A 20-year-old man was referred to our clinic for elevated serum urea and creatinine levels. He had complained of painful red eye and decreased vision in both eyes for 2 months. There was no history of ingestion of any drugs. There was no significant past medical history. Physical examination was unremarkable except for the bilateral red eye. Laboratory findings were as followed; urea 51 mg/dl, serum creatinine 1.6 mg/dl. Other biochemical and haematological tests were normal. Urinalysis showed a pH of 6, specific gravity 1032, glucose positive, protein 34 mg/dl, 15–20 red blood cells/high-power field. Twenty four hour urinary protein was 680 mg/day and estimated creatinine clearance was 63.5 ml/min. Serum glucose levels, glycosylated haemoglobin, immunoglobulin levels, complement fractions C3 and C4 and urinary elimination of β2-microglobulin were normal. Serological tests for the infectious and non-infectious causes of AIN were negative. An ophthalmological examination revealed bilateral non-granulomatous anterior and posterior uveitis with posterior synchiae and posterior subcapsular cataract on left eye. Abdominal ultrasonography was normal except increased parenchymal echo patterns in both kidneys. In light microscopy of a kidney biopsy, mild mesangial proliferation and a moderate mononuclear cell infiltration in the interstitium were observed. Amyloid, IgA, IgG3, IgM, C3, C4 and fibrin deposits were not detected and a diagnosis of AIN was made. The presence of unilateral uveitis confirmed the diagnosis of TINU. The patient was treated with 1 mg/kg/day oral prednisone and topical corticosteroids. Six weeks after therapy, 24 h urinary protein was reduced glomerular filtration rate. Kidney biopsy confirmed AIN [2,3]. Functional improvement after prednisone treatment is typical of the TINU syndrome. However, stopping therapy may induce ophthalmological relapse [3]. TINU syndrome should be considered in the differential diagnosis of unexplained tubulointerstitial nephritis, especially in the presence of ocular findings.

Comment

Acute interstitial nephritis may have various causes [1]. TINU is a syndrome characterized with diagnostic anterior uveitis concomitant with or late onset nephropathy. The present case had proximal tubular dysfunctions and a reduced glomerular filtration rate. Kidney biopsy confirmed AIN [2,3]. Functional improvement after prednisone treatment is typical of the TINU syndrome. However, stopping therapy may induce ophthalmological relapse [3]. TINU syndrome should be considered in the differential diagnosis of unexplained tubulointerstitial nephritis, especially in the presence of ocular findings.

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Vitamin E, 5-lipoxygenase and oxidative stress in haemodialysis patients: facts, not fancies

Sir,

A daily supplement of 800 IU of vitamin E is now recommended only for secondary prevention of cardiovascular events in ESRD patients on maintenance haemodialysis (MHD) [1]. However, we wish to emphasize the possible role of vitamin E supplements in primary and secondary prevention of major acute cardiovascular events in all MHD patients, even though its efficacy in the general population has never been clearly demonstrated.

Atherosclerosis is a leading cause of cardiovascular morbidity and mortality in ESRD patients. Vitamin E (α and γ tocopherols) is a main lipid-soluble antioxidant of cell membranes [2]. Oral vitamin E supplements have been shown to prevent oxidative stress and to increase LDL resistance to ex vivo oxidation in HD patients [3]. Peripheral blood mononuclear cell (PBMC) 5-lipoxygenase (5-Lox) activity is involved in low-density lipoproteins (LDL) oxidation in the early phases of the atherosclerotic arterial lesion [4]. 5-Lox activity and molecular expression are up-regulated in PBMC of HD patients [2]; 5-Lox is involved in lipid peroxidation, reactive oxygen species (ROS) production, mitochondrial damage and apoptosis of PBMC, which are also enhanced in HD patients compared to healthy controls [2]. This may contribute to the increased susceptibility of ESRD patients to atherosclerosis, compared to the age-matched general population. Finally, PBMC 5-Lox activity, but not its molecular expression, is specifically inhibited by vitamin E both in vitro and in vivo with an enzymatic, non-oxidative mechanism, regardless of its administration route [2]. An analogous enzymatic, non-oxidative inhibition of 5-Lox exerted by N–3 polyunsaturated fatty acids (PUFAS) was recently reported [5], and may also contribute to the effect of fish oil derivatives in the secondary prevention of coronary heart disease. Conflicting results are observed when the effects of vitamin E supplements on cardiovascular protection are investigated in selected groups of ESRD patients on MHD and in large randomized trials, where a clear-cut relationship between vitamin E supply and cardiovascular morbidity and mortality has never been demonstrated [6]. In a recent meta-analysis of seven large clinical trials, vitamin E supplements failed to show any significant improvement in cardiovascular primary or secondary prevention [7]. However, the authors themselves admitted that they were not able to assess the actual effect of antioxidant vitamins in selected cohorts of high-risk high-oxidative stress patients, such as ESRD patients under MHD, and that no trial assessed the efficacy of antioxidants supply by measuring markers of lipid peroxidation, as we did in previous investigations [2]. Moreover, recent reports suggest that serum γ tocopherol is more consistently related to decreased cardiovascular risk, and vitamin E supplements lead to a significantly higher increase in serum γ rather than α tocopherol in both ESRD patients and healthy controls. A significant elevation in serum phytyl anti-inflammatory anti-atherogenic active metabolites of γ and α tocopherol (i.e. γ and α carboxyethyl-hydroxycromans) was also reported in ESRD patients before and after HD, compared to healthy controls [8]. All these reports may contribute to a better response of ESRD patients to vitamin E supplements.
Supplementation of natural antioxidants such as vitamin E may thus be beneficial to all ESRD patients on MHD, even though its real benefit in the general population remains a matter for debate.

**Conflict of interest statement.** We have had no involvements that might raise the question of bias in the work reported or in the conclusions, implications or opinions stated.

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