SPONTANEOUS INTRACRANIAL HAEMORRHAGE AS PART OF THE INITIAL MANIFESTATION OF CHILDHOOD SYSTEMIC LUPUS ERYTHEMATOSUS: AN UNUSUAL CLINICAL PRESENTATION

Bibi Nabiilah Auckburally1,2, Anis Munirah Mohd Kori1,2, Ahmad Hadif Zaidin Samsudin1,2, Mohamad Ikram Ilias1,2*

Abstract
Childhood-onset systemic lupus erythematosus is a systemic autoimmune disorder with a variety of clinical manifestations. Most children and adolescents experience the gradual onset of prolonged fever, weight loss, fatigue, and arthralgia over weeks or months. Nonetheless, isolated haematological abnormalities are unusual as an initial clinical manifestation. We report a case of spontaneous intracranial haemorrhage due to severe thrombocytopenia as part of the initial manifestation of SLE in childhood. A high index of suspicion is necessary to diagnose systemic lupus erythematosus in children who present with unexplained spontaneous intracranial haemorrhage and isolated thrombocytopenia as an initial presentation.

Keywords: Childhood-onset systemic lupus erythematosus; discoid rash; gingival bleeding; intracranial hemorrhage; petechiae; thrombocytopenia
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Introduction
The pathogenesis of systemic lupus erythematosus (SLE) is multifactorial and comprises environmental and genetic factors, a breach in immunologic self-tolerance, and the development of autoimmunity. Childhood-onset SLE (cSLE) is associated with a more severe disease phenotype than adult-onset SLE [1]. Those diagnosed with cSLE at a younger age (less than 10 years) have a worse prognosis [2]. Approximately 50% of adolescents with SLE have thrombocytopenia, but it is typically mild, with platelet counts between 100 and 150 x 10⁹/L, and haemorrhage is uncommon [1]. Nonetheless, platelet counts below 10 x 10⁹/L and associated mucocutaneous haemorrhage are possible. Childhood-onset systemic lupus erythematosus is a systemic autoimmune disorder with a variety of clinical manifestations. Most children and adolescents experience the gradual onset of prolonged fever, weight loss, fatigue, and arthralgia over weeks or months. Nevertheless, isolated haematological abnormalities are uncommon. We report a case of spontaneous intracranial haemorrhage due to severe thrombocytopenia as part of the initial manifestation of SLE in childhood.

Case report
A 10-year-old Malay girl presented with fever and persistent gingival bleeding for 1 week following tooth extraction. She recalls having easy bruising all over her body and spontaneous bleeding when brushing her teeth for years, but she never sought medical attention. She is the youngest of seven siblings, and her eldest sister passed away at the age of 16 with an intracranial bleed secondary to SLE. Upon physical examination, multiple petechial rashes were discovered on her face and upper chest (Figure 1). Other systemic examinations were unremarkable. Her first full blood count revealed pancytopenia. A full blood picture confirmed the absence of blast cells.

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1Department of Pediatrics, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kota Bharu, Kelantan, Malaysia
2Hospital Universiti Sains Malaysia (HUSM), Health Campus, Kubang Kerian, 16150 Kota Bharu, Kelantan, Malaysia
3Department of Radiology, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kota Bharu, Kelantan, Malaysia
*Corresponding Author:
Mohamad Ikram Ilias, Department of Pediatrics, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kota Bharu, Kelantan, Malaysia
Hospital Universiti Sains Malaysia (HUSM), Health Campus, Kubang Kerian, 16150 Kota Bharu, Kelantan, Malaysia
Telephone: 609-767 6537 Email: dirikram@usm.my
The coagulation profile was normal, and a few infectious screenings were negative. Screening for connective tissue disease showed positive results for antinuclear antibody (ANA) and anti-double-stranded deoxyribonucleic acid antibodies (anti-dsDNA Abs). A summary of the laboratory analysis is shown in Table 1.

The patient initially received multiple platelet transfusions, but the platelet count remained unchanged. On day 10 of admission, she received one dose of intravenous immunoglobulin, with a modest increase in platelet count but still below 50 x 10^9/L. During her hospitalisation, she also developed a neutropenic fever that necessitated the intravenous administration of imipenem and amphotericin B. Serial cultures of blood and urine were negative. On day 11 of her hospitalization, she presented with a persistent fever, an intermittent mild headache, and minimal post-prandial vomiting. She was referred to an ophthalmologist to exclude the possibility of eye involvement. The ophthalmologic examination revealed normal visual acuity in both eyes. Fundoscopy revealed bilateral tortuous veins, an elevated optic disc, and a splinter haemorrhage in the left eye. As a result, we proceeded with brain imaging. A computerised tomography (CT) scan of the brain (Figure 2) revealed acute subdural haemorrhage in the bilateral parietal and right frontal regions, extending into the interhemispheric fissure. The optic nerve sheath diameters on both sides were within the normal range.

Due to the presence of positive ANA and anti-dsDNA, a discoid rash on her face, and haematological involvement, she met SLE criteria and was treated with intravenous methylprednisolone for three days and prophylactic levetiracetam. Her symptoms improved as the pancytopenia resolved, and she was subsequently discharged on hydroxychloroquine and prednisolone.

