are associated with the patients’ predisposition, due to possible anomalies in the renal collecting system, infections, urolithiasis or hydronephrosis (6). For this reason, infections and reflux will be treated equally as in any other patient. However, in the case of lithiasis, if process allows it and there are no contraindications, lithotripsy (ESWL) will be used as a first option, but without disregarding the need of a transperitoneal approach surgery (6).

REFERENCES AND RECOMMENDED READINGS (*of special interest, **of outstanding interest)


** INTRACTABLE HEMATURIA SECONDARY TO SYSTEMIC AMYLOIDOSIS WITH BLADDER INVOLVEMENT

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Summary.- OBJECTIVE: To present the therapeutic management of intractable hematuria secondary to systemic amyloidosis with bladder involvement.

METHODS: We describe the clinical case, the medical management, the endo-urological technique used, and the results supported by relevant published literature.

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RESULTS: A 50-year-old woman with a 20-year history of rheumatoid arthritis in chronic treatment with corticosteroids and non-steroidal anti-inflammatory drugs in addition to chronic renal insufficiency not requiring hemodialysis. Twenty-four hours after resection of a hepatic hydatid cyst she presented intractable hematuria. The ultrasound and CT scan showed the formation of a large blood clot in the bladder not affecting the upper urinary tract. An intra-operative cystoscopy revealed a distended bladder showing signs of inflammation with diffuse, widespread bleeding. Hemostasis was achieved and a biopsy of the mucosa was taken, associated to bladder irrigation with potassium alum as a hemostatic. Given the persistence of the hematuria, further revision in the operating room as well as blood transfusion were carried out and, due to the hemodynamic instability that could not be controlled, finally selective embolization was performed. Intravesical instillation of dimethyl sulphoxide every 72 hours was used to control any remaining hematuria. The biopsy showed bladder amyloidosis. The addition of intravenous steroids and orally administered colchicine successfully controlled the patient's clinical status.

CONCLUSIONES: Secondary amyloidosis of the bladder is a condition associated with hematuria that is difficult to manage. Hematuria control is often difficult, requiring aggressive treatment in addition to more conservative approaches.

**Keywords:** Hematuria. Amyloidosis. Rheumatoid arthritis.

**RESUMEN.- OBJETIVO:** Presentar el manejo terapéutico de la hematuria incórcerible generada en la amiloidosis sistémica con afectación vesical.

**MÉTODO:** Descripción del caso clínico, el manejo médico, la técnica endourológica utilizada y de los resultados con apoyo de la literatura publicada al respecto.

**RESULTADOS:** Mujer de 50 años con antecedentes personales de artritis reumatoide (AR) de 20 años de evolución en tratamiento crónico con corticoides y AINES así como insuficiencia renal crónica sin necesidad de hemodiálisis, que tras 24 horas de la resección de un quiste hidatídico hepático presenta hematuria incórcerible. Ecografía y TAC revelan gran coágulo vesical organizado sin repercusión de la vía urinaria. La cistoscopia intraoperatoria muestra una vejiga distendida de aspecto inflamatorio con sangrado difuso generalizado. Se realiza hemostasia y toma de biopsias de la mucosa asociando al lavado vesical albúmina potásmica como hemostático. Dada la persistencia de la hematuria se procede a nueva revisión en quirófano más transmisión de hemoderivados en vista de la inestabilidad hemodinámica sin lograr control de la misma por lo que se realiza embolización selectiva. Se asocia instilación vesical con DMSO cada 72 hrs. para el control de la hematuria remanente. La biopsia revela el hallazgo de amiloidosis vesical agregándose al tratamiento corticoide intravenoso y colchicina oral controlando satisfactoriamente la clínica de la paciente.

**INTRODUCTION**

Amyloidosis is a disease characterized by extracellular deposits of hyaline protein material visible with Congo red staining. Several classifications of this condition exist according to distribution, i.e. localized and systemic forms, which in turn can be of primary or secondary origin. There are also familiar and senile forms of amyloidosis. Rarely, the urinary system is affected, causing deposits in the connective tissue and blood vessels beneath the urothelium. If the damage occurs in the bladder, hematuria or urinary dysfunction of the lower urinary tract may be present (1).

