Chinese herbal uropathy and nephropathy

Chris Laing, Sally Hamour, Michael Sheaff, Ron Miller, Robin Woolfson

In July, 2003, a 30-year-old Chinese man was referred to our outpatients department. He had reported macroscopic haematuria to his family physician, who confirmed haematuria on urine dipstick; his blood tests at that time showed a high serum creatinine concentration (200 µmol/L). He was then referred to our nephrology clinic. There were no other symptoms or medical history and no family history of renal disease. For at least 5 years, he had been taking the Chinese herb Longdan Xieganwan to “enhance” his liver. He was normotensive, and physical examination was unremarkable. Nephritic screen and urine culture were negative with normal renal-tract ultrasonography.

A few days after his initial assessment, he returned to clinic with a large fragment of solid material that he had passed per urethram. Histopathology showed a mass of transitional-cell carcinoma cells. Urgent cystoscopy showed a limited bladder tumour, which was resected. There was no extravesical extension of tumour on pelvic CT, and he received intravesical chemotherapy. Despite avoidance of Chinese herbs, he has developed recurrent transitional-cell carcinomas in the bladder, which have been treated by repeated cystoscopic resection; he has declined cystectomy. A renal biopsy done in April, 2004, showed interstitial fibrosis consistent with Chinese herbal nephropathy (figure). He has progressed to end-stage renal failure, and when seen in June, 2006, was preparing for renal replacement therapy.

Longdan Xieganwan contains Caulis aristolochia manshuriensis, of which aristolochic acid is an active ingredient. Although this compound has previously been recognised as nephrotoxic, public awareness was increased after end-stage renal failure was reported in nine women who had inadvertently been exposed to it as part of a weight-reduction programme.1 The renal lesion is a non-inflammatory interstitial fibrosis,2 and patients can present with abnormal renal function, hypertension, urinary leucocytosis, and moderate proteinuria. Progression to renal failure, despite avoidance of the herb, is well recognised. After exposure to aristolochic acid, there is also a very high incidence of uroepithelial atypia and transitional-cell carcinoma, and this substance is now recognised as a potent urological carcinogen. Although urothelial lesions can present with macroscopic haematuria, many lesions will be asymptomatic. In one series of 39 patients, 18 had carcinomas and a further 19 had dysplastic lesions.3 The carcinogenic role of Chinese herbs was confirmed by the presence of aristolochic-acid-related DNA adducts in tissue samples. The authors concluded that cumulative doses exceeding 200 g were highly associated with urothelial carcinoma.4 Poisons have also been implicated in the pathogenesis of Balkan nephropathy and analgesic nephropathy and, intriguingly, both these entities are also associated with urothelial carcinoma. Longdan Xieganwan is manufactured by China Tong Ren Tang, China’s oldest supplier of traditional medicine. After a warning about nephrotoxicity issued by the US Food and Drug Administration against aristolochic acid in May, 2000, the company replaced the herb in Longdan Xieganwan in 2002. Recently, more than 100 Chinese renal patients initiated a class-action lawsuit against the manufacturer—the first such consumer action China has seen.5 Aristolochic acid has been banned in many countries but continues to be available on the internet.6 This case emphasises the importance of an adequate environmental and dietary history in uropathological disease and highlights the dangers of unregulated herbal therapy.

References:

Figure: Renal biopsy

Interstitial fibrosis (pink) with no inflammatory-cell infiltrate. Elastic van Gieson x400.