EXTENDED REPORT

Catastrophic antiphospholipid syndrome during pregnancy and puerperium: maternal and fetal characteristics of 15 cases

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Ann Rheum Dis 2007;**66**:740–746. doi: 10.1136/ard.2006.061671

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Accepted 25 December 2006
Published Online First 11 January 2007

Background: The catastrophic variant of the antiphospholipid syndrome (APS) is a life-threatening form of presentation of this syndrome that can be triggered by several factors.
Aim: To describe the characteristics of patients who developed catastrophic APS triggered during pregnancy and puerperium.
Methods: A review of the first 255 cases collected in the website-based ''CAPS Registry'' was undertaken. Three new and unpublished cases of catastrophic APS developed during pregnancy and puerperium were added.
Results: Fifteen cases were identified. The mean (range) age was 27 (17–38) years. Most patients had a previous unsuccessful obstetric history. In 7 of 14 (50%) cases with available medical history, the catastrophic APS appeared during pregnancy, in 6 (43%) during the puerperium and in 1 (7%) after curettage for a fetal death. The main clinical and serological characteristics were similar to those patients with catastrophic APS triggered by other factors, except for a history of a higher prevalence of previous abortions ($p<0.01$). Several specific features were found, including the HELLP (haemolysis, elevated liver enzymes, low platelets) syndrome in 8 (53%) patients, placental infarctions in 4 (27%) patients, and pelvic vein thrombosis and myometrium thrombotic microangiopathy in 1 (7%) patient each. Mortality rate was high for the mothers (46%), and for the babies (54%).
Conclusions: It is important to consider the possibility of the development of catastrophic APS in those patients with signs of HELLP syndrome and multiorgan failure during pregnancy or puerperium, especially in those patients with previous history of abortions and/or thrombosis.

The antiphospholipid syndrome (APS) is a systemic autoimmune disorder characterised by a combination of arterial and/or venous thrombosis, pregnancy morbidity, usually accompanied by a mild-to-moderate thrombocytopenia, and raised titres of antiphospholipid antibodies (aPL)—namely, the lupus anticoagulant (LA) and/or anticardiolipin antibodies (aCL).[1]

The most characteristic feature of obstetrical APS is miscarriage. Currently, recurrent miscarriage is a potentially treatable condition when it is associated with aPL.[2] Additionally, several other serious obstetric complications have been associated with APS, including pre-eclampsia, fetal growth restriction, uteroplacental insufficiency, fetal distress and medically induced preterm delivery.[3 4]

Catastrophic APS (also known as ''Asherson's syndrome'') is an unusual (<1%) but usually a life-threatening variant of APS, characterised by rapid appearance of multiple thromboses (mainly small-vessel thrombosis) that lead to multiorgan failure.[5] Since its first description in 1992,[5] several large series have been published,[6 7] and more than 250 patients have been collected in the international registry of patients with catastrophic APS (Catastrophic Antiphospholipid Syndrome (CAPS) Registry. Catastrophic events may be triggered, in >50% of patients, by a recognised factor, mainly infections, trauma or surgery, anticoagulation withdrawal, malignancies and lupus ''flares'', or appear infrequently during pregnancy (ie, after a caesarean section or fetal loss).

No previous publications have focused on the setting of catastrophic APS during the obstetric period. Our objective in this study was to assess the clinical and laboratory characteristics of the catastrophic APS triggered or presented during pregnancy and puerperium obstetric periods by analysing three new and unpublished cases in addition to 12 already published cases collected from the ''CAPS Registry'', with special interest in maternal and fetal outcome.

