CASE REPORT

Catastrophic antiphospholipid syndrome in a young girl with lupus

Ines Zendah a,*, Ahlem Rebeha a, Samira Meraia a, Hafaoua Daghfous a, Sadok Yaalaoui b, Sonia Ben Mrad a, Fatma Tritar a

a Pneumology Department C, Abderrahmene Mami Hospital of Pneumology, 2080 Tunis, Tunisia
b Immunology Department, Abderrahmene Mami Hospital of Pneumology. 2080 Tunis, Tunisia

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Summary
Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disorder, still of unknown cause, that can affect the respiratory system with variable manifestations, course and prognosis. Catastrophic antiphospholipid syndrome is an uncommon feature in SLE and is often fatal. We report a case of fatal systemic lupus erythematosus in a 17-year-old girl with a catastrophic antiphospholipid syndrome who presented a pulmonary embolism and septic shock due to a urinary tract infection. We discuss the nosology, clinical features, immune disorders, treatment and prognosis of the disease.

Introduction
Systemic lupus erythematosus (SLE) is a multisystemic disease involving mainly the joints. Respiratory involvement is rare apart from pleural. The disease is rare in persons younger than 20 years old. Catastrophic antiphospholipid syndrome (CAPS) is an uncommon feature in SLE associated with antiphospholipid syndrome (APS).1–3 It also has a high mortality.2 We report a case of fatal SLE in a 17-year-old girl with CAPS who presented with septic shock and acute respiratory distress syndrome (ARDS).

Case report
A 17-year-old girl, without significant medical history, was transferred to our department for suspicion of anaphylaxis as she developed facial edema and maculopapular lesions that appeared 5 days after being treated by amoxicillin and clavulanic acid. This drug was administered since she complained from fever, cough, left chest pain and fatigue. On admission there were skin lesions, ulcerations of the labial mucosa, edema of the face and the inferior limbs, pyrexia (temperature 38°C), low blood pressure (blood pressure = 100/60 mmHg) and tachycardia (pulse rate = 114 beats/min). Chest radiography showed a basal pleuro-parenchymal consolidation. Laboratory findings revealed anemia with hemoglobin level...
of 85 g/l, leukopenia (white blood cells = 3 × 10⁹ cells/l) and thrombopenia (platelets = 10¹ × 10⁹ cells/l). Erythrocyte sedimentation rate was 70 mm. Blood gas analysis showed PaO₂ = 79 mmHg, PaCO₂ = 28 mmHg. An electrocardiogram showed tachycardia (pulse rate = 116 beats/min) and right branch block. On echocardiography, pulmonary arterial pressure was 40 mmHg and there was a small pericardial effusion. A pulmonary embolism was then suspected and heparin was given but the ultrasound imaging of the venous system of the inferior limbs did not reveal thrombosis. Protein electrophoresis showed: protidemia = 42 g/l, albuminemia = 17 g/l and proteinuria = 3 g/l. A nephrotic syndrome was then diagnosed. There was no renal insufficiency. Antinuclear, antinative DNA, anti-Sm, anti-RNP and anticardiolipin antibodies were positive. Thoracic CT scan angiography demonstrated arterial pulmonary embolism of the left latero- and posterobasal arteries, a pericardial effusion and a consolidation of the right superior lobe, and a right pleural effusion (Fig. 1).

The diagnosis of SLE was made and prednisone 1 mg/kg per day was administered on the seventh day of admission. On the second day of treatment, the patient presented an acute respiratory failure with SaO₂ = 86%, a fever (temperature 39.5 °C) and diffuse abdominal pain. Chest radiograph revealed a worsening of the abnormalities with hilo-axillar alveolar and pleural condensations. An abdominal ultrasonography revealed a peritoneal effusion. The patient was transferred to the intensive care unit (ICU). A purulent pleural effusion was diagnosed. Bronchoalveolar lavage showed total cell count = 420 × 10³ cells/l, neutrophils = 18%, lymphocytes = 15%, eosinophils = 2% and macrophages = 65%. Golde score was 40. The culture of the bronchial liquid, the hemocultures and the urine culture revealed Escherichia coli.

The diagnosis of catastrophic antiphospholipid syndrome associated with sepsis was made. Cefotaxim and Ciproflaxcin were administered. Nevertheless, the patient presented hemodynamic instability requiring intubation and ventilation. Heparin, corticosteroids and vasoactive drugs were administered and hemodialysis was undergone because of metabolic acidosis (pH = 7.1, lactates 19 mmol/l). The volume of the pericardial effusion increased without tamponade. There was no worsening of the pulmonary arterial hypertension. Hemoglobin failed to 42 g/l and platelets to 14,000/mm³. The patient presented an ARDS. The chest X-ray film showed a consolidation of the right hemithorax (Fig. 2). Finally, the patient died 16 h after her admission to the ICU as a result of septic shock and multiorgan failure.

