Medical Case Reports and Reviews

Case Report ISSN: 2517-7214

Acute interstitial nephritis due to Ciclosporin a toxicity during Behçet's disease

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Abstract

Introduction: Ciclosporin A is an immunosuppressive molecule widely used in Behçet's disease (BD), especially for severe ocular and/or neurological disorders. Its particular toxicity in this field has, however, largely limited its use during this vasculitis. We report an aspect.

Case report: 26-year-old patient followed since the age of 20 for BD with severe ocular involvement (bilateral posterior steroid-resistant uveitis with a significant decrease in visual acuity) requiring treatment with Ciclosporin A at a dose of 5mg/kg/twice daily during the first month and then 5mg/kg/day as a maintenance dose to control uveitis. The one-year control report noted a creatinine at 147µmol/l with aseptic leucocyturia at 400 elements/l. blood pressure was normal and there was no associated hematuria or proteinuria. The infectious and toxic investigation was normal. The ultrasound showed two kidneys of normal size and echo-structure. Renal biopsy revealed acute interstitial nephritis with images of toxic tubular necrosis. Cyclosporine was discontinued and replaced with azathioprine. Renal function normalized three weeks after stopping the molecule.

Conclusion: periodic and regular monitoring of renal function (blood and urine tests) is strongly recommended in order to detect renal damage early in the BD; especially if Ciclosporin A treatment.

Introduction

Behçet's disease (BD) is a chronic inflammatory disease that progresses by relapses, and is most likely to affect young male, with a classic historical triad of recurrent oral aphthous ulcers, genital ulcers, and anterior uveitis with hypopyon [1]. Its anatomical substratum is a systemic vasculitis affecting the vessels of the body of all types (arteries and veins) and any size (large, medium, and small); it has been officially recognized as a systemic vasculitis since the last Chapel Hill consensus for the nomenclature and classification of systemic vasculitis in 2012 [2].

Various systemic visceral disorders (cardiovascular, neurological, gastrointestinal, renal, pulmonary, ocular, ...) can be seen during the evolution of this disease,and be potentially fatal [3]. Some of these serious disorders require the use of immunosuppressive treatments including ciclosporin A [4], a treatment that is not without sometimes severe adverse effects [5,6].

We report the observation of ciclosporin A-induced acute interstitial nephritis in a patient with BD.

Case Report

Our patient is aged 26 and was followed since the age of 20 for BD with severe ocular involvement: bilateral posterior steroid-resistant uveitis with a significant decrease in visual acuity. This ocular complication of the disease necessitated the treatment with Ciclosporin A at the initial dose of 10 mg/kg/day for one month, then 5 mg/kg/day as a maintenance dose for the control of uveitis.

The one-year control report noted a creatinine at 147µmol/l with aseptic leucocyturia at 400 elements/l. Blood pressure was normal and there was no associated hematuria or proteinuria.

Other basic biological tests (total blood count, erythrocyte sedimentation rate, C-reactive protein, ionogram, serum calcium, fasting blood glucose, liver enzymes, muscle enzymes, and electrophoresis of serum proteins) were within normal limits.

The infectious, immunological, and toxic investigations were negative. The ultrasound showed two kidneys of normal size and echo-structure, and Doppler examination of renal vessels was without abnormalities.

Thus, renal biopsy was indicated, and histological exam revealed acute interstitial nephritis with images of toxic tubular necrosis.

Based on the clinical context, the negativity of etiologic investigations for this acute renal failure, and literature data, the diagnosis of cyclosporin A-induced toxic acute interstitial nephritis was retained.

Cyclosporine was discontinued and replaced with azathioprine with good outcome. Renal function was normalized three weeks after stopping the molecule.

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Key words: *Behcet's disease, cyclosporine A, interstitial nephritis, nephrotoxicity, side effect*

Received: February 07, 2019; **Accepted:** February 11, 2019; **Published:** February 15, 2019

Discussion

The specific renal involvement of BD is exceptional [7,8]. In the large series, its frequency is estimated between 1.23% [9] and 2.6% [10], but often conditions the prognosis of the disease [7-11]. The clinical spectrum of this nephropathy may include microscopic hematuria, proteinuria, nephrotic syndrome, arterial hypertension, and acute or chronic renal failure [7-11].

Histologically, nephropathy during BD may be secondary amyloidosis, proliferative glomerulonephritis, mesangial nephropathy, extracapillary glomerulonephritis with crescents, focal segmental glomerulosclerosis and hyalinosis, thrombotic microangiopathy, or linear IgA nephropathy [7-13].

Ciclosporin A is an immunosuppressive molecule widely used during BD, especially if associated ocular and/or neurological involvement [4-6]; however, this molecule is not without risk, particularly demonstrated increased neurotoxicity [5] and nephrotoxicity [6] in patients with BD. Indeed, in the literature review by Akapilat T *et al*, five of the 23 patients with BD who developed renal impairment with renal failure had already received treatment with ciclosporin A [14]. Similarly, 45% of Sajjadi H, *et al*., patients with BD treated with low doses of cyclosporine A had elevations of serum creatinine [4].

As for histologically proven acute tubule-interstitial nephritis, it has only been reported once in BD [7].

This observation draws attention to the nephrotoxicity of Ciclosporin A in BD, which does not appear to be dependent on the duration of treatment or the total dose received [6].

Thus, regular clinical and biological renal monitoring is required in any patient followed for BD and receiving ciclosporin A therapy. In-time detection allows the recovery of renal function following decay and stopping this immunosuppressant [4].

Conclusion

As rare as it may be, this particular renal complication of cyclosporine A treatment in BD must be known by clinicians managing this disease.

Cyclosporine A treatment should be restricted to cases of BD refractory to any other immunosuppressive or immunomodulatory therapies. In these cases regular clinical and laboratory monitoring is strongly recommended in order to detect early abnormalities of renal function parameters.

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