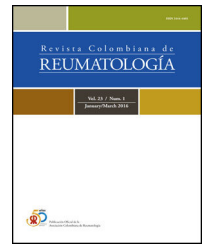




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Case report

Rhupus syndrome. A rare combination[☆]

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ABSTRACT

Rhupus syndrome is a rare combination of rheumatoid arthritis and systemic lupus erythematosus, and is characterized by the presence of erosive arthritis together with symptoms and signs of systemic lupus erythematosus. Among its complications, is the presence of rheumatoid nodules, and neurological and renal involvement that further complicates its prognosis, thus significantly reducing the perception of health-related quality of life in patients who suffer from it. The case is presented of a female patient diagnosed with lupus erythematosus, who during the course of the disease, developed clinical and humoral signs that led to the diagnosis of syndrome Rhupus syndrome. This is believed to be of relevance to the knowledge of the medical community.

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Síndrome de Rhupus. Una superposición infrecuente

RESUMEN

El síndrome de Rhupus es una rara superposición de artritis reumatoide y lupus eritematoso sistémico, que se caracteriza por la presencia de una poliartritis erosiva asociada a síntomas y signos de lupus eritematoso sistémico. Entre sus complicaciones destaca la presencia de nódulos reumatoideos, afectación neurológica y renal que complican más aún la evolución

Palabras clave:

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del caso, disminuyendo considerablemente la percepción de la calidad de vida relacionada con la salud de los pacientes que lo padecen. Se presenta el caso de una paciente mujer con diagnóstico de lupus eritematoso, que desarrolla en el curso de la enfermedad manifestaciones clínicas y humorales que permiten llegar al diagnóstico de un síndrome de Rhupus, lo cual consideramos sea de importancia para el conocimiento de la comunidad médica.

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Introduction

Rheumatic diseases (RD) include a group of about 250 conditions that primarily affect the bones, muscles and joints, being characterized clinically by the presence of pain, inflammation, stiffness, deformity and different degrees of disability, that cause a decreased perception of the health related quality of life (HRQoL).^{1,2}

Despite the fact that there are well-established diagnostic criteria, up to 25% of patients with RD, with systemic symptoms, cannot be clearly diagnosed. They are patients who share clinical and pathological characteristics of systemic inflammation without meeting the criteria for a specific disease.³ One of the elements that brings more difficulty in this regard is the overlap of RD in a single entity. Multiple overlaps are described, that even come to be considered as an independent entity, as it is the case of the mixed connective tissue disease.^{4,5}

Other overlaps are reported, among them, one of the most discussed and infrequent is the one that combines clinical and laboratory elements of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). The first reports on this disease date back to the year 1960 when the first clinical observations that helped to identify this entity were made. However, it was not until the year 1971 when the term Rhupus was used for the first time to refer to this condition.⁴⁻⁶

Overlap syndromes are considered a rare phenomenon. Rhupus syndrome (RhS) has been estimated at between 0.01% and 2% of patients with RD. There is a variant of overlap between juvenile idiopathic arthritis and SLE, which is described as a rare clinical condition in children.^{7,8}

RhS is defined as a deforming and erosive symmetric polyarthritis accompanied by symptoms of SLE and the presence of antibodies of high diagnostic specificity, such as anti-double stranded DNA, anti-Smith and anti-cyclic citrullinated peptide (anti CCP) antibodies.⁹ Renal involvement is characteristic of this syndrome; several authors have encountered findings of type IV lupus nephritis in patients diagnosed with RhS,^{9,10} which together with the neurological manifestations causes a decrease in the perception of HRQoL.¹¹⁻¹⁴

That is why, taking into account the infrequent occurrence of this condition, its repercussion on the osteo-musculo-articular system and the renal complications that it causes, the impact on the perception of the HRQoL in the patients who suffer from it and the scarcity of reports about the disease in Ecuador, it was decided to carry out this work with the purpose to let the medical community know the clinical and humoral manifestations of RhS.

