

Clinical Features and Diagnosis-Treatment Strategy of Childhood Systemic Lupus Erythematosus Complicated with Hypoprothrombinemia-Lupus Anticoagulant Syndrome

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Abstract

Objective

This study aimed to analyze the clinical features, laboratory findings, diagnostic approaches, and treatment strategies of childhood Systemic Lupus Erythematosus (cSLE) complicated with Hypoprothrombinemia-Lupus Anticoagulant Syndrome (HLAS). The goal was to enhance the early recognition and standardized management of this rare complication.

Methods

A retrospective analysis was conducted on the clinical data of a 10-year-old female child diagnosed with cSLE and HLAS. Additionally, a systematic review of relevant literature was performed by searching PubMed, CNKI, and Wanfang databases from their inception up to September 2025.

Results

The child initially presented with skin ecchymosis and rash. Coagulation tests revealed a significant reduction in the activity of multiple coagulation factors (factor II [FII]: 17.5%, factor III [FIII]: 4.9%), accompanied by marked prolongation of activated partial thromboplastin time (APTT) and prothrombin time (PT). Lupus Anticoagulant (LA) testing showed LA1 of 122.0 s and LA2 of 57.5 s, resulting in an LA1/LA2 ratio of 2.12—indicating the presence of high-titer LA. Thromboelastography (TEG) demonstrated a hypocoagulable state (R time: 12.8 min, Angle: 43.9°, Coagulation Index [CI]: -8.1%), which was consistent with the pathophysiological mechanisms of coagulation factor consumption and LA interference. Following confirmation by a multidisciplinary team, the child was treated with glucocorticoids, hydroxychloroquine, and belimumab, without prophylactic coagulation factor replacement. As the cSLE condition was controlled, coagulation parameters gradually improved. Literature review indicated that HLAS primarily manifests with bleeding symptoms, is prone to misdiagnosis, and requires immunosuppressive therapy as the cornerstone of treatment.

Conclusion

HLAS is a significant complication of cSLE, driven by autoimmune-mediated coagulation factor consumption. Diagnosis relies on the combination of LA detection, coagulation factor activity assays, and TEG assessment. Management should focus on immunosuppressive therapy, and multidisciplinary collaboration is essential to balance the risks of bleeding and thrombosis.

1. Introduction

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease characterized by multi-organ involvement and the production of various autoantibodies. Compared with adult-onset SLE, childhood-onset SLE (cSLE) typically has a more acute onset, faster progression, and more severe disease course. It is also more likely to involve the kidneys and hematological system [1]. Hematological abnormalities are common in children with cSLE; in addition to leukopenia, anemia, and thrombocytopenia, coagulation dysfunction also requires close attention [2].

Hypoprothrombinemia-Lupus Anticoagulant Syndrome (HLAS) is a rare but potentially life-threatening complication in patients with SLE. First described by Rapaport et al. in 1960, its core features include the coexistence of Lupus Anticoagulant (LA)—an antiphospholipid antibody that prolongs phospholipid-dependent coagulation time in vitro—and a significant reduction in prothrombin (factor II) activity, ultimately leading to a bleeding tendency [3]. In 2009, Hua et al. reported the first case of HLAS in China [4]. Unlike the Antiphospholipid Syndrome (APS)—which is usually associated with SLE and causes a hypercoagulable state—HLAS exhibits the opposite pathological characteristics, presenting a unique clinical paradox [5].

Due to the extremely low incidence of HLAS in children and insufficient clinical awareness, it is easily confused with hemophilia, vitamin K deficiency, liver failure, or disseminated intravascular coagulation (DIC), leading to inappropriate treatment [6]. By analyzing the clinical data of a child with cSLE complicated with HLAS and reviewing relevant literature, this study explores the pathogenesis, clinical features, diagnostic approaches, and treatment strategies of HLAS. The aim is to provide references for early clinical recognition and standardized management, and to improve the diagnosis and treatment of this syndrome among pediatric clinicians.

2. Case Data

2.1 Basic Information

A 10-year-and-6-month-old female child was admitted to the hospital on September 15, 2025, due to "persistent skin ecchymosis for more than 1 month, accompanied by rash for 1 week".

