Sir,

Sirolimus is being used increasingly in calcineurin inhibitor-free regimens in solid organ transplant immunosuppression [1,2]. However, it has potential pulmonary toxicity due to a capillary leak syndrome [3,4]. We report for the first time one such case with involvement of the paranasal sinuses and retina in addition to sirolimus-induced pneumonitis, all probably related to the same underlying pathophysiology.

A 54-year-old male with presumed chronic tubulointerstitial nephritis and end-stage renal disease (ESRD) on intermittent haemodialysis treatment underwent cadaver renal transplantation in August 2003. He was given daclizumab induction, followed by mycophenolate mofetil (MMF) 1000 mg per day and sirolimus (6 mg loading followed by 2 mg once daily) and low dose prednisolone as immunosuppression. Cyclosporin was avoided due to delayed graft function. MMF was withdrawn and cyclosporin (3 mg/kg) was introduced after 2 weeks once adequate graft function was established. His baseline serum creatinine at this time was 1.8 mg/dl. One month post-transplant, he was found to have diabetes mellitus for which he was put on insulin therapy. Two months post-transplant, he presented with complaints of increasing breathlessness and headache. He was afebrile, normotensive and had no systemic oedema. Chest examination revealed bilateral crepitations. Fundoscopy showed bilateral macular oedema. Blood chemistry showed a haemoglobin of 11.2 g/dl, TLC 11 300/mm³, serum urea 83 mg/dl and creatinine 1.8 mg/dl. Chest X-ray showed bilateral non-homogeneous opacities in the middle and lower zones, and X-ray of the paranasal sinuses revealed bilateral opaque maxillary sinuses and hazy frontal sinuses. Computed tomography (CT) scan showed mucosal oedema and thickening of all the sinuses (frontal, ethmoid, sphenoid and maxillary). Sputum cultures were sterile. Fluorescein fundus angiography showed pooling of contrast suggestive of central serous retinopathy.

Sirolimus was stopped and he was managed conservatively without antibiotics as there was no evidence of infection. A sirolimus trough level was not done as we did not have the facility at our centre. Bronchial alveolar lavage was not done due to rapid resolution of symptoms. His breathlessness and headache subsided during the next 48 h. At repeat X-rays of chest and paranasal sinuses, the initial findings were almost cleared up and at fundus examination a decreased macular oedema was found.

There have been several case reports of pneumonopathy with the usage of sirolimus [3–5]. None of them have reported involvement of paranasal sinuses and the retina, probably because this was not looked for in view of the dominant pulmonary symptomatology. Case reports mention high drug levels, graft dysfunction and hypervolaemia to be possible risk factors [2,3].

This case reminds us of the importance of identification of potential toxicities of the immunosuppressive regimens, e.g. sirolimus. The acute toxic effects as a rule are reversible, and cessation of the drug usually leads to resolution of the side effects.

Conflict of interest statement. None declared.

Old-time features are back in renal transplanted patients

Sir,

Uraemic stomatitis is a very rare oral mucosal disorder probably because nowadays patients are seldom left without dialysis at advanced and prolonged stages of renal failure. The present report details the features of uraemic stomatitis in a patient with longstanding chronic renal failure.

A 46-year-old male was referred by the nephrology department of Hospital das Clinicas to the oral medicine unit of UFPE, Recife, Brazil, complaining of a burning sensation of the oral mucosa and dysgeusia. The patient had developed chronic renal disease due to non-specific nephritis associated with severe hypertension in 1991, at which time he commenced haemodialysis. In the same year the patient underwent renal transplantation but the renal allograft was rejected 4 years later. The patient continued haemodialysis for 10 years until he underwent a further renal transplant in 2001. Perhaps surprisingly, at the time of referral his renal disease was considered stable, aside from elevation of plasma urea (288 mg/ml: normal range 18–21 mg/ml) and creatinine. Unfortunately, no details of calcium, phosphate or haemoglobin were available at that time. Intra-oral examination
revealed adherent white plaques of the floor of the mouth, bolcal mucosae, lateral borders of the tongue and gingivae. To establish the precise diagnosis, incisional biopsies of the tongue were undertaken. Histopathological examination revealed an epithelium markedly acanthotic, with most of the suprabasal layers comprising pale staining degenerate keratinocytes. The surface layers showed sloughing, and there was hyperplasia of the basal cell component. Fungal stains, immunohistochemistry for human papillomavirus (HPV) and EpsteinBarr virus (EBV) late membrane protein, and in situ hybridization for EBV early RNA were all negative. Based upon the clinical and histopathological features a final diagnosis of uraemic stomatitis seemed appropriate.

Uraemic stomatitis has been suggested to arise when blood urea levels are more than 300 mg/ml [1], although there have been reports of mucosal changes at urea levels of <200 mg/ml [2,3]. Patients with uraemia may have dysgeusia and an altered perception to sweet and sour taste [4], and a burning sensation of the lips and tongue possibly caused by pain pathway activation [5]. Younger patients usually have more significant impairment in taste modalities, but may have a better recovery of neural taste function following dialysis [6]. Zinc deficiency can arise in renal failure [7], however, there is no evidence that mild zinc deficiency gives rise to oral mucosal changes nor oral pain.

Uraemic stomatitis responds to treatment of underlying renal failure. The present patient had resolution of oral mucosal lesions and symptoms following hydrogen peroxide therapy. This response perhaps reflects an antimicrobial effect thus reducing the local levels of bacterially derived ureases. The aetiology of this oral disorder is unclear; however, as transplant failure is an increasingly frequent condition, the reappearance of such lesions may be expected.

Acknowledgements. J.C.L. is partially funded by a grant from CNPq (Ministry of Science and Technology, Brazil).


doi:10.1093/ndt/gfh476