Case presentation

A 47-year-old female patient with a diagnosis of SLE for 6 years, currently treated with 50 mg of azathioprine daily, 7.5 mg of prednisone daily, 250 mg of chloroquine daily and 100 mg of acetylsalicylic acid daily. At the time of the onset of the disease she met 5 diagnostic criteria for SLE (malar rash, oral ulcers, positive antinuclear antibodies [ANAs], complement consumption and thrombocytopenia). During the 6 years of evolution of the disease she presented periods of exacerbation with predominance of joint manifestations and constitutional symptoms, given by the presence of asthenia, anorexia, weight loss and low-grade fever in the evening, which resolved with the increase in the dose of steroids, which in some occasions reached up to 20 mg daily.

On this occasion she attends the consultation reporting that for approximately 5 months she has had a polyarticular additive inflammatory clinical picture that involves primarily the small joints of the hands and feet, as well as the left elbow, the right knee and both temporomandibular joints. It is accompanied by morning stiffness for about 90 min and exacerbation of the constitutional symptoms given by asthenia, anorexia and low-grade fever in the evening. The patient states that she has had these symptoms in other occasions, but of less intensity and duration, which disappear when the dose of steroids is increased. In addition she has right frontal-occipital headache of moderate intensity, photosensitivity, sleep disorders, irritability and affective lability.

On physical examination are found as significant data the presence of slight malar rash, alopecia of 2 cm in diameter in the right frontal-parietal region, limited mobility of the cervical segment and limitation of the flexion/extension of both wrists (30°). The left elbow shows inflammatory signs given by pain both spontaneous and induced by mobilization, heat and increase of volume; at the level of the hands can be observed atrophy of the interosseous muscles, bilateral swelling of the second and third metacarpophalangeal joints and the proximal interphalangeal joints (PIPs), hyperflexion deformity in distal interphalangeal joints (DIPs) and bilateral ulnar deviation of the fingers (Fig. 1). It can be observed the presence of joint effusion in the right knee, with increased local temperature, pain at digital pressure in the articular interline with predominance of the internal compartment, with pain at digital pressure on the surface of the internal femoral condyle; in addition, pain at digital pressure of the right anserine bursa. In the feet is found thrusting of the 2nd finger over the 3rd finger of the right foot, bilateral hallux valgus and bilateral positive pullison maneuver.



Fig. 1 – Swelling of metacarpophalangeal and proximal interphalangeal joints, ulnar deviation of the fingers, flexion deformity of distal interphalangeal joints. Source: Authors.

The complementary tests in this case provide as data of interest an increase in the erythrocyte sedimentation rate (62 mm/h) and in the C-reactive protein (128 mg/l). Positivity of ANAs (156 U/ml), anti-Smith (U/ml), anti CCP (75 U/ml), rheumatoid factor (latex) in 1024 IU/ml and complement consumption (C3 in 56 mg/dl). Another datum of interest is the presence of anemia (9.7 g/l) and thrombocytosis (479,000/mm³). The rest of the hemochemical studies carried out are within normal parameters.

The imaging studies reveal joint space narrowing at the level of the carpal and PIP joints, bone cysts and medial erosion at the 2nd metacarpophalangeal joint of the right hand and juxta-articular bone demineralization in both hands. The X-ray of both feet in anteroposterior projection shows the presence of bilateral subluxation of the 1st metatarsophalangeal joint and the above-mentioned thrust.

Clinimetric instruments are applied, obtaining a SLEDAI of 16 points (disease activity) and a DAS28 of 5.14 (activity between moderate).

Taking into account the clinical elements described above and the results of immunological and imaging studies, the case is diagnosed as an RhS and it is decided to increase the dose of steroid to 15 mg daily and to add to the treatment 10 mg of methotrexate weekly, with the consequent folic acid supplementation. At this time, after 3 months of treatment, the patient has evolved favorably without presenting new periods of exacerbation of the disease. There is also

evidence of improvement from the viewpoint of laboratory tests.

