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CASE REPORT

A Case of Childhood Lupus Anticoagulant-Hypoprothrombinemia Syndrome with Diagnostic and Therapeutic Insight

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Introduction: Lupus anticoagulant-hypoprothrombinemia syndrome (LAHPS) is a rare coagulation disorder characterized predominantly by hemorrhagic manifestations. The laboratory findings of LAHPS are complex, including notably reduced prothrombin activity and a positive lupus anticoagulant test, making early recognition challenging. This article reports the diagnosis and treatment process of a pediatric LAHPS case, aiming to enhance clinicians' understanding and management of this disease.

Materials and Methods: Clinical data and treatment details of the patient were retrospectively collected. A literature search was performed using the keywords "lupus anticoagulant", "LAHPS", and "PIVKA-II" in the PubMed database to retrieve evidence supporting clinical decision-making.

Results: A 3-year-and-10-month-old male with no remarkable past or family medical history was admitted due to "multiple skin ecchymoses". Initial management included transfusions of cryoprecipitate, hemocoagulase, and vitamin K. Although his coagulation parameters initially normalized, they later became aberrant again. Further testing of coagulation factor activity, lupus anticoagulant, anticardiolipin antibodies, and protein induced by vitamin K absence/antagonist-II (PIVKA-II) confirmed the diagnosis. Treatment with prothrombin complex concentrate and glucocorticoids led to gradual resolution of symptoms, signs, and laboratory abnormalities without recurrence.

Conclusion: LAHPS should be considered in children presenting with multisite bleeding such as cutaneous bruising. With early diagnosis and timely intervention, the prognosis is generally favorable. PIVKA-II may serve as a valuable marker in the diagnosis and management of this condition.

Keywords: children, lupus anticoagulant-hypoprothrombinemia syndrome, bleeding, PIVKA-II

Introduction

Lupus anticoagulant-hypoprothrombinemia syndrome (LAHPS) is a rare acquired coagulation disorder characterized by the presence of lupus anticoagulant (LA) and deficiency of prothrombin (Factor II). Studies have identified bleeding as the predominant symptom in pediatric LAHPS, with varying severity and sites of hemorrhage. Notably, 29.4% of patients present with multi-site bleeding, while 20.6% experience events of varying severity; this is particularly evident when comorbid with other autoimmune diseases.[1] In an analysis of 53 LAHPS patients by Wang et al, 64.2% exhibited bleeding manifestations—primarily subcutaneous hemorrhage, urinary tract bleeding, and epistaxis. Severe cases may involve intracranial, gastrointestinal, or multi-site bleeding, while approximately 36% of patients remain asymptomatic for hemorrhage; Importantly, besides hemorrhagic tendencies, two pediatric cases developed deep vein thrombosis, highlighting the clinical paradox wherein LAHPS patients may also present with thrombotic complications due to the presence of LA[2,3] Furthermore, the etiology of LAHPS differs across pediatric age groups, children aged ≥9 years frequently have underlying autoimmune diseases, particularly systemic lupus erythematosus (SLE), these patients

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typically exhibit prothrombin levels below 10%, correlating with an increased risk of severe bleeding, In contrast, those under 9 years of age are often triggered by infectious diseases and generally present with milder symptoms.[3]

Currently, no unified diagnostic criteria exist for LAHPS, and early identification remains challenging. Diagnosis relies on multiple laboratory parameters, including coagulation profiles with mixing studies, lupus anticoagulant detection, prothrombin activity, and anti-prothrombin antibody testing, the limited availability of these specialized assays in most hospital laboratories—often necessitating outsourcing to specialized centers—further increases diagnostic time and complexity.[4] Regarding treatment, although no standardized guidelines exist, glucocorticoids serve as the primary first-line therapy. For refractory cases, immunosuppressants (eg, cyclophosphamide, mycophenolate mofetil) and biologics (eg, rituximab) have demonstrated therapeutic efficacy.[4,5] Critically, therapeutic decision-making must balance hemorrhagic and thrombotic risks, underscoring the necessity for timely and individualized management. Enhanced clinician awareness of pediatric LAHPS—coupled with prompt initiation of essential laboratory investigations—is crucial to shortening diagnostic delays, identifying underlying etiology, and ultimately improving prognosis.

This article details the diagnostic and therapeutic course of a 3-year-and-10-month-old boy with LAHPS. In response to specific clinical questions encountered during management, we conducted a PubMed database search to provide and synthesize scientific evidence for clinical decision-making in this case.

Materials and Methods

Case Presentation

A 3-year-and-10-month-old boy was admitted to the hospital due to "cutaneous ecchymoses for 3 days" (Figure 1). One week prior to admission, he had experienced diarrhea and received anti-infective therapy and fluid replacement at a local hospital for two days, after which his condition resolved. Three days before admission, his parents noticed scattered purplish-red petechiae on his trunk, which progressively increased in number and spread to his back and upper limbs. The lesions enlarged, with the largest ecchymosis measuring approximately 6 cm in diameter. No epistaxis, hematuria, hematochezia, fever, or cough were reported. His appetite and sleep remained normal. He was born full-term via vaginal delivery (G2P2). There was no history of underlying diseases, trauma, blood transfusion, or allergies. Both parents and an older brother were healthy, with no notable medical conditions.

Physical Examination on Admission: Temperature: 36.6°C; pulse: 112 beats/min; respiratory rate: 26 breaths/min; weight: 17.5 kg; blood pressure: 90/59 mmHg. He was conscious, alert, and well-nourished. Physical examination revealed scattered petechiae and ecchymoses of varying sizes on the skin, with the largest measuring 4×6 cm, presenting as dark purple lesions without significant swelling or abnormal skin temperature. His lips, oral mucosa, and nail beds were pink. Cardiopulmonary, abdominal, and neurological examinations were unremarkable. The liver and spleen were not palpable below the costal margin, and no joint swelling was observed.

Initial Laboratory Findings: See Table 1.

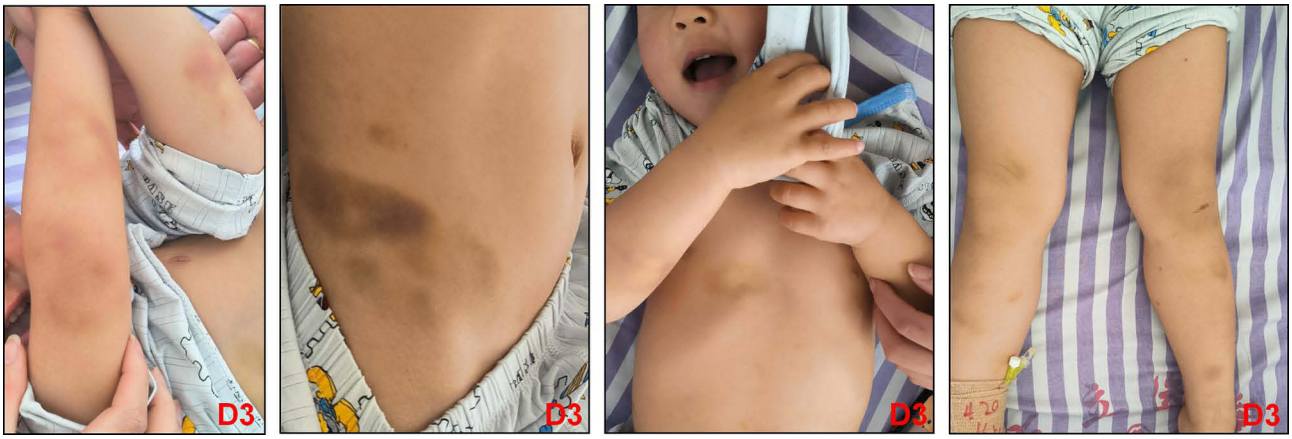

Figure 1 Photograph of the child on the third day of hospitalization.