METHODS

We reviewed the 255 cases that were included in the website-based CAPS Registry on 1 November 2005. This registry was created by the European Forum on Antiphospholipid Antibodies, a study group devoted to the development of multicentre projects with large populations of patients with catastrophic APS. The website contains clinical, laboratory and

Abbreviations: aCL, anticardiolipin antibodies; aPL, antiphospholipid antibodies; APS, antiphospholipid syndrome; CAPS Registry, Catastrophic Antiphospholipid Syndrome Registry; CNS, central nervous system; DIC, disseminated intravascular coagulation; HELLP, haemolysis, elevated liver enzymes, low platelets; LA, lupus anticoagulant; TMA, thrombotic microangiopathy; TTP, thrombotic thrombocytopenic purpura

therapeutic data on all reported cases of patients with catastrophic APS and can be freely accessed through the internet (http://www.med.ub.es/MIMMUN/FORUM/CAPS.HTM). The sources of information are the personal communications of the physician who treated these patients and the periodically computer-assisted search (Medline, National Library of Medicine, Bethesda, Maryland, USA) of published reports to locate all cases of patients with catastrophic APS. Patients included in the CAPS Registry fulfil the classification criteria for catastrophic APS[8] (box 1). Cases were summarised using a standardised data form, including age, diagnosis of the underlying condition, time of presentation of catastrophic APS features (during pregnancy or puerperium periods), clinical manifestations, serological features, treatment and outcome.

We selected those patients who developed the catastrophic APS during pregnancy and puerperium. The list of precipitating factors in the CAPS registry was used as a guide for case identification; however, only those cases with a close relationship between pregnancy and/or puerperium and the development of the catastrophic APS event were included. Three previously unpublished cases with catastrophic APS occurring during pregnancy or puerperium were added to the review and subsequently included into the registry. The diagnosis of HELLP (haemolysis, elevated liver enzymes, low platelets) syndrome was established if patients fulfilled the laboratory criteria proposed by Sibai *et al*,[9] including: (1) platelet count <100 000/mm^3, (2) aspartate aminotransferase >70 IU/l and (3) lactate dehydrogenase >600 U/l. Severity of HELLP syndrome was classified according to Martin *et al*'s[10] criteria based on platelet count. Class 1 (severe) was considered when platelet count was $<50\times10^9$/mm^3, class 2 (moderate) when platelet count was between 51×10^9 and 100×10^9/mm^3 and class 3 (mild) when platelet count was $>100\times10^9$/mm^3.

In order to identify whether patients with catastrophic APS triggered during pregnancy or puerperium correspond to a special subset of patients with catastrophic APS, we compared them with the rest of patients (n = 240) included in the CAPS Registry (χ^2 test, SPSS V.11.0).

Box 1: Preliminary criteria for the classification of catastrophic antiphospholipid syndrome

- Evidence of involvement of three or more organs, systems and/or tissues. Usually, clinical evidence of vessel occlusions, confirmed by imaging techniques when appropriate. Renal involvement is defined by a 50% rise in serum creatinine, severe systemic hypertension (>180/100 mm Hg) and/or proteinuria (> 500 mg/24 h).
- Development of manifestations simultaneously or in <1 week
- Confirmation of small-vessel occlusion in at least one organ or tissue by histopathology. For histopathological confirmation, significant evidence of thrombosis must be present, although vasculitis may coexist occasionally.
- Laboratory confirmation of the presence of antiphospholipid antibodies (aPL): lupus anticoagulant and/or anticardiolipin antibodies. If the patient was not previously diagnosed as with an antiphospholipid syndrome (APS), the laboratory confirmation requires that aPL is detected on two or more occasions at least 6 weeks apart (not necessarily at the time of the event), according to the proposed preliminary criteria for the classification of definite APS.

Definite catastrophic APS

- All four criteria

Probable catastrophic APS

- All four criteria, except for only two organs, systems and/or tissues involvement
- All four criteria, except for the absence of laboratory confirmation at least 6 weeks apart due to the early death of a patient never tested for aPL before the catastrophic APS
- Criteria 1, 2 and 4
- Criteria 1, 3 and 4, and the development of a third event in >1 week but in <1 month, despite anticoagulation

RESULTS

We analysed 15 cases of catastrophic APS that appeared during pregnancy or puerperium. (3 previously unpublished cases and 12 from the CAPS Registry[5 11–19]). Tables 1 and 2 summarise the data from these cases.

