disease involving the kidneys; it develops due to deposits of cryoglobulins. The course is often fatal or leads to end-stage renal disease. The disease tends to relapse. Women with this disorder rarely become pregnant and conclude successfully the pregnancy.

Our experience: a 30-year-old woman suffering from HCV-cirrhosis was admitted for severe peripheral edema with proteinuria 7g/day and albumin 2.3g/dL. The glomerular filtration rate was in the normal range. Renal biopsy showed a membranous-proliferative glomerulonephritis. The patient received 1 cycle of 12 plasmapheresis associated with Mycophenolate Mofetil (MM) 2g/day and prednisone 12.5mg/day therapy. After 1 month, we observed a partial remission of proteinuria (3g/day). The MM therapy was continued. After 2 years, the patient reported amenorrhea lasting for 3 months. The beta-HCG test and U.S. scan confirmed the pregnancy. The MM was interrupted whereas prednisone therapy was maintained at 5mg/day. During pregnancy, proteinuria was always less than 2g/day and renal function was regular. The pregnancy continued without major problems. A cesarean section was performed at the thirty-sixth week of pregnancy. Laboratory tests showed: white blood cells: 3.170/mmc, Hb: 8.2g/dL. PLT: 46.000/mmc, AST: 60IU/L, ALT 33IU/L, gammaGT: 14IU/L, total bilirubine: 1.84mg/dL, total protein: 4.1g/dl, albumin: 2.16g/dL. The fetus was healthy and growth corresponded to the twenty-eighth week of pregnancy. Anti-HCV antibodies detection was negative and the child follow-up did not show any significant diseases after 3 years from birth. The patient resumed MM and prednisone therapy. One year after the child's birth, the patient showed good health with proteinuria 1 g/day; she continued MM 2g/day and prednisone 5mg/day. After 18 months postpartum, proteinuria increased to 4g/day. We carried out again a cycle of six plasmapheresis, achieving a reduction of proteinuria (<1g/day). Therefore, we carried out the maintenance of MM and prednisone therapy at the same dose. Although pregnancy in patient with cirrhosis remains rare, recent improvements in the treatment of cirrhosis led to an increase in life expectancy and quality of life, making pregnancy a most frequent event. Outcomes of pregnancy in patients with cirrhosis are poorly described. Regarding neonatal well-being, there is no association between vertical transmission of HCV and gestational age at delivery or the presence of chorioamnionitis. There is no evidence demonstrating an increased risk of HCV transmission in HIV-negative women who breast feed.[4] There are some reports regarding a worsening of HCV-liver disease after pregnancy.[5] Regarding immunological pathology, the prognosis associated with many forms of systemic vasculitides was quite grim. Advances in this field have allowed us to focus on issues related to quality of life such as fertility, conception, and pregnancy among women with vasculitis.[6] This case report shows the possibility of a favourable outcome, if the pregnancy occurs during a clinical stabilization phase of cirrhosis and vasculitis.

### Conflict of interest

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


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## Severe hypocalcaemia post-denosumab


Nefrologia 2013;33(4):614-5
doi:10.3265/Nefrologia.pre2013.Apr.11922


**To the Editor:**

Denosumab is a human IgG2 monoclonal antibody that binds to RANKL (receptor activator of nuclear factor KB ligand gene), thus causing a reduction in osteoclast activity. It has been approved since 2010 for use in osteoporosis and does not require adjustment in accordance with renal function, although several studies indicate an increase of hypocalcaemia in patients with renal failure (RF). It is administered subcutaneously biannually.[1]

We report the case of a 46-year-old woman with high blood pressure, dyslipidaemia, stage 5 chronic kidney disease (CKD), focal segmental glomerulonephritis and severe seronegative rheumatoid arthritis resistant to different drugs. Due to the presence of pathologic fractures to the pelvis, the Department of Rheumatology decided to start treatment with 60mg denosumab. She received treatment with 2.4g/12 hours sevelamer, 0.50mg Rocaltrol®: 5 tablets/week, 1 tablet/8 hours Mastical®, 266µg/15 days calcifediol, antihypertensive drugs and painkillers. The analytical data were: urea 205mg/dl, creatinine 5.95mg/dl, calcium 8.8mg/dl, albumin 3.8g/dl, intact

parathyroid hormone 581pg/ml, 25-OH vitamin D 9.2ng/ml, alkaline phosphatase 221U/l.

One week after the drug was administered, we detected hypocalcaemia (6.7mg/dl corrected calcium) in a routine clinic blood test. The patient was asymptomatic and because of significant history of poor adherence to treatment, she was urged to adhere to treatment as prescribed.

Two weeks later, the patient came to the Emergency department with general weakness, dizziness, tremors and nausea. Corrected calcium of 5.2mg/dl was detected. Physical examination revealed no signs of hypocalcaemia (Trousseau or Chvostek) or peribuccal paresthesia.

It was decided to admit the patient for intravenous treatment, which yielded good clinical and laboratory results.

Bisphosphonates are commonly used to reduce bone loss but they are mainly eliminated through the kidney, and as such, their use is not recommended in patients with severe RF.[2] Denosumab significantly reduces the risk of fractures[3] and it has been shown to increase bone mineral density and reduce resorption markers. Furthermore, preclinical studies have revealed that, unlike bisphosphonate, it is not nephrotoxic at levels of 100µmol/l[4] and is independent of the degree of RF, since its pharmacokinetic and pharmacodynamic profile does not vary significantly according to the degree of renal function.[1]

It has been hypothesised that patients with CKD and bone disease due to hyperparathyroidism may be at greater risk of hypocalcaemia with denosumab, since their serum calcium levels will depend to a greater extent on bone resorption mediated by the parathyroid hormone. As such, inhibition of osteoclast activity following administration of the first dose of denosumab could lead to a syndrome similar to hungry bone, with the rapid decrease in serum calcium levels due to its uptake by bone.[5] At this time, calcium and vitamin D supplements are required, until the formation of osteoclasts leads to proper mineralisation.

In a study[6] conducted on 46 patients with varying degrees of RF, pain in limbs and hypocalcaemia were observed as the most common adverse effects. The latter appeared in 15% of participants, with only two patients requiring hospitalisation for intravenous treatment and in only one, hypocalcaemia was symptomatic.

The use of denosumab in patients with CRF is convenient, as it requires no dose adjustment and it is not nephrotoxic; as such, its use is expected to increase. In this group of patients, we should administer appropriate calcium and vitamin D supplements before beginning treatment with denosumab, in addition to monitoring these parameters in the laboratory after treatment begins, since a non-negligible number of patients will develop hypocalcaemia, which will be asymptomatic in the majority of cases.

### Conflicts of interest

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


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## Passenger lymphocyte syndrome: an uncommon form of anaemia in renal transplantation


Nefrologia 2013;33(4):615-6
doi:10.3265/Nefrologia.pre2013.May.11930


**To the Editor:**

Passenger lymphocyte syndrome (PLS) is an alloimmune haemolytic anaemia in solid organ transplantation (SOT) caused by alloantibodies derived from a donor B cell clone, that are transferred with the graft, resulting in a secondary immune response against the recipient's red blood cells in SOT with compatible but not identical blood groups.[1-5] It is an uncommon entity whose frequency has been related to the size (in terms of lymphoid content) of the transplanted organ and is much more common in heart/lung (70%) and liver (29%) than in renal transplantation (RT) (9%).[2,3] The antibodies are normally anti-ABO, uncommonly anti-D, and there are isolated cases of anti-C, anti-E, anti-Kell, anti-Jk and anti-Fy.[3]