2.2 Present Illness

On August 2, 2025, the child developed ecchymosis on both lower limbs without an obvious inducement. Coagulation tests at another hospital showed a significantly prolonged APTT (73.3 s), but no special treatment was administered. Subsequent monitoring revealed that APTT fluctuated between 68.4 and 80.3 s. Coagulation factor activity testing indicated decreased levels of multiple factors (factor II [FII]: 31%, factor III [FIII]: 35.1%, FIV: 15.8%, factor V [FV]: 18.4%). In the past 3 weeks, she developed migratory joint pain involving the knees, ankles, and wrists; in the past 1 week, polymorphous rash appeared on the extremities, some accompanied by induration, without pruritus. On September 15, 2025, a complete blood count at another hospital showed leukopenia ($2.29 \times 10^9/\text{L}$), hemoglobin of 116 g/L, and platelets

of $154 \times 10^9/L$; erythrocyte sedimentation rate (ESR) was elevated (110 mm/h); immunoglobulin G (IgG) was increased (20.96 g/L). The child was transferred to our hospital for further diagnosis and treatment.

2.3 Past History, Personal History, and Family History

The child's father and paternal grandfather had polycystic kidney disease; there was no history of other genetic diseases or similar family conditions.

2.4 Physical Examination on Admission

Vital signs were stable, and the child was alert with a normal mental state. Multiple enlarged lymph nodes were palpable in the neck, the largest measuring approximately $2.0 \text{ cm} \times 1.0 \text{ cm}$, without tenderness. Polymorphous rash was scattered on the extremities, some accompanied by induration, which did not fade with pressure; scattered ecchymosis and petechiae were present on both lower limbs. No obvious abnormalities were found in the cardiopulmonary, abdominal, or neurological examinations.

2.5 Auxiliary Examinations

2.5.1 Hematological Tests

Persistent leukopenia ($2.29\text{--}3.56 \times 10^9/L$); mild anemia (hemoglobin: 109–116 g/L); direct antiglobulin test (Coombs test) was positive.

2.5.2 Coagulation Function Tests

APTT was persistently prolonged (68.4–80.3 s), and PT was also prolonged (18.1–21.5 s); international normalized ratio (INR) was elevated (1.62–1.94).

A recheck of coagulation factor activity on September 19, 2025, showed: FⅡ 17.5%, factor Ⅲ (FⅢ) 76.4%, factor Ⅳ (FⅣ) 76.2%, FⅤ 29.8%, FⅥ 20.2%, factor Ⅶ (FⅦ) 66.7%, FⅧ 4.9%, FⅨ 12.0%—indicating a significant reduction in the activity of multiple factors.

LA function confirmation test results: LA1 was 122.0 s (reference range: 31.0–44.0 s), significantly prolonged; LA2 was 57.5 s (reference range: 30.0–38.0 s), prolonged; standardized ratio (LA1/LA2) was 2.12 (reference range: 0.80–1.20), which was > 1.2 . This confirmed LA positivity and indicated the presence of high-titer LA.

TEG indicated a hypocoagulable state (see Section 2.5.6 for details).

2.5.3 Immunological Tests

Antinuclear antibody (ANA) was positive at a titer of 1:320 (homogeneous pattern); anti-double-stranded DNA (anti-ds-DNA) antibody was 346.77 IU/mL; anti-cardiolipin antibody (ACA) was $> 400.0 \text{ U/mL}$; anti-ribosomal P protein antibody was positive; complement C3 (0.26 g/L) and complement C4 (0.02 g/L) were significantly reduced.

2.5.4 Kidney-Related Tests

Urinalysis showed occult blood (3+), with 2–5 red blood cells per high-power field (HPF) under microscopy, and approximately 70% of the red blood cells were abnormal in shape; urinary microalbumin was elevated (80 mg/L). Imaging examinations revealed multiple cysts in both kidneys, consistent with the manifestations of polycystic kidney disease.

2.5.5 Other Examinations

Bone marrow aspiration and biopsy ruled out hematological malignancies; echocardiography and electrocardiography showed no abnormalities.

2.5.6 Thromboelastography (TEG) Assessment

TEG results on September 24, 2025: R time 12.8 min (reference range: 5–10 min, prolonged); K time 4 min (reference range: 1–3 min, prolonged); Angle 43.9° (reference range: 53–72°, decreased); Maximum Amplitude (MA) 50.5 mm (reference range: 50–70 mm, at the lower limit of normal); CI -8.1% (reference range: -3 to 3%, indicating hypocoagulability); A 50.9 mm; G 5099.4 d/sc; LY30 0% (normal). Overall, TEG indicated delayed coagulation initiation, slowed fibrin formation, and a hypocoagulable state—consistent with the mechanisms of factor activity reduction and LA interference. Fibrinolysis was normal, ruling out bleeding caused by hyperfibrinolysis.

