Intracranial hypertension and antiphospholipid antibodies

Antiphospholipid syndrome is a clinical entity defined by vascular events and circulating antiphospholipid antibodies in peripheral blood. Intracranial hypertension has been associated with venous thrombosis in patients suffering from antiphospholipid syndrome. We present the case of a patient with intracranial hypertension probably related to antiphospholipid antibodies and without venous thrombosis.

KEYWORDS: antiphospholipid antibodies ■ antiphospholipid syndrome ■ intracranial hypertension ■ pseudotumor-cerebri ■ systemic lupus erythematosus

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Case report

Antiphospholipid syndrome (APS) is a clinical entity defined by vascular events and circulating antiphospholipid antibodies (APA) in peripheral blood [1]. Stroke is the most frequently found neurological condition, followed by cognitive deficit.

Intracranial hypertension has been associated with venous thrombosis in patients suffering from APS, but there are few cases of intracranial hypertension (ICH) reported without thrombosis [2].

We present the case of a 46-year-old woman without relevant clinical history. She had normal BMI (22 kg/m^2). She was not under medical treatment and had no clinical signs or symptoms suggesting pulmonary artery thrombosis.

She complained of tinnitus and pulsatile headache accompanied by neck stiffness 7 years ago. She did not have nausea, vomiting or visual deficits. During the last month, headache episodes had occasionally appeared and tinnitus had worsened. General, neurological and otoneurological examinations were normal. Ophthalmologic exploration showed mild bilateral papilledema with normal visual function (Figure 1). A brain MRI showed arachnoid granulations. Initial laboratory test yielded the following results: hemoglobin 13.8 g/dl ([11.5–15.3]; mean corpuscular volume 91 fl [80.0–97.0]; white blood cell count, 6.3 × 109/l [3.70–11.60]) with normal differential; platelet count 199 × 109/l (7.6–10.8); sodium 141 mEq/l (136–146); potassium 4.1 mEq/l (3.5–5.1); glucose 95 mg/dl (74–115); blood urea 27 mg/dl (17–43); creatinine 1.0 mg/dl (0.7–1.1); and liver function test results were within normal limits. Antinuclear antibodies were negative, complement C3 and C4 were within normal limits. She had high titers of anticardiolipin IgM antibodies (46 MPI) that maintained after 12 weeks (51 MPI units). Lupus anticoagulant and IgM anti-β2 GPI antibodies were both negative.

As symptoms mantained, a lumbar puncture was carried out and intracranial pressure was 30 cm H_2O. Cerebrospinal fluid did not show inflammation or infection (white cells 0/mm^3 red cells 0/mm^3, proteins 10.5 mg/dl, and glucose 56 mg/dl). Venous thrombosis or ischemic lesions were ruled out by MR venogram.

Finally, a diagnosis of intracranial hypertension associated with APA was established and antiaggregant treatment was initiated. After 6 months a lumbar puncture was performed, showing 15 cm H_2O pressure. Papilledema had disappeared and symptoms had improved.

Discussion

We present the case of a patient with intracranial hypertension probably related to APA. She showed great clinical improvement with antiaggregant treatment.

APS has been defined by two components: APA and at least one thrombotic vascular event, clinically diagnosed or found by other diagnostic procedures [1,3]. It is classically characterized by arterial or venous thrombosis, and may show related clinical manifestations such as stroke, livedo reticularis, transient ischemic attack or fetal loss [3]. CNS manifestations, apart from stroke, include white matter lesions [4] and, more frequently, cognitive deficits.

Intracranial hypertension is the term used to describe the presence of raised intracranial pressure, usually due to obstruction to cerebrospinal fluid. It can appear as headache, visual deficits and tinnitus. ICH has been described as a rare complication of systemic lupus erythematosus

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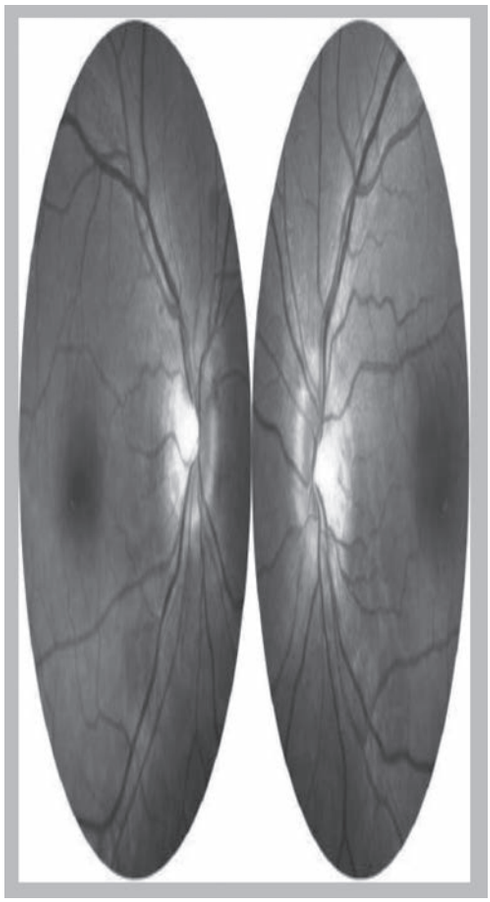

Figure 1. Bilateral papilledema.

(SLE) [5], perhaps as a consequence of cerebral venous sinus thrombosis. Idiopathic ICH has also anecdotally been associated with APA, especially with anticardiolipin. In a previous study that included 14 patients with ICH, positive APA were proven in six of them [6]. When comparing those with positive and negative APA, no statistical differences were found regarding clinical presentation, laboratory test or neuroimaging results. As with our patient, those with positive APA initiated antiaggregant treatment and no thrombotic events appeared during follow-up. This was followed by an investigation into ICH [7], which showed high titers of APA; however, no MRI was performed to rule out cerebral venous thrombosis. However, in our patient, associated connective tissue diseases were ruled out and neuroimaging did not show venous thrombosis.

Intracranial hypertension has been postulated as an APS with limited expression. Nowadays, the pathogenic mechanism underlying ICH in patients with positive APA is not clear. It is known to be an imbalance between procoagulant and anticoagulant systems in APS. Some authors propose that APA would bring out a hyperviscosity state similar to policytemia vera without evidence of a thrombotic event. In patients with SLE this pathogenic mechanism has been widely studied. Furthermore, APA have been suggested as one of twenty types of brain-specific and systemic autoantibodies associated with neuropsychiatric SLE [8]. On the contrary, despite some authors suggesting a relationship between these entities, they propose that ICH could be a manifestation of lupus activity [9] as the majority of patients improved in their clinical condition with steroids. It is noteworthy that our patient improved with antiaggregant treatment and there has not been a need for a new lumbar puncture. It was prescribed because of clinical evidence of its protective effect in asymptomatic antiphospholipid carriers with systemic SLE [10,11].

Conclusion & future perspective

APS has been classically characterized by arterial or venous thrombosis. CNS manifestations apart from classical ones are rare. ICH has been described as a rare complication of SLE but has anecdotally been associated with APA without evidence of autoimmune systemic disease or venous thrombosis.

Nowadays the pathogenic mechanism underlying intracranial hypertension in these patients is not clear. Future research should focus on providing more clinical evidence with new investigations to extend the knowledge of this clinical association to establish a recommendation about screening and treatment with ICH and positive antibodies.

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Executive summary

- Antiphospholipid antibodies are associated with a wide spectrum of clinical manifestations affecting the CNS.
- It is possible that intracranial hypertension may represent a restricted form of antiphospholipid syndrome limited to the CNS.
- Antiphospholipid antibodies may predispose patients to the development of intracranial hypertension although new studies are needed in the future.

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