Case Report
Multiple spontaneous intracranial hemorrhages in a patient with systemic lupus erythematosus: a case report

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Abstract: Spontaneous intracranial hemorrhage (ICH) has been reported in systemic lupus erythematosus (SLE) and is the important diagnostic evidence of neuropsychiatric systemic lupus erythematosus (NPSLE). Multiple spontaneous ICHs are uncommon in SLE. We report flare up of a left hemisphere spontaneous epidural hematoma (EDH) in a 45-year-old female patient with SLE. Active surgery and other treatments were performed, but new spontaneous ICHs in different locations were observed. The patient died as a result. To the authors’ knowledge, we have the first pathological report of cerebral dura mater vascular in SLE with spontaneous EDH. In SLE, cerebral dura mater vasculature can be involved, which may be an important cause of spontaneous EDH. Multiple spontaneous ICHs are very rare, but fatal in patients with SLE even after neurosurgery operations.

Keywords: Neurosurgery, intracranial hemorrhage, systemic lupus erythematosus

Introduction
SLE is a common kind of inflammatory autoimmune disease characterized by a heterogeneous clinical presentation. Previous studies have reported that patients with SLE are have an increased risk of spontaneous ICH [1]. Spontaneous ICH, which may result from thrombocytopenia, hypertension and hyperlipidemia, is a serious comorbidity of patients with SLE. Here we present a rare case of multiple spontaneous ICHs in a female SLE patient, whose first diagnosis was EDH, with the pathological report of cerebral dura mater vasculature.

Case report

History and presentation
A 45-year-old woman presented with a history of fever and cough followed by chest distress over 1 week for evaluation. The female was first admitted to the Department of Rheumatology, for her 6-year history of SLE. Her pulmonary computed tomography (CT) revealed infection.

On admission, her leukocyte count was 1.7×10⁹/l, and C-reactive protein (CRP) was 58.3 mg/l. She had positive anti-dsDNA and antinuclear antibodies. Antibiotics and glucocorticoids were given for her treatment. A bone marrow aspiration was performed by hematologists and the diagnosis of leukemia was excluded.

On day 7, the patient developed a severe headache with nausea and vomiting, followed by rapid unconsciousness. CT of the head demonstrated a left temporal-parietal spontaneous epidural hematoma (EDH) (Figure 1). Her family denied any history of head trauma.

Surgical procedure
The patient was treated with tracheal intubation and mechanical ventilation. Emergent craniotomy surgery was performed to clean up the EDH under general anesthesia. In the surgical procedure, we didn’t find any skull fracture line or congenital structure deformity. After the anesthesia recovery, she was conscious.

But just several hours later, the patient fell into unconsciousness again. Repeated CT scans showed a new left frontal EDH and occipital EDH with obvious shift of brain midline (Figure 2). After a comprehensive evaluation, we performed another emergency craniotomy surgery to remove the frontal EDH, followed by some
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Figure 1. Preoperative head CT scan demonstrating spindle high density shadow under left temporal parietal bone.

Figure 2. Postoperative head CT scan demonstrating new spindle high density shadows under left frontal and occipital bones.

Figure 3. After second surgery, first reviewed head CT scan demonstrating remission of brain midline shift.

After second surgery, first reviewed head CT scan demonstrating remission of brain midline shift. During the second operation, intracranial pressure was still not high. Postoperative CT scanning revealed remission of the brain midline shift (Figure 3). Although the occipital epidural hematoma enlarged a little, a new surgery was not necessary according to the surgery index.

Several hours later, review of head CT scan revealed severe changes that included increased spontaneous ICHs, global cerebral edema, multiple cerebral infarctions and serious shift of the brain midline (Figure 4). The patient had bilateral dilated pupils with severe intracranial hypertension. We planned an emergency decompressive hemicraniectomy, but the family rejected the procedure.

Histopathological findings of cerebral dura mater vasculature

During the second surgery, we took a cerebral dura mater sample (1 cm × 1 cm) with a section of larger artery which was filled with thrombosis and inflammatory cells. Few inflammatory cells were found infiltrating the vascular wall. Thrombosis and inflammatory cells were also found in vasa vasorum. Routine (H & E) stains showed a bit of calcification of the vessel wall. This is the first pathological report about cerebral dura mater vasculature in SLE with spontaneous EDH (Figure 5).

Other treatment strategies and clinical outcome

Besides the surgeries, we gave the patient hemostatic therapy, antibiotics to prevent infection, nutrition, glucocorticoids and other supporting treatments. Laboratory findings are summarized in Table 1. Blood transfusions were given. The condition of the patient continued to get worse. In the end, the patient died.

Discussion

In SLE, the brain may suffer from various damages that can result in NPSLE. The American
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1999. This case meets the inclusion criteria for NPSLE, which can present as either hemorrhagic or thrombotic stroke [2]. Headaches were the most common manifestation of NPSLE, followed by cerebrovascular disease (CVD) and seizure [3].

Eswar Krishnan reported that the rate of acute stroke in hospitalized patients (age ≤50 years) with SLE is 1.23%. It showed that patients with lupus are more likely to be hospitalized for the risk of ICH compared with the general population.

Table 1. Laboratory findings

<table>
<thead>
<tr>
<th></th>
<th>On admission</th>
<th>1 day before surgery</th>
<th>The day of surgery</th>
<th>After 1st surgery</th>
<th>After 2nd surgery</th>
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<tr>
<td>White blood cell count (× 10^9/l)</td>
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<td>9.40</td>
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<td>Red blood cell count (× 10^{12}/l)</td>
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<td>3.85</td>
<td>3.89</td>
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<tr>
<td>Platelet count (× 10^9/l)</td>
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<td>150.00</td>
<td>66.00</td>
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<tr>
<td>D-dimer (mg/l)</td>
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<td>Procalcitonin (ng/ml)</td>
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<td>Immunoglobulin G (g/l)</td>
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<td>Immunoglobulin A (g/l)</td>
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<td>Immunoglobulin M (g/l)</td>
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<td>Complement factor 3 (C3) (g/l)</td>
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<td>Complement factor 4 (C4) (g/l)</td>
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<td>C-reactive protein (mg/l)</td>
<td>58.30</td>
<td>83.20</td>
<td>25.30</td>
<td>16.80</td>
<td>31.50</td>
</tr>
</tbody>
</table>

Figure 4. After second surgery, second reviewed head CT scan demonstrating high density shadows in multiple lesions, multiple low density shadows, global cerebral swelling and obvious shift of brain midline.

Figure 5. Histopathology of vascular of dura mater showing thrombosis, inflammatory cells and calcification.
Either stable or active SLE patients could suffer from spontaneous ICH. N Gao et al. reported that the ICH prevalence of SLE was 0.39% in Peking Union Medical College Hospital in a 18-year period. 88.5% of the patients were female in that study and short-term prognosis was very poor, with a rate of in-hospital fatality of 23.1%. Headache, disturbance of consciousness and multiple hemorrhages are common in many patients. Cerebral infarction was presented in a considerable portion of SLE patients with ICH [4].

The causes of ICH in SLE are complex, which may include thrombocytopenia, hemorrhagic infarction, hypertension, disturbance of blood coagulation and CVDs. Thrombocytopenia presented more frequently in SLE patients with ICH than ones without ICH, and it was an independent risk factor [4]. The pathogeneses of thrombocytopenia may include antibodies in platelet destruction, administration of immunosuppressive agents, antiphospholipid antibodies, thrombotic microangiopathy, bone marrow depression and megakaryocyte maturation disorders. In the report of Yoshiyuki Arinuma about ICH in SLE, it suggested that ICH was induced by thrombosis and arteritis [5].

Antibodies could cause cerebrovascular injury, which may be an important cause of ICH [2]. Previous studies revealed the evidence of widespread likely multifactorial vasculopathy. Cerebral vascular pathological changes caused by development of autoimmunity were characterized by cerebral thrombosis, cerebral infarction and cerebral hemorrhage [6]. Researchers have demonstrated the existence of inflammation in intracranial arteries in SLE with ICH through pathological findings [7]. However, classic vasculitis and immune deposits were found to be rare. In the study of Yoshiyuki Arinuma, the histopathological examination revealed a necrotizing vasculature, which filled with thrombi and infiltrated with inflammatory cells, and disrupted lamina elastica interna [5]. It was thought that ICH could be induced by thrombosis and arteritis and that chronically repeated thromboses could lead to multiple cerebral infarctions in SLE.

In Irene Rozet’s case report, the patient had similar development to this case that included initial ICH and relative surgery, then new ICHs, with progressive cerebral swelling and infarctions, and again in the end the patient died. This suggested that prominent endothelial dysfunction with hypercoagulation played a major role in active SLE and contributes to the development of cerebral infarcts. There may be a vicious circle that could result in ICH, uncontrolled progressive global brain swelling, development of cerebral infarction and herniation in SLE patients [8].

How to predict ICH in SLE? Magnetic resonance imaging (MRI) may be a helpful neuroimaging technique and could provide useful information in the study of spontaneous ICH in SLE. Common MRI findings in SLE include white matter hyperintensity, brain atrophy, and infarction. A recent study suggested that punctate white matter hyperintensity reflected vasculopathy [9]. SLE patients with CVD were more likely to exhibit gray matter hyperintensities, parenchymal defects, and abnormal diffusion-weighted imaging [10].

In conclusion, spontaneous ICH is a kind of severe complication of SLE due to the multiple bleeding tendency. Headaches in SLE patients should be paid careful attention, and MRI could provide useful clues to spontaneous ICH. Autoimmune pathogenesis can cause diffuse brain injury, that would make the brain more vulnerable compared with the general population. Cerebral dura mater vasculature could be involved, which may be an important cause of spontaneous EDH. Various types of cerebrovascular events, including cerebral thrombosis, cerebral infarction and cerebral hemorrhage, could expand in SLE patients and result in poor prognosis, like this patient. Neurosurgeons should be more cautious when a SLE patient presents with spontaneous ICH for its greater instability compared with the general population. In this case, besides removing the hematoma, decompressive craniectomy may be considered earlier, even when initial intracranial pressure is not high, to alleviate the possibly of multiple spontaneous ICHs and cerebral swelling.

Disclosure of conflict of interest

None.

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References