General characteristics and obstetric history

In all, 7 (47%) patients had primary APS, 7 (47%) had SLE and 1 (6%) had lupus-like syndrome. The mean (SD, range) age at the time of the catastrophic APS event was 27 (6 (17–38)) years. Past obstetric history was available in 14 cases. Only 1 patient had a previous successful pregnancy, 9 patients had previous abortions or fetal losses, and in 4 cases[11 13 16 19] there were no previous pregnancies. In 7 of the 14 (50%) cases catastrophic APS appeared during pregnancy (ranging from the 17th to 38th weeks of gestation), in 6 (43%) cases it presented during puerperium (ranging from the 2nd day until 3 weeks after delivery) and in 1 (7%) case it presented, 2 days after dilatation and curettage for a fetal death at 18 weeks of pregnancy. In 4 (26%) cases the catastrophic APS event was the first manifestation of the APS (cases 1, 6, 11 and 13). Only 6 (40%) patients fulfilled the diagnostic criteria for APS prior to the catastrophic APS event. The remaining patients had some features suggestive of APS or previous aPL-positive determinations. At the moment of the catastrophic APS event, only 2 patients (cases 2 and 10) were under treatment (aspirin 325 mg/day and warfarin, respectively).

Thrombotic and APS-related features

The main clinical symptoms were renal involvement in 11 (73%) patients (in 3 of them in the form of renal thrombotic microangiopathy (TMA)) pulmonary involvement in 11 (73%) patients (acute respiratory distress syndrome (ARDS) in four patients, respiratory failure in three, pulmonary embolism in two, and alveolar hemorrhage, pulmonary infarcts and pulmonary TMA in one case each), central nervous system (CNS) involvement in 9 (60%) patients (cerebral infarcts in five cases, encephalopathy in two cases, cerebral haemorrhage in two cases, transient ischaemic attack in one case, cerebral TMA in one case and status epilepticus in one case) and HELLP syndrome in 8 (53%) patients. Seven patients had a class 1 HELLP syndrome, whereas only 1 patient had class 2. The mean platelet count among patients with HELLP syndrome was 29 000/mm^3 (ranging from 6000 to 59 000).

Intra-abdominal and pelvic features included placental infarctions in 4 (27%) patients, gastrointestinal thrombosis in 4 (27%; including mesenteric and intestinal thrombosis), hepatic thrombosis in 3 (20%), adrenal involvement in 2 (13%; haemorrhage in one case and adrenal infarcts in another), portal vein thrombosis in 1 (7%), inferior vena cava

Table 1 General characteristics of patients with catastrophic antiphospholipid syndrome during pregnancy or puerperium

	Age (year)	Diagnosis	Previous obstetric history	Time of onset
Bendon *et al*[11]	22	SLE	No previous pregnancies	30 weeks of gestation
Hochfeld *et al*[12]	37	PAPS	Three previous spontaneous abortions	2nd day after fetal death
Kupferminc *et al*[13]	17	PAPS	No previous pregnancies	5th day of puerperium
Kitchens[14]	38	SLE	NR	38 weeks of gestation
Wislowska[15]	26	SLE	One previous successful pregnancy	25 weeks of gestation
Sinha *et al*[16]	22	SLE	No previous pregnancies	25 weeks of gestation
Asherson *et al*[5]	22	SLE	One spontaneous abortion	20 wks of gestation
Asherson *et al*[5]	27	PAPS	One fetal loss	Post-fetal loss
Ortiz *et al*[17]	32	Lupus-like	One second trimester fetal loss	2nd day of puerperium
Koenig *et al*[18]	19	PAPS	One miscarriage	17 weeks of gestation
Coward *et al*[19]	30	PAPS	No previous pregnancies	3rd weeks of puerperium
Wieser M *et al**	33	PAPS	One first trimester spontaneous abortion	5th day of puerperium
Present case 1	29	SLE	Eight previous spontaneous abortions	28 weeks of gestation
Present case 2	26	SLE	Two previous fetal losses	3rd day of puerperium
Present case 3	28	PAPS	One second trimester fetal loss	6th day of puerperium

NR, not reported; PAPS, primary antiphospholipid syndrome; Ref, reference; SLE, systemic lupus erythematosus.
*Included previously in the ''CAPS Registry''.

thrombosis in 1 (7%), splenic infarcts in 1 (7%), pelvic vein thrombosis in 1 (7%) and myometrium TMA in 1 (7%).

Other manifestations were skin involvement in 5 (33%) patients (livedo reticularis in two cases, and skin ulcers, skin thrombosis and digital necrosis in one case), heart involvement in 3 (20%) patients in the form of myocardial infarction, valve disease and myocardial TMA in one case each, deep vein thrombosis in 3 (20%) patients, bone marrow involvement in 2 (13%) patients (bone marrow necrosis in one and bone marrow hypoplasia in the other) and bone necrosis in 1 (7%) patient.

Laboratory features

Severe thrombocytopenia was found in 2 (13%) patients without HELLP syndrome, schistocytes were found in 3 (20%) patients, disseminated intravascular coagulation (DIC) features in 3 (20%), haemolytic anaemia in 2 (13%) and severe pancytopenia in 2 (13%). In all, 14 (93%) patients were positive for aCL, 12 (80%) for the IgG isotype and 4 (27%) for the IgM isotype. LA was found in 10 (73%) patients, and anti-β2 glycoprotein I (GPI) antibodies in 3 (20%).

Treatment and maternal and fetal outcomes

A total of 6 (40%) patients (cases 2, 6, 9, 10, 11 and 13) were under anticoagulation treatment (low molecular weight heparin) before a catastrophic APS event. Specific treatment for the catastrophic APS events was available in 14 cases. In all, 11 (79%) out of 14 patients received anticoagulation, 10 (71%) steroids, 4 (29%) plasma exchange, 3 (21%) dialysis, 3 (21%) cyclophosphamide, 3 (21%) intravenous immunoglobulins, 2 (14%) fresh frozen plasma and 1 (7%) fibrinolysis.

In all, 7 (46%) mothers died due to the catastrophic APS. Fetal outcome was available in 13 cases. Only 6 (46%) babies survived (3 of them were premature newborns), whereas 7 (54%) babies died. Neither the mothers nor the babies had different outcomes regarding the previous presence of HELLP syndrome or the treatment received (non-statistically significant differences), including the combined therapies (anticoagulation and plasma exchange). Regarding the babies who survived, in 2 cases their mothers had received plasma exchange. However, in 2 of the babies who died, their mothers had also received plasma exchange therapy.

Comparison between patients with pregnancy or puerperium-associated catastrophic APS

Fifteen patients with catastrophic APS events associated with pregnancy or puerperium were compared with 240 patients with catastrophic APS events not associated with pregnancy or puerperium that were included in the CAPS Registry (table 3). In the former group, there was a higher prevalence of previous abortions ($p<0.001$). In those patients with catastrophic APS events not related to pregnancy or puerperium, there was a higher prevalence of cardiac involvement ($p = 0.02$) and livedo reticularis ($p = 0.025$), and they had a higher prevalence of catastrophic events as the initial manifestation of APS ($p = 0.05$).

DISCUSSION

Pregnancy is a well-recognised hypercoagulable state that encompasses a period of 10–11 months (including puerperium). This hypercoagulability is explained by many factors, including alterations in coagulation proteins (increased levels of factors II, V, VII, VIII, X and XII as well as von Willebrand factor, and decreased levels of protein S and activated protein C) and alterations in fibrinolytic systems (low plasma fibrinolytic activity during pregnancy, labour and delivery), with a decreased activity of tissue plasminogen activator.[20 21] The presence of microparticles derived from maternal endothelial cells, platelets and placental trophoblasts may also contribute to the procoagulant situation.[20] Additionally, the reduction of venous flow in lower extremities as a result of compression by the gravid uterus and the prolonged bed rest (especially during labour and postpartum) induces venous stasis and contributes to the formation of thrombosis. The risk of venous thrombosis is 5–6-fold higher during pregnancy compared with non-pregnant women of similar age.[21] Despite this situation, deep venous thrombosis is not commonly reported during pregnancy, occurring in 1 in 1000 to 1 in 2000 pregnancies;[21] however, this prevalence may be higher in the presence of any thrombophilic factor.

Thrombophilic disorders notably increase gestational vascular complications, leading to pre-eclampsia, retardation of fetal growth, placental abruption, placental thrombosis and recurrent miscarriages. Several thrombophilic disorders have been described during pregnancy, including antithrombin deficiency, protein S and protein C deficiency, factor V Leiden and prothrombin gene mutation, hyperhomocysteinaemia and aPL, among others.[22] Routine assessment of these factors is not currently recommended in healthy pregnant women. It is only indicated in those women with previous thrombosis and/or recurrent pregnancy losses.[22]

HELLP syndrome is a manifestation of pre-eclampsia occurring in approximately 0.6% of all pregnancies.[23] It involves smaller terminal arterioles and is a process with characteristic histological features. The microangiopathic haemolytic anaemia and the raised liver enzymes are explained by platelet-fibrin

Table 2 Clinical and serological characteristics and outcome of patients with catastrophic antiphospholipid syndrome during pregnancy or puerperium

Author (CAPS registry number)	Catastrophic APS features	Laboratory findings	Treatment	Outcome	
				Maternal	Fetal
Bendon *et al*[11]*(6)	Placental infarctions myocardium, renal, gastrointestinal and myometrium TMA	Severe thrombocytopenia Schistocytes aCL positive LA: ND	NR	Death	Intrauterine fetal death
Hochfeld *et al*[12] (22)	HELLP, iliac, pelvic vein and skin thrombosis Renal failure, cerebral, cardiac Pulmonary, splenic and adrenal Infarcts, cerebral haemorrhage	DIC LA positive IgG aCL (high titres)	Anticoagulation (IV heparin) Steroids Cyclo Plasma exchange	Death	Intrauterine fetal death
Kupferminc *et al*[13]†(31)	HELLP, ARDS Placental infarcts, renal failure Alveolar haemorrhage	LA positive IgG aCL (26.5 GPL)	Steroids Plasma exchange Dialysis	Recovery	Prematurity
Kitchens[14]*(65)	HELLP, portal vein Inferior cava, hepatic and mesenteric vein thrombosis	aCL strongly positive LA negative	Anticoagulation (IV hepatin) Streptokinase	Recovery	NR
Wislowska *et al*[15]* (82)	ARDS, encephalopathy Rapid progressive nephritis Skin ulcers	LA positive IgG aCL moderate levels	Anticoagulation (LMWH) Steroids Cyclo	Recovery	Miscarriage
Sinha *et al*[16]* (100)	HELLP Placental infarcts Cerebral infarcts Bone marrow necrosis	Severe pancytopenia IgG aCL (203 GPL) IgM aCL (10 MPL) LA positive, B2GP1 IgG	Steroids Plasma exchange IVIG	Death	Death (intracerebral haemorrhage)
Asherson *et al*[7]*(110)	HELLP Renal TMA, ARDS Cerebral infarcts	Thrombocytopenia Schistocytes, LA positive IgG and IgM aCL positive	Steroids Cyclo Anticoagulation (IV heparin)	Recovery	Death
Asherson *et al*[7] (121)	PE, digital necrosis Hepatic, renal, intestinal and mesenteric thrombosis	Haemolytic anaemia IgG aCL (72 GPL) LA negative	Steroids Anticoagulation	Death	Death
Ortiz *et al*[17]† (240)	Renal TMA, valve lesions Multiple cerebral infarcts	Thrombocytopenia Haemolytic anaemia Schistocytes, LA positive IgG aCL (>120 GPL) IgM aCL (19.2 MPL)	Steroids, FFP Anticoagulation (LMWH)	Recovery	NR
Koenig *et al*[18]*(251)	HELLP Hepatic infarctions Bone necrosis, bowel TMA	Severe thrombocytopenia IgG and IgM aCL positive B2GP1, LA positive	Anticoagulation (LMWH) FFP	Recovery	Death
Coward *et al*[19]†(252)	TIA, status epilepticus Renal failure, brain and pulmonary TMA Adrenal haemorrhage	LA positive	Anticonvulsants Dyalysis	Death	Healthy child
Weiser M(‡)†(99)	HELLP, ARDS Renal failure, cerebral infarctions and haemorrhage	Severe thrombocytopenia IgG aCL (>100 GPL) LA positive	Steroids, IVIG Anticoagulation Dyalysis	Death	Healthy child
Present case 1*	HELLP, bone marrow hypoplasia, renal failure DVT, respiratory failure Livedo reticularis	DIC Pancytopenia IgG aCL high titres LA negative	Steroids Anticoagulation (LMWH)	Death	Prematurity
Present case 2†	DVT, PE TIA, respiratory failure	IgG aCL high titres LA negative	Anticoagulation (LMWH) Steroids, IVIG	Recovery	Healthy child
Present case 3†	Placental infarctions Renal failure, encephalopathy Respiratory failure	Severe thrombocytopenia LA positive, DIC, aCL IgG (24 U/ml) B2GP1 IgG (44.9 U/ml)	Anticoagulation (LMWH) Plasma exchange	Recovery	Healthy child

aCL, anticardiolipin antibodies; APS, antiphospholipid syndrome; ARDS, acute respiratory distress syndrome, B2GP1, β2-glycoprotein 1 antibodies; Cyclo, cyclophosphamide; DIC, disseminated intravascular coagulation; DVT, deep vein thrombosis; FFP, fresh frozen plasma; HELLP, haemolysis, elevated liver enzymes, low platelet count; IVIG, intravenous immunoglobulins; LA, lupus anticoagulant; LMWH, low molecular weight heparin; ND, not done; NR, not reported; PE, pulmonary embolism; TIA, transient ischaemic attack; TMA, thrombotic microangiopathy.
*Presenting during pregnancy.
†Presenting during puerperium.
‡This case was included in the CAPS registry by Manfred Weiser, Salzburg, Austria.

deposits and thrombi causing fragmentation of red cells as they pass through interrupted arterioles and hepatic sinusoid blood flow restrictions, respectively. Thrombocytopenia is due to the increased consumption of platelets after their adhesion to damaged endothelium and intravascular aggregation.[24]

The real incidence of HELLP syndrome in APS is difficult to estimate. Around 50 well-documented cases are reported with both conditions. Von Tempelhoff *et al*[25] studied several thrombophilic factors, including LA and aCL, in a series of 32 patients with HELLP syndrome. Of these, 17 (53%) patients were positive for LA and 15 (47%) were positive for aCL. Thuong *et al*[26] described 16 episodes of HELLP in 15 patients with APS. In 8 of these cases, HELLP syndrome revealed an APS (patients with previously unknown APS). In all, 11 (69%) and 3 (19%) patients had pre-eclampsia and eclampsia, respectively. In a significant proportion of cases (44%) HELLP syndrome occurred during the second trimester, and in 12% during 18–20 weeks of gestation. The authors concluded that HELLP appears in a more severe form in early stages of pregnancy in patients with APS than in the general population.

In the present study, we found eight patients with HELLP syndrome; most of them were classifiable as class 1 (severe)

Table 3 Comparison between patients with catastrophic antiphospholipid syndrome related and those not related to pregnancy or puerperium

	Catastrophic APS related to pregnancy and puerperium n = 15 (%)	Catastrophic APS not related to pregnancy or puerperium n = 240 (%)	p Value
Feature			
Catastrophic APS as a first manifestation	3 (20)	114 (47)	0.05
Previous APS features	10 (67)	127 (53)	NS
Previous abortions	9 (60)	41 (17)	<0.001
DVT	3 (20)	76 (32)	NS
Peripheral arterial thrombosis	0 (0)	27 (11)	NS
Cardiac involvement	3 (20)	128 (33)	0.02
Valvular disease	1 (7)	49 (20)	NS
Pulmonary involvement	11 (73)	159 (66)	NS
ARDS	5 (33)	60 (25)	NS
Renal involvement	10 (67)	175 (73)	NS
Cerebral involvement	9 (60)	151 (63)	NS
Cutaneous involvement	5 (33)	124 (52)	NS
Livedo reticularis	2 (13)	66 (27)	0.025
Death	7 (47)	111 (46)	NS

ARDS, acute respiratory distress syndrome; DVT, deep venous thrombosis; NS, not significant.

