NDT Plus (2008) 1: 55–62

NDT PLUS
Nephrology Dialysis Transplantation

Letters

Advance Access publication 11 December 2007

Lipomatosis and focal segmental glomerulosclerosis: causation, association or coincidence?

Sir,

Lipomatosis is an extremely rare disorder [1]. Affected persons develop multiple symmetrical, diffuse deposits of fat in the subcutaneous tissue. The lipomata cause physical disfigurement, without tendency to malignancy [1].

Little is known about secondary co-morbidity, with no previous reports of associated renal disease. We describe three patients with lipomatosis who developed biopsy-proven focal segmental glomerulosclerosis (FSGS).

A 41-year-old man with lipomatosis since age 18 was incidentally found to have proteinuria (1.36 g/day). Blood pressure and lipid levels were normal. Serum creatinine was 132 mmol/l. Renal biopsy showed FSGS. Prednisone and ramipril led to mild proteinuria reduction. After 110 months, creatinine was 154 mmol/l and proteinuria was 1.92 g/day.

Patient 2 developed proteinuria and anasarca at age 7. These rapidly resolved with prednisone and diuretics. There was no follow-up. Lipomatosis appeared at 25. Urinalysis and blood pressure at 32 were normal. Asymptomatic proteinuria (0.79 g/day) was again noted at 34. Blood pressure, kidney function and albumin remained normal. Renal biopsy showed FSGS. Enalapril led to modest proteinuria reduction. After 134 months, creatinine was 190 mmol/l with proteinuria of 0.79 g/day.

The third patient also had undiagnosed childhood renal disease, with peripheral oedema and proteinuria. Symptoms and proteinuria were resolved with herbs. Lipomatosis became apparent at 20. Asymptomatic proteinuria (2.2 g/day) was again noted at 37. Blood pressure was 120/80, serum creatinine was 136 mmol/l and albumin was normal. Renal biopsy showed FSGS. There was minimal response to prednisone, but with subsequent ramipril, proteinuria fell to 0.53 g/day. After 86 months, creatinine had risen to 280 mmol/l with proteinuria of 2.94 g/day.

The slow deterioration in all patients occurred despite ACE inhibitor therapy and optimal blood pressure and lipid control.

FSGS is a common renal diagnosis, with non-specific histological findings. Of interest here is the unifying association with lipomatosis. FSGS can be primary or secondary. Clinical and biopsy features usually allow distinction. In our patients, the lack of symptoms, degree of proteinuria, electron microscopic findings and slow progression suggested secondary disease.

In patient 1, we were unable to identify any coexisting disorders associated with secondary FSGS. The other two patients had undiagnosed childhood renal disease, which, despite apparent resolution with therapy, may have been predisposing. Regardless, the rarity of lipomatosis makes the chance of finding the same renal lesion in the three patients less likely. Further, the same renal lesion occurs in obesity, a condition also associated with adipocyte excess. The mechanism underlying this association remains unclear, but the effects of adipocyte-derived hormones on glomerular structure and function have been suggested, with leptin, TNF-α and angiotensin II being identified as potential mediators [2,3].

We suggest a possible link between adipocyte tumour cell hormone production and the development and/or progression of FSGS in our patients. Increased reporting of similar cases is needed to confirm this association.

Conflict of interest statement. None declared.

[1]Department of Nephrology
Vancouver General Hospital
Vancouver, Canada

Katherine Barraclough[1]
Choi Kit Yeung[1]

E-mail: arbieb@hotmail.com

1. Harsch IA, Schahin SP, Fuchs FS *et al*. Insulin resistance, hyperleptinemia, and obstructive sleep apnea in Launois–Bensaude syndrome. *Obes Res* 2002; 10: 625–632
2. Wolf G. After all those fat years: renal consequences of obesity. *Nephrol Dial Transplant* 2003; 18: 2471–2474
3. Weicek A, Kokot F, Chuduk J *et al*. The adipose tissue—a novel endocrine organ of interest to the nephrologist. *Nephrol Dial Transplant* 2002; 17: 191–195

doi: 10.1093/ndtplus/sfm002

Advance Access publication 11 December 2007

Simultaneous allergic interstitial nephritis and cardiomyopathy in a patient on clozapine

Sir,

Clozapine is an atypical anti-psychotic, currently indicated for patients with schizophrenia who are non-responsive to, or intolerant of, other neuroleptics. Apart from striking sedation and lowered seizure threshold, the most serious side effect is agranulocytosis. It is also rarely associated with myocarditis, cardiomyopathy and allergic interstitial nephritis [1–4]. We report a case of concomitant allergic

interstitial nephritis and cardiomyopathy in a patient recently started on clozapine.

