EDITORIAL

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Tubulointerstitial Nephritis and TINU syndrome: A rising cause of acute kidney injury

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Much is written and studied about the glomerulus. Nevertheless, tubulointerstitial fibrosis leads to renal dysfunction a lot more quickly than glomeruloesclerosis. Among the diseases that affect the renal interstitium is acute tubulointerstitial nephritis (ATIN). ATIN is a known cause of acute kidney injury (AKI), accounting for 10 to 27% of the AKI cases without an obvious aetiology[1]. As AKI has very important implications for kidney future health and patient morbid-mortality[2], early diagnosis and treatment of AKI is mandatory.

ATIN diagnosis can be a challenge and a high index of suspicion is necessary, especially in young patients, as symptoms are nonspecific, physical examination findings evasive, and blood and urine and imaging tests not always helpful. Definitive diagnosis is made through a kidney biopsy. Renal interstitium inflammatory infiltrate of T-lymphocytes and monocytes, as well eosinophils, neutrophils and plasma cells, with tubulitis and edema the expected findings.

Several factors can precipitate ATIN, more than two thirds drug-induced[3], but infections and auto-immune diseases are other frequent factors. Because of its triggers, ATIN seems to be increasing among older patients[3], as we can verify in the 2014 and 2015 kidney biopsies national report[4,5]. ATIN hasn't appeared in the top 10 of histologic diagnosis since 2008 (for instance, in 2012 ATIN occupied the 15th place, in 2013 the 13th), but when a sub-analysis is made based on the age of the patients, it ascends to the top 10, and in 2014 was the 6th more frequent diagnosis, alongside cast nephropathy and diabetic nephropathy.

Tubulointerstitial nephritis with uveitis (TINU) syndrome is an uncommon cause of ATIN (9 – 22% of ATIN cases) and even rarer cause of uveitis (less than 2% of uveitis cases) and is thought to be a multisystemic autoimmune disorder, usually precipitated by drugs, mostly antibiotics and NSAIDs, and flu-like infections (coincidently all factors that cause ATIN *per se*)[6]. In addition to the presence of ATIN and uveitis, it is required the absence of other systemic disorders that are also associated with ATIN and ocular symptoms, as some infections – tuberculosis would be an example – or other autoimmune diseases, as sarcoidosis. TINU syndrome is an exclusion diagnosis. This is important to note because it has treatment implications.

Although a rare disease, in this issue of the *Portuguese Journal of Nephrology and Hypertension*, two group of authors, one from the north and the other from the south of the country, describe 4 cases of TINU syndrome[7,8]. If we go back to 2003, 5 additional cases were reported in our Journal[9-12]; the first in 2007. Possibly more cases are diagnosed in our country (and around the world) that simply aren't reported, and it is possible that its prevalence is underestimated. The pathogenesis of this disease is not completely understood; the possibility for autoantibodies is studied, but cellular immunity appears to be central[6].

While these cases from the *Portuguese Journal of Nephrology and Hypertension* seem to be straightforward, some of their features are worth highlighting: 1) TINU syndrome has a predilection for young female

patients, but we cannot rule out the entity in older patients; 2) while kidney manifestations of TINU often precedes ophthalmologic manifestations[6], in three of these cases ocular manifestation appeared first, and ophthalmologists should order kidney function tests in the laboratory investigation of uveitis; 3) ocular manifestations can be asymptomatic, so every ATIN patient should be referred for an ocular evaluation; 4) with steroid therapy, recovery of renal function is the rule, and relapses are infrequent, but uveitis tends to persist or relapse in 50% of the TINU patients[13], as reported in one of those cases.

In conclusion, the epidemiology of TINU syndrome is changing and, despite it being a more typical paediatric disease of, more cases in adults and elderly adults are emerging. In parallel, the incidence of ATIN cases, especially in the elderly, is also increasing. We need to learn more about these diseases and how to prevent them to reduce cases of acute kidney injury.

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