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Case Report

Amyloid Vasculopathy Revealed by Episodes of Severe Arterial Hypotension Complicating Crohn's Disease

K El Montacer[1]*, W Hliwa[1], Ri Seydou[1], F Haddad[1], FZ El Rhaoussi[1], M Tahiri[1], A Bellabah[1], W Badre[1] and M Regragui[2]

[1]Hepato-Gastroenterology Department of the University Hospital Center IBN ROCHD of Casablanca, Morocco

[2]Anatomopathology Department of the University Hospital Center IBN ROCHD of Casablanca, Morocco

***Corresponding Author:** K El Montacer, Hepato-Gastroenterology Department of the University Hospital Center IBN ROCHD of Casablanca, Morocco.

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Abstract

Background: Renal failure secondary to AA amyloidosis is a common cause of death among patients with untreated Crohn's disease. Once amyloid deposits set in, they are irreversible; however, controlling the inflammation limits the progression of tissue damage and stabilizes the disease.

Aim of the study: To describe the case of Crohn's disease with a delayed diagnosis reaching complication stage: renal and vascular amyloidosis with a poor prognosis, in order to make practitioners aware of the importance of systematic screening for this severe complication and the establishment as soon as possible of a specific therapeutic strategy aimed at controlling inflammation and slowing progression to end-stage chronic renal disease.

Case report: A 50years old male patient diagnosed, simultaneously, after 20 years of symptom progression, with stenosing ileocolic Crohn's disease complicated by systemic AA amyloidosis revealed by renal failure and episodes of vasoplegia. Ileo-caecal resection and control of inflammation with steroids and immunosuppressive therapy resulted in stabilization of renal status and decreased frequency of orthostatic hypotension episodes.

Conclusion: Screening for proteinuria and impaired renal function in patients with chronic inflammatory diseases, particularly Crohn's disease, allows early diagnosis of secondary amyloidosis. Although no treatment has been proven effective for the reversibility of amyloid deposits; control of inflammation seems to stop amyloidogenesis and consequently limits the progression of organ dysfunction.

Keywords: Crohn's Disease; Arterial Hypotension; AA Amyloidosis; Immunosuppressant

Introduction

AA amyloidosis is a rare and potentially fatal complication of chronic inflammatory bowel syndrome [1,2]. Renal symptoms, including proteinuria and renal failure, are revealed late, in some cases at more than 20 years of evolution of the disease [1,2].

Case Report

Mr. R.M., 50 years old, followed since 2019 for a Crohn's disease classified A3L3B2 according to the Montreal classification, revealed clinically by chronic liquid diarrhea, a Koening syndrome of the right iliac fossa and an alteration of the general state; and biologically by an inflammatory syndrome and malabsorption.

The patient underwent colonoscopy, which revealed exulcerated ileitis with nonspecific inflammatory changes. The quantification of the bacterial genome by PCR method did not reveal any Koch bacillus. Abdominal CT scan showed a thickening of the last ileal loop with inflammatory appearance and infiltration of the mesenteric fat, associated with a left lower polar renal cyst classified as Bosniak IV.

The diagnosis of Crohn's disease was retained, but treatment with corticosteroids and azathioprine could not be started because of the strong suspicion that the renal lesion was malignant.

The patient underwent an ileo-caecal resection with terminal-lateral anastomosis taking out 12cm of the ileum and 5cm of the cecum. The histological study of the surgical specimen showed a transparietal inflammation with mononuclear cells and a Sclerolipomatosis with identification of an epithelio-giganto-cellular granuloma. A nephrectomy was deferred due to the occurrence of a vasoplegia during surgery.

These episodes of arterial hypotension profoundly altered the patient's quality of life and sometimes required noradrenaline infusions. Their etiological work-up did not identify any cardiac abnormalities, nor any metabolic disorder such as hypothyroidism (TSHus at 1.29mUI/l, T3 at 2umol/l and T4 at 13umol/l), adrenal insufficiency (8 h cortisol level at 11.6ug/dl, normal natraemia and kalaemia), or vitamins deficiencies (vitamin B12 at 288pmol/l and vitamin D at 39nmol/l). Brain magnetic resonance imaging (MRI) was unremarkable.

Renal function was disturbed with urea at 0.51g/l, creatinine at 28mg/l, glomerular filtration rate at 25ml/min/1.73m2 and moderate proteinuria at 0.36g/24h. Renal ultrasound with renal artery Doppler and renal artery angioscanner showed normal sized kidneys, fairly well differentiated with a small but permeable renal artery.

