In addition, homocysteine thiolactone, homocysteine metabolite, can cause cell damage by inducing intracellular accumulation of free radicals and methylmalonic acid can interfere in the mitochondrial metabolism of renal cells. Association with HUS is uncommon, although described, above all, in newborns[3,4], as was confirmed in case 1 and suspected in case 2. At birth, many patients already have kidney failure, which could be reversible with early treatment (hydroxocobalamin, trimethylglycine, folate and protein restriction), which did not occur in our cases given the late diagnosis[4,5]. Consequently, early clinical suspicion is fundamental for trying to improve renal function as much as possible.

Conflict of interest

The authors declare that they have no conflicts of interest related to the contents of this article.

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Table 1. Biochemical and genetic data

	Case 1	Case 2
Methylmalonic acid (urine) Normal: 0.8-8.5mmol/mol Cr	124mmol/mol Cr	2150mmol/mol Cr
Homocysteine (serum) Normal: 3.7-7.5mcmol/l	85mcmol/l	109mcmol/l
Homozygous mutation in MMACHC gene (type cblC)	c.271dupA/c.271dupA	c.271dupA/c.271dupA

An uncommon cause of linfadenopathy in a kidney transplant patient: Cat-scratch disease

Dear Editor,
Cat scratch disease (CSD) is an infectious disease that usually presents

as a self-limiting illness characterized by regional lymphadenopathy, fever and constitutional symptoms in association with a cat scratch or bite.[1-4] In most cases, Bartonella henselae is the etiologic agent and cats are important reservoirs.[2-5]

We report a case of CSD in a 38-year-old Caucasian female recipient of a deceased kidney transplant since 2006 due to chronic renal failure of unknown etiology. Her maintenance immunosuppressive treatment was mycophenolate mofetil and cyclosporine. She was also medicated with calcium carbonate, vitamin D, atenolol, folic acid, fluoxetine, omeprazole, ferrous sulfate.

Six years post transplantation the patient was admitted to the hospital with a 4-week history of asthenia, low fever, loss of weight and multiple painful cervical ganglions. There was no previous history of tuberculosis. She had close contact at home with cats. On physical examination, the patient had a temperature of 37,3ºC, pulse rate of 84/min, blood pressure of 134/88mmHg, respiratory rate of 16/min and pulse oximetry of 100% in ambient air. She had multiple bilateral painful ganglions only in cervical region (node size ≤4cm). There was no rash. Examination of the lungs, heart and abdomen revealed no abnormalities including hepatosplenomegaly. The graft was painless. Laboratory tests revealed a white blood cell count 11,81×10^3/L (neutrophils 65,8%, lymphocytes 23,6%, monocytes 10%, eosinophils 0,1%), normochromic-normocytic anemia (Hgb 9,6g/dL); creatinine 1,2mg/dL (basal value), blood urea nitrogen 39mg/dL; protein C reactive 143mg/L; LDH, SGOT, SGPT, total bilirubin and alkaline phosphate without alterations. Ultrasound cervical ecography demonstrated multiple ganglion formations.

She was observed on admission by an otorhinolaryngologist who prescribed metronidazole plus amoxicillin and clavulanate for a nasopharynx´s infection. Serologies for Epstein-Barr
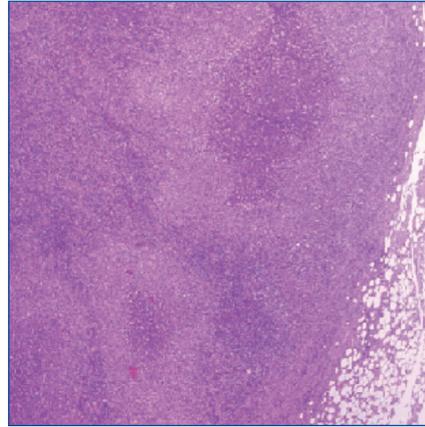

Figure 1. Ganglion biopsy – Focus of necrosis, some surrounded by granulomatous inflammation in cortical region (H&E, original magnification x40).

virus, herpes virus, cytomegalovirus, toxoplasmosis, brucella, leishmania, and HIV infection were negative. Blood culture was sterile. Chest and abdominal CT scan without changes. Quantiferon test for tuberculosis was indeterminate. Peripheral blood cytometry and cytometry of ganglion did not showed immunophenotypic alterations compatible with lymphoma. An ganglion biopsy was performed and histological examination revealed reactive lymphadenitis with central necrosis (Ziehl neelsen was negative) alterations compatible with CSD (Figures 1 and 2). She stopped the initial antibiotherapy on the 6th of
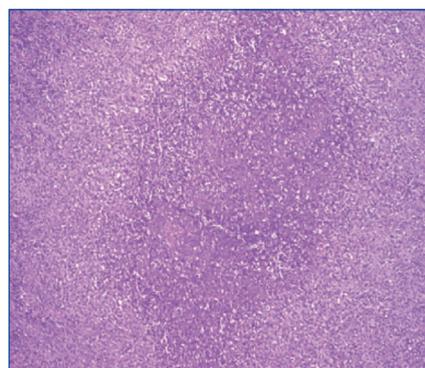

Figure 2. Ganglion biopsy – Focus of stellate aspect necrosis with epithelioid macrophages in the periphery (H&E, original magnification x100).

internment (without improvement of complains) and began azithromycin 500mg on day one, followed by 250mg for four days. There has been a good clinic improvement with involution of ganglion swelling and resolution of the pain and fever. One month later the patient was asymptomatic, without any signs of recurrence.

