

# Antiphospholipid syndrome and dermatomyositis/polymyositis: a rare association

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## ABSTRACT

The association between antiphospholipid syndrome and idiopathic inflammatory myopathies has been rarely reported in the literature. In this paper we report two patients with antiphospholipid syndrome diagnosed with concomitant dermatomyositis or polymyositis. We also reviewed the literature on this overlapping of two systemic autoimmune entities.

**Keywords:** dermatomyositis, polymyositis, antiphospholipid syndrome, case studies.

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## INTRODUCTION

Antiphospholipid syndrome (APLS) can be primary or secondary to several conditions such as neoplasias, infectious diseases, drugs,<sup>1</sup> or even to other autoimmune diseases such as systemic lupus erythematosus (SLE).<sup>2,3</sup> Dermatomyositis (DM) and polymyositis (PM) also occur alone or in association with other autoimmune diseases, of which SLE and Sjögren's syndrome are the most frequently observed.<sup>4</sup>

However, only a few studies have reported the association between APLS and DM or PM<sup>5-7</sup> as follows: four cases of the APLS-PM overlap,<sup>5-7</sup> two of which associated with transverse myelitis;<sup>7,8</sup> and one case of APLS associated with DM.<sup>5</sup>

Because of the rarity of that overlapping, we report the case of two patients with simultaneous APLS and DM or PM and provide literature review.

## CASE REPORT

### Case 1

The patient is a 40-year-old male complaining of proximal muscle weakness of all four limbs and constitutional symptoms for three months. On the occasion the patient showed increased levels of muscle enzymes [creatine kinase (CK): 1,876 U/L (reference value: 26–190 U/L); aldolase: 146 U/L

(reference value: up to 7.6 U/L)] and electroneuromyography (ENMG) and biopsy of the brachial biceps muscle compatible with inflammatory myopathy. Infections and neoplasias were excluded. Based on the hypothesis of PM, prednisone (1 mg/kg/day) and methotrexate (maximal dose: 25 mg/week) were initiated. Later, because of lack of clinical and laboratory response, a second immunosuppressive agent, azathioprine (maximal dose: 3 mg/kg/day), was added along with disease activity control.

One year after being diagnosed with PM the patient had deep venous thrombosis (DVT) of the right lower limb (RLL), confirmed on Doppler ultrasound, of no apparent cause. On that occasion his anticardiolipin IgM level was 110 MPL (reference value: < 20 MPL) and, thus, coumarin was initiated with adequate control by use of coagulogram. Twelve weeks after the thrombotic event, anticardiolipin IgM level was 100 MPL, confirming the diagnosis of APLS.

Currently, the patient is stable from the clinical and laboratory viewpoints. He has not been on prednisone for only one year, being currently on azathioprine (3 mg/kg/day), methotrexate (10 mg/week), and warfarin (5 mg/day).

### Case 2

The patient is a 48-year-old female complaining of proximal muscle weakness of all four limbs and heliotrope and Gottron's

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sign for seven months. On her first medical assessment she showed CK of 3,500 U/L and aldolase of 376 U/L and her biopsy of the brachial biceps muscle was compatible with DM. Prednisone (1 mg/kg/day) and azathioprine (maximal dose: 3 mg/kg/day, weight of 50 kg) were initiated. However, after six months, because of little clinical and laboratory response, pulse therapy with methylprednisolone (1 g/day for three consecutive days) was initiated and methotrexate was associated, with progressive dose increase up to 25 mg/week.

During follow-up the disease relapsed after a corticosteroid dose reduction, when a single dose of human intravenous immunoglobulin (1 g/kg/day for two consecutive days) was administered, with an improvement in clinical and laboratory findings. During that same period, cyclosporine (100 mg/day) was associated with good response.

Two years after the diagnosis of DM the patient developed DVT of the RLL, confirmed on Doppler ultrasound, with no apparent cause. In addition, she reported abortion on the 16<sup>th</sup> gestational week and neonatal death, with a morphologically normal fetus. After clinical reassessment, positivity for lupus anticoagulant antibody was observed (two positive samples at an interval greater than 12 weeks). Coumarin was initiated, satisfactory control was achieved, and no other thrombotic episodes occurred.

