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Tubulo-interstitial nephritis and uveitis syndrome

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ABSTRACT

Acute tubulo-interstitial nephritis with concomitant uveitis is a rare condition. While its aetiology is unknown, cellular immunological mechanisms have been implicated in its pathogenesis.

The authors describe a case report of a forty-nine year-old patient who presented with ocular symptoms that preceded a constitutional syndrome and acute renal failure (serum creatinine 6.6 mg/dl). The renal pathology study showed acute tubulointerstitial nephritis with an inflammatory infiltrate, with predominant lymphocytes. The immunofluorescence was negative. Administration of corticosteroids led to a clinical and biochemical improvement.

We stress the importance of diagnosing this clinical entity, the role of kidney biopsy, and the success of steroid treatment when started early.

Key-Words:
Tubulointerstitial nephritis; uveitis.

INTRODUCTION

Acute interstitial nephritis (AIN) is an acute disease characterised by the presence of inflammatory infiltrates within the interstitium which can cause acute renal failure. There is evidence that it is an immunologically-induced hypersensitivity reaction to an antigen that is classically a drug or an infectious agent. Less often it may be secondary to immune reactions to a renal antigen.

The association of idiopathic AIN with anterior uveitis (TINU syndrome) has been reported as a distinct clinical entity. It is a rare condition and was first described in 1975 by Dobrin[1]. This syndrome is found most commonly in pubertal girls and young women but it also appears in young males and in adults.

Approximately 140 cases have now been reported. The majority have been documented in ophthalmology and paediatric nephrology literature in case reports and small descriptive series.

Initial symptoms are generally of a systemic nature with fever myalgia and asthenia but ocular pain and visual impairment may also be present at presentation. Acute renal failure, which may range from mild to severe, develops as the disease progresses.

Renal biopsy shows interstitial inflammatory infiltrate with mononuclear cells, such as lymphocytes, plasma cells, and histiocytes. Eosinophils and non-caseating granulomas are rarely seen. There are no immune deposits. Granuloma may be present in bone marrow, lymph-nodes kidney and liver[1,2].

The pathogenesis of this disorder is not well understood. Delayed-type hypersensitivity and suppressed cell-mediated immunity with a predominance of T-lymphocytes seems to be implicated with proliferation and activation of T-lymphocytes by IL-2[3,4].

We report the case of a forty-nine year-old male patient who presented with acute renal failure due

to idiopathic tubulo-interstitial nephritis documented by renal biopsy and uveitis. We excluded all diseases causing acute tubulo-interstitial nephritis such as Behçet's disease, Sjögren's syndrome, hypersensitivity to drugs, systemic drugs or vasculitis and systemic infection. The patient recovered after corticotherapy.

CASE REPORT

A forty-nine year-old male patient came to our hospital with fatigue, anorexia and fever of two weeks duration. He had been losing weight since the previous month. Since then he had complained of severe pain in the right eye, with no precipitating factors, accompanied by photophobia, weeping and impaired vision. He had no evidence of recent infection, articular pain or skin rash.

He had been treated for hypertension with lisinopril since the age of 30 with reasonable results; dyslipidemia had recently been diagnosed and he was taking a statin. He denied taking other drugs or being exposed to toxic substances.

Examination revealed normal body temperature (36.5ºC) and blood pressure (120/60 mmHg) and normal cardio-pulmonar findings. There was a moderate malleolar oedema. There were no skin changes or enlarged lymph-nodes. He was not oliguric.

The main baseline laboratory findings were anaemia (Hb 9.6 g/dl), a rapid sedimentation rate, decreased renal function, creatinine 6.6mg/dl, urea 180 mg/dl, and urinalysis positive for proteinuria with no blood or casts. Blood electrolytes were normal. There was moderate hypoalbuminemia (3.8mg/dl). Liver tests and iron metabolism were normal. Urine culture was negative.

Further laboratorial investigation included immunological and virological study. He had normal complement levels. ANA, anti-DNA, ANCA and RA test were negative. Levels of immunoglobulins were respectively IgG 1700mg/dl, IgA 335mg/dl and IgM 270 mg/dl. Quantitative proteinuria was 4.2g per day.

Serologic tests were negative for HBV, HCV, CMV, Epstein Barr virus, HIV and toxoplasmosis.

Renal echography showed kidneys normal in size and morphology. Ophthamological examination showed anterior uveitis of the right eye.

The renal biopsy showed inflammatory interstitial infiltrate with lymphocytes and eosinophils. Tubulitis was present with scarce infiltrating lymphocytes. Glomeruli were normal and there were no vascular changes. There were no immune deposits. The diagnosis of acute interstitial nephritis was made (Fig. 1, 2).

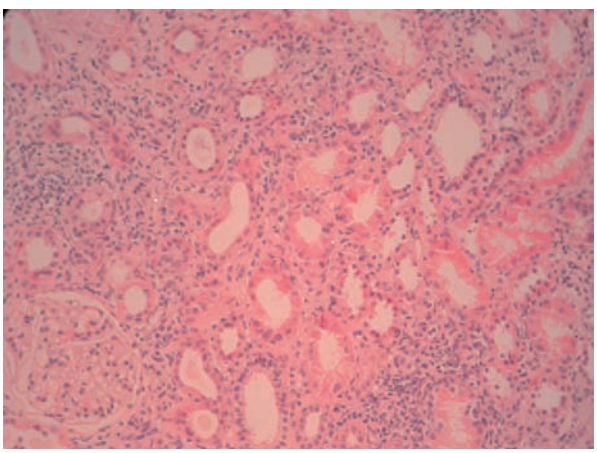

Figure 1

Renal biopsy with an acute interstitial infiltrate

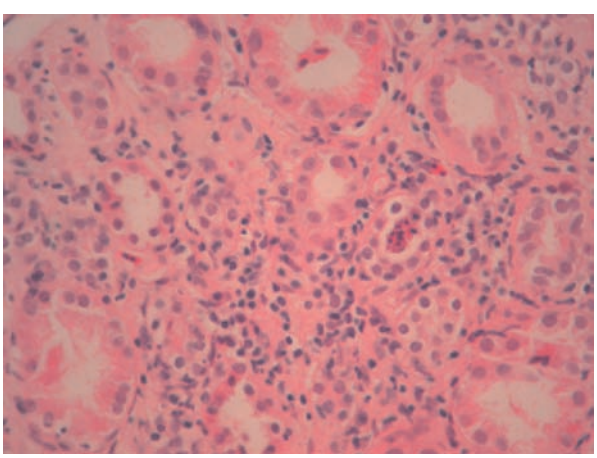

Figure 2

Presence of interstitial eosinophils

The patient was treated with pulse methylprednisolone 1g i.v q.i.d. for three consecutive days followed by oral prednisolone 1 mg per Kg per day for two months. Then the dose was tapered off to a maintenance dose of 10 mg q.i.d. There was rapid amelioration of ocular pain and of visual acuity which recovered completely. Peripheral oedema disappeared and renal function and urinary changes showed progressive recovery. At the end of the second month of therapy there was no anaemia, serum creatinine was 1.8 mg/dl and there was only trace proteinuria. Therapy was maintained unchanged for one year. At that time serum creatinine was 1.3mg/dl and there were no urinary changes. Only anti-hypertensive therapy was maintained.

At 36 months follow-up renal function remains stable (serum creatinine 1.2 mg/dl) and ocular symptoms did not relapse.

DISCUSSION

TINU syndrome is a distinct clinical entity which is characterised by the association of idiopathic acute interstitial nephritis with anterior uveitis. For its diagnosis infection and drug allergy must be excluded.

The patient described above had symptoms of uveitis associated with systemic changes followed by acute renal failure one month afterwards. Drug exposure and infection were excluded by patient history and laboratory tests. While uveitis may be associated with Sjögren, Behçet or Reiter syndromes as well as with sarcoidosis, there were no clinical or laboratory findings here suggesting the presence of any of these diseases.

Renal biopsy showed acute tubulointerstitial nephritis with an inflammatory infiltrate, with predominant lymphocytes. The immunofluorescence was negative. These findings associated with the diagnosis of anterior uveitis are typical of TINU syndrome. The onset of uveitis most commonly follows the onset of interstitial nephritis but may also precede interstitial nephritis or occur concurrently.

The finding of transient nephrotic range proteinuria is not commonly seen and may be related to glomerular changes which were not evident at the light microscopy level.

The patient responded well to corticotherapy with recovery of systemic, renal and ocular changes. Similar results have been reported in other TINU syndrome patients[5-7]. Patients who have been reported to recover spontaneously were most often in the paediatric age range[8,9]. On the other hand some patients did not recover completely[3] and some were even on dialysis for some time[4].

The therapy for TINU syndrome is not well established in general and neither the dose and duration of corticotherapy or the use of other immunosupressor drugs[5] are well established in particular. In the cases reported so far therapy has been established based on clinical grounds. In this particular patient renal function was severely impaired and he had severe systemic and ocular symptoms. High doses of corticosteroids were given and a rapid response was observed. However renal function remained moderately impaired after two months and for this reason low dose steroids were maintained for one year. Similar results have been described in literature[10].

Conclusion: Urine analysis and evaluation of renal function are recommended in patients with uveitis at presentation and during long term follow-up. The diagnosis of TINU syndrome is based on renal biopsy. Early treatment can prevent chronic renal disease.

Conflict of interest statement. None declared.

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