Catastrophic antiphospholipid syndrome with massive cerebral venous sinus thrombosis

Sirs,

Catastrophic antiphospholipid syndrome (CAPS) is a rare variant of the antiphospholipid syndrome (APS), characterised by disseminated thrombosis evolving over a short period of time, histopathological evidence of multiple microthrombosis and laboratory confirmation of antiphospholipid antibodies (aPL). CAPS occurs in 1% of patients with APS (1). Early diagnosis and treatment are important due to the high associated mortality (1).

A 17-year-old woman was admitted to the Emergency Department with non-specific fatigue and malaise, with no fever or constitutional symptoms. She did not smoke, consume illegal drugs or use oral contraceptives nor did she suffer from any systemic autoimmune disease. The physical examination was normal except for purpuric lesions in both thumbs.

Laboratory tests revealed 33.000 platelets / mm^3, prothrombin time 66% and fibrinogen 293 mg/dL. Peripheral blood smear showed <1 schistocytes/field. Within 24 hours, the skin lesions progressed and the patient suffered a sudden neurological deterioration with disorientation, inappropriate behaviour, paresis of her left arm and bilateral reactive mydriasis. An urgent cerebral CT scan showed a massive thrombosis of the dural sinuses with a right fronto-parietal haemorrhage. Treatment was started with unfractionated heparin, platelet transfusion, intravenous methylprednisolone 2 mg/kg/day and broad-spectrum antibiotics.

She was transferred to Hospital Universitario Cruces, a reference centre for neurosurgery, to be managed by a multidisplinary team, including internists from the Autoimmune Diseases Unit. Upon admission, she was given an intravenous pulse of methylprednisolone (MP) of 250 mg, an emergency mechanical thrombectomy with full recanalisation of the dural sinuses was performed and aPL were tested and reported on the day, with lupus anticoagulant (LA) being positive by Russell Viper Venom Time, with the remaining aPL testing negative. The patient was transferred to the Intensive Care Unit and the therapeutic scheme for CAPS, based on MP, plasma exchange, intravenous immunoglobulins (IVIG), anticoagulation and hydroxychloroquine (HCQ), was started (Table I).

A full-body angio-CT showed a bilateral segmental pulmonary thromboembolism, a large thrombus in the inferior cava vein extending to the left supra-hepatic vein and the right atrium and a splenic infarction. The skin biopsy revealed small vessel thrombosis. The trans-esophageal echocardiography was normal.

Table I. Treatment protocol for catastrophic antiphospholipid syndrome.

Day 1	Pulse of methylprednisolone 250-500 mg + mechanical thrombectomy + **plasma exchange** with replacement with FFP	LMWH 1mg/kg/bid
Day 2	Pulse of methylprednisolone 250-500 mg + **plasma exchange** with replacement with FFP	LMWH, same dose
Day 3	Pulse of methylprednisolone 250-500 mg + IVIG 200 mg/kg)	LMWH, same dose
Day 4	Methylprednisolone 20 mg/day+ **plasma exchange** with replacement with FFP	LMWH, same dose
Day 5	Methylprednisolone 20 mg/day	LMWH, same dose
Day 6	Methylprednisolone 20 mg/day+ **plasma exchange** with replacement with FFP	LMWH, same dose
Day 7	Methylprednisolone 20 mg/day + IVIG 200 mg/kg	LMWH, same dose
Day 8	Methylprednisolone 20 mg/day+ **plasma exchange** with replacement with FFP	LMWH, same dose
Day 9	Methylprednisolone 20 mg/day	LMWH, same dose + HCQ 200 mg/day
Day 10	Methylprednisolone 20 mg/day+ **plasma exchange** with replacement with FFP	LMWH, same dose + HCQ 200 mg/day
Day 11	Methylprednisolone 15 mg/day + IVIG 200 mg/kg	LMWH, same dose + HCQ 200 mg/day
Day 12 and on the following days	Prednisone 15 mg/day one week, then 10 mg/day with tapering to 5 mg/day over 4-8 weeks + LMWH 1mg/kg/12h + HCQ 200 mg/day	

FFP: fresh-frozen plasma; LMWH: low molecular weight heparin; IVIG: intravenous immunoglobulins; HCQ: hydroxychloroquine..

The patient presented a favourable clinical course, with full neurological recovery and resolution of the visceral thromboses. She was discharged after three weeks, on treatment with enoxaparin 1.5 mg/kg/day, prednisone 10 mg/day, HCQ 200 mg/day and vitamin-D. Over the following month, prednisone was tapered down to 5 mg/day and enoxaparin was changed to acenocumarol (target INR 2.0–3.0) plus AAS 100 mg/d. LA tested positive in several determinations during the follow-up, although oral anticoagulant therapy had to be transiently changed to enoxaparin to avoid the interference with the test. aCL and anti-ß2-GPI remained negative.

Prednisone was eventually discontinued. She has had no thrombotic recurrences within the 5-year follow-up and continues a completely normal life, on maintenance therapy with acenocumarol, AAS 100 mg/d, HCQ 200 mg/d and vitamin D.

CAPS is a rare condition with high-mortality rates, thus early suspicion and aggressive treatment are key for a successful outcome (2-4). Treatment is based on supportive care, identification and correction of the precipitating factor and specific therapy (3-4). Triple therapy, which includes anticoagulants, glucocorticoids, plasma exchange and/or IVIG, is the recommended regime (4-6). Early anticoagulation with heparin is essential. The duration of plasma exchange after at least 3–6 courses should be guided by clinical response (3). Rituximab and eculizumab may have a role as second-and/or third-line therapy (4-8).

Two additional factors played a crucial role in the good outcome of the patient: multidisciplinary teamwork, that prevented long-term neurological sequelae, and the restrictive use of glucocorticoids (9), which helped decrease the risk of infectious complications in a clinical scenario needing an aggressive immunosuppressive regimen within an intensive care setting (10).

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