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B) CASOS CLÍNICOS BREVES

Renal amyloidosis in common variable immunodeficiency

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Dear Editor:

Common variable immunodeficiency (CVID) is the most prevalent symptomatic primary antibody deficiency, characterized by hypogamaglobulinemia, normal or decreased B-cell number and impaired antibody response leading to chronic and recurrent infections, mostly in the respiratory and gastrointestinal tracts[1,2]. However, a significant proportion of patients manifest features of immune dysregulation, including polyclonal lymphocytic infiltration, autoimmunity, enteropathy and malignancy[3].

Secondary amyloidosis is an extremely rare complication of CVID[4], mostly reported in middle aged males[5-7]. This manifestation refers to the extra-cellular tissue deposition of serum amyloid A (SAA) protein fibrils with β-sheet structure, which could be due to chronic and recurrent infections in this group of patients[8]. The self-assembly by amyloid proteins cannot progress in the soluble condition of dissembled precursor proteins alone, while it is speeded up by seeding with preformed amyloid fibrils[9] which described as «seeding mechanism». Also, enzyme inhibitory function against SAA proteins was confirmed in AA type of amyloid formation and deposition[10]. All reported CVID cases with amyloidosis had a sever status of infectious disease or underling complications like cor pulmonale, congestive hepatomegaly, bilateral bronchiectasis, severe respiratory failure[7] and tuberculosis[6]. Recurrent infections could be considered as the main cause of the amyloidosis development; although recurrent infections could be as a consequence of inadequate IVIG therapy, long delay diagnosis can also prone patient to chronic and recurrent infections[7].

We report herein a 50-year old male with a history of recurrent respiratory tract infections and diarrhea from early childhood. The diagnosis of amyloidosis was made for this patient based on histopathological findings of renal biopsy, once he hospitalized due to edema and massive proteinuria at the age of 48 years. Renal fine needle aspiration biopsy revealed deposition of amorphous pink hyaline eosinophilic material in glomerulus, tubular basement membrane (TBM), interstitial area and vessel walls of arterioles; it was documented by green appearance fibrils under polarized light which stained and bind with Congo red (figure 1). As the patient experienced several episodes of infections, immunological studies were performed which showed significant decreased in all serum immunoglobulin levels, compatible with diagnosis of CVID (table 1). Regular hypo-osmolar

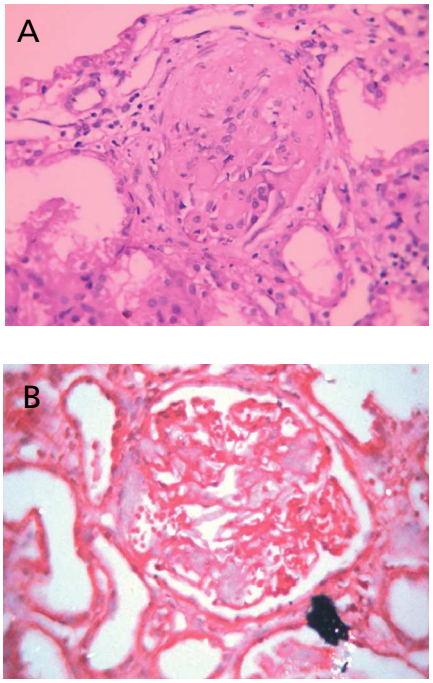

Figure 1. Renal glomerule with deposition of amorphous pink material proved to be amyloid by Hematoxyline, Eosin staining (A. X400) and special reacting to Congo-red stain (B. X400).

Table 1. Patients laboratory finding

Normal range	Patient	Finding
4-10,000	11,000	WBC (count/mm^3)
1,000-6,000	7,700	PMN (count/mm^3)
1,000-4,800	3,080	Lymphocyte (count/mm^3)
12-16	13.2	Hemoglobin (mg/dl)
450-450 (x106)	288 (x10^6)	Plt (count/mm^3)
28-77	88	CD3 (%)
32-62	27	CD4 (%)
2-36	59	CD8 (%)
5-19	10	CD16 (%)
3-14	5	CD19 (%)
700-1,600	251	Serum IgG (mg/dl)
70-400	5	Serum IgA (mg/dl)
40-230	34	Serum IgM (mg/dl)
90-100	98	NBT (%)
50-150	110	CH50 (%)
0.89-1.87	1.31	C3 (g/L)
0.16-0.38	0.31	C4 (g/L)
Up to 20	55	ESR (mm)
Less than 200	347	Triglycerides (mg/dl)
Less than 240	229	Cholesterol (mg/dl)

intravenous immunoglobulin was started in addition to prophylactic antibiotics and cholchicin, which controlled his renal disease. Moreover, he has not experienced further episode of serious infection since last two years.

The clinical manifestations of amyloidosis are widely dependent to the type of deposited protein and amount of amyloid deposition. Variation in the clinical picture of amyloidosis is related to the type of precursor involved[8,11]. Moreover, the clinical features of amyloidosis vary by the organ affected; the most common organ involvement in CVID patients, which are complicated with amyloidosis, is kidney[5,12]. Gastrointestinal (malabsorption, perforation, hemorrhage and obstruction)[6], joints (arthropathy)[13], thyroid[7], and gum were other sites which could be affected by secondary amyloidosis in CVID. Kidney organ function does not change with small amounts of AA amyloid deposition, while the prognosis of excessive deposition of AA renal amyloidosis is generally poor and potentially fatal[14].