Amyloid deposits by Congo red staining and birefringence were identified on salivary gland biopsies with expression of anti-PAA antibodies.

The patient underwent a partial nephrectomy with removal of the lesion whose histological examination was in favor of a papillary adenomatous disease, without signs of malignancy with identification of amyloid deposits type AA with a vascular predominance (Figure 1-3).

Figure 1: Hematoxylin eosin stain x200: diffuse mononuclear inflammatory infiltrate with eossinophilic amorphous material surrounding tubules and vessels.

Figure 2: Congo red stain showing Green birefringence.

Figure 3: Congo red stain showing Pink amorphous deposits surrounding blood vessels.

The patient was put on corticosteroid therapy and on azathioprine. The evolution is marked by a clinical remission, a stabilization of the GFR and a decrease in the frequency of arterial hypotension episodes after 6 months.

Discussion

AA amyloid protein is derived from the cleavage of serum amyloid-associated protein (SAA), one of the major proteins of the inflammatory reaction. AA amyloidosis is an architectural and tissue disruption of organs where extracellular deposits of this abnormal fibrillar insoluble protein material are formed in response to chronic inappropriate systemic inflammation [1,2].

The first case of amyloidosis related to Crohn's disease was reported by Moschcowitz in 1936 [3]. It is a rare and potentially fatal complication, occurring in 0.5-6% of cases [4]. It is much less frequent in ulcerative colitis [5]. The time interval between the diagnosis of Crohn's disease and the development of AA amyloidosis varies between 1 and 42 years; sometimes they are diagnosed simultaneously [5], as in the case of our patient whose symptoms had been evolving for over 20 years.

The phenotype most frequently associated with this complication is the stenosing and fistulizing form complicated by suppurations [6]. Our patient presented with stenosing ileo-caecal Crohn's disease that led to ileo-caecal resection for diagnostic and therapeutic purposes.

The most frequent localization of AA amyloidosis is renal. Its clinical phenotype is variable: positive proteinuria, nephrotic syndrome, renal failure [8]. Amyloid deposits are mainly glomerular, but in 15-25% of cases, they can be exclusively vascular, characterized by the appearance of renal failure without proteinuria. It has a better prognosis than the glomerular form [9-11]. Our patient had severe renal failure without significant proteinuria or morphological abnormalities on ultrasound. Histology confirmed the predominance of amyloid type AA deposits at the vascular level.

Increased AAS in Crohn's disease is a prognostic indicator predictive of the occurrence of AA amyloidosis, which could be used to screen and monitor individuals at risk [8]. This biological marker has a better value than C-reactive protein, which could be normal even in case of persistent inflammatory activity [7]. Its determination could not be done in our case due to lack of financial means.

Confirmatory diagnosis of AA amyloidosis is based on the demonstration of amyloid deposits by Congo red staining and birefringence on biopsy samples from organs suspected of being affected by the disease, and identification of the protein subtype by immunohistochemistry. I-serum amyloid P scintigraphy has recently proven to be a non-invasive alternative with 100% sensitivity [12,13]. In our observation, amyloid deposits were identified on salivary gland biopsy and the partial nephrectomy specimen.

To date, no drug is considered effective in the treatment of amyloidosis (Azathioprine, colchicine, Dimethyl sulfoxide) [14,15]. However, Yoon Kyung Park., *et al.* reported a favorable outcome of ileocolic Crohn's disease with ano-perineal manifestations complicated by renal, colonic and thyroid AA amyloidosis on Infliximab, marked by improved renal function, decreased proteinuria and SAA levels [16].

Renal transplantation remains the best therapeutic choice for end-stage renal disease [17].

Due to the unavailability of biotherapy, our patient was put on Azathioprine 2mg/kg/d and corticosteroids. The evolution is marked by a clinical remission and a stabilization of the GFR at 25ml/min/1.73m2.

Conclusion

Renal involvement conditions the prognosis during Crohn's disease because of its severity and insidious onset. Early diagnosis of IBD as well as early detection of amyloid deposits allows to avoid the progression of renal amyloidosis towards renal failure.

Compliance with Ethical Standards

Conflict of Interest

No Conflict of Interest

Author Contributions and Agreements

I confirm that all authors of the manuscript have read and agreed on its contents and that the reproducible material described in the manuscript would be freely available to all scientists wishing to use it for non-commercial purposes.

Informed consent was obtained for this publication.

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