Primary or localized bladder amyloidosis can be recurrent and requires a long monitoring period, although it is generally benign (1). Treatment in these cases is usually medical, administering oral colchicine and performing instillation of dimethyl sulfoxide (DMSO). Occasionally, it is necessary to perform a transurethral resection and induce hemostasis (10).

More severe symptoms are observed in the secondary form in which a systemic amyloidosis associated with chronic diseases, such as rheumatoid arthritis or ankylosing spondylitis, occurs. The hematuria is usually more abundant because of the extent of amyloid deposits that generate diffuse damage of the vascular walls. This type of hematuria may be intractable, causing hemodynamic compromise and requiring significant blood transfusion (1). Consequently, a more aggressive therapeutic approach is required, in some cases involving arterial embolization, bladder formalization or even cystectomy.

**CASE REPORT**

A 50-year-old woman with a 20-year history of rheumatoid arthritis (RA) in chronic treatment with corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs) in addition to chronic renal insufficiency not requiring hemodialysis is described. Twenty-four hours after resection of a hepatic hydatid cyst, she presented insidious hematuria that became intractable.
The patient was stable with regard to the rheumatologic disease and the anesthesiological assessment prior to surgery was normal. In her family history it is notable that her mother was a carrier of systemic lupus erythematosus (SLE) and her father a controlled type 2 diabetic. The patient had no descendants or high-risk toxic habits.

Initially, conservative measures were taken. This included manual bladder irrigation with 1000 ml of saline, followed by continuous bladder irrigation with saline and subsequent evaluation with analytical controls. In addition, the treatment using heparin of low molecular weight prescribed after hepatic surgery was stopped.

After 48 hours the patient presented acute anemia (hemoglobin <8 g/dl) and the hematuria persisted, requiring the transfusion of three (3) hemoconcentrates. An ultrasound scan showed a large blood clot in the bladder with no bilateral ureterohydronephrosis or morphological changes in the kidneys.

The resulting persistent severe anemia despite the transfusion of seven hemoconcentrates and the hemodynamic instability generated was the basis for performing bladder irrigation under anesthesia (removal of 700ml of blood clots) and a cystoscopy in which the orthotopic meatus were observed to have no hematuria in the ejaculate, and no evidence of any mass lesion was found. Profuse bleeding occurred when performing hydrodistention and inflammation in some areas of the bladder mucosa was observed. Hemostasis was achieved and biopsies were taken. After the procedure, continuous bladder irrigation with potassium alum was started. At 72 hours the patient presented severe hematuria once more, and a new blood transfusion was required. A contrast CT scan and URO-CT images in the late phases showed no evidence of kidney lesions or ureteral filling defects, but new blood clots in the bladder were detected (Figure 1). For this reason, it was decided to proceed to surgical maneuvers (bladder irrigation and hemostasis induction) with the subsequent instillation of potassium alum. This produced partial clinical improvement for 72 hours, at which point the patient presented hematuria again, followed by a further hemodynamic deterioration with worsening of the anemia (5.6 g/dl). A further blood transfusion was carried out and selective embolization of the bladder was performed by the Department of Interventional Radiology at the hospital.

Following this, the patient presented mild hematuria, coinciding with the appearance of edema that was successfully controlled with diuretics and a decrease in administered liquids. Given the persistence of the hematuria, the intravesical instillation of DMSO for 30 minutes every 72 hours was carried out to control the remaining hematuria.

Based on the suspicion of basic coagulopathy and autoimmune diseases, in addition to those already known, extensive analytical studies were carried out and did not reflect significant alterations.

The patho-anatomical description is as follows: a pink, homogenous proteinaceous deposit in the lamina propria and in the blood vessel walls along with focal areas of hemorrhage; Congo red positive for amyloid (Figure 2) with subsequent confirmation of type AA secondary amyloidosis of the bladder.

Treatment with intravenous corticosteroids and oral colchicine was carried out, improving the clinical status of the patient and producing remission of hematuria.