This case report intends to illustrate that the investigation of an immunocompromised kidney transplant patient presenting with lymphadenopathy may constitute a challenge given the wide differential diagnosis possible. The presence of enlarged lymph nodes in those patients should lead to post-transplant lymphoproliferative disorders (PTLD) as a first hypothesis; however more benign and unsuspected causes must be the cause.

The risk of PTLD is associated with the degree of immunosupression, time post transplant and the presence of Epstein-Barr virus.[6-9] Their incidence is approximately 30 to 50 times greater than in the general population and comprises a wide histological spectrum from hyperplastic appearing lesions, non-Hodgkin lymphoma or multiple myeloma histology.[6,8]

Regional lymphadenopathy is the hallmark of CSD in association with mild constitutional symptoms and a previous history of cat scratch or bite.[1-3] In our case the investigation was wide and extensive once this disease can mimic the more common PTLD disease or others infectious causes.[2-4] In addition to serological tests a lymph node biopsy was performed to exclude lymphoma or other malignant causes. It has been proposed that at least three of four criteria must be present to establish the diagnosis of CSD: a) cat or flea contact; b) negative serology for other causes of adenopathy or sterile pus aspirated from a node or a positive Bartonella PCR assay or liver or spleen lesions on CT scan; c) positive serology for Bartonella henselae (EIA or IFA≥1:64); d) biopsy showing granulomatous

inflammation consistent with CSD or a positive Warthin-Starry silver stain.[2,3,10] The diagnosis of CSD in our patient was based on the presence of a cat contact history, negative serology for other causes and a ganglion biopsy compatible with CSD (Figures 1 and 2). Serologic methods for detection of Bartonella henselae were not available in our hospital and it was not possible to isolate this agent by culture. The treatment of this entity is recommended in immunocompromised patients due to high risk for disseminated and recurrent CSD.[2,3]

Although CSD had rarely been reported in kidney transplant patients it should be considered in the differential diagnosis of patients with lymphadenopathy and a history of cat exposure.[5] The absence of easy complementary tests, the difficulty in isolating the bacteria and the need of tissue biopsy makes a difficult diagnosis.

Conflict of interest

The authors declare that they have no conflicts of interest related to the contents of this article.

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Extreme hypocalcaemia and hyperparathyroidism following denosumab. Is this drug safe in chronic kidney disease?

To the Editor,

Nefrología has recently published a case of post-denosumab hypocalcaemia and we would like to contribute to this subject[1]. Denosumab is an anti-RANKL (receptor activator of nuclear factor-$\varkappa$ B ligand) monoclonal antibody used in osteoporosis treatment as an antiresorptive agent. Unlike bisphosphonates, denosumab does not appear to be nephrotoxic[2], nor does it require dosage adjustments in kidney failure due to its favourable pharmacokinetic and pharmacodynamic profile[1,3]. However, the qualitative bone changes in osteoporosis patients are not comparable with the wide spectrum of alterations in bone turnover that accompanies chronic kidney disease (CKD)[4]. For this reason and in relation to the changes in mineral metabolism caused by denosumab, its safety in this population could be questioned. We describe a patient with advanced CKD with extreme hypocalcaemia and hyperparathyroidism following continuous administration of denosumab.

The patient is a 75-year-old female who sought treatment for tremors, muscle spasms and paraesthesia in the limbs. Stage 5 CKD, probably secondary to nephroangiosclerosis and diabetes mellitus, stands out in her medical history. She is allergic to penicillin and is treated with insulin, doxazosin, nifedipine GITS, torsemide, acetylsalicyclic acid, oral iron, erythropoietin, paricalcitol and calcifediol. She was treated, until 7 months before, with 70mg alendronic acid, which was suspended on starting six-monthly subcutaneous 60mg denosumab. Her nephrologist was unaware of the prescription of this drug. She presented the following analysis: creatinine 3.6mg/dl, total corrected calcium 10.06mg/dl, ionic calcium 5.1mg/dl, phosphate 5.1mg/dl, alkaline phosphatase 157U/l, bicarbonate 27.6mmol/l, parathyroid hormone (PTH) 436pg/ml, 25-vitamin D 30.2ng/ml. The evolution of the biochemical parameters until the last analysis 14 days after denosumab is shown in Figure 1. The patient did not attend this last evaluation due to not feeling well. Six days later,