Isolated positivity for anti-ribosomal P antibodies and its utility in clinical practice: a literature review and description of 16 cases

Sirs,

Anti-ribosomal P (aRibP) antibodies are autoantibodies targeting ribosomal phosphoproteins (P-proteins), components of the ribosome involved in protein synthesis. These antibodies are mainly seen in autoimmune diseases, particularly systemic lupus erythematosus (SLE), where they are present in 15–30% of patients. They are considered a marker of high specificity for SLE, especially in cases with renal, psychiatric, or hepatic involvement (1, 2). These antibodies may also be found in ANA-negative SLE patients. Their role in lupus nephritis is debated, with some studies associating them with poor prognosis, while others suggest a beneficial effect (3).

The isolated presence of aRibP antibodies, without other hallmark autoantibodies like anti-dsDNA or anti-Smith, is less understood. This fact raises questions about its clinical relevance and value in the diagnosis and follow-up of autoimmune diseases.

The present study aimed to assess the clinical and laboratory characteristics of patients with isolated aRibP antibodies in a cohort from a tertiary hospital.

The positivity criterion for aRibP included the observation of a compatible pattern through indirect immunofluorescence on HEp-2 cells (AC-19) and confirmation using at least two solid-phase immunoassay techniques (immunoblot (Euroimmun®/DTEK®) and Biorad-Bioplex® or ELiA-Thermofisher) (4). Patients with concurrent antibodies (anti-SSA/Ro52, anti-SSA/Ro60, anti-SSB/La, anti-CENPB, anti-Sm, anti-U1RNP, anti-dsDNA, antinucleosomes, and antihistones) were excluded.

A descriptive review of the patients with isolated aRibP antibodies was performed to identify their characteristics, establish the underlying pathologies and determine the associated manifestations.

The study was approved by the Clinical Research Ethics Committee of Fundación Jiménez Díaz, Madrid (protocol no. PIC135-23).

Out of a total of 404,599 aRibP antibody determinations, 172 were positive based on the study's inclusion criteria. Among these, 141 were associated with other antibodies, while 31 corresponded to 16 patients with isolated aRibP antibodies.

The medical records of the 16 patients with isolated aRibP antibodies were reviewed (Table I).

Eleven of the 16 patients (68.75%) with isolated aRibP antibodies had autoimmune diseases. Six were diagnosed with SLE, with various manifestations including cutaneous involvement, arthralgia/arthritis, lupus nephritis, neuropsychiatric symptoms (such as lupus psychosis and seizures), lymphopenia, and neutropenia. One patient with lupus nephritis achieved complete remission after treatment with corticosteroids, hydroxychloroquine, cyclophosphamide, mycophenolate mofetil, and belimumab. In four of the six SLE patients for whom these antibodies were prospectively assessed, aRibP antibody levels fluctuated without any correlation to clinical relapses or with disease activity assessed by SLEDAI (data not shown). The remaining five patients had autoimmune hypothyroidism, autoimmune thrombocytopenic purpura, interstitial pneumonia with autoimmune features (IPAF), and two cases of mixed cryoglobulinaemia related to hepatitis C virus infection.

Table I. Clinical description of the patients included in the study.

Cases	Sex	Age	Clinical presentation	Diagnosis and main clinical manifestations
1	F	27	Nephrotic syndrome	SLE (renal and haematological involvement)
2	M	49	Photosensitivity	SLE (articular and cutaneous involvement)
3	F	29	Thrombocytopenia and haematoma	Autoimmune thrombocytopenic purpura
4	F	60	Constitutional symptoms	Pancreatic cancer
5	M	76	Renal function impairment	No specific disease*
6	F	56	Oral ulcers	SLE (articular, cutaneous, haematological and central nervous system involvement)
7	F	76	Arthralgia	Mixed cryoglobulinaemia due to HCV
8	F	44	Skin lesions	SLE (cutaneous involvement)
9	F	33	Arthritis, lymphopenia	SLE (articular and haematological involvement)
10	M	49	Cough	Pneumonia
11	M	76	Haemoptysis	Interstitial pneumonia with autoimmune features
12	F	69	Arthralgia	Autoimmune hypothyroidism
13	F	65	Arthralgia	No specific disease*
14	F	57	Nonspecific skin lesions, arthralgia	No specific disease*
15	F	69	Raynaud's phenomenon	SLE (cutaneous involvement)
16	M	77	Skin lesions and arthralgia	Mixed cryoglobulinaemia due to HCV

CNS: central nervous system; HCV: hepatitis C virus; SLE: systemic lupus erythematosus; M: male; F: female.
*No specific disease during follow-up.

In five individuals, the presence of isolated aRibP antibodies was unrelated to an autoimmune disease (Table I). In three of these individuals, no underlying disease was identified after a median follow-up of 14.5 months (range: 7–143 months).

This study confirms that isolated aRibP antibodies are uncommon and mostly found in association with other antibodies. While the isolated occurrence is rare, it is more frequently seen in autoimmune diseases, particularly SLE. In this cohort, aRibP antibodies were associated with renal and neuropsychiatric involvement in SLE, in line with previous reports (5, 6). However, it should be pointed out that other studies have not found an association between aRibP and renal manifestations (7), and that the correlation with more prevalent neuropsychiatric manifestations has been controversial (8).

In our series, we also identified patients with autoimmune diseases other than SLE, such as mixed cryoglobulinaemia, IPAF, and autoimmune hypothyroidism. In this regard, other studies have reported the presence of aRibP antibodies in patients with other autoimmune diseases, such as autoimmune hepatitis (9).

Interestingly, our study also indicates that, in some cases, isolated aRibP antibodies may be observed without any underlying disease or may be associated with conditions other than autoimmune diseases. A literature search revealed that patients without any autoimmune condition may also test positive for these antibodies (10).

In conclusion, our study highlights that the presence of isolated ARibP antibodies is uncommon, mostly associated with autoimmune diseases, in particular with SLE. However, the presence of these antibodies does not always indicate an underlying autoimmune disease.

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