SAFDGS data. Genotypic data of rs7493 and rs12704795 were polymorphic and verified for Mendelian inconsistencies and allele and genotype frequencies were measured using the programme PEDSYS subroutines. The allele frequencies of rs7493 were 77% (C) and 23% (G). In regard to the rs12704795, the A and C allele frequencies were 76% and 24%, respectively. Genotypic data of rs7493 [CC (60%), CG (35%), GG (5%)] and rs12704795 [AA (55%), AC (39%), CC (6%)] were consistent with the Hardy–Weinberg Equilibrium expectations, and there was no evidence for hidden population stratification. Association analysis in our family data was carried out using the measured genotype approach within the variance components analytical framework implemented in SOLAR [5]. Of the phenotypes examined for association [T2DM, body mass index (BMI), blood pressure measures, total cholesterol, high density lipoprotein-cholesterol, triglycerides and ln ACR], the C/G variant (rs7493) exhibited significant association only with ACR ($P = 0.013$) after adjusting for the effects of age, age$^2 \times$ sex, diabetes, duration of diabetes, systolic blood pressure, and antihypertensive treatment with ACE inhibitors or AT1R antagonists. The mean ACR values of the groups, the genetic influences attributable to this polymorphism, is found in different ethnic variants in the flanking genes. These possibilities remain to be explored. In conclusion, our data support the findings by others [1,2] that the Cys(311)Ser variant of PON2 may contribute to albumin excretion rate. Although the susceptibility to albuminuria due to this variant is found in different ethnic groups, the genetic influences attributable to this polymorphism appear to be rather minor in their magnitude.

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Posterior reversible encephalopathy induced by intravenous immunoglobulin

Sir,

Intravenous immunoglobulin (IvIg) is commonly used in nephrology units for the treatment of auto-immune diseases, antibody-mediated renal allograft rejection and immune deficiencies. Minor adverse effects, such as myalgia, headache, shiver, nausea, vomiting or fever occur in <20% of patients. Major reactions including renal failure, thromboembolism, aseptic meningitis and anaphylaxis are less common. Whereas osmotic nephropathy resulting from maltose and saccharose toxicity is well-known to nephrologists, posterior reversible encephalopathy syndrome (PRES) is a rare and potentially severe adverse event of IvIg therapy.

A 42-year-old man was admitted for end-stage renal failure secondary to myeloma cast nephropathy in the context of plasma cell leukaemia, diagnosed 2 months previously. His past medical history was otherwise unremarkable. Haematological tests showed increased white blood cells (12380/mm$^3$) with 27% of circulating plasma...
cells. Immunoelectrophoresis revealed a serum monoclonal IgG-k with a urine-k Bence–Jones protein and serum levels of k-free light chains of 9760 mg/l. Gammaglobulin level was 13 g/l. Bone marrow smears and biopsy demonstrated massive plasma cell infiltration (67%). X-ray examination revealed diffuse osteolytic bone lesions. Serum creatinine was 450 μmol/l with severe hyperkalaemia (7%).

Because of persistent hypogammaglobulinaemia (5 g/l), the patient developed headache, nausea, fever (38 °C), visual loss with horizontal nystagmus and hypertension (170/80 mmHg). Four hours later, confusion and generalized seizures occurred, which required intravenous clonazepam and phenytoin and assisted ventilation. A plasmapheresis session with serum albumin was performed. After 24 h, complete resolution of neurological symptoms was achieved.

At the onset of neurological symptoms, laboratory data showed: glucose 1 g/l, sodium 140 mmol/l, potassium 3.5 mmol/l, serum creatinine 450 μmol/l, total protein 66 g/l, albumin 28 g/l, calcium 2.2 mmol/l, phosphorus 1.53 mmol/l, CRP 7 mg/l, white blood cell 14 500/mm³, haemoglobin 9.7 g/dl, haematocrit 30% and platelet 379 000/mm³. Fundoscopic examination was normal. Brain MRI revealed increased signal in the white matter of left parieto-occipital lobe on T2 weighted sequences. Unfortunately, lumbar puncture and plasma viscosity was not performed. One month later, neurological examination and brain MRI were normal.

PRES, initially described by Hinchey et al. in 1996 [1], is defined by the association of neurological signs (headache, vomiting, visual disturbance, confusion and seizures) and radiological abnormalities of occipital white matter, usually bilateral, characterized by cerebral oedema with hypodense signals on CT scan and hyperintense signals on T2 weighted images by MRI. Electroencephalographic examination shows non-specific slow wave activity, while lumbar puncture reveals raised protein concentration with mononuclear pleocytosis [2,3]. The most commonly reported causes of PRES are immunosuppressive drugs (cyclosporin A and tacrolimus), interferon-α, malignant hypertension with encephalopathy and eclampsia. By definition, clinical neurological and radiological signs are reversible after resolution of the underlying cause.