**Figure 1.** Petechiae rash (arrow) and discoid rash (arrow head) on the face.

**Figure 2.** Axial (Figs 2a and 2c) and coronal (2b) views of a CT scan of the brain showed bilateral subdural hemorrhage (arrow head) in the bilateral parietal region, the frontal region (*) and the interhemispheric fissure (arrow).
Table 1. Laboratory analysis

<table>
<thead>
<tr>
<th>Blood</th>
<th>Result</th>
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<tr>
<td>WBC (10^9/L)</td>
<td>4.6</td>
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<tr>
<td>Haemoglobin (g/L)</td>
<td>9.4</td>
</tr>
<tr>
<td>MCV</td>
<td>78</td>
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<tr>
<td>MCH</td>
<td>34</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>28</td>
</tr>
<tr>
<td>Platelets (10^9/L)</td>
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<th>Connective tissue disease screening</th>
<th>C3 (g/L)</th>
<th>C4 (g/L)</th>
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<td>Positive</td>
<td>1.1</td>
<td>0.2</td>
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<table>
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<tr>
<th>Anti-dsDNA antibody</th>
<th>Positive</th>
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<tr>
<td>(titre 573.8)</td>
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<tr>
<th>RF§</th>
<th>Negative</th>
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<tr>
<td>IPF¶</td>
<td>2.4%</td>
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<tr>
<td>EBV IgM</td>
<td>Negative</td>
<td></td>
<td></td>
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<tr>
<td>CMV IgM</td>
<td>Negative</td>
<td></td>
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<tr>
<td>Mycoplasma IgM</td>
<td>Negative</td>
<td></td>
<td></td>
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<tr>
<td>HepBs Ag§</td>
<td>Negative</td>
<td></td>
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<tr>
<td>Anti-HCV¶</td>
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<tr>
<td>VDRL</td>
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<td></td>
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<tr>
<td>ELISA for HIV</td>
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<td>Prothrombin time (sec)</td>
<td>13</td>
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<tr>
<td>Active partial thromboplastine</td>
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<tr>
<td>time (sec)</td>
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<tr>
<td>INR§</td>
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<tbody>
<tr>
<td>Anti-double-stranded deoxyribonucleic acid (anti-dsDNA), Cytomegalovirus (CMV), enzyme-linked immunosorbent assay (ELISA) for human immunodeficiency virus (HIV)</td>
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<tr>
<td>§ rheumatoid factor (RF), Hepatitis B surface antigen (HepBs Ag)</td>
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<tr>
<td>¶ immature platelet fraction (IPF), anti-Hepatitis C virus antibody (Anti-HCV)</td>
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Discussion

Intracranial haemorrhage continues to be a rare but potentially fatal manifestation of cSLE. Komvilaisak et al. reported cases of intracranial haemorrhage in patients with SLE and the lupus anticoagulant-hypoprothrombinaemia syndrome [3]. This syndrome increases the risk of haemorrhage due to the presence of anti-prothrombin antibodies, as demonstrated by a prolonged prothrombin time and partial thromboplastin time [4]. In our case study, however, the INR and prothrombin time were normal, and the partial thromboplastin time was slightly prolonged. Therefore, the intracranial haemorrhage is most likely caused by severe thrombocytopenia. N Gao et al. analysed the clinical characteristics and risk factors of intracranial haemorrhage in SLE; headache was the most prevalent symptom (53.5%), the anatomical localization of the cerebral haemorrhages was predominately in the cerebrum, intracranial haemorrhage could occur in patients with stable or active SLE. Furthermore, SLE patients with intracranial haemorrhage presented with neuropsychiatric syndromes, thrombocytopenia and antiphospholipid syndrome more frequently than SLE without intracranial haemorrhage [5]. In this case, we should conduct additional testing for antiphospholipid syndrome and screen for neuropsychiatric disorder.

In some cases, primary immune thrombocytopenia has been found to be a precursor to full-blown SLE [6]. In our case study, the patient's history of bleeding extends back several years, but she did not seek medical attention. Therefore, we were unable to identify any underlying immune thrombocytopenia prior to the patient’s presentation. This case demonstrates the significance of ophthalmological evaluation in assisting and guiding the evaluation of additional disease symptoms. The patient's symptoms are not indicative of a typical intracranial haemorrhage, but the results of the fundoscopy suggest that brain imaging is warranted. This child presents with a diagnostic conundrum of severe thrombocytopenia. Despite undergoing several platelet transfusions, the platelet count remained unchanged. She was given intravenous immunoglobulin along with a slight increase in platelets. Despite a negative septic screening, she presented with neutropenic fever and was receiving intravenous administration of imipenem and amphotericin B.

CNS involvement is relatively prevalent in SLE. The nature of vasculitis that impacts intracranial vessels remains unknown [7]. However, there has been a case report of a cerebral aneurysm [8].

Conclusion

SLE in children can manifest with atypical symptoms; therefore, a high index of suspicion is required for diagnosis. Prompt diagnosis and aggressive initial treatment can aid in preventing the morbidity and mortality associated with SLE in children.

List of abbreviations

Anti-double-stranded deoxyribonucleic acid antibodies (anti-dsDNA Abs).
Antinuclear antibody (ANA)
Childhood-onset SLE (cSLE)
Computerised tomography (CT)
Systemic lupus erythematosus (SLE)
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Conflict of interest
We have no conflict of interest to declare.

Ethical approval
There is no ethical issue.

Consent
The parent gives written informed consent for publication of the manuscript and photos.

Author contribution
MII, AHZS and BNA conceived, provided materials and designed the case report. BNA and MII wrote the initial and final draft of the article. AMMK edited and submitted the report to the journal. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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References