Table 1 Initial Laboratory and Diagnostic Test Results Upon Admission

Category	Parameter	Patient Value	Reference Range	Notes
Complete Blood Count	HB (g/L)	123	112–149	
	RBC (10^{12}/L)	4.42	4.0–5.0	
	MCV (fL)	78	76–88	
	MCH (pg)	27.8	24–30	
	MCHC (g/L)	357	310–355	Elevated
	PLT (10^{9}/L)	297	188–472	
Coagulation Profile (D1)	PT (s)	17.4	11–14	Prolonged
	APTT (s)	77.2	24–39	Prolonged
	INR	1.39	0.8–1.2	Elevated
	FIB (g/L)	2.75	2–4	
	TT (s)	18.7	14–21	
	D-Dime (ug/mL)	0.54	0–1	
	FDP (ug/mL)	2.2	0–5	
Coagulation Profile (D2)	PT (s)	16.2	11–14	Prolonged
	APTT (s)	87.8	24–39	Prolonged
	INR	1.30	0.8–1.2	Elevated
	FIB (g/L)	2.61	2–4	
	TT (s)	18.2	14–21	
	D-Dime (ug/mL)	0.58	0–1	
	FDP (ug/mL)	2.62	0–5	
Mixing Study	APTT 1:1 (s)	55.0	24–39	No correction
	APTT 1:1 2h (s)	64.5	24–39	
	Rosner's Test	17.3%	≤ 15%	
Other Tests	Urine OB	1+	Negative	Weakly positive
	Stool Rt	Normal		
	Urine CMV-DNA	Normal		
	Blood chemistry panel	Normal		
	Serum ferritin	Normal		
	ESR	Normal		

Diagnostic Decision-Making

The patient presented with extensive cutaneous ecchymoses and significant coagulation abnormalities, suggesting a hemorrhagic disorder. Hemorrhagic diseases are broadly categorized into three types: capillary/platelet abnormalities, coagulation factor deficiencies, and mixed types (eg, disseminated intravascular coagulation). In this case, the normal platelet count, markedly prolonged APTT, and mildly prolonged PT indicated a coagulation factor deficiency-related hemorrhage. The elevated APTT and PT suggested abnormalities in common pathway factors (X, V, II, I) or vitamin K deficiency. The prolonged APTT uncorrected by normal plasma raised the possibility of circulating anticoagulants, such as LA or antiphospholipid antibodies. Additionally, normal liver function excluded impaired synthesis of coagulation factors due to hepatic dysfunction. The absence of family history argued against an inherited coagulation factor deficiency, and no recent exposure to anticoagulants ruled out drug-induced coagulopathy.

Based on the clinical and laboratory findings, further testing was performed, including antinuclear antibody profiling, coagulation factor activities, von Willebrand factor activity, antiphospholipid antibodies, and lupus anticoagulant testing (Table 2). A diagnosis of LAHPS was established based on the following criteria: 1) widespread ecchymoses; 2) significantly prolonged APTT and PT (predominantly APTT) uncorrected by normal plasma; 3) normal thrombin time and platelet count; 4) markedly reduced factor II activity; 5) normal liver function and vitamin K1 levels with elevated PIVKA-II; 6) negative antiphospholipid antibody panel; 7) negative antinuclear antibody panel; 8) positive lupus anticoagulant; and 9) gradual normalization of clinical and laboratory parameters following glucocorticoid therapy.

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Table 2 Results of Additional Diagnostic Investigations

Category	Parameter	Value	Reference Range	Notes
Complete Blood Count	ANA Profile (13 items)	All Negative	Negative	
	vWF: Ag (%)	59	50–160	
Coagulation Factor Activity (%)	F II	14.9	70–120	Decreased
	F V	76.3	70–120	
	F VII	91.1	70–120	
	F VIII	50.3	70–150	
	F XI	62.8	70–120	
	F X	86.8	70–120	
	F XI	85.5	70–120	
	F XII	61.2	70–150	
Lupus Anticoagulant (LA) Tests	LA Screening Test (s)	66.2	31–44	Prolonged
	LA Confirmatory Test (s)	59.4	30–38	Prolonged
	dRVVT Screen Ratio	1.78	<1.28	Elevated
	dRVVT Confirm Ratio	1.65	<1.14	Elevated
	dRVVT Normalized Ratio	1.08	<1.20	
Vitamin K Related	Vitamin K1 (ng/mL)	1.04	0.13–1.39	
	PIVKA-II (mAU/mL)	4472.21	<40	Elevated
Antiphospholipid Antibodies	ACAIgA (U/mL)	2.95	0–12	
	ACAIgG (U/mL)	3.12	0–12	
	ACAIgM (U/mL)	2.55	0–12	
	β2GPI-IgA (U/mL)	2.68	0–20	
	β2GPI-IgG (U/mL)	2.14	0–20	
	β2GPI-IgM (U/mL)	3.18	0–20	

Treatment and Prognosis

On admission (Day 1), the child presented with multiple cutaneous petechiae and ecchymoses, accompanied by a significantly prolonged APTT. Initial management included administration of vitamin K, tranexamic acid, etamsylate, hemocoagulase, and cryoprecipitate transfusion. By hospital Day 3, the skin petechiae and ecchymoses had begun to fade in color, and a repeat APTT test showed a notable decrease from the initial level. On Day 5, the ecchymotic areas had reduced in size with no new hemorrhagic lesions. Coagulation testing indicated that the APTT had essentially normalized. The family subsequently declined further inpatient treatment and requested discharge. On Day 13, new petechiae emerged, and APTT was found to be re-elevated to 62 seconds. Treatment was initiated with prothrombin complex concentrate and methylprednisolone (2 mg/kg). By Day 18, follow-up APTT had returned to normal, and the petechiae had lightened in color. Intravenous methylprednisolone was discontinued and switched to oral prednisone tablets (1.5 mg/kg). Subsequent weekly coagulation tests remained within normal limits. The prednisone dosage was tapered by half each week. By Day 45, the skin petechiae and ecchymoses had resolved completely, and on Day 52, prednisone was fully discontinued (Figure 2). Furthermore, coagulation factor II activity, PIVKA-II levels, and lupus anticoagulant activity all returned to and remained within normal ranges.

Literature Search

A literature search was conducted using the PubMed database with the keywords “lupus anticoagulant”, “LAHPS”, and “PIVKA-II”, alone or in combination. The search focused specifically on pediatric cases and review articles. The retrieved results were systematically analyzed to extract relevant evidence supporting clinical decision-making for the present case.

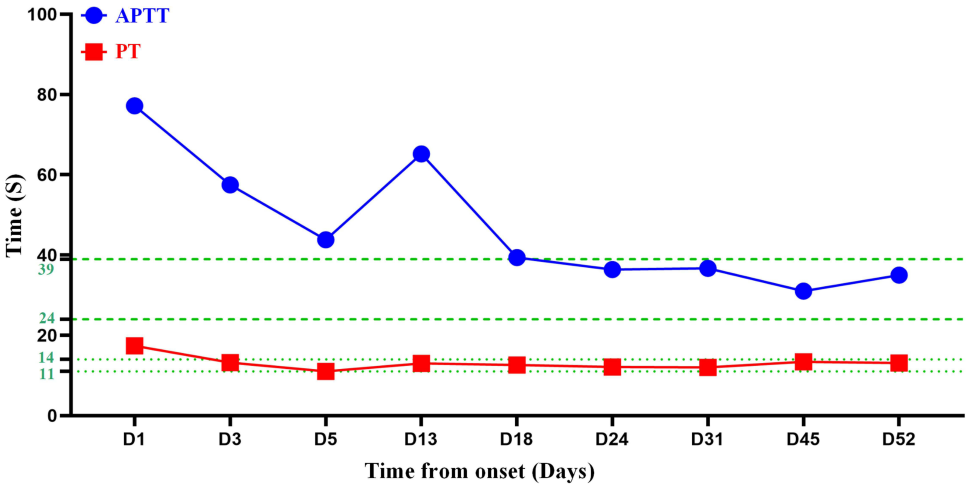

Figure 2 The diagnosis and treatment process of the hospitalized child and the dynamic changes in coagulation indicators.

Ethics Statement

Written informed consent was obtained from the patient's parents (his legal guardians) for the publication of this case report. All patient information has been de-identified to protect privacy. This study was approved by the Ethics Committee of Suzhou Hospital of Anhui Medical University (Approval No. KY-YJ-2025-013).

Discussion

Early Recognition of LAHPS

LAHPS is a rare acquired coagulopathy characterized by the presence of anticoagulant substances and deficiency of prothrombin (Factor II). Patients may present with both hemorrhagic and thrombotic tendencies. Due to its rarity, no unified diagnostic or therapeutic criteria currently exist, posing challenges for early recognition.[3,6]

The present case involved a child admitted with cutaneous ecchymoses. During the acute phase, both APTT and PT were markedly prolonged (predominantly APTT), while FDP and D-dimer levels remained normal, initially suggesting a coagulation factor deficiency. Subsequent normal liver function tests and failure of APTT correction with normal plasma indicated potential anticoagulant substances. Further laboratory evaluation revealed positive lupus anticoagulant, normal antiphospholipid antibodies, and reduced Factor II activity, supporting the diagnosis of LAHPS. Given the unavailability of anti-prothrombin antibody testing, PIVKA-II was measured and found to be 20-fold higher than the normal range (Figure 3).

For children with coagulopathy, prompt mixing studies are essential. These tests differentiate between factor deficiencies and inhibitor presence based on the correction of coagulation parameters after mixing patient plasma with normal plasma: complete or significant correction suggests factor deficiency (eg, hemophilia, vitamin K-dependent factor deficiency), whereas partial or absent correction indicates inhibitors such as specific factor antibodies (eg, FVIII inhibitors) or broad-spectrum anticoagulants like lupus anticoagulant or antiphospholipid antibodies. Thus, mixing studies enable efficient preliminary classification of coagulation disorders.

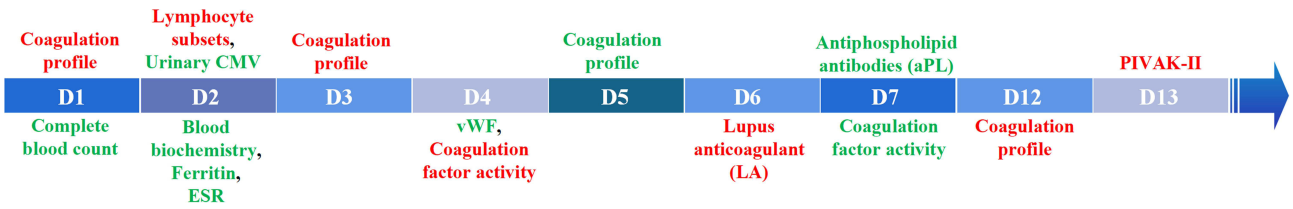

Figure 3 Timeline of relevant diagnostic test results during treatment.

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Role of PIVKA-II in LAHPS Diagnosis and Management

The diagnosis of LAHPS relies on complex laboratory parameters. Tests such as coagulation factor/vWF activities, lupus anticoagulant, antiphospholipid antibodies, and anti-prothrombin antibodies are often unavailable in routine hospital laboratories, requiring outsourcing and increasing diagnostic time and complexity. In this case, mildly reduced activities of FVIII, FIX, and FXII alongside FII (12.9%) raised the possibility of consumption due to bleeding from venipuncture or mucosal injury, initially diverting attention from LAHPS. Anti-prothrombin antibody testing was also unavailable.

Given these limitations, PIVKA-II was measured and found to be significantly elevated. PIVKA-II, an abnormal prothrombin precursor, is synthesized in the liver. Its N-terminal Gla domain contains 10 glutamate residues that undergo vitamin K-dependent γ-carboxylation to form functional prothrombin. Impairment of this process—due to vitamin K deficiency, vitamin K antagonists, severe liver disease, or autoimmune interference—results in incompletely carboxylated PIVKA-II, which cannot bind calcium and thus lacks procoagulant activity.[7] Although widely studied as a biomarker for hepatocellular carcinoma early detection and prognosis,[8,9] PIVKA-II remains underexplored in acquired autoimmune bleeding disorders like LAHPS.

In this patient, normal liver function, vitamin K1 levels, and absence of relevant drug exposure argued against common causes of PIVKA-II elevation. The normalization of lupus anticoagulant, PIVKA-II, and coagulation parameters following glucocorticoid therapy suggested an autoimmune etiology. Autoantibodies may recognize the calcium-stabilized conformational epitope of the Gla domain, potentially interfering with vitamin K-dependent carboxylation. This could lead to accumulation of uncarboxylated/partially carboxylated prothrombin (PIVKA-II) and accelerated clearance of functional prothrombin, culminating in bleeding manifestations.[10] The parallel resolution of clinical symptoms and laboratory abnormalities with immunosuppression underscores the potential utility of PIVKA-II as a diagnostic and monitoring biomarker in LAHPS. Moreover, PIVKA-II exhibits greater stability under delayed sample processing compared to FII:C, which is particularly prone to preanalytical degradation.[11] This advantage is critical for hospitals lacking specialized LAHPS testing capabilities.

In summary, while PIVKA-II research has predominantly focused on hepatocellular carcinoma and vitamin K status,[12,13] its role in LAHPS and other acquired autoimmune coagulopathies remains inadequately investigated. Future studies should prioritize systematic PIVKA-II evaluation in such disorders to clarify its potential in therapeutic monitoring, prognosis assessment, and personalized management.

Treatment and Prognosis of LAHPS

LA is an antibody closely associated with autoimmune diseases, particularly SLE. First, LA may form complexes with coagulation factors (eg, Factor II), inhibiting their activity and prolonging coagulation times.[14] Second, LA can trigger autoimmune responses, leading to specific factor-neutralizing antibodies that exacerbate coagulopathy.[3] Additionally, LA may dysregulate physiological anticoagulant mechanisms (eg, protein C and S pathways), further reducing prothrombin levels.[15]

LAHPS manifests differently in children and adults. Pediatric cases exhibit more prominent bleeding and lower thrombotic risk. A study of 84 children by Hanna et al reported median ages of 11.5 years for autoimmune-associated LAHPS and 3 years for infection-triggered cases, with thrombosis occurring exclusively in the autoimmune subgroup, which also showed higher treatment resistance and relapse rates.[16] The higher prevalence of autoimmune diseases in adults may partly explain their more severe symptoms and poorer prognosis.[3,4,17] Tian et al[4] retrospectively analyzed 70 pediatric LAHPS cases: 80% presented with bleeding, 13 were asymptomatic, and only one had thrombosis. Etiologies included autoimmune diseases (15 cases), infections (51 cases), and unknown causes (4 cases). All patients achieved normalization of symptoms and laboratory parameters after treatment, without bleeding recurrence or thrombosis, indicating favorable prognosis with timely intervention. Our patient presented with bleeding and a recent diarrheal history, suggesting infection-associated LAHPS, though no active infection was detected at admission.

The clinical challenge in LAHPS lies in balancing hemorrhagic and thrombotic risks. Chronic inflammation may activate platelets and endothelial cells, upregulate procogulant factors, and promote vasoconstriction, increasing

thrombosis susceptibility. Post-hemorrhagic thrombotic events appear more common in adults with comorbid autoimmune diseases.[3,18,19]

Our patient received cryoprecipitate, vitamin K, and hemostatic adjuvants during the acute phase. Upon confirming LAHPS, glucocorticoid therapy was initiated, leading to normalized parameters within one week and sustained remission during follow-up. The favorable outcome may relate to the confinement of bleeding to cutaneous sites without vital organ involvement. Early transfusion of cryoprecipitate/fresh frozen plasma provides critical factor replacement before definitive diagnosis.[20] Glucocorticoids remain first-line therapy, particularly in severe or acute cases, with rapid tapering to the lowest effective dose upon stabilization to minimize side effects.[21,22] Vitamin K not only enhances coagulation factor synthesis but may also modulate immune cell function.[23,24] Refractory cases may require immunosuppressants (eg, cyclophosphamide, mycophenolate mofetil) or biologics (eg, rituximab).[5]

Conclusion

Pediatric LAHPS is a complex rare disorder with unclear etiology, often secondary to infections or autoimmune diseases. Diagnosis relies on coagulation profiles and specific