

## CASE REPORT

# Reflex sympathetic dystrophy in a patient with the antiphospholipid syndrome

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We describe a 50-year-old woman who developed severe pain of the left lower limb after an episode of thrombophlebitis. Bone scintigraphy and thermography showed results indicative of reflex sympathetic dystrophy. Laboratory analysis revealed the presence of the lupus anticoagulant. The patient was diagnosed as antiphospholipid syndrome complicated with reflex sympathetic dystrophy of the left lower limb. To our knowledge, this is the first report of a patient with reflex sympathetic dystrophy with underlying antiphospholipid syndrome.

**Keywords:** reflex sympathetic dystrophy; antiphospholipid syndrome; lupus anticoagulant; thrombophlebitis

Reflex sympathetic dystrophy (RSD) is a chronic pain syndrome with impaired sympathetic nerve function, often occurring after some trauma. A variety of conditions causing RSD are known, such as minor trauma in the limb, bullet wounds, surgical procedures, gout,<sup>1</sup> arterial blood gas sampling,<sup>2</sup> or even impact from inflation of airbags in traffic accidents.<sup>3</sup> There are also some case reports of RSD occurring after episodes of deep vein thrombosis.<sup>4-5</sup> The pathogenesis of this condition is not clearly understood.

We present here an unusual case of RSD, where severe pain on the left lower limb appeared after an episode of thrombophlebitis. Laboratory analysis revealed the presence of lupus anticoagulant (LAC). She was diagnosed as antiphospholipid syndrome (APS), complicated with RSD of the left lower limb. To our knowledge, this is the first report of a patient with RSD with underlying APS.

### Case report

A 50-year-old Japanese woman presented with pain and swelling of her left leg in December 1995. Examination at another hospital revealed deep vein

thrombosis of the left femoral and the left popliteal veins, and defect at right segment 6 by perfusion scintigram of the lung. She was treated with anticoagulants, and redness and swelling of her left leg improved. However, pain of the left leg did not improve, and she complained of increasing pain, which did not respond to nonsteroidal anti-inflammatory drugs (NSAIDs), and only slightly to morphine. Anticoagulants were discontinued in May 1996.

On January 1997, there was an episode of thrombophlebitis of the left leg. Warfarin administration resulted with improvement of swelling of the left leg, but severe pain in her left leg continued. RSD was suspected, and sympathetic nerve block, epidural anesthesia was performed without success. On December 3, 1997, she was admitted to our department for evaluation of her leg pain and repetitive thrombophlebitis.

On admission, her body temperature was 37°C. Her left ankle and foot was edematous. Muscle atrophy of her left lower leg was evident (Figure 1). She complained of severe pain of her left leg from under the knee. Her walking ability was greatly impaired. Laboratory analysis revealed normal blood count, liver and renal functions. Antinuclear, anti-DNA, anti-RNP, anti-Sm, anti-SS-A and anti-SS-B antibodies were negative. IgG, A and IgM anti- $\beta_2$  Glycoprotein I antibodies were not detected. Prothrombin time was normal, and activated partial thromboplastin time (APTT) was slightly prolonged to 30.8 s (reference values: 29.0 s). Kaolin clotting time (KCT) was greatly prolonged to 260 s (reference values: 86 s).

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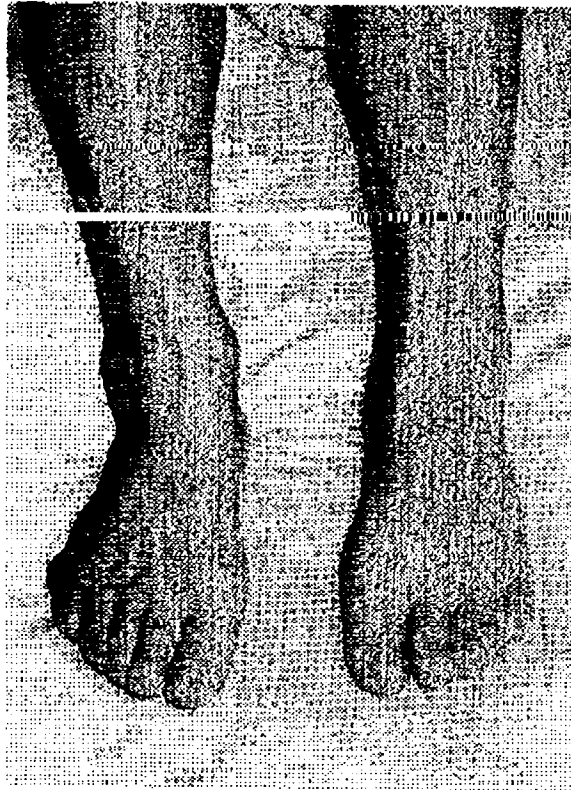


Figure 1 Edema and muscle atrophy of the left leg.

The presence of lupus anticoagulant (LAC) was evaluated, and mixing test for KCT showed LAC positive pattern. Diluted aPTT test also showed LAC positive pattern. LAC was repeatedly positive in two different occasions three months apart. She had three healthy children, and did not have history of fetal loss.

Bone scintigram revealed abnormal uptake in the left ankle (Figure 2). Thermography showed that the skin temperature on her left leg was higher than that on her right leg. RI venography did not reveal new lesions of deep vein thrombosis. During a 3 months period, no growth of the nails in the left foot was noticed. RSD of the left leg was diagnosed. Although her thrombophlebitis was well controlled with 5 mg/d of warfarin, various therapies including NSAIDs, antidepressants, minor tranquilisers, morphine and laser showed very little effect for continuous pain.

### Discussion

RSD, also known as complex regional pain syndrome, or causalgia, was first reported in 1864, in a patient in whom severe pain and muscle atrophy developed after a bullet wound in the leg. Three criteria are used for

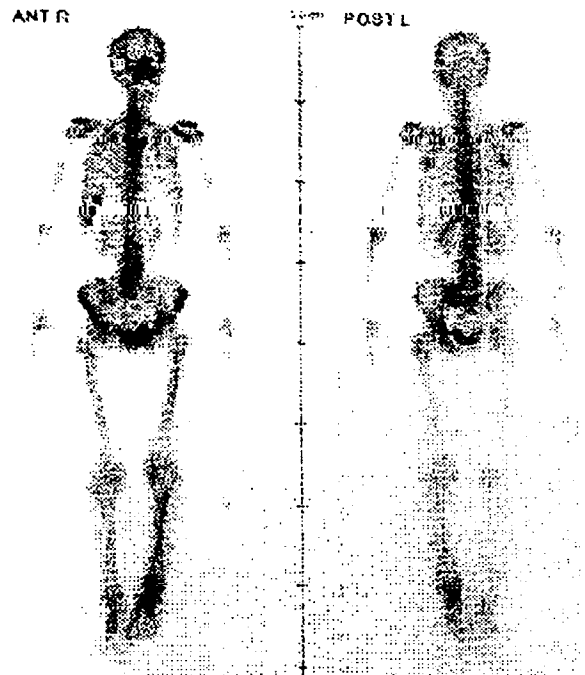


Figure 2 Bone scintigram showing abnormal uptake in the left ankle.

the definition of this condition.<sup>6-8</sup> (1) Diffuse pain in an anatomic area not corresponding to the distribution of a peripheral nerve. (2) Diminished function of the affected area and stiffness of involved joints. (3) Characteristic skin and soft tissue changes, ranging from swelling, rubor, hyperhidrosis, and warmth in early stages to atrophy, stiffness, and coldness as the syndrome progresses; vasomotor instability is usually present. Our patient fulfilled these criteria.

Treatment of RSD is often extremely difficult. NSAIDs, steroids,  $\alpha$  or  $\beta$  blockers are used with limited success. Early diagnosis and treatment are considered to be important. Stellate ganglion block, intravenous sympathetic block and surgical sympathectomy are reported as useful procedures to relieve continuous and severe pain.<sup>6</sup> However, in many cases, severe pain persists for an indefinite period, possibly for life, leading to complete impairment of the affected area. A case where amputation of the affected limb was inevitable has been reported.<sup>9</sup>

In our case, as far as we could confirm, acute thrombophlebitis was the cause of her RSD. We cannot rule out the possibility that continuous pain after the episode of deep vein thrombosis on December 1995 was due to onset of RSD. Both her deep vein thrombosis and her thrombophlebitis are considered to have occurred from APS.

APS is characterised by presence of antibodies toward phospholipids and thrombotic episodes.<sup>10-11</sup> Antiphospholipid antibodies are generally detected by two methods; enzyme immunoassays (EIA) such as anticardiolipin (aCL) EIA or anti- $\beta_2$ -Glycoprotein I EIA,<sup>12-16</sup> and LAC assays. Both assays are reliable and detect overlapping but distinct population of antiphospholipid antibodies. However, in some occasions, only EIA is done for the screening of APS. In this patient, presence of antiphospholipid antibodies was confirmed by the KCT mixing test. On the other hand, we could not detect anti- $\beta_2$ -Glycoprotein I in this patient. These results confirm the importance of testing for both antiphospholipid EIA and LAC in patients suspected of having APS.

Thrombophlebitis is fairly commonly seen in APS. In many cases, deep vein thrombosis and thrombophlebitis caused by APS is favourably controlled by adequate doses of warfarin, and although recurrences of thrombophlebitis occasionally occur, to our knowledge, RSD caused by this condition is not reported. When an APS patient complains of prolonged pain after a thrombotic episode, occurrence of RSD should be taken in consideration.

## References

- Zucchi F, Varenna M, Binelli L, Sraigaglia L. Reflex sympathetic dystrophy syndrome following acute gouty arthritis. *Clin Exp Rheumatol* 1996; 14: 417-420.
- Crisuolo C, Nepper G, Bachalter S. Reflex sympathetic dystrophy followed arterial blood gas sampling in the intensive care setting. *Chest* 1995; 108: 578-580.
- Shah N, Weinstein A. Reflex sympathetic dystrophy syndrome following air-bag inflation [letter]. *N Engl J Med* 1997; 337: 574.
- Bulry F, Chazerain P, Magnin J et al. Algodystrophy and venous thrombosis of the lower limbs: diagnostic problems. Apropos of 5 cases. (In French) *Rev Rhum Mal Osteoartic* 1989; 56: 403.
- Bulry F, Baudouveau B, Cleinert R et al. Algodystrophy and venous thrombosis of the lower extremities. Diagnostic discussion. Apropos of 3 cases. (In French) *Phlebologie* 1987; 40: 251.
- Nath RH, Mackinnon SE, Steinicki E. Reflex sympathetic dystrophy. The controversy continues. *Clin Plast Surg* 1996; 23: 435-446.
- Mackinnon SE, Dellon AL. Painful sequelae of peripheral nerve injury. In: Mackinnon SE, Dellon AL: *Surgery of the peripheral nerve*. Thieme Medical Publishers, New York, 1988; pp 492-504.
- Poplawski ZI, Wiley AM, Murray JF. Post-traumatic dystrophy of the extremities. *J Bone Joint Surg Am* 1983; 65: 642.
- Geertzen JH, Rietman JS, Smit AJ, Zimmerman KW. A young female patient with reflex sympathetic dystrophy of the upper limb in whom amputation became inevitable. *Prosthet Ortho Int* 1997; 21: 159-161.
- Asherson RA, Cervera R. Anticardiolipin antibodies, chronic biologic false-positive tests for syphilis and other antiphospholipid antibodies. In: *Dubois's lupus erythematosus fourth edition*. Lea and Febiger, Philadelphia, USA, 1993; pp 233-245.
- Hughes GRV. The antiphospholipid antibody syndrome: 10 years on. *Lancet* 1993; 342: 341-344.
- Tsutsumi A, Matsura E, Ishikawa K et al. Antibodies to  $\beta_2$ -glycoprotein I and clinical manifestations in patients with systemic lupus erythematosus. *Arthritis Rheum* 1996; 39: 1466-1474.
- Roubey RAS, Maldonado MA, Byrd SN. Comparison of an enzyme-linked immunosorbent assay for antibodies to  $\beta_2$ -glycoprotein I and a conventional anticardiolipin immunoassay. *Arthritis Rheum* 1996; 39: 1606-1607.
- McNally T, Purdy G, Mackie U et al. The use of an anti- $\beta_2$ -glycoprotein-I assay for discrimination between anticardiolipin antibodies associated with infection and increased risk of thrombosis. *Br J Haematol* 1995; 91: 471-477.
- Pengo V, Biasiolo A, Fior MO. Autoimmune antiphospholipid antibodies are directed against a cryptic epitope expressed when  $\beta_2$ -glycoprotein I is bound to a suitable surface. *Thrombosis Haemostasis* 1993; 73: 29-34.
- Amengual O, Atarri T, Khamashta MA et al. Specificity of ELISA to  $\beta_2$ -glycoprotein I in patients with antiphospholipid syndrome. *Br J Rheumatol* 1996; 35: 1239-1243.