

Amyloïdosis Complicating Behcet's Disease

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Abstract

Background: Behcet's disease is a vasculitis affecting several organs. A renal involvement is rarely described. It is most of the time about a renal amyloidosis. **Patients and methods:** It is a descriptive retrospective study concerning the patients followed in our department for a Behcet's disease having presented a renal amyloidosis. **Results:** It is about 4 men with average age of 38.25 years old. The renal involvement was revealed after an average delay of 5.7 years by a nephrotic syndrome in all cases. A renal insufficiency was noted in 3 cases with an average serum creatinine of 587 $\mu\text{mol/l}$ (127 - 1490). The type of the amyloidosis was AA in 2 cases. The treatment contained colchicines in every case. The evolution was marked by the worsening of the renal function leading to end stage renal disease in 3 cases. Death occurred in 1 case and one patient lost to follow up. **Discussion:** Renal amyloidosis can complicate the evolution of a Behcet's disease. It occurs generally 1 to 10 years after the beginning of the disease. Once installed, it evolves generally towards the chronic renal insufficiency and can condition the forecast of this affection. **Conclusion:** Amyloidosis is a rare complication of the Behcet's disease. Its screening is so desirable to improve the renal prognosis of these patients.

Keywords

Amyloidosis, Prognosis, Behcet's Disease

1. Introduction

Behcet's disease is a vasculitis involving several organs [1] [2]. It was originally described as a triad of oral and genital aphthae with uveitis. Renal involvement is rarely described in this disease [3]. This is most often of renal amyloidosis [4]. We conducted a retrospective descriptive study of patients followed in our department for Behcet's

disease who presented renal amyloidosis proved by histology.

2. Case Reports

In this report, four cases with Behcet's disease were followed during the period between 1990 and 2014. All our patients met the criteria of the international study group for Behcet's disease (ISG) [5]. The features of the patients are shown in **Table 1**.

2.1. Case 1

A 58-year-old man had recurrent oral aphthae with genital ulceration at the age of 42 years.

He had surgery for retinal detachment. He presented later panuveitis with hypopyon.

Treatment consisted of infusion of methylprednisolone (1 g) during the first three days followed by steroids and intravenous pulses of cyclophosphamide (1 g monthly) for six months. He was later under Colchicine (1 mg/day). He presented gross hematuria leading to diagnosis of carcinoma of the right kidney for which nephrectomy was done. Seven years later he presented edema of lower limb. Biology showed renal insufficiency (serum creatinin at 433 $\mu\text{mol/l}$) with a nephrotic syndrome. Renal ultrasound showed the left kidney increased in size and poorly differentiated. Thoraco abdominal CT angiography showed the presence of an aneurysm of the descending thoracic aorta with parietal thrombus and an aneurysm of the abdominal aorta. A labial salivary gland biopsy showed amyloid AA protein.

Evolution was marked by the deterioration of renal function leading to end stage renal disease (ESRD).

2.2. Case 2

A 34-year old man presented recurrent oral aphthae with fever, arthralgia and

Table 1. Patients' data at diagnosis of amyloidosis.

	Age/gender	Symptoms	Biology	Histology	Treatment	Outcome
Case 1	58/M	Macroglossia, BP = 110/60 mmHg	SC = 1490 $\mu\text{mol/L}$, Pt = 42 g/l, SA = 15 g/l, Prot = 4 g/day	Labial	Colchicine	ESRD
Case 2	34/M	BP = 110/60 mmHg, OHT, edema, hepatomegaly, splenomegaly	Pt = 54 g/l, SA = 18 g/l, Prot = 12 g/day, SC = 127 $\mu\text{mol/l}$	Renal	Colchicine	ESRD, death
Case 3	26/M	BP = 130/80 mmHg, Edema	SC = 50 $\mu\text{mol/l}$, Pt = 60 g/l, SA = 16 g/l, Prot = 10 g/day	Renal		Loss to follow up
Case 4	35/M	Edema, BP = 110/60 mmHg, OHT, arthritis, lymph node	Pt = 39 g/l, SA = 9 g/l, Prot = 8 g/day, SC = 144 $\mu\text{mol/L}$	Renal	Colchicine	ESRD

M = male, BP = blood pressure, SC = serum creatinine (normal value: 53 - 97 $\mu\text{mol/l}$), Pt = protidemia (normal value: 55.5 - 87.7 g/l), SA = serum albumin (normal value: 35 - 50 g/l), Prot = proteinuria (normal value: <0.3 g/day), OHT = orthostatic hypotension, ESRD = end stage renal disease.

folliculitis. Diagnosis of Behcet's disease was then retained. Treatment consisted of steroids with good outcome. He was operated on a right atrial myxoma with valve replacement.

He presented five years later edema with fever. Biology showed a nephrotic syndrome. Renal histology concluded to a vascular and glomerular amyloidosis.

He was treated with Colchicine (1 mg/day). Unfortunately, evolution was marked by worsening of renal function leading to ESRD after 15 months.

2.3. Case 3

A 26-year old man presented Behcet's disease which was diagnosed inside of recurrent oral apthae with folliculitis and uveitis. He was treated by steroids but it was badly followed. He presented 36 months after diagnosis, edema without triggering factor. On biology, there was a nephrotic syndrome. Renal histology showed renal amyloidosis of type AA. Unfortunately he was lost to follow up.

2.4. Case 4

A 35-year-old male presented with recurrent oral and genial apthae with a positive pathergy test. The vascular involvement consisted of thrombophlebitis. The diagnosis of Behcet's disease was made and treatment consisted of steroids. He presented edema after a delay of 96 months. Laboratory analysis revealed a nephrotic syndrome. Renal histology concluded to renal amyloidosis. Treatment comprised Colchicine (1mg/day). However, there was no improvement with a progressive worsening of renal function leading to ESRD after a delay of 132 months.

3. Discussion

Behcet's disease is a systemic vasculitis which the most important events are eye, skin, joint, neurological and vascular [1]-[3]. The usual age of onset is around 30 and the male to female ratio varies with the ethnic background. Our report is particular by the male tendency.

Outside the eye, its course is characterized by recurrent self-limiting episodes of acute inflammation that can lead to significant disability.

Renal involvement is rare in this disease. Renal symptoms can range from nephrotic syndrome with renal failure until asymptomatic urinary abnormalities, hematuria and/or proteinuria that can lead to disregarding latent kidney damage [4] [6].

These renal manifestations may be intermittent and observed with variable frequency from 20% to 49% [6]. Renal parenchymal lesions are dominated by amyloidosis [7].

The frequency of amyloidosis in the Behcet's disease varies from 0.5% to 3% [3] [4] [8] [9]. It appears to be related to the long duration of the disease. It is much more common in the Mediterranean area where there is a recurrent disease [3] [4].

It occurs between 1 and 10 years after the start of Behcet's disease and most often is manifested by proteinuria and/or nephrotic syndrome [3] [4] [8]. In our series, amyloidosis happened after 3 - 8 years and it manifested by nephrotic syndrome in all cases.

Amyloid protein is type AA as in other chronic inflammatory and infectious processes [10]. Once installed amyloidosis progresses to kidney failure and is one of the causes of death with their extra-renal localization and severe states of cachexia observed in Behcet's disease [6] [7]. This poor renal prognosis is supported by our report since three of our patients evolved to end stage renal disease.

The management of patients with behcet's disease has evolved considerably over the last decade, with more insight into the better use of older agents and the development of newer remedies such as biologics. Despite that, treatment remains challenging as it continues to be largely based on case reports, case series, and only a few randomized clinical trials. All our patients were treated with traditional treatments like corticosteroids and none with biologics since they were not yet available in our department.

Colchicine has not always proved its effectiveness in the treatment of amyloidosis [11]. Its prescription can be justified, however, to stabilize amyloid lesions. Meanwhile, in our series colchicine didn't improve the prognosis of our patients.

4. Conclusion

Amyloidosis is a rare but serious complication of Behçet's disease. Once installed, it usually progresses to chronic renal failure. Its detection is thus desirable to improve the renal prognosis of these patients.

Ethical Approval

All procedures performed in our study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration.

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