HELLP syndrome. This is, however, not a very helpful classification tool in this particular group of patients (SLE, aPL, related septic process, etc). Nonetheless, severe HELLP syndrome seems to be a major feature of catastrophic APS during the obstetric period. This is supported by data observed in six of eight collected cases with HELLP syndrome. In the case described by Hochfeld *et al*,[12] HELLP syndrome was characterised by a persistent thrombocytopenia. In the case described by Kupferminc *et al*,[13] HELLP syndrome improved only after plasma exchange sessions. Portal and hepatic vein thrombosis and an inferior vena cava thrombosis accompanied the HELLP syndrome in the patient documented by Kitchens *et al*.[14] In the case described by Koenig *et al*,[18] the patient had abdominal pain, requiring a laparotomy, which did not reveal any abnormality. Only a CT scan revealed concomitant hepatic infarctions. Interestingly, in the case described by Sinha *et al*,[16] the HELLP syndrome deteriorated despite the termination of pregnancy. Finally, in our first case, HELLP had an unsatisfactory course in relation to surgical wound infection and haematoma formation.

As these microangiopathic disorders share several clinical and serological characteristics, the differential diagnosis in pregnant patients may be difficult, but necessary, because it carries different therapeutic strategies—eg, plasma exchange sessions for those cases with thrombotic thrombocytopenic purpura (TTP) and prompt delivery for those cases of HELLP syndrome. There are several clinical features that may differentiate each disorder. In TTP, the involvement of the CNS is higher than in HELLP syndrome, which involves mainly liver parenchyma. TTP induces a more severe thrombocytopenia and haemolytic anemia than HELLP syndrome. Anti-thrombin and D-dimers are normal in TTP, whereas they are abnormal in patients with HELLP syndrome. In some severe HELLP syndrome and pre-eclampsia cases, diverse organs may be affected, leading to acute renal failure, myocardial dysfunction, DIC, ascites, pulmonary oedema, cerebral oedema, subcapsular liver haematoma and ARDS, among others.[26] There are additional diagnostic challenges for clinicians. Patients with catastrophic APS develop a wide spectrum of clinical and haematological features including CNS involvement, HELLP syndrome, DIC[27] and microangiopathic thrombosis. In patients with catastrophic APS, combined treatments are needed, including, in many cases, plasma exchange sessions, as well as termination of pregnancy in those cases with related pre-eclampsia or eclampsia.

Catastrophic APS during pregnancy or puerperium represents almost 6% of all cases (15/255) described with catastrophic APS. This represents a life-threatening situation with a high mortality rate in these young women of childbearing age. This also represents a unique scenario where many factors may participate as additional potential trigger factors, including infections such as endometritis, caesarean wound or episiotomy wound infection or mastitis, lupus flares, anticoagulation withdrawal during the actual labour, among others.

The relatively small number of patients with catastrophic APS during the obstetric period makes it difficult to definitely conclude whether this group corresponds to or singles out a different subset of patients with catastrophic APS. However, these patients seem to have a higher prevalence of previous abortions than the non-pregnant patients with catastrophic APS.

On the basis of present data and as per previous guidelines for the treatment of catastrophic APS,[8] we propose the following scheme for the management of catastrophic APS during pregnancy (management of catastrophic APS during puerperium could be similar to that in other scenarios). First, it is essential to prevent any potential trigger factor, mainly infections, and to maintain an adequate anticoagulation in those patients with previous thromboses and aPL. The second aspect is to evaluate fetus maturation. When pulmonary fetal maturation is ready, a prompt delivery is recommended. In those cases with HELLP or other microangiopathic features, plasma exchange sessions are certainly strongly indicated. Plasma exchange sessions have been used previously in mothers with other life-threatening conditions.[28 29] The remaining therapeutic measures recommended in catastrophic APS are also useful, specially steroids and intravenous immunoglobulins. It is important to bear in mind that pre-term delivery is the strongest risk factor for an adverse neonatal outcome, but it can be life saving for the mother and the fetus.

In conclusion, it is important to consider the possibility of the development of catastrophic APS in those patients with signs of TMA (with or without HELLP syndrome) and/or multiorgan failure during pregnancy or puerperium, particularly in those patients with a history of abortions and/or thrombosis.

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Competing interests: None declared.

*The complete list of members of the ''CAPS Registry'' Project Group is given in the appendix.

Funding: Supported in part by grant p1030280 from ISCIII of Spain.

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APPENDIX

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