Discussion

RhS has been considered as a rare overlap between RA and SLE which has its own clinical and laboratory characteristics.¹⁵ Since the first description of the term (1960) there are difficulties to identify those patients, given the lack of clear parameters that define this entity.⁴⁻⁶ Studies conducted in patients with RA and SLE found a very low percentage of patients with evidence to support the diagnosis of Rhupus.⁶

In general, the syndrome is described with higher incidence in women, although it may occur in male patients,¹⁶ appearing first the manifestations of RA and then those of SLE, in most cases, another important group of patients begins with manifestations of the 2 entities simultaneously, and patients who begin with manifestations of SLE and later of RA are reported rarely.⁶ In our case, despite being a female patient, she has had a diagnosis of SLE for 6 years and began having articular manifestations given by a chronic, symmetric, bilateral, erosive and seropositive polyarthritis, and for this reason it differs from the generality of cases of RhS previously reported.

With regard to the time of appearance of the manifestations of one or another disease, it is reported that in the patients with RA the time for the onset of the clinical manifestations of SLE ranges between 4 and 7 years.^{6,8} In the case of the patients with initial SLE, is reported a period of approximately 4 years for the onset of the articular manifestations of RA.^{6,7,16} In the case studied this period was longer, since the joint articular manifestations started 6 years after the initial diagnosis of SLE.

The most commonly reported clinical manifestations in the cases of RhS are the presence of erosive polyarthritis, rheumatoid nodules, malar rash, photosensitivity, alopecia and presence of constitutional symptoms; renal and neurological involvement are more rarely described.^{9,10} In this patient, the erosive polyarthritis appeared as the predominant form of RA, whereas the manifestations of SLE, the malar rash and the photosensitivity were those of greater clinical significance. There were no complications related with the underlying diseases, such as the presence of neurological or kidney involvement or the presence of rheumatoid nodules, among others.

It is described that in the clinical course of SLE can occur different types of joint affectation, being more frequent the appearance of arthralgias; persistent oligo or polyarticular clinical pictures can occur on certain occasions, and an erosive polyarthritis is present only in 1% of cases.^{17,18}

The results of the diagnostic methods played a key role in the definitive diagnosis of the disease. It could be observed the presence of molecules that have been considered until now specific markers of one or another nosological entity separately, such as anti-Smith or anti-CCP. In addition, there are other results that reinforce even more the diagnosis, such as the positivity of ANAs, complement consumption, positivity of rheumatoid factor, C-reactive protein and erythrocyte

sedimentation rate, as well as thrombocytosis and anemia. The presence of anti-CCP has been used to distinguish RA and Rhupus syndrome from SLE.³ In our case, the positivity of anti-Smith and anti-CCP antibodies supports the criterion that Rhupus syndrome is an overlap syndrome and not a variable of SLE.

Imaging studies show an erosive joint pattern with the presence of radiological signs, such as juxta-articular bone demineralization and the presence of erosions which are part of the diagnostic criteria for RA.¹⁹

With regard to the therapeutic approach, the incorporation of methotrexate is justified by the presence of the polyarticular, erosive and seropositive inflammatory picture; with the addition of folic acid supplements and the increase in the dose of steroids in order to control, in the short term, the articular inflammatory process and to achieve an improvement in constitutional symptoms. Other drugs such as mycophenolate mofetil and biologic therapy have been used, especially if there is renal involvement.²⁰

RhS is an infrequent condition, but when occurs it can cause complications that determine different degrees of disability in the patients who suffer from it, the constant monitoring of the clinical manifestations of this entity becomes the most secure way to prevent the complications derived from it.

Conclusions

RhS is considered an overlap of RA and SLE. The clinical and serological characteristics that allow us to reach its diagnosis evidence a progression toward an erosive joint damage, which leads to greater articular destruction with an increase in the degrees of disability and a decrease in the perception of the HRQoL of the patients who suffer from it. Despite being a rare entity, it is important to know the clinical and humoral elements that allow its early diagnosis, making it easier to start treatment in a timely manner and reduce its possible complications.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Conflict of interest

The authors declare they do not have any conflict of interest.

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