It is considerable that renal AA amyloidosis in CVID patients commonly presented with asymptomatic proteinuria, whilst nephrotic syndrome is present in more than one fourth of patients at the time of diagnosis[15]. Also, red blood cells count in urinary sediments and microscopic haematuria may present in CVID patients with the AA type, which more prominent than primary amyloidosis (AL type)[15].

The incidence of AA amyloidosis could be increased with duration of the underlying disease condition and associated factors such as long delay diagnosis. The mean duration of inflammation before the diagnosis of amyloidosis is estimated about 8-14 years[15]. CVID patients usually experience several episodes of infections since childhood; it is expected that the patients had a history of many years inflammation without appropriate treatment, which is enough for progression of AA amyloidosis. The average age of reported CVID patients with renal secondary amyloidosis was 40.7 ± 10.9 years[5-7], which is much lower than the age of other renal amyloidosis population (70.7 ± 12.0 years)[15].

Glomerular deposition of amyloid substances in CVID patients had a significant differentiation from other individuals with renal amyloidosis. In these patients, immunoglobulins are not accompanied in intraglomerular deposition, while in other diseases associated with renal amyloidosis, deposition of IgG and C3 occurred at a rate of 60% and 45%, respectively. Furthermore, IgA deposition can be seen in 50-60% of cases with AA type[9].

Control of the underlying inflammatory disease is the preferred therapy of AA amyloid, but patients who have diagnostic criteria of CVID should receive immunoglobulin replacement therapy. Administration of IVIG could dramatically reduce recurrent infections and subsequent complications in the patients with antibody deficiency[1,2]. Although the usual initial dosage for IVIG therapy is 300-400 mg/kg per month, higher doses of 600-800 mg/kg may be needed in subgroup of patients, especially in patients with bronchiectasis or chronic sinusitis. Nonetheless, IVIG may induce renal damage, especially in patients with preexisting renal insufficiency. Increased level of sucrose, blood viscosity and deposition of immune complex in renal tissue are the main causes of renal damage due to IVIG. Therefore treatment of CVID patients with amyloidosis is a subject of debate. However, high dosage of hypo-osmolar IVIG without sucrose (such as Gummunex or Octagam) is recommended for prevention of renal damage in addition with adjustment of dosage of antibiotics and colchicines. It is expected that new therapeutic strategies in addition to IVIG should be commenced in CVID-amyloidosis patients[15]. The biological agents such as tumor necrosis factor alpha (TNF-α) blocker, Etanercept, Iododoxorubicin and low-molecular-weight sulfates (Fbrilex) have been shown to be effective in treatment of AA-type renal amyloidosis[9], which should be tried in CVID-amyloidosis patients as well.

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Infección por *Cryptosporidium parvum* en un receptor de trasplante renal

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Sr. Director:

Cryptosporidium parvum es un protozoo intracelular que puede producir gastroenteritis en humanos. En huéspedes inmunodeprimidos, la infección puede ser severa y conducir a diarrea persistente y comprometer la vida. La experiencia en el tratamiento de esta infección en los receptores de trasplantes de órgano sólido es limitada. Describimos, en el caso de un receptor de trasplante renal con severa criptosporidiosis, la importancia del diagnóstico y tratamiento precoz. El tratamiento antibiótico, junto con la reducción en la inmunosupresión, permite optimizar el estado inmunológico y conducir a la resolución de la infección.

Presentamos el caso de una mujer de 78 años con enfermedad renal crónica, secundaria a nefropatía intersticial crónica en hemodiálisis desde febrero de 2003. Recibió un trasplante renal de donante cadáver en diciembre de 2003 con Crp basal de 2 mg/dl. En tratamiento con esteroides, micofenolato mofetil y tacrolimus. Los esteroides se suspendieron a los 31 meses postrasplante. En junio de 2008 ingresa por diarrea acuosa sin productos patológicos de 7 días de evolución, sin fiebre, vómitos o dolor abdominal. Se acompañaba de inestabilidad hemodinámica con tensión arterial de 80/50 mmHg, disminución del ritmo de diuresis y deterioro de la función renal hasta cifras de Cr y urea plasmáticas de 4,3 y 177 mg/dl, respectivamente. Al persistir la diarrea a pesar de dieta absoluta y sueroterapia, se inicia tratamiento con metronidazol y ciprofloxacino. La detección de antígeno de adenovirus y rotavirus en heces, y el cultivo y la citotoxicidad en muestra directa de heces para *Clostridium difficile* fueron negativos. En el examen en fresco de heces no se observaron parásitos. La antigenemia y la PCR cuantitativa para citomegalovirus (CMV) fueron negativas. Finalmente y ante la mala evolución se realizó tinción de Kinyoun modificada (figura 1), observándose ooquistes de *Cryptosporidium* en heces, por lo que se inició tratamiento con paramomicina y azitromicina hasta completar 14 días. Posteriormente se administró nitazoxanida durante 6 días y se redujeron las dosis de tacrolimus y micofenolato mofetil. Tras estas medidas, desapareció la diarrea y la función renal se recuperó hasta sus cifras basales, permaneciendo asintomática 17 meses después.

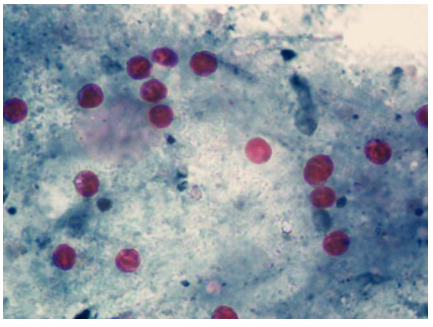

Figura 1. Tinción de Kinyoun modificada.