Discussion

The diagnosis of APS was made in our patient on the basis of the presence of SLE criteria with positive anticardiolipin antibody and pulmonary thrombosis. CAPS is a rapidly progressive life-threatening disease that causes:

1. Multiple organ thrombosis (usually within a week) resulting in multiple organ dysfunction syndrome (MODS)
2. Pathological evidence of small vessel thrombosis
3. Evidence of systemic inflammatory response syndrome (SIRS)
4. High risk of unusual organ involvement
5. Laboratory confirmation of the presence of anti-phospholipid antibodies (aPL)

Though microthrombosis is one of the typical markers of a CAPS event, it may be difficult to confirm and the diagnosis in our patient could only be labeled as “probable” CAPS.² The nephrotic syndrome could be due to the lupus or to thrombosis of microvessels of the kidney, or to both of these.
CAPS was first described in 1992. As it is rare, an international registry of patients (the CAPS registry) was created in 2000, supported by the European Forum on Antiphospholipid Antibodies. As of July 2005, a total of 252 cases had been reported. Cervera et al., in a series comprising 220 patients included in website-based CAPS, found that CAPS occurs most of the time in women aged from 7 to 74 years. The majority of patients present with multiple organ involvement at the time of CAPS. The main clinical manifestations included renal (70%), pulmonary (66%), cutaneous (47%), cerebral (60%) and cardiac (52%) involvement. Our patient presented with pulmonary, cutaneous, cardiac and renal involvement.

Acute respiratory distress syndrome (ARDS) is the most common manifestation seen in 34% of CAPS patients with a mortality rate of 52%. Thus some authors recommend that the existence of ARDS in the context of an APS makes it necessary to rule out the presence of the catastrophic variant of this syndrome.

Pulmonary embolism is encountered in 16% of patients with CAPS. Cervera et al. reported on 100 patients with APS associated with infections; there was pulmonary involvement in 39 of them including ARDS in 24 cases, pulmonary embolism in 18, pulmonary hemorrhage in 3 and pulmonary hypertension in 1.

The occlusion of the vessels can affect not only pulmonary arteries and small vessels but also large vessels, and may affect several aortic branches.

Anticardiolipin antibodies (aCL) are detected in 84% of the patients, the lupus anticoagulant in 76%, the antinuclear antibodies in 62%, anti-double-stranded DNA in 36% and anti RNP in 8% of CAPS patients. Thrombocytopenia is found in 63–68% of the patients and hemolytic anemia in 26–32%. All those abnormalities were found in our patient.

As in our patient, in the 220 patients reported from the CAPS registry, more than half had an infection as a precipitating factor to the CAPS and 4% had lupus flares. Patients with lupus are prone to infections, and some authors have found that infection is the first cause of death in lupus patients. Presumed immunodeficiency mechanisms added to the disease by itself appear to predispose to this complication.

CAPS may be preceded by urinary tract infection in 4% of the cases, and general sepsis in 1% of cases. Urinary tract infection, especially due to E. coli, is the first or second cause of infection followed by respiratory tract infections in SLE patients. Our patient presented with septic shock with pulmonary involvement due to a urinary infection by E. coli.

APS and CAPS can be challenging to treat. Mortality reaches almost half of the cases especially those presenting with cardiac, renal, splenic, and adrenal involvement and those havingSLE such as in our patient. The site and the extension of the vascular occlusions and the degree of systemic inflammatory response are the determinants of the treatment.

The combination of anticoagulation, steroids and drugs reducing the aPL titers (plasmapheresis and/or intravenous gammaglobulins) have the highest survival rate (70%). The treatment of any precipitating factor is mandatory, especially antibiotic therapy if an infection is suspected. Annane et al. showed that the use of steroids reduced the risk of death in patients with septic shock.

Our patient received corticotherapy for SLE and heparin for pulmonary embolism. Nevertheless, she developed a multiorgan failure due to a CAPS within 48 h and even continuing to be administered those treatments, she died in 16 h. Unfortunately, no plasmapheresis nor gammaglobulins were administered.

Conclusion

SLE associated with CAPS is an extremely rare, distinct cause of multiple organ failure resulting from widespread thrombosis and SIRS; it may be revealed by many presentations and may be fatal. The diagnosis and the treatment are challenging for physicians. Awareness of this rare syndrome would facilitate an early diagnosis to prescribe life-saving multimodal therapies including anticoagulation, corticosteroids and plasma exchange. A further understanding of the etiopathogenesis of CAPS might lead to novel targeted therapies and further reduce the mortality rate, which remains too high.

Conflict of interest statement

None of the authors have a conflict of interest to declare in relation to this work.

References

fatal stroke in a patient with systemic lupus erythematosus: