

Case Report

Reynolds syndrome: case report and literature review


Síndrome de Reynolds: reporte de caso y revisión de la literatura


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 Chantong Villacrés Luis Alberto ^{a, b, c}, luischv5@hotmail.com

 Arana Candela Izaskun, Izaskun_arana@hotmail.com ^d,

 Macías Tomalá Maria Fernanda ^e, dramfmaciast@outlook.com

 Farfán Cano Galo Guillermo ^{a, c, e}, galo.farfanc@iess.gob.ec

a. University of Guayaquil, Ecuador.

b. Catholic University of Santiago de Guayaquil, Ecuador.

c. General Hospital of the North of Guayaquil Los Ceibos, Ecuador.

d. Ministry of Public Health. Ecuador.

e. Rey Juan Carlos University, Spain.

Correspondence: Luis Alberto Chantong Villacrés Email: luischv5@hotmail.com

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Abstract

Reynolds syndrome is an autoimmune condition, characterized by a combination of CREST-type systemic sclerosis (skin calcifications, calcinosis, Raynaud's phenomenon, digital ulcers, facial telangiectasias, esophageal involvement, and sclerodactyly), and primary biliary cholangitis (PBC), very poorly documented in Ecuador. We present a case of this pathological entity, its management and also a brief review of the literature.

Keywords: CREST Syndrome; Limited Scleroderma; Primary Biliary Cholangitis; Collagen Diseases; Connective Tissue Diseases.

Resumen

El síndrome de Reynolds es una condición autoinmune, caracterizada por una combinación de esclerosis sistémica tipo CREST (calcificaciones cutáneas, calcinosis, fenómeno de Raynaud, úlceras digitales, telangiectasias faciales, afectación esofágica y esclerodactilia) y colangitis biliar primaria (CBP), muy escasamente documentada en Ecuador. Se presenta un caso de esta entidad patológica, su manejo y además una revisión breve de la literatura.

Palabras claves: Síndrome CREST; Esclerodermia Limitada; Colangitis Biliar Primaria; Enfermedades del Colágeno; Enfermedades del Tejido Conjuntivo.

Introduction

Reynolds syndrome (SR), described in 1971, is a rare autoimmune disorder defined by the overlap of primary biliary cholangitis (predominant in a ratio of 10: 1 in middle-aged women to men) and CREST-type systemic sclerosis (skin calcifications, calcinosis, Raynaud's phenomenon, digital ulcers, facial telangiectasias, esophageal involvement, and sclerodactyly). It can present more frequently as incomplete CREST scleroderma. It tends to appear between the ages of 30 and 65, between 5 and 15% of cases correspond to systemic sclerosis¹⁻⁴.

Clinical case

60-year-old female patient, originally and resident of Guayaquil, with a 16-month history of evolution, which began with intermittent behavioral jaundice, colicky abdominal pain (mild to moderate intensity) in the right upper quadrant and epigastrium, accompanied by coluria and fatigue. He went to the hospital unit due to dyspnea, headache, unquantified thermal rise, low back pain, and myalgias (predominantly in the shoulders), a feeling of easy fatigue with minimal physical activities.

When questioning the patient, he reported that at the beginning of 2017, he presented pruritic skin lesions with scaly plaques, lichenified on the legs, keratoderma and plantar fissures; On physical examination, bilateral eyelid edema was observed; hyperpigmented macules, dark brown in color, with frontal distribution and facial center on the face; Indurated skin on the forearms and thighs with an edematous consistency, sausage fingers (Figure 1), erythematous and scaly plaques on the back of the feet, as well as plantar keratoderma



Figure 1. Puffy skin, edema of the left hand.

(stiff) (Figure 2). Decreased mouth opening (2 cm) was also observed. There were no added noises or signs consistent with cardiorespiratory involvement.



Figure 2. Hyperchromic lesions with irregular borders in the lower extremities.

Within the paraclinical findings, no alterations were observed within the hemogram, however, the reactivity of Ab was striking. Antinuclear with centromeric pattern (positivity for anti-mitochondrial M2 and anti-centromere antibodies). In addition, the marked increase in cholestasis enzymes, that is, alkaline phosphatase and gamma-glutamyl tranpeptidase, is striking. As well as cytolysis parameters and alteration of the lipid profile and muscle enzymes (Table 1).

Table 1. Laboratory results of a patient with Reynolds syndrome.

Leukocytes	8.74x10x / ul	AST	85IU / L
Hemoglobin	15.4g / dl	ALT	193UI / L
Hematocrit	44.70%	GGT	1113U / I
Platelets	170x10x / ul	FA	535U / L
Glucose	98mg / dl	TP	12.1sec
Urea	25mg / dl	TPT	33.2sec
Creatinine	1.38mg / dl	INR	1.01
Chlorine	92mmol / L	CPK	2614U / L
Sodium	138mmol / L	CK-MB	40U / L
Potassium	3.53mEq / L	Myoglobin	258.2ng / ml
Triglycerides	214mg / ml	Ac. (Antibodies) by immunofluorescence	
Cholesterol	252mg / ml	Ac. antinuclear, centromeric pattern	3,597222222
HDL	84mg / ml	Ac. anti-mitochondrial M2	122.41 (positive)
Direct bilirubin	0.2mg / dl	Ac. Anti Centromer	122.20 (positive)
Indirect bilirubin	0.39mg / dl	Ac. Anti Scl70	10.61 (negative)
Total bilirubin	0.59mg / dl	Ac. lkm-1	0.87 (negative)

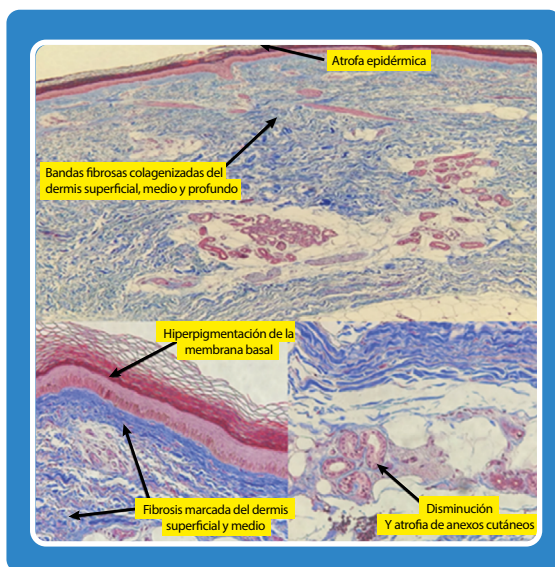


Figure 3. Photomicrograph of skin biopsy of the right forearm.

Masson's trichome stain Courtesy of Dra. Perón, anatomopathology service of the Hospital General del Norte de Guayaquil "Los Ceibos"

With the laboratory results obtained, it was considered to take a sample for biopsy of the skin of the right forearm; the histopathological findings were compatible with scleroderma (epidermal atrophy covered by orthokeratotic layer plus

hyperpigmentation of the basal layer, marked fibrosis of the superficial and deep dermis, reduction and atrophy of skin adnexa, positive Masson trichrome for fibrosis with proliferation of thickened collagen fibers in the dermis shallow and deep)(Figure 3).

In a second biopsy sample from the skin of the right foot, an irregular epidermal hyperplasia was observed, covered by a thick hyper parakeratotic layer, which contained isolated focal pustules, spongiosis and mild focal epidermal exocytosis, focal vacuolar degeneration accompanied by hyperpigmentation of the baseline and infiltrate. chronic inflammatory lymphocyte in the papillary dermis. Additionally, pigmentary incontinence was found with marked fibrosis of the superficial and deep dermis, reduction, and atrophy of skin attachments, and in Masson's trichrome positive for fibrosis, marked proliferation of thickened collagen fibers in superficial and deep dermis. Based on the symptoms of 16 months of evolution and the previously mentioned laboratory results for antibodies, —the suspicion of Primary biliary cholangitis and limited systemic sclerosis. Thus, the diagnosis of Reynolds syndrome was established. Treatment with poral red nisone 40 mg (8 am), 20 mg (2 pm) and ursodeoxycholic acid 500 mg each day; and at hospital discharge, methotrexate 10 mg orally was added every week. On the nineteenth day of treatment, evident improvement was observed,

with remission of dyspnea, IV + / V muscle strength, less indurated skin, significant decrease in muscle enzymes (CPK 76 U / L, myoglobin 127.3ng / ml) and alkaline phosphatase (493U / L). The patient concluded her hospital stay, without complications derived from the treatment, consequently she was discharged with an indication for outpatient follow-up.

Discussion

The definition of SR is made by exclusion of other autoimmune diseases, in the presence of systemic sclerosis or CREST-type scleroderma, in conjunction with CPB. In general, it presents with jaundice, dermatological lesions such as facial erythema, induration, sclerosis, skin ulcers, angiectasis or telangiectasia in the mucosa and / or areas of skin hyperpigmentation^{2,4,5}. In most clinical case reports of SR, an elevation of the serum values of liver enzymes: ALT, AST, GGT and alkaline phosphatase has been observed. Hence the high diagnostic suspicion of RS in patients with cholestasis and positive anti-mitochondrial antibodies (AMA). It is common for the appearance of collagen disease symptoms such as Raynaud's phenomenon, xerostomia and / or xerophthalmia, to precede the appearance of primary biliary cirrhosis by months or years¹⁻⁷. Although AMAs are elevated in 25% of RS cases and are considered the marker with the highest specificity and sensitivity⁸, the presence of positivity of anti-smooth muscle (ASMA) and anti-smooth muscle antibodies has also been described. -nuclear (ANA). Furthermore, hypercholesterolemia is described as a consequence of chronic cholestasis⁽⁸⁾. Indeed, this syndrome may be linked to a possible genetic substrate for laminopathy, described through the discovery of a mutation in the laminin B receptor^(9,10). Regarding the therapeutic management of this mixed entity, for PBC the drug of choice is ursodexocolic acid, at doses of 13-15 mg / kg / day, as it contributes to reducing the inflammation of the bile ducts and the symptoms associated with their obstruction⁷. For the manifestations of scleroderma, NSAIDs are administered, in addition to corticosteroids at a dose of 1mg / kg bodyweight per day at the beginning of treatment and then reduced until reaching the minimum expected dose. At the same time, a corticosteroid-sparing drug is added, such as methotrexate at low or moderate doses (10 to 15 mg every week), as long as the upper limits of transaminases do not exceed their value by three^{2,4,6,7}. In general terms, this was the treatment

indicated for the patient at hospital discharge.

Conclusion

Reynolds syndrome is a rare pathology, even if it is considered within the group of autoimmune rheumatic diseases. But it is easily identifiable after clinical suspicion, in the context of a middle-aged female patient with long-standing intermittent behavioral jaundice, indurated skin, muscle weakness, and high bile stasis markers and liver damage when performing laboratory tests. Although there is no cure for SR, treatment will be instituted to prolong the quality of life of the patient.

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