**DISCUSSION**

In 1883, Virchow, in continuing the studies of Rokitansky, described what is now known as amyloidosis based on its histopathological similarity with starch. Defined as extracellular deposits of amyloid, this disease can be classified from the clinical point of view as follows: primary or idiopathic amyloidosis (type AL), secondary amyloidosis (type AA), and other forms of amyloidosis that include hereditary types, those associated with multiple myeloma, and senile forms, among other infrequent variations.

The first description of amyloidosis of the bladder was made by Solomin in 1887. Corbitt et al. provided the first endoscopic image of the disease in 1944. Symptomatic bladder involvement in the context of other systemic diseases, such as rheumatoid arthritis or ankylosing spondylitis (secondary forms), is quite rare. In fact, there are less than 25 cases reported in the literature. Bender and Kelly first reported a case of secondary bladder amyloidosis in a patient with rheumatoid arthritis in 1969 (4). The systemic disease most commonly associated with this condition is rheumatoid arthritis, which occurs in the

![Figure 1. URO-CT scan showing no evidence of kidney lesions or ureteral filling defects. A large blood clot in the bladder is observed.](image-url)
case described in our review. Despite the lack of clinical expression of this disease, amyloidosis of the bladder is actually more common than previously thought. This has been demonstrated by reviews of autopsies in patients with systemic amyloidosis (1,3). Nevertheless, it is important to note that in terms of frequency, published cases of primary bladder amyloidosis significantly exceed those of secondary bladder amyloidosis (2,4,6).

The star symptom of the disease is hematuria that is usually intense, severe, intractable and difficult to manage clinically. The usual trigger is unknown, although some authors have suggested irritation of the bladder mucosa by various factors such as urinary tract infection (2,6), endoscopic instrumentation, and/or catheterization, which occurs in our case report. This symptom, although present in both forms of bladder amyloidosis, is usually of greater importance and worse outcome in the secondary form of the disease. It is believed that this is related to the deposit of amyloid material around the capillaries of the submucosa, a situation that hinders the hemostatic vasoconstriction of these capillaries in response to hemorrhage (1,2,4,6).

The cystoscopic imaging of bladder amyloidosis is usually nonspecific (9,10) and can produce many findings, such hemorrhagic areas with surrounding areas of edema that give the appearance of an ulcerating, inflammatory process or even acquire the morphology of pseudotumor lesions that simulate a solid tumor (9). Likewise, in some cases raised yellowish-white plaques (9) that correspond to the amyloid deposits in the vessel wall are seen. In this case, the only way to obtain a definitive diagnosis, once the disease is suspected and samples of bladder mucosa are taken, is to proceed to patho-anatomical studies (4,9) to demonstrate the presence of amyloid material using various techniques (hematoxylin-eosin, Congo red). We must highlight the importance of immunohistochemistry techniques (Figure 3) in the diagnosis because they allow AL and AA amyloids to be distinguished and permit primary amyloidosis (AL amyloid) or secondary amyloidosis (AA) to be considered specifically. With regard to treatment, in symptomatic cases the main objective is to control the hematuria by first using conservative treatment. In cases of persistent or abundant hematuria, various procedures may be employed, ranging from the instillation of DMSO (5), hemostatic transurethral resection (1,2,6,7), selective embolization of the bladder, hypogastric artery ligation (1,2,3), and even cystectomy in extreme cases (3,6,7,8). In our case, embolization was a decisive measure in addition to the subsequent bladder instillation of DMSO. Once the histopathological diagnosis was made, the use of corticosteroids and colchicine allowed us to stabilize the disease and control the remaining hematuria.

Finally, timely monitoring of patients for possible recurrence of the disease while discarding the possibility...
of concomitant bladder carcinoma is of great clinical interest (4).

CONCLUSIONS

Secondary bladder amyloidosis is a rare entity in the world and often involves hematuria that is difficult to manage and must be suspected in patients with a suggestive history. Controlling hematuria is often difficult. Apart from the common conservative treatments (irrigation, intravesicular hemostatics), more aggressive surgical treatment is sometimes required.

REFERENCES AND RECOMMENDED READINGS
(*of special interest, **of outstanding interest)