Tubulointerstitial nephritis and uveitis syndrome (TINU): a step forward to understanding an elusive oculorenal syndrome

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In this issue of NDT, Sartelet et al. [1] provide an interesting study on Tubulointerstitial Nephritis and Uveitis Syndrome (TINU), an oculorenal syndrome the pathophysiology of which is still poorly understood.

TINU is a rare disease, first described in 1975 by Dobrin [2] in two adolescent girls, in whom non-caseating granulomas were found in the bone marrow and in the lymph nodes, in association with anterior uveitis and tubulointerstitial nephritis. Since then, more than 200 cases have been
The differential diagnosis for interstitial nephritis associated with uveitis is broad (Table 1). Further ocular findings, in addition to those that characterize uveitis, help suggest the correct diagnosis in these cases [7,8]. Sarcoidosis and Sjögren’s syndrome expression is close to that of TINU, making an accurate diagnosis difficult in the absence of a specific involvement of other organs.

The pathophysiology of TINU is still unknown. Renal tubular and ciliary body epithelia share several functions, including those pertaining to electrolyte transporters sensitive to carbonic anhydrase inhibitors. It is conceivable that they share closely related antigens that account for a cross-reactivity. Specific basement membrane antigens have been found to be immunogenic in animal models of acute interstitial nephritis, and some patients with acute interstitial nephritis express antibodies to the tubular basement membranes (TBMs) [4]. Immunofluorescence using sera from patients with anti-TBM nephritis revealed their localization in the TBMs of the proximal and, to a lesser extent, the distal tubule and Bowman’s capsule, and also the basal membrane of the intestinal mucosa [9,10]. Although rare, human anti-TBM nephritis has been reported in some cases related to drugs [11], in transplanted patients [12]; some cases occur in the absence of any detectable underlying disease [13]. Only few patients with TINU were specifically reported to have immunofluorescent TBM staining indicating antibody deposition [14,15].

Sartelet et al. [1] report for the first time the presence of autoantibodies recognizing a common antigen found in reported in the ophthalmologic and paediatric literature, in the form of case reports and small series. Epidaemiology, diagnosis, pathophysiology and management of TINU syndrome have been reviewed in a recent issue of NDT Plus by Sinnamon et al. [3]. Ocular symptoms are forerunners of systemic symptoms in ~20% of cases and follow systemic symptoms by up to 14 months in 65% of cases. Uveitis is limited to the anterior segment in 80% of cases. Uveitis is bilateral at presentation in 77% of cases. The visual prognosis appears to be good. However, uveitis recurs or follows a chronic course in 56% of the patients and persists for several years in some cases. Ocular complications (including posterior synechiae, cataract and higher than normal intraocular pressure) have been reported in one-fifth of cases [4]. The kidney involvement consists of a tubulointerstitial nephritis with a mononuclear infiltrate in the majority of cases. In general, the renal disease tends to resolve either spontaneously or with corticosteroids. Few cases were characterized by the recurrence of acute interstitial nephritis. Persistent renal dysfunction has been reported in 11% of cases, including several patients who required transient dialysis for a period of time (2 weeks to 5 months) [4]. However, two out of five affected patients evolved to renal replacement therapy [4,5]. There are arguments suggesting that TINU is underdiagnosed and may be far more common than currently appreciated, especially in young patients in whom mild renal disease does not become symptomatic and/or if diagnostic tests regarding renal involvement are not performed at the time of presentation [6].
tubular and uveal cells, in the serum of a 15-year-old girl suffering from TINU. After a negative standard direct immunofluorescence, the serum of the patient and that of a normal healthy human control were deposited on frozen sections of the normal human kidney and normal mouse eye. Immunofluorescence microscopy showed focal cytoplasmic IgG deposits on proximal and distal tubular epithelial cells along with membranous IgG deposits in uveal cells (ciliary body and iris) incubated with the patient’s serum. There were no IgA or IgM deposits and no deposits in sections incubated with a normal serum. This forms an original set of findings in TINU.

However, the presence of autoantibodies does not necessarily indicate the presence of an autoimmune disease. As an example, natural anti-glomerular basement membrane autoantibodies exist in normal human sera [16]. More information is therefore required to establish the causative role of the antibodies observed by Sartelet et al. Nevertheless, the identification of circulating antibodies against uveal proteins, even when their precise nature has not been elucidated, incites to attribute an autoimmune background to the patient’s illness. The unique case presented by Sartelet et al. is of particular interest in that it adduces arguments for a pathophysiologic role of concomitant anti-uveal and anti-renal tubule antibodies.

The experience to date indicates that continued search for, and identification of, anti-TBM antibodies, in the renal tissue and in the serum of patients with TINU syndrome, is warranted. In this respect, Sartelet et al.’s case provides a strong incentive to pursue this quest with renewed conviction.

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References

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