

## Review

## Subarachnoid hemorrhage in systemic lupus erythematosus: Systematic review and report of three cases



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## ABSTRACT

**Objective:** Systemic lupus erythematosus (SLE) is an autoimmune disorder of multifactorial etiology with a broad range of clinical manifestations. Cerebral disorders such as psychosis, seizures and cerebrovascular accidents are commonly described in SLE patients. Subarachnoid hemorrhage (SAH) presents a higher incidence than in the general population. Saccular aneurysms are the most frequent cause, but uncommon forms of SAH had been repeatedly reported in SLE patients. Through three case examples we outline these uncommon patterns, which we hypothesized, might be responsible for the higher incidence of SAH in SLE patients.

**Methods:** We present three patients previously diagnosed with SLE, who suffered a SAH and we perform a systematic literature review.

**Results:** All three cases presented with a Fisher grade IV bleeding. One harbored a distal middle cerebral artery aneurysm, another had multiple aneurysms, and the youngest patient had no findings on the cerebral angiography. A focal vasculitic process seemed most likely responsible for the two aneurysmal cases. The angiography negative case was attributed to severe SLE systemic complications and had an unexpected bad outcome. Literature review yielded 39 previously reported cases.

**Conclusions:** The uncommon SAH patterns make etiological diagnosis challenging. Management can also be daunting due to both local and systemic consequences of SLE. Awareness of these uncommon patterns, management challenges, and higher likelihood of bad outcomes may help physicians dealing with this disease. Further research to unveil the mechanisms behind it is granted to fully understand SAH in SLE patients.

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**Abbreviations:** ACA, anterior cerebral artery; AICA, anterior inferior cerebellar artery; CNS, central nervous system; CT, computed tomography; EVD, external ventricular drain; GCS, Glasgow Coma Scale; ICG, indocyanine green; MRSA, methicillin-resistant staphylococcus; MCA, middle cerebral artery; mRS, modified rankin score; PCoA, posterior communicating artery; SAH, subarachnoid hemorrhage; SLE, systemic lupus erythematosus.

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## 1. Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by complex-mediated lesions of blood vessels in multiple body organs, leading to different types of vascular complications. Incidence rate of SLE is quoted between 1 and 10/100,000 per year depending on the population studied (sex, ethnicity, geographical location and age). The incidence is markedly higher in non-Caucasian population [1]. Immune complexes that cause vasculitis in Lupus may contain DNA and Anti-DNA antigens, or Ro and Anti-Ro antigens and usually affect small vessels; medium and large vessels are only exceptionally affected [2]. The central nervous system (CNS) can be affected in 25–50% of SLE patients mostly due to seizures, psychosis, and cerebrovascular accidents [3]. Incidence of subarachnoid hemorrhage (SAH) is considered higher in SLE patients than in the general population, with a rate of 49.4 vs. 10.2 per 100,000 person-years [4]. However, the underlying cerebral vasculitis described in SLE does not justify the pathophysiology of all the SAH cases, and the causes leading to this increased incidence remain unclear [5,6].

In this manuscript, we review case reports of SAH in SLE patients found in the medical literature. While we do not have enough information to assess the causes of SAH in SLE patients, we hypothesized that there would be a few clinical identifiable patterns whose detailed description may help improving diagnostic and management strategies of these complex cases. Bad prognostic spontaneous SAH, multiple aneurysms and fusiform or uncommon aneurysm might reflect the characteristic behavior of SAH in SLE. We also review our own experience with SAH in SLE patients and report three additional cases that we managed in our department.

## 2. Methods

### 2.1. Literature review

We have conducted a systematic literature search in PubMed and MedLine using “systemic lupus erythematosus” and “subarachnoid hemorrhage” as key words and free text searches. We limited language to English, French and Spanish and publication period from January 1980 to December 2013. Abstracts of identified references were initially screened and full publications of potentially relevant articles were obtained for further examination. The references of each included report were also screened for additional manuscripts. The initial search strategy identified 25 manuscripts. We eliminated 9 of them that were not written in English, French or Spanish. Full text of the remaining 16 articles were obtained and 4 of them were excluded for reporting other causes of SAH (such as traumatic vertebral dissection) not corresponding with aneurysmatic or angio-negative SAH. References of the remaining

12 articles yielded 6 extra manuscripts meeting our search criteria. Out of them, one article by a Japanese author reported two new cases in English and reviewed 55 more from the Japanese literature. Detailed data for the two cases reported in English was extracted but original data for the remaining 55 cases was either incomplete or written in Japanese and therefore, was excluded. Overall, we found 18 unique articles reporting SAH in 39 SLE patients.

### 2.2. Cases report

Between January 1996 and December 2013, we identified 3 patients previously diagnosed with SLE out of the 641 who were admitted with non-traumatic SAH and prospectively collected in our service database. Their demographic features, clinical presentation, management strategy and outcomes were thoroughly reviewed.

Clinical outcomes were assessed using the modified Rankin Score (mRS). Good outcomes were defined as a final mRS score of 0–2, and poor outcomes were defined as a final mRS greater than 2. Improvement was defined as a decrease in mRS score (change in the mRS of less than or equal to zero), and deterioration was defined as an increase in mRS score (change in the mRS of greater than zero).

## 3. Results

To the best of our knowledge, 39 patients with SLE and SAH have been described in English, Spanish or French articles. Table 1 summarizes the main features, treatment strategy and outcomes of all these reported cases. Eleven cases presented an angiographically negative SAH and 5 out of those 11 had a bad outcome (4 deaths, 1 severe disability). Out of the remaining 27 reported cases, all with a confirmed aneurysmatic SAH, 6 patients presented with multiple aneurysms and 6 had a either a fusiform aneurysm, an aneurysm in an atypical location or both.

The analysis of this search revealed that three main patterns have been consistently reported as leading to SAH in SLE patients. First, distal fusiform aneurysms with aberrant morphology in uncommon locations [7,8]; second, multiple saccular aneurysms [9]; and third, angiographically negative SAH with an unexpected bad prognosis [10].

### 3.1. Illustrative cases

Each of these cases illustrate one of the aforementioned 3 main patterns usually responsible for SAH in SLE patients.

**Table 1**  
Summary of main SAH features, SLE activity, management strategy and outcomes of previously reported cases.

Case reports	Asian patients	No. of patients	Type of aneurysm	Location	Systemic disease	Treatment	Outcome
Asai et al. (1989)	Yes	1	Multiple, saccular	PCoA, BA, ACA aneurysm	Transmural angitis by pathology	All clipped except the BA aneurysm	Dead
Atanes et al. (1989)	No	1	Multiple, saccular	Left ACA, Left PCoA aneurysms	Active SLE	Steroids and cyclophosphamide	No neurological deficits
Baizabal Carvallo et al. (2007)	No	10	5 aneurysms, 5 negative SAH	4 MCA, 1 PCoA	4 with active SLE	2 aneurysms were not treated, 2 clipped, 1 endovascular embolization	1 DSA negative SAH and 3 patients with aneurysm died, the other survived
Brah et al. (2012)	No	1	Multiple, fusiform	SCA and lenticulostriated arteries	Active SLE	Embolization	Dead
Gillard et al. (2002)	No	1	Multiple, fusiform	Left SCA, fusiform ACA, saccular MCA	Active SLE	Left SCA was clipped, ACA and MCA aneurysms were not treated.	NA
Hashimoto et al. (1986)	Yes	2	Saccular	BA, ACA aneurysms	Active SLE	Both clipped	1 Hemiplegic, 1 without deficits
Kelley et al. (1980)	No	1	Fusiform aneurysm	PCoA aneurysm	Transmural angitis by pathology	Medical treatment with steroids	Dead
Mimori et al. (2000)	Yes	10	4 saccular, 4 Spontaneous SAH, an 2 with not angiography done	MCA, 2 PCoA, 1 ACA aneurysm	5 with active SLE	3 clipped, and 1 patient died before a surgical treatment could be done	7 Deaths, 3 survived
Nagayama et al. (1989)	Yes	1	Saccular	Basilar artery	No SLE activity	Clipped	Left hemiplegia
Nakai et al. (2000)	Yes	1	Saccular	Left SCA	No SLE activity	Embolization	Good recovery
Lim et al. (2013)	Yes	1	Blister Aneurysm	ICA	NA	Stents with coiling	Dead
Owada et al. (2009)	Yes	2	1 Multiple aneurysms, 1 saccular aneurysm	Bilateral MCA and Carotid aneurysm. One PCoA aneurysm	Active SLE (both)	Both patients were clipped	Both good recovery
Refai et al. (2008)	No	1	Spontaneous SAH	No	Active SLE	Steroids	No neurological deficits
Rozet et al. (2004)	Yes	1	Saccular	PICA	Active SLE	Clipped	Dead
Sakaki et al. (1990)	Yes	2	Saccular	MCA, ACA	Transmural angitis by pathology in both cases	1 Clipped, 1 conservative treatment	1 good recovery, the other was dead
Sánchez-Ojanguren et al. (1999)	No	1	Saccular	ACA aneurysm	Active SLE	Clipped	Dead
Segura et al. (1998)	No	1	Spontaneous SAH	No aneurysm in two angiographies	Active SLE	Steroids, gamma globulins and plasmapheresis	No neurological deficits
Tang et al. (2011)	Yes	1	Multiple fusiform dilatations	Multifocal (ICA, MCA, ...)	Active SLE	Conservative treatment	Gait disturbance

*Abbreviations:* PCoA: posterior communicating artery; BA: basilar artery; ACA: anterior cerebral artery; SLE: Systemic Lupus Erythematosus; MCA: middle cerebral artery; DSA: digital subtraction angiography SCA: superior cerebellar artery; EC-IC: extracranial-to-intracranial, ICA: internal carotid artery; PICA: posterior inferior cerebellar artery; NA: not available.

#### 4. Case 1: Distal fusiform aneurysm

##### 4.1. History and examination

A 34-year-old man complained of sudden severe headache and left-sided hemihypoesthesia. He had been diagnosed with SLE six months prior, and was being treated with prednisone, azathioprine and hydrochloroquine for his disease. On the neurological exam, he was alert and oriented. He had left hemibody hypoesthesia but no motor deficit was observed.

##### 4.2. Diagnostic studies

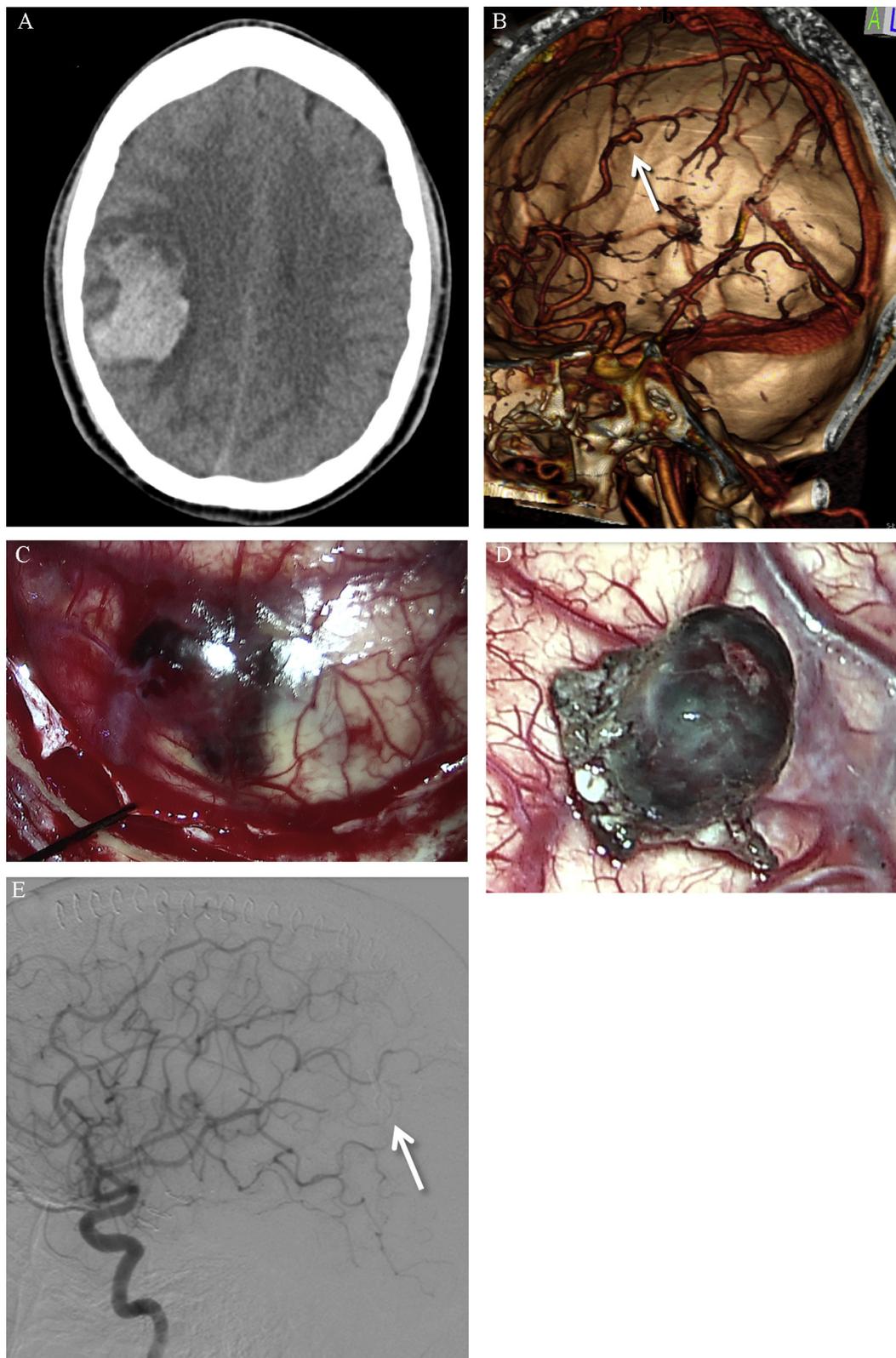
Head CT scan revealed a right-sided 25 cm<sup>3</sup> parietal hemorrhage with cortical SAH (Fig. 1a). CT angiography showed a 5 mm fusiform aneurysm of a right middle cerebral artery (MCA) M4 segment (Fig. 1b). The rest of the distal MCA and its branches had

normal caliber and course. No other vascular abnormalities were observed.

##### 4.3. Management

A right fronto-parietal craniotomy was performed and a wide dural opening exposed a tortuous, thickened angular artery with a 5 mm fusiform aneurysm (Fig. 1c and d). The aneurysm morphology prevented it from being occluded with regular neck clipping and therefore it was trapped. The inflow and outflow ends of the parent artery were too small and friable to suture, therefore, end-to-end re-anastomosis or any other direct revascularization options were discarded. The intraparenchymal hematoma was evacuated through a corticotomy in the parietal lobe to relieve the mass effect.

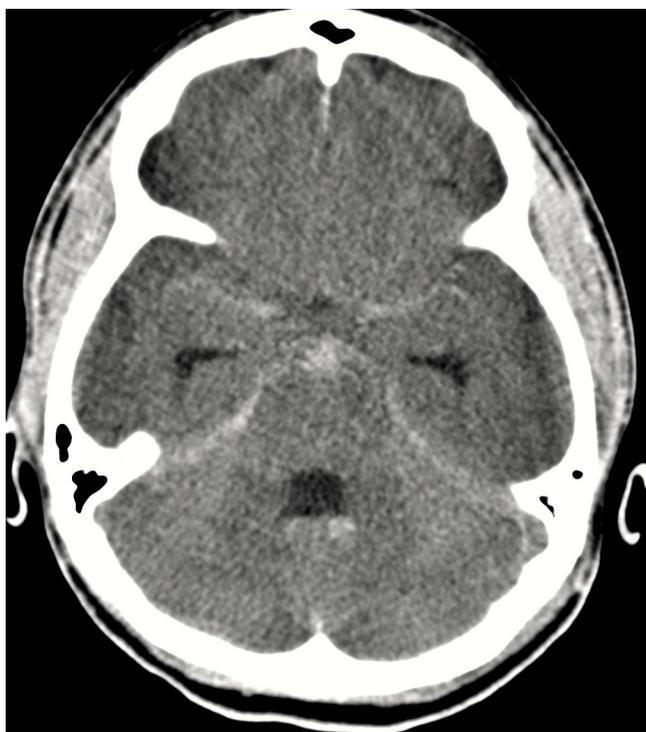
A postoperative angiogram demonstrated complete exclusion of the aneurysm and adequate filling of the entire right MCA territory despite the M4 occlusion (Fig. 1e). Histological examination



**Figure 1.** Imaging studies and intraoperative pictures of case 1. A: Preoperative brain CT-scan (axial view) showing the right parietal hematoma. B: Preoperative brain CT angiography (3D reconstruction) revealing a distal MCA M4 segment fusiform aneurysm (arrow). C: Postoperative imaging. Right internal carotid injection angiogram (lateral view) demonstrating complete occlusion of the aneurysm (arrow). D: Intraoperative picture showing the subarachnoid blood around the aneurysm prior to beginning of the dissection. E: Intraoperative picture showing the excluded and resected aneurysm that was sent to pathology for further study.

of the aneurysm wall demonstrated an intimal layer thickening, severe fragmentation and disappearance of elastic fibers suggesting a likely previous injury that originated the pseudoaneurysm. No fibrinoid necrosis was seen. Neither lymphocytes nor plasma

cells suggesting active vaculitis were identified. Postoperatively, the patient's hyposensitivity in the left side improved and he was discharged on postoperative day 11 with a modified Rankin Score (mRS) of 1.



**Figure 2.** Imaging studies of case 2. A: Brain CT scan (axial view) showing the initial Fisher IV subarachnoid hemorrhage.

## 5. Case 2: Angiographically negative SAH

### 5.1. History and examination

A 24-year-old woman was transferred to our hospital after a sudden severe headache and a generalized seizure. At the time of onset, she was admitted in another hospital where she was being studied for fever, nephritis, hypertension, arthritis and pleuropericarditis that finally led to a SLE diagnosis. Once in our hospital, the neurological exam revealed that she was disoriented both in time and space. No other neurological deficits were present at the time, but she developed severe agitation during the next few hours finally prompting orotracheal intubation for management. Head CT scan revealed a Fisher IV subarachnoid hemorrhage with an incipient ventricular dilatation (Fig. 2a). A four-vessels cerebral angiography revealed an infundibular origin of the right AICA as the only finding. But no aneurysms, arteriovenous malformations or dural arteriovenous-fistula were observed. Angiography revealed no findings consistent with vasculitis.

### 5.2. Management

Subsequent CT imaging confirmed the onset of hydrocephalus, which prompted placement of an external ventricular drain. The patient also presented a severe autoimmune leucopenia and thrombopenia (as low as 10,000 platelets) that was medically treated with steroids and danazol. Ten days after being admitted in the ICU, she developed a *Corynebacterium* sp ventriculitis and a methicillin-resistant *Staphylococcus* (MRSA) sepsis. These caused a severe worsening of her neurological status. Despite proper placing verified by CT, the EVD stopped working and required revision. In the setting of low platelet count, the revision provoked an intraventricular hemorrhage that slowly cleared over the course of two weeks. However the patient did not tolerate the closure of the ventricular drainage and a definitive ventriculo-peritoneal shunt was placed. Three months after her admission, she was transferred to a regular

hospitalization floor where she slowly recovered from a myopathic tetraparesis and bradypsychia secondary to the intraventricular hemorrhage. After spending a total of six months at our institution, she was transferred to a rehabilitation facility with a mRS of 4. Nineteen months after discharge she had improved to mRS 3. During a reevaluation of her SLE and a new severe drop of her platelet count to 15,000, she presented with another intraventricular hemorrhage and sepsis that finally led to her exitus.

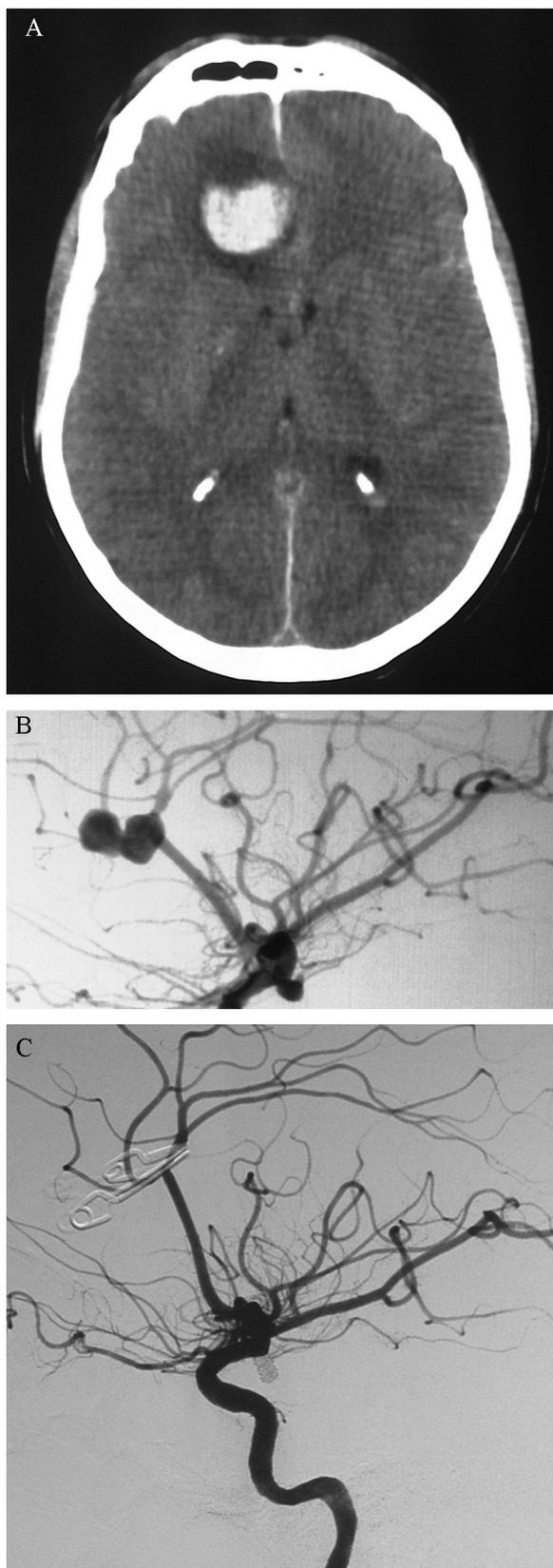
## 6. Case 3: Multiple aneurysms

The family of a 55-year-old man with a history of SLE, hypertension, smoking and alcohol abuse called the emergency services because he had suffered a sudden severe headache followed by a generalized seizure and a loss of consciousness. The emergency services found him in a Glasgow Coma Scale (GCS) 7 (eyes 1, verbal 1, motor 5); proceeded to orotracheal intubation and transfer to our center. Head CT scan revealed a Fisher IV subarachnoid hemorrhage with a 50 mm right frontal hematoma related to the genu of the corpus callosum with no midline shift or mass effect (Fig. 3a). A cerebral angiography showed a right 13 mm Anterior Cerebral Artery (ACA) pericallosal segment aneurysm and a 5 mm right Posterior Communicating Artery (PCoA) aneurysm (Fig. 3b).

The SAH distribution and the hematoma pointed toward the pericallosal aneurysm as responsible for the acute bleed. Considering the distal location and the wide neck of the aneurysm, surgical management was preferred as the first therapeutic option. A bifrontal craniotomy with a subarachnoid interhemispheric approach was performed. The course of the distal ACA branches were followed down the interhemispheric fissure and around the corpus callosum until the aneurysm was exposed at the pericallosal bifurcation and proximal control was gained. A straight 10 mm clip stacked up with another 5 mm straight clip was placed through the aneurysm neck. The surrounding hematoma was then evacuated. The PCoA aneurysm was considered unruptured and occluded endovascularly in a delayed fashion. A postoperative angiogram confirmed complete occlusion of the aneurysm and patency of the parent vessel (Fig. 3c). Initially the patient needed a ventricular drainage for acute hydrocephalus management, but no permanent shunt was necessary in the long term. He improved postoperatively and was discharged home 4 weeks after admission with a mRS of 3. At the last available follow-up, two years after the SAH, the patient had a mRS of 1.

## 7. Discussion

Central nervous system (CNS) involvement in systemic lupus erythematosus (SLE) is relatively common. Almost half of the patients suffer some kind of symptoms from CNS manifestations. Stroke, mostly ischemic but also hemorrhagic, accounts for 15% of CNS disease [11]. However, proof of vasculitis affecting the intracranial vessels and justifying the incidence of stroke is rare. Therefore, the real causes behind the CNS involvement remain unclear. Among the hemorrhagic strokes, the higher incidence of SAH in SLE patients is an even more intriguing matter. There are SLE patients with a SAH due to a saccular aneurysm as it occurs in the general population [12]. But most case reports of SLE patients presenting a SAH do not describe this as the source of the subarachnoid bleed. Uncommon lesions like distal fusiform aneurysms [7,9,13–16] or clinical entities like angio-negative SAH with an unusual torpid clinical course [10,17] are frequently described when SAH occurs in SLE. Multiple aneurysms outside the typical branching sites, are also frequently reported as the pathological finding in SLE patients with SAH [9,13,18–20]. Here we aim to summarize all this literature by describing what we found to be



**Figure 3.** Preoperative and postoperative imaging studies of case 3. A: Preoperative brain CT-scan (axial view) showing the right frontal hematoma abutting the genu of the corpus callosum and subarachnoid blood in the interhemispheric cistern. B: Right internal carotid artery angiogram, (lateral view). A 13 mm bilobulated pericallosal aneurysm and 5 mm PCoA aneurysm can be seen. C: Postoperative imaging. Right internal carotid injection angiogram (lateral view) demonstrating complete occlusion of both the pericallosal aneurysm and the PCoA aneurysms.

the three most typical clinical scenarios reported in patients with SAH and SLE. This tendency warrants further research that could establish a new clinical classification for SAH in SLE patients.

### 7.1. Etiology of SAH in SLE patients

These three unusual forms of SAH affecting SLE patients point toward an uncommon underlying physiopathology most likely related to the systemic disease. However, the real terms of this relationship and the reasons for the aforementioned increased SAH incidence in SLE patients remain unclear.

Classical risk factors for SAH such as atherosclerosis and hypertension happen to be relevant complications also seen in SLE. The treatment of SLE in the acute phases consists mostly of medical therapy with steroids and/or cytotoxic immunosuppressants. It is well known that these drugs can cause hypertension as a side effect [7,8,21], which could result in aneurysm formation and rupture, and therefore, could be one of the explanations for the higher rate of SAH in SLE patients. This hypothesis is also supported by the fact that higher daily steroid use (>10 mg) has been reported as an independent risk factor for increased incidence of SAH [4,9].

Vasculitis, when present, could also influence the incidence of SAH. Inflammation of arteries narrows the arterial lumen, compromises cerebral blood flow, and causes a variety of atherosclerotic-like symptoms leading to ischemia and hemodynamic stress, which have also been previously identified as aneurysms inducers. Furthermore, focal vasculitis could be the cause of the uncommon aneurysms in unusual locations that are frequently described in patients with SLE [10,22–24]. However, only three authors have been able to prove anatomopathological findings supporting focal transmural angiitis in fusiform aneurysms [14,19,24]. Our case #1—distal fusiform aneurysm—, represents one of these uncommon lesions. Anatomopathological findings in our patient revealed a pseudoaneurysm with a wall defect but without lymphocytic infiltration, and thus an active focal vasculitic process was ruled out. Therefore, although focal vasculitis might be a plausible explanation for the higher incidence of fusiform aneurysms in SLE patients, the inconsistent pathology reports should make us think of other primary and/or concomitant causes that we have missed so far [7,8,13,16].

Multiple aneurysms seem to occur more frequently in SLE patients. From our knowledge, only Owada et al. reviewed an incidence of single and multiple aneurysms of 69.5% and 31.6%, respectively, among Japanese SLE reports [10,20,25]. Saccular or berry aneurysms would be explained by an increased incidence of hypertension; fusiform distal aneurysms could be somehow related to focal vasculitis; but the higher incidence of multiple aneurysms in SLE patients lacks a plausible explanation. Unexpectedly, Akio Asai et al. [19] found a transmural angiitis in one of the saccular aneurysms of a SLE patient harboring multiple aneurysms. We presented a patient with multiple aneurysms (case #3) but no specimen was delivered to pathology in the surgical aneurysm and the other one was treated with endovascular procedures. Despite the lack of a solid evidence, the higher incidence of multiple aneurysms in SLE patients and the eventual presence of vasculitic pathological findings point toward a vasculitic component behind these SAH in SLE patients.

Several cases of SLE patients and SAH without pathological findings in the angiography have been reported [26,27]. Furthermore, most of these “angio-negative” cases rarely have a perimesencephalic blood distribution and some of them even had autopsy confirming the absence of cerebral aneurysms [10,28]. In the general population, angio-negative SAH is thought to be of venous origin, usually happens in older patients, has a typical perimesencephalic blood distribution, a benign clinical course and patients usually do not rebleed [29]. Case #2 of our report is an angio-negative

SAH in a very young patient. Her clinical course was extremely complicated due to low platelet count and various systemic complications. The patient spent six months admitted in the hospital dealing with all the consequences of what we initially thought would be a benign angio-negative SAH. Moreover, a year and a half later she was admitted again with another angio-negative SAH and ended up dying from systemic complications. Previous reports also describe an extremely high mortality rate in SLE patients with angio-negative SAH unless the patient has a venous-like perimesencephalic bleed [10,17].

### 7.2. Management strategy

Therapeutic management of SAH in these patients is not well established and depends highly on the underlying lesion causing the bleed and on the patient's clinical condition. The frequent hematologic and renal complications are important comorbidities for any kind of invasive procedure. The intraventricular hemorrhage described in patient #2 is a clear example what should have been a low risk procedure such as an EVD revision, turned into a serious complication due to an extremely low platelet count.

When an aneurysm is present and requires occlusion, both surgical and endovascular options are challenging [30]. Unexpectedly fragile intracranial arterial walls due to multifocal spread disease make them difficult to handle and could prompt a rupture during both surgical and endovascular procedures. Due to a non-saccular morphology, the aforementioned fragility and uncommon locations [7] these aneurysms are rarely amenable to direct clipping and instead require occlusion techniques like trapping and excision with or without revascularization. On top of that, in case a bypass is needed, selecting the appropriate donor and recipient vessels can be challenging due to the general distribution of the disease [31]. In Case #1, the aneurysm was distal enough to allow trapping of the MCA M4 segment without needing a revascularization bypass. In truth, the inflow and outflow ends of the vessel seemed too fragile and friable to even attempt re-anastomosis. Collateral circulation took over and the patient did not experience any new deficits from his arterial occlusion. However, neurosurgeons should be aware of these difficulties and plan several alternative bypasses in case a revascularization therapy is needed either as a primary or as a rescue therapy.

The development of saccular aneurysms in SLE patients may be unrelated to their systemic disease and account instead for a defect in the arterial wall just as it occurs in the general population [32,33]. The rupture, on the other hand, might be closely related to the SLE activity mainly due to complications like arterial hypertension secondary to active vasculitis. Therefore, in order to prevent SAH in SLE patients, not only the treatment of active SLE and its systemic complications is important but also a strict control of cardiovascular risks factors (smoking, hypertension, hypercholesterolemia) must be a core part of management strategy.

### 7.3. Clinical outcomes

Despite their younger age and regardless of the type of aneurysm they harbored, patient with SLE and SAH have a higher mortality rate than other SAH patients. In the only available population study, the in-hospital mortality rate for SLE patients was 60% vs. a 39% for the general population suffering a SAH [19]. Not only in aneurysmatic SAH hemorrhage, but also and surprisingly, in those with negative angiographies. This worst outcome could be explained due to the severe medical problems such as infections and hematologic issues related to the systemic disease. Case #2 was a young woman who presented with SAH and a good GCS, yet was admitted for more than 6 months in our hospital for multiple medical complications such as severe thrombopenia with multiple systemic bleedings and

nephritis. The poor prognosis in these patients, independently of their younger age, should be made part of the discussion in the decision making with the family and internal medicine colleagues. Obviously, we should achieve the best possible hematological status prior to invasive treatment.

Vasculitis when present and treatments like immunosuppressants or glucocorticoids could also influence the incidence of SAH. It seems that in some populations, older age, high dose (>10 mg daily) steroid intake, and previous transfusions of red blood cells or platelets are independent risk factors for SAH [4,34].

## 8. Conclusion

SAH is an infrequent but important manifestation of cerebral involvement in SLE and neurosurgeons should be aware of the special characteristics and technical difficulties associated with these patients. The angiography should be carefully reviewed looking for fusiform aneurysms in uncommon locations and searching all the vascular territories to rule out multiple aneurysms.

SLE patients might present SAH with no evidence of an aneurysm. Frequent systemic SLE complications like extremely low platelet count, or treatment related complications due to corticotherapy could be held accountable for these "angio-negative" forms of SAH. The scarce literature about it and the lack of definitive evidence prevent us from inferring a causality relationship. However, bad outcome of this form of "angio-negative" SAH may be expected and should be regarded by the physician.

Strict control of cardiovascular risk factors (smoking, hypertension, hypercholesterolemia), hematologic complications, and SLE reactivations could improve the outcome in these patients and should therefore be made a management priority.

This study of SAH in SLE patients is descriptive and does not allow us to explain their unique morphology and etiology. However, we provide a simple way of classifying the uncommon clinical patterns that are usually faced when dealing with SAH in a SLE patient. The real causes underlying the higher incidence of SAH in SLE patients remain yet unclear. Several physiopathological hypotheses provide a partial explanation, but further research is granted to fully understand the mechanisms behind this morbid form of hemorrhagic stroke. Prospective studies focused on the incidence of SAH, its clinical characteristics, aneurysm morphology and number, are warranted to fully understand the patterns of subarachnoid hemorrhage in this rheumatologic disease.

## Conflict of interest

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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## Author contributions

Torné was responsible for the conception and design of the study as well as for the acquisition, analysis and interpretation of data. He also drafted the article along with Rodríguez-Hernández and Bernard who were also responsible for other study aspects; Rodríguez-Hernández carried out the analysis and interpretation of data while Bernard in association with Aríkan, and Vilalta performed the Acquisition of data. Sahuquillo supervised the study. All authors critically revised the article.

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