The patient is currently on cyclosporine (200 mg/day), azathioprine (75 mg/day – reduced dose due to lymphopenia already reversed), and prednisone (15 mg/day), experiencing difficulty in dose reduction. The last relapse was five years ago.

## DISCUSSION

Adding to the few clinical cases reported in the literature, we report two cases of patients with APLS with concomitant idiopathic inflammatory myopathy (DM or PM).

The association between APLS and other systemic autoimmune diseases has been reported. Tarr et al.<sup>8</sup> have found approximately 30% of APLS in their 362 patients with SLE. In addition, that overlap determines higher rates of DVT, stroke/transient ischemic attack, recurring fetal loss, and acute myocardial infarction, as compared with patients with only SLE.

The coexistence of APLS has also been reported in 10% of the patients with Sjögren’s syndrome who have antiphospholipid antibodies.<sup>9</sup> Those patients have more Raynaud’s phenomenon, skin lesions (purpura and *livedo reticularis*), and cytopenias.<sup>9</sup>

APLS has also been described in patients with mixed connective tissue disease (MCTD).<sup>10–12</sup> However, even in those cases, when PM-like findings were included, the diagnosis of MCTD was established due to high levels of specific antibodies.

However, the association between APLS and idiopathic inflammatory myopathies is extremely rare. So far, only five cases (four with PM and one with DM) of that overlapping have been described.<sup>5–7</sup> Such cases are shown in Table 1.

Whether the association between APLS and DM/PM is marked by myositis-specific antibodies or whether such antibodies

**Table 1**  
Association between APLS and idiopathic inflammatory myopathies reported in the literature

	Gender	Age	Myopathy	Antiphospholipid syndrome	Overlap	Medications
<b>Sherer et al. (2000)</b>						
1	M	24	PM	TM; aCL IgG (+)	No	CS, MTX, CPP, ACO
2	F	61	DM	PE; aCL IgG (+)	No	CS, ACO
3	F	50	PM	stroke, recurrent abortions; LAC, aCL IgG (+)	No	CS, MTX, ACO
<b>Ponyi et al. (2004)</b>						
1	F	41	PM	DVT LLL, aCL IgM (+), IgG (+)	RA, antisynthetase	CS, SSZ, CYCL, ACO
<b>Mori et al. (2010)</b>						
1	M	46	PM	TM, Anti-β2GPI	No	CS
<b>Souza et al. (2011)</b>						
1	M	40	PM	DVT RLL, aCL IgM (+)		CS, AZA, MTX, ACO
2	F	48	DM	DVT RLL, gestational, LAC (+)		CS, AZA, MTX, IVIg, CYCL, ACO

M: male; F: female; PM: polymyositis; DM: dermatomyositis; TM: transverse myelitis; aCL: anticardiolipin antibody; CS: corticosteroid (IV,VO); MTX: methotrexate; CPP: cyclophosphamide; ACO: oral anticoagulant; PE: pulmonary embolism; LAC: lupus anticoagulant antibody; DVT: deep venous thrombosis; LLL: left lower limb; SSZ: sulfasalazine; CYCL: cyclosporine; Anti-β2GPI: anti-β2-glycoprotein I antibody; RLL: right lower limb; AZA: azathioprine; IVIg: intravenous immunoglobulin.

play a pathogenic role in myopathies have not been clarified, endothelial damage being undoubtedly the basic pathogenic process of DM.<sup>13</sup>

It is worth noting the common refractoriness to therapy observed in our patients and in literature reports, all of whom having received high corticosteroid doses either orally or as pulse therapy.<sup>5-7</sup> Four of those patients have experienced disease relapse, requiring the use of at least two immunosuppressive drugs (azathioprine, methotrexate, and/or cyclosporine).<sup>5-7</sup>

Doubt remains as to whether the association of those entities worsens the prognosis of DM/PM. Future studies are required.

Intravenous immunoglobulin can be a treatment option for patients with coexisting APLS and refractory myopathy, being currently accepted for treating DM/PM, with some descriptions of its use in APLS.<sup>14,15</sup> Our patient with DM, because of refractoriness to conventional medicamentous therapy, received intravenous immunoglobulin and had a good clinical and laboratory response.

In conclusion, the concomitance of APLS and DM/PM has been rarely reported. This paper reports two cases in which a relatively more aggressive course of myopathy was observed, in accordance with those already described.

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