2.6 Diagnostic Results

After discussion by the multidisciplinary team, the final diagnoses were:

1. Childhood Systemic Lupus Erythematosus (cSLE)
2. Hypoprothrombinemia-Lupus Anticoagulant Syndrome (HLAS)
3. Autosomal Dominant Polycystic Kidney Disease (ADPKD)
4. Tonsillar Hypertrophy with Adenoidal Hypertrophy

2.7 Treatment and Outcome

After diagnosis, the treatment focus was shifted to immunosuppression to control SLE activity. The child was given oral prednisone (0.75-1 mg/kg/day) combined with hydroxychloroquine; belimumab was added later. No prophylactic infusion of plasma or coagulation factor products was administered. Meanwhile, symptomatic support measures such as calcium supplementation and kidney protection were provided, and bleeding prevention was strengthened. After treatment, the child had no new bleeding episodes, and coagulation parameters gradually improved. After the condition stabilized, the child was transferred to the Department of Nephrology and Rheumatology for long-term follow-up management.

3. Discussion

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease, whose core pathogenesis involves immune dysregulation leading to the massive production of autoantibodies that attack multiple

organs. Childhood-onset SLE (cSLE) is generally more severe than adult-onset SLE, with a more acute onset, more frequent organ involvement (especially the kidneys and central nervous system), and high disease activity—seriously affecting the child's growth and development as well as quality of life [7]. Hematological abnormalities are a common manifestation of cSLE, occurring in more than half of affected children. These abnormalities include autoimmune hemolytic anemia, leukopenia, lymphopenia, and thrombocytopenia; some children even present with hematological abnormalities as the initial symptom [8].

Among hematological abnormalities, the management of coagulation dysfunction is particularly complex and presents obvious contradictions. Traditionally, antiphospholipid antibodies (aPLs) associated with SLE—especially LA—interfere with phospholipid-dependent coagulation reactions in vitro, leading to prolongation of indices such as APTT. However, this in vitro "anticoagulant" phenomenon is inconsistent with the in vivo effect: in vivo, LA can induce Antiphospholipid Syndrome (APS), leading to a hypercoagulable state and increased thrombotic risk [9]. This contradiction between "anticoagulation in vitro and procoagulation in vivo" has long been a focus of research [10].

Against this background, the occurrence of HLAS further complicates the management of coagulation in cSLE. Characterized by the coexistence of abnormal LA activity and a significant reduction in prothrombin (FII) activity [5], this syndrome breaks the traditional understanding that LA is usually associated with thrombosis, shifting the clinical manifestation to a bleeding tendency. It thus represents a unique clinical paradox in SLE-related coagulation dysfunction [5].

The pathophysiological core of HLAS is autoimmune-mediated coagulation factor consumption. Currently, it is believed that HLAS is closely related to anti-prothrombin autoantibodies. These antibodies cause bleeding through two main mechanisms: first, they bind to prothrombin to form complexes, which are rapidly cleared by the mononuclear phagocyte system—resulting in a sharp decrease in plasma prothrombin concentration and activity [5]; second, some antibodies directly interfere with the conversion of prothrombin to thrombin or block the assembly of the prothrombinase complex, inhibiting the common coagulation pathway. The coexistence of LA may further aggravate coagulation disorders on the phospholipid surface, collectively leading to severe bleeding [11, 12].

Pediatric HLAS is extremely rare, and its incidence in cSLE remains unclear. Most literature consists of case reports, with an estimated incidence of approximately 0.7%-1.8% [13]. Despite its rarity, HLAS is potentially life-threatening. Insufficient clinical awareness often leads to misdiagnosis: when children with cSLE present with unexplained bleeding accompanied by significant prolongation of PT and APTT, HLAS should be suspected to avoid misdiagnosis as hereditary coagulation factor deficiency, vitamin K deficiency, liver failure, or DIC. Inappropriate treatment—such as blind infusion of blood products—not only has a short-term effect but may also exacerbate the disease due to the "antibody enhancement effect" or induce thrombosis [14].

Therefore, the accurate diagnosis of HLAS requires a high degree of vigilance and the integration of precise laboratory assessments. For suspected cases, in addition to routine coagulation screening (PT,

APTT), it is essential to perform coagulation factor activity assays (especially FⅢ:C) and standardized LA function confirmation tests. The LA results of this case (LA1 122.0 s, LA2 57.5 s, ratio 2.12) met the LA positivity criteria of the International Society on Thrombosis and Haemostasis (ISTH) [16, 17]. The coexistence of a significant reduction in FⅢ:C and strongly positive LA (e.g., ratio > 2) is the key laboratory basis for diagnosing HLAS [15, 16].

