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## Case report

# Childhood-onset systemic polyarteritis nodosa and systemic lupus erythematosus: an overlap syndrome?



## Poliartrite nodosa sistêmica e lúpus eritematoso sistêmico de início na infância: uma síndrome de sobreposição?

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### ARTICLE INFO

#### Article history:

Received 7 August 2014

Accepted 11 January 2015

Available online 13 July 2015

### Introduction

Childhood-onset systemic polyarteritis nodosa (c-PAN) is a rare necrotizing arteritis characterized by the presence of aneurismal nodules, stenosis or occlusion of small and medium-sized vessels of the entire body.<sup>1-3</sup> Recently, the European League Against Rheumatism (EULAR)/Paediatric Rheumatology International Trials Organisation (PRINTO)/Paediatric Rheumatology European Society (PRES) proposed new validated criteria for c-PAN diagnosis. This new criteria studied 150 patients with c-PAN worldwide and demonstrated high sensitivity and specificity for the diagnosis of this systemic vasculitis.<sup>3</sup>

Childhood-onset systemic lupus erythematosus (c-SLE) is an autoimmune and multisystemic disorder.<sup>4,5</sup> Inflammation of the blood vessels is a common disease manifestation and may affect small, medium and large-sized vessels.<sup>4-7</sup>

Moreover, c-SLE and c-PAN may present similar clinical manifestations and laboratory alterations. However, to our knowledge the overlap syndrome of these two diseases has not previously been described. Therefore, we reviewed our data from January 1983 to July 2013 and included 5593 patients followed at our Pediatric Rheumatology Unit. We identified 289 (5.1%) c-SLE patients that fulfilled the American College of Rheumatology (ACR)<sup>6</sup> classification criteria and 15 c-PAN patients that fulfilled the EULAR/PRINTO/PRES criteria.<sup>7</sup> We

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<http://dx.doi.org/10.1016/j.rbre.2015.01.004>

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described herein a patient (0.34%) who presented a possible c-PAN and c-SLE overlap.

## Case report

A 9-year-old girl presented tender subcutaneous nodules on the feet, arterial hypertension, right hemiplegia and dysarthric speech. She was hospitalized due to stroke, numbness in her extremities and left foot drop. Brain computer tomography showed ischemic stroke. Magnetic resonance angiography revealed stenosis in the middle cerebral and internal carotid arteries. Electroneuromyography identified a mononeuropathy of the left posterior tibial nerve. Therefore, C-PAN was diagnosed according to the EULAR/PRINTO/PRES criteria.<sup>3</sup> Laboratory tests showed hemoglobin 12 g/dL, white blood cell count (WBC) 5500/mm<sup>3</sup> (75% neutrophils, 19% lymphocytes, 5% monocytes and 1% eosinophils), platelets 264,000/mm<sup>3</sup>, erythrocyte sedimentation rate (ESR) 45 mm/1st hour, C-reactive protein (CRP) 0.9 mg/dL (normal 0–0.3), aspartate aminotransferase 22 U/L (normal 15–40), alanine aminotransferase 21 U/L (normal 10–35), urea 26 mg/dL (normal range 15–45 mg/dL) and creatinine 0.7 mg/dL (normal range 0.6–0.9 mg/dL). Urinalysis and 24-h proteinuria were normal. Immunological tests showed antinuclear antibodies (ANA) 1:320 (fine speckled pattern), and negative anti-double-stranded DNA (anti-dsDNA), anti-Sm, anti-RNP, antineutrophil cytoplasmic autoantibodies (ANCA), IgG and IgM anticardiolipin antibodies, and lupus anticoagulant. She received three intravenous methylprednisolone pulse therapy, followed by prednisone (1.4 mg/kg/day) that was progressively tapered, aspirin (150 mg/day), six months of intravenous cyclophosphamide (500 mg/m<sup>2</sup>/month) and after that she was treated with azathioprine (1.6 mg/kg/day) for 19 months. At 13 years and 10 months, she presented multiple erythematous scaly plaques over the malar area, ears and chest. The skin biopsy from the left ear evidenced focal psoriasiform hyperplasia with perivascular mononuclear infiltrate and direct immunofluorescence showed granular immunoglobulin G (IgG), IgA, IgM and C3 deposits at the dermoepidermal junction. She was treated with topical hydrocortisone 1% with improvement of skin lesions after 3 months. At the age of 14 years and 9 months, she presented malar rash, photosensitivity, edema in lower limbs and arterial hypertension. At that moment, hemoglobin was 11.61 g/dL, WBC was 3500/mm<sup>3</sup> (80% neutrophils, 15% lymphocytes and 5% monocytes), platelets 391,000/mm<sup>3</sup>, ESR was 54 mm/1st hour, CRP 7.0 mg/dL, urea 20 mg/dL and creatinine 0.4 mg/dL. Urinalysis showed leukocyturia and hematuria. The proteinuria was 1.7 g/day. ANA was 1/1280 (homogeneous nuclear pattern) and anti-dsDNA antibodies were positive. Anti-Sm, anti-RNP, ANCA, IgG and IgM anticardiolipin antibodies and lupus anticoagulant were negative. C3 was 41 mg/dL (range 79–152) and C4 was 4.5 mg/dL (range 16–38). Renal biopsy showed focal proliferative and membranous glomerulonephritis with immune deposits of C1q, C3, IgG, IgM and IgA. She fulfilled the American College of Rheumatology classification criteria for SLE<sup>8</sup> and the SLE Disease Activity Index 2000 (SLEDAI-2K)<sup>9</sup> was 18. She was treated with

prednisone (0.6 mg/kg/day), hydroxychloroquine (6.0 mg/kg/day) and mycophenolate mofetil (2.0 g/day).

## Discussion

We reported herein a unique case of a possible c-PAN and c-SLE overlap over a period of 30 years at our tertiary hospital.

It was observed that our patient had stenosis in the middle cerebral and internal carotid arteries compatible with c-PAN 5 years before the c-SLE diagnosis, thus suggesting the presence of two different autoimmune diseases over a long period of time.

Primary vasculitis has been rarely reported in association with SLE.<sup>6,7</sup> Of note, Kawasaki disease is an acute childhood systemic vasculitis that mainly affects the medium vessels, particularly coronary arteries, and may overlap with c-SLE.<sup>6</sup>

Moreover, subacute cutaneous lupus erythematosus occurs in 7–27% of adults with SLE and has been rarely reported in pediatric lupus population. The lesions are papulosquamous, affecting areas exposed to sunlight, as evidenced in our patient.<sup>10</sup> Interestingly, the subacute cutaneous lupus is a new topic of the recent Systemic Lupus International Collaborating Clinics (SLICC) criteria, validated for adult and c-SLE populations.<sup>11,12</sup>

Our case fulfilled the c-PAN diagnosis criteria. According to the new pediatric EULAR/PRINTO/PRES criteria,<sup>3</sup> a patient is classified with c-PAN if presents necrotizing vasculitis involving medium or small arteries or an angiographic abnormality showing aneurysm, stenosis, or occlusion of a medium or small-sized artery, plus one of these following criteria: skin involvement (livedo reticularis, skin nodules or infarcts), peripheral neuropathy, arterial hypertension, myalgia or muscle tenderness and renal involvement. Remarkably, sensitivity and specificity of these new criteria for c-PAN diagnosis were 89.6% and 99.6%, respectively.<sup>3</sup>

Since the two diseases coexisted over a long period time, the association between them may suggest an overlap syndrome. Indeed, the subsequent change of clinical and laboratorial abnormalities with the presence of specific autoantibodies, decreased complement levels,<sup>13</sup> and skin and kidney biopsies confirmed the c-SLE diagnosis. Furthermore, the presence of ANCA was reported in six out of 47 tested c-PAN patients in a multicenter study<sup>2</sup> and ANA is generally negative in c-PAN.<sup>1</sup>

However, all of c-PAN manifestations of our patient may be evidenced in c-SLE and we cannot exclude the possibility that the first signs and symptoms may be attributed solely to lupus. Therefore, this patient may be suffering from c-SLE with visceral manifestations of vasculitis mimicking c-PAN.

In conclusion, we described herein a possible overlap syndrome of two autoimmune diseases, where c-PAN occurred five years before the c-SLE diagnosis.

## Funding

This study was supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP – grants 2008/58238-4 to C.A.S. and 2011/12471-2 to C.A.S.), by Conselho Nacional

do Desenvolvimento Científico e Tecnológico (CNPQ – grant 302724/2011-7 to C.A.S.), by Federico Foundation to C.A.S. and by Núcleo de Apoio à Pesquisa “Saúde da Criança e do Adolescente” da USP (NAP-CriAd).

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### Conflicts of interest

The authors declare no conflicts of interest.

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