Neurological complications of IV Ig therapy include mainly aseptic meningitis, cerebral infarction and PRES [2]. In our case, the presence of suggestive neurological signs with unilateral parieto-occipital changes on MRI, strongly suggested the diagnosis of PRES. IV Ig was first implicated as a cause of PRES in 1996 [4]. Since then, four additional cases have been reported [2,3,5,6], two of them with unilateral occipital white matter changes on MRI [3,5]. Although a latency of 3 [4] to 4 [5] days between IV Ig infusion and onset of PRES has been reported, neurological signs may appear in the first hours of treatment, as in our case [2,3]. Complete recovery of neurological symptoms occurs within 2 days [2,3,5] to several weeks [1,6]. Little is known about the pathophysiology of IV Ig-induced PRES. A role for hypertensive encephalopathy is unlikely in our case. Vasogenic oedema, cerebral vasospasm and serum hyperviscosity [2,4] have been proposed as probable mechanisms of PRES. Unfortunately, in previous and present cases, plasma viscosity was not measured. In our patient, although hyperviscosity secondary to myeloma was ruled out by evidence of low serum protein, albumin and gammaglobulin levels, we postulated that a brutal change of plasma viscosity induced by IV Ig perfusion might be involved in the sudden occurrence of PRES. However, a role for cerebral vasospasm or vasogenic oedema was not excluded. Two previously reported patients were treated successfully with intravenous corticosteroids [4,5], but evidence for their use remains uncertain, as withdrawal of the offending agent may be sufficient for neurological recovery. Whether or not plasmapheresis had a beneficial effect on clinical symptoms remains also unproven in the present case.

In summary, PRES should be suspected in patients with neurological signs, especially visual disturbance after IV Ig infusion and adequately confirmed by MRI. Nephrologists need to be aware of this unusual neurological complication, as early recognition may improve prognosis.
A supernumerary parathyroid gland located in an unusual site, parapharyngeal space, in a patient with persistent renal hyperparathyroidism

Sir,

Sometimes it is difficult to detect pathological parathyroid glands both in primary and secondary hyperparathyroidism (HPT). We are reporting a case of persistent renal HPT due to a supernumerary gland located in the parapharyngeal space.

The patient was a 58-year-old female, who had continued haemodialysis (HD) for 25 years and referred to our department due to advanced renal HPT. She underwent total PTx with forearm autograft and four parathyroid glands could be removed. However, a high intact parathyroid hormone (PTH) level was persistent on the first day after PTx. To detect missed glands, image diagnostic examinations, including MIBI scintigram, ultrasonography (US), computed tomography (CT) and magnetic resonance imaging (MRI) were performed several times. Finally, we recognized an abnormal uptake of MIBI scintigram in her face, and we detected a mass located in the parapharyngeal space by CT (Figure 1). The mass was removed by an operation from the oral cavity. Histopathological examination confirmed that the mass represented a parathyroid gland. The high intact PTH level decreased dramatically. It is suggested that the gland may be an undescended parathyroid gland. This case may be the first to report a parathyroid gland located high up in the neck at the level of the parapharyngeal space. In 1995, Simeone et al. [1] reported a case with an undescended parathyroid gland located within or in close approximation to the parapharyngeal wall, but the parapharyngeal space has a higher position in the neck than that area. The inferior parathyroid glands arise from the third pharyngeal pouch along with the thymus. During the course of normal development, the inferior parathyroid glands descend through the neck with the thymus. The loss of expression of some genes that induce descending of the parathyroid glands may be a cause why the gland remained in the parapharyngeal space. It has been confirmed that a gene, Hoxa3, is involved in the descent of the parathyroid glands [2].

An undescended parathyroid gland is one of many pitfalls that may cause the missing of an abnormal parathyroid glands. Undescended parathyroid glands are most commonly found within the carotid sheath at the level of the carotid bifurcation [3]. In our large series, the frequency of undescended glands was 0.97%, and half of them could be removed at reneck exploration [4]. In 1998, we reported that the frequency of supernumerary glands in renal HPT was 92 of 570 glands (16.1%) and of these 92 glands, 12 were removed at reoperation [5].

The risk of persistent/recurrent HPT due to remaining parathyroid tissue is not negligible, especially in patients who require long-term maintenance HD after PTx. Therefore, supernumerary glands have special significance during surgery for renal HPT, either as a cause for persistent or recurrent HPT.

We conclude that one should keep in mind that parathyroid glands can be located in the parapharyngeal space and that one should look for this possibility, when pathological glands in the usual sites are not detected.