A healthy 26-year-old man with bipolar-type schizoaffective disorder presented with bizarre, threatening behaviour and paranoid hallucinations. He was started on valproic acid, lithium, risperidone and clonazepam. Minimal improvement was noted, and after 8 weeks he was gradually switched from risperidone to 125 mg of clozapine. At this point all his blood work was normal and he had good exercise tolerance. After 2 weeks of initiating clozapine, he was transferred to our hospital for a fever of 104.2 F. On admission he was found to be hypertensive (BP 167/107) and tachycardiac. His physical exam was unremarkable, without any signs of fluid overload. He had an elevated serum creatinine (1.5 mg/dl) and WBC (13 000/mm^3) with peripheral eosinophilia (820/mm^3). His urinalysis showed 2+ protein, 5–10 white cell casts and >50 WBC with significant eosinophiluria. Chest X-ray and urine, blood and CSF cultures were negative. All medications were stopped, and he was given intravenous hydration. Intravenous steroids were started for presumed clozapine-induced interstitial nephritis. On Day 6, his creatinine peaked to 5 mg/dl. He maintained good urine output throughout his stay. A renal biopsy was scheduled but was cancelled because of subsequent complicated course and improving renal function thereafter.

On Day 8 he developed dyspnea and bilateral inspiratory rales. He denied chest pain. Chest X-ray and CT-scan were consistent with pulmonary oedema. His pro-BNP was 27 727 pg/ml. EKG and cardiac enzymes remained normal and viral titers were negative. He was started on intravenous diuretics. An echocardiogram showed moderate global left ventricular dysfunction with an EF of 40% and left ventricular diastolic internal dimension of 5 cm. Next day, he was intubated for respiratory distress from CHF and was transferred to ICU. His respiratory status gradually improved with diuresis and he was extubated after 3 days. Beta-blockers, hydralazine and nitrates were initiated for CHF. At discharge, his eosinophilia resolved, creatinine was 1.36 mg/dl and pro-BNP was 812 pg/ml. Two weeks later, an echocardiogram showed some recovery (EF 50%).

The patient's previous tolerance of all other medications, the chronological onset of his symptoms after initiating clozapine and the fact that there was no previous cardiac history suggest that this case most likely represents clozapine-induced acute interstitial nephritis and cardiomyopathy. While dilated cardiomyopathy is more common with clozapine, a third of patients develop non-dilated cardiomyopathy [5], as seen in our patient. Both the processes are probably related to IgE-mediated hypersensitivity reaction, and hence the simultaneous occurrence is not surprising [1,3,5]. To the best of our knowledge, this is the first case of simultaneous clozapine-induced interstitial nephritis and cardiomyopathy. Clozapine maybe associated with fatal complications in healthy young adults and it is imperative that physicians are aware of these potentially lethal side effects.

Conflict of interest statement. None declared.

Bilal K Siddiqui[1]
Syed Asim[2]
Afroz Shamim[3]
Nisha Pillai[1]
Sujatha Rajan[1]

[1]Department of Internal Medicine, Long Island Jewish Medical Center, New York, USA
[2]Department of Medicine, Danbury Hospital, Danbury, CT, USA
[3]Department of Psychiatry, Zucker Hillside Hospital, Glen Oaks, New York, USA

E-mail: bilalkarim81@yahoo.com

1. Elias TJ, Bannister KM, Clarkson AR *et al*. Clozapine-induced acute interstitial nephritis. *Lancet* 1999 Oct 2; 354: 1180–1181
2. Au AF, Luthra V, Stem R. Clozapine-induced acute interstitial nephritis. *Am J Psychiatry* 2004; 161: 1501
3. Killian JG, Kerr K, Lawrence C *et al*. Myocarditis and cardiomyopathy associated with clozapine. *Lancet* 1999; 354: 1841–1845
4. La Grenade L, Graham D, Trontell A. Myocarditis and cardiomyopathy associated with clozapine use in the United States. *N Engl J Med* 2001; 345: 224–225
5. Wooltorton E. Antipsychotic clozapine (Clozaril): myocarditis and cardiovascular toxicity. *CMAJ* 2002; 166: 1185–1186

doi: 10.1093/ndtplus/sfm003

Advance Access publication 11 December 2007

Sorafenib treatment and intracaval neoplastic thrombosis regression

Sir,

Up to 10% of patients with renal clear cell carcinoma (RCC) have intracaval neoplastic extension (ICNE). Caval thrombectomy is associated with a 7.5% early mortality and requires a multidisciplinary surgical team, with the use of cardiopulmonary bypass (CPB). Furthermore, this surgical option has not revealed any substantial impact on the long-term survival of patients [1]. We report a favourable outcome of recurrent ICNE under sorafenib treatment, in a patient who had previously undergone surgery.

A 62-year-old man was diagnosed in May 2006 with ICNE secondary to left RCC. He underwent a nephrectomy and removal of intracaval thrombosis extending into the right atrium. Postoperative serum creatinine level was 1.70 mg/dL. Pathological exam confirmed the neoplastic nature of the thrombus related to RCC. Despite thrombolytic agents followed by anticoagulant treatment, ICNE recurred 2 months later, with right renal vena extension inducing oliguric acute renal failure (serum creatinine, 7.38 mg/dL), and required iterative haemodialysis. Despite a 5-month compassionate use of sunitinib 37.5 mg daily and maintained anticoagulation, ICNE remained stable (Figure 1A) and the patient remained haemodialysis dependent. In January 2007, he was then treated with sorafenib 400 mg twice a day. Three months after the start of the treatment, his pre-haemodialysis serum creatinine level decreased from 5.63 to 1.77 mg/dL, and he became free of dialysis up to the present. Magnetic resonance nuclear imaging revealed a reduction of the thrombus mass