Unusual association of diseases/symptoms

Cerebral embolism from libman–sacks endocarditis

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Summary

Libman–Sacks endocarditis consists of aseptic valvular abnormalities, associated with systemic lupus erythematosus and antiphospholipid syndrome. Embolic ischaemic stroke is a possible clinical presentation. The authors present the case of a woman in her fourth decade who developed central facial palsy after several transient ischaemic attacks with visual loss. Cerebral imaging revealed multiple small ischaemic lesions in the right hemisphere. The transoesophageal echocardiogram showed mitral vegetations and she tested positive for antiphospholipid antibodies. She underwent mitral valve replacement for a mechanical prosthesis due to extensive valvular damage and started anticoagulation. The valve's microbiological exams were negative establishing the diagnosis of libman–sacks endocarditis. Endocarditis should be suspected with sequential cerebral ischaemia in patients of all ages. Valvular surgery is the mainstay of treatment in recurrent embolic events. Association with antiphospholipid antibodies is common yet a poor-known fact. The patient is currently asymptomatic on warfarin and aspirin, with a normal functioning mitral prosthesis.

BACKGROUND

Libman–Sacks endocarditis is commonly associated with elevated titers of antiphospholipid antibodies and studies suggest a role for these autoantibodies in the pathogenesis of aseptic endocarditis. Stroke due to cardiac emboli from libman–sacks endocarditis is not a rare pathogenic factor of the central nervous system disease in systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS) and should be investigated along with cerebral arterial and venous thrombosis, small-vessel angiopathy and vasculitis. Investigation of the literature discloses a high incidence of both valvular and cerebral abnormalities in patients with antiphospholipid antibodies. This paper demonstrates the importance of such findings in young patients, even in the absence of a clear-cut diagnosis of lupus or APS, which is frequently only established after years of follow-up, as other clinical features are elicited.

CASE PRESENTATION

A 33-year-old woman recurred to her physician with muscle weakness on the left side of her face, with deviation of the mouth to the right. She had suffered three transient episodes of abrupt and complete visual loss in the recent weeks, each lasting less than 1 h.

In the past 3 months, she had been feeling tiresome. Fever, weight loss, night sweats, swelling and chest or leg pain were absent. She had no history of abortions or premature births, limb arterial or venous thrombosis, ischaemic heart disease or pulmonary thromboembolism. She denied having joint pain or swelling, skin rash, photosensitivity or oral ulcers. She had had an oral infection 12 months earlier, following a tongue piercing, resolved with antibiotics. The patient smoked 20 cigarettes per day and was on oral contraceptive.

The initial physical examination was remarkably normal, except for the presence of slight left central facial

palsy, with normal speech and understanding. A complete neurological examination excluded other motor or sensitivity deficits and cognitive dysfunctions.

In the routine blood tests there was a slight decrease in platelet count— 140×10^6 / μ l and activated partial thromboplastin time and prothrombin time were prolonged to 55 and 24 s, respectively. Anaemia was absent (haemoglobin 11.7 g/dl). C reactive protein was negative and erythrocyte sedimentation rate was 16 mm.

Cerebrospinal fluid had normal cell count and biochemistry, without oligoclonal bands or other abnormal results in immune electrophoresis. The cerebral MRI showed multiple small cortical and subcortical acute ischaemic lesions disperse in the right cerebral hemisphere affecting the frontal operculum, corona radiata and semioval centre figure 1A,B.

Blood cultures were negative for bacteria and fungus. Viral and bacterial serologies—cytomegalovirus, Coxsackie, Epstein–Barr virus, herpes simplex virus, Borrelia, Brucella, Legionella were negative for recent infection. The patient had positive lupus anticoagulant and a high titre of antinuclear (1/320) and anticardiolipin antibodies (604 U_{gpl}/ml). Complement fractions C3 and C4 were normal and antibodies against double-stranded DNA (anti-dsDNA) and Smith antigen (anti-Sm) negative. Investigation of coagulation disorders only disclosed a low activity of S protein (31%).

Transoesophageal echocardiogram revealed three nodular images in the mitral valve, the largest adherent to the anterior leaflet, with 1×1.5 cm in diameter and 2 millimetrical lesions on the posterior leaflet. There was no evident pedicle for these masses and their irregular surface with friable appearance suggested a vegetation of endocarditis with 'kissing lesion' figure 2. These lesions determined a mild mitral regurgitation. The aortic, tricuspid and pulmonary valves were normal.

Figure 1 (A,B) Several lesions circumscribed to the right cerebral hemisphere – frontal operculae, corona radiata and semioval centre; hypersignal in T2 and diffusion-weighted images.

She was referred to a cardiothoracic surgical centre for removal. During the procedure, the surgeon noticed the friable, verrucous, ‘active’ appearance of the nodular masses, affecting the subvalvular structure. A mitral valve replacement for a mechanical prosthesis was performed due to the extensive valvular damage.

Microbiological stains and cultures of the surgical samples of the native valve were negative. Pathological examination was suggestive of sterile verrucous vegetations.