The value of Thromboelastography (TEG) in HLAS management: TEG can comprehensively assess the entire coagulation process and has unique advantages in the diagnosis and treatment of HLAS. Unlike traditional tests that only reflect partial links of coagulation, TEG enables dynamic monitoring of the coagulation process. In this case, TEG showed a hypocoagulable state (prolonged R time, decreased Angle, negative CI)—consistent with the mechanisms of factor consumption and LA interference. This helped to accurately assess bleeding risk and rule out other causes such as DIC and hyperfibrinolysis. Especially in the presence of LA, traditional coagulation tests may show false prolongation due to interference, while TEG can more truly reflect the in vivo coagulation balance. In addition, TEG results can guide treatment: for example, a hypocoagulable pattern supports prioritizing immunosuppressive therapy, avoiding blind infusion of blood products. Therefore, for children with suspected HLAS, TEG is recommended as an important supplementary assessment tool to facilitate the precise balance of bleeding and thrombotic risks [17].

Based on the autoimmune nature of HLAS, its treatment strategy differs fundamentally from that of hereditary coagulation factor deficiency. The core goal is to rapidly and effectively inhibit abnormal immune responses. Glucocorticoids, as first-line drugs, can quickly suppress antibody production and the clearance of immune complexes; combined with hydroxychloroquine, they help control the underlying SLE condition and exert immunomodulatory effects. For severe cases or those unresponsive to glucocorticoids, second-line immunosuppressants or biological agents should be considered [18]. The infusion of blood products should be strictly indicated: it is only used for active, life-threatening bleeding as "bridging" support before the onset of immunosuppressive effects, and close monitoring of thrombotic risks is required [19]. The entire diagnosis and treatment process emphasizes collaboration among a multidisciplinary team (MDT) including rheumatology and immunology, hematology, transfusion medicine, and intensive care units. Through joint assessment, the MDT achieves a precise balance between bleeding and thrombotic risks, and between the intensity of immunosuppression and infection risks [20].

4. Conclusion

Childhood Systemic Lupus Erythematosus complicated with HLAS (cSLE-HLAS) is a rare clinical disease but potentially fatal, belonging to a clinical emergency.

1. The paradoxical nature of clinical features and their warning significance: The most prominent feature of HLAS is a bleeding tendency, which contradicts the traditional understanding that LA is usually associated with thrombosis. Therefore, for children with confirmed or suspected cSLE, if

they present with bleeding that cannot be explained by common causes and is accompanied by significant prolongation of PT and APTT, HLAS should be considered first.

2. Precise laboratory assessment is the key to diagnosis: The diagnosis of HLAS relies on a characteristic "triad": $\square$ positive LA; $\square$ significant reduction in F $\square$:C (often < 20%); $\square$ exclusion of other causes of coagulation dysfunction. It is necessary to complete coagulation factor activity assays, standardized LA function verification, and antiphospholipid antibody profile testing. TEG can comprehensively assess coagulation function, reduce misjudgment caused by LA interference, and more truly reflect the hypocoagulable state—providing important references for diagnosis and risk balance.
3. Immunosuppression is the core treatment strategy: The core of HLAS treatment is to control the active phase of the underlying SLE disease. An immunosuppressive regimen combining low-to-moderate dose glucocorticoids with hydroxychloroquine is the main approach, which can effectively inhibit the production of autoantibodies and promote the recovery of prothrombin levels, and most children respond well to this regimen.
4. Blood product infusion should follow a prudent principle: Prophylactic or routine infusion of fresh frozen plasma and prothrombin complex concentrate in children with HLAS should be avoided. Such infusions are only used as bridging support before the onset of immunosuppressive effects in cases of active, life-threatening bleeding, while related risks should be vigilantly monitored [22].
5. Multidisciplinary collaborative management is crucial: The effective management of cSLE-HLAS depends on close collaboration among MDT members including rheumatology and immunology, hematology, transfusion medicine, and intensive care units. The MDT model enables the optimization of the entire process from rapid recognition and accurate diagnosis to individualized treatment, providing higher-quality diagnosis and treatment for children.

5. Clinical Implications and Prospects

Improving clinicians' awareness and vigilance of cSLE-HLAS is a prerequisite for avoiding misdiagnosis and mistreatment. It is necessary to deeply understand the immunological mechanism of cSLE-HLAS and establish a treatment concept centered on immunosuppression. In the future, it will be necessary to establish a large-scale case registration system for childhood cSLE-HLAS to clarify its epidemiological characteristics; conduct in-depth exploration of its pathogenic mechanism; and optimize treatment regimens to provide more evidence for improving prognosis.

Declarations

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Changzhou Children's Hospital Affiliated to Nantong University. Informed consent was obtained from the patient's legal guardian.

Consent for Publication

Written informed consent for publication of clinical details was obtained from the patient's legal guardian.

Competing Interests

The authors declare that they have no competing interests.

Authors' Information

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Authors' Contributions

YQ designed the study, drafted and revised the manuscript. LD collected and analyzed the data. JZ, ZGZ, YQY, JZ, NW, JW, and YDL participated in case data collection and literature review. All authors read and approved the final manuscript.

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Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

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