OUTCOME AND FOLLOW-UP

The patient began therapy with aspirin and warfarin after surgery, with a moderate international normalised ratio (INR) target of 2.6–3.0. She was released from hospital without any postsurgical complications. She remained

asymptomatic, always with positive antiphospholipid antibody (aPL). Subsequent echocardiograms confirmed a normal functioning mitral prosthesis. Her facial palsy resolved and at re-evaluation neurological deficits were absent.

DISCUSSION

The diagnosis of APS and SLE, like most autoimmune disorders is based on clinical criteria. Definite APS is considered present if at least one of the following clinical criteria and at least one of the following laboratory criteria are satisfied in the below table.¹

Diagnostic criteria for APS

Clinical criteria

Vascular thrombosis

≥1 Clinical episodes of arterial, venous, or small vessel thrombosis

Unexplained pregnancy loss

≥1 Unexplained deaths of a normal fetus ≥ tenth week

≥2 Premature births of a normal neonate < thirty-fourth week due to severe pre-eclampsia or placental insufficiency

≥3 Unexplained, consecutive abortions < tenth week of gestation (maternal anatomic or hormonal abnormalities and chromosomal causes excluded)

Laboratory criteria (on at least two occasions, at least 12 weeks apart)

Lupus anticoagulant positive

aCL > 19 GPL (immunoglobulin G)

Anti-β₂GP1 > 20 GPL (immunoglobulin G)

The absence of clinical history prior to the thromboembolic episodes described makes a definite diagnosis impossible at this stage, with long and close follow-up needed. In this case of heart valve disease associated with aPL, the diagnosis of primary APS is probable, since there is no associated autoimmune, rheumatic or infectious disease or drug use known to induce aPL.

Although extensive, the valvular abnormalities produced only a mild regurgitation jet, which explains the absence of a heart murmur and symptoms of heart failure. This is in agreement with the statement that Libman–Sacks endocarditis is often clinically silent. Lupus anticoagulant was positive and a high titre of aCL of the immunoglobulin G type was present, favouring the diagnosis of APS. Anti-dsDNA antibody and complement components C3 and C4 were normal, rendering the diagnosis of SLE unlikely. Patients with aPL may also develop antibodies against protein S, as seems to be the case of our patient and low protein S levels correlate with a higher risk for thrombotic events.²

Endocarditis is a possible cause of cerebral infarction in patients of all ages and should be suspected with simultaneous or sequential cerebral ischaemia. The small size and disperse unilateral pattern of the ischaemic cerebral lesions is characteristic of a cardioembolic origin. Stroke rates are higher in patients with SLE and APS, but multifactorial pathological lesions contribute to this high rate, rendering the determination of the specific role of valvular abnormalities impossible.³ Cerebrovascular disease in young patients without significant risk factors should raise suspicion for APS. In two reports, aPL were found in 25 and 20 per cent of patients with stroke of unclear aetiology, under the age of 45 and 50, respectively.^{4 5}

Valvular abnormalities are fairly common among these patients. Systematic echocardiography detects some form of valvular lesion in 30–68% of patients with primary APS,

Figure 2 Nodular masses with adherence to the mitral (A2, the largest) and posterior (P2) leaflets 1074×775 mm.

with vegetations occurring in 6–10%. Transoesophageal imaging can usually detect these complications in higher rates.⁶

Prophylaxis of secondary infectious endocarditis, antiplatelet and anticoagulant medication are current treatment recommendations. There are case reports of resolution of vegetations in APS with warfarin therapy alone,⁷ but these findings are contradicted by long-term prospective studies.⁶ Initiation of oral anticoagulation is mandatory in APS, after the first event. In the case of an initial venous event, a low dose (target INR between 2.0 and 2.6) may suffice, but intermediate dose anticoagulation (target INR between 2.6 and 3.0) is recommended after an initial arterial or recurrent venous events. Moderated to high intensity anticoagulation is also necessary in patients with cardiac embolism.^{8–9} Therapy must be prolonged, usually lifelong, but there are no definite guidelines for the exact duration. Aspirin use is becoming increasingly frequent in the secondary prevention of embolic phenomena in these patients, but more data is needed.¹⁰

The role of corticosteroid and other immune-modulating drugs is still unclear in the outcome of SLE secondary APS valvulopathy, with small case series showing that it may prevent the development of cardiac lesions in long-term follow-up, as histological active lesions are identified less frequently.¹¹ In primary APS, however, no immunosuppressant therapy is advocated. Valvular surgery should be considered in patients with large mobile vegetations, significant valvular dysfunction or recurrent embolic events.¹²

Prognosis is dependent on the underlying disease and associated myocardial dysfunction. Resistant patients with recurrent thrombotic events, despite anticoagulant and antiplatelet therapy have an increased risk of death. The long-term prognosis for this patient is good, as she improved with treatment.

Learning points

- ▶ Positive aPL antibodies is a common finding in young stroke patients.
- ▶ Aseptic endocarditis is a complication in patients with aPL antibodies even in the absence of diagnostic criteria for SLE and APS.
- ▶ Prophylaxis of secondary infectious endocarditis, antiplatelet and anticoagulant medication are the current treatment recommendations.
- ▶ Valvular surgery is considered for large mobile vegetations, significant valvular dysfunction or recurrent embolic events.

Competing interests None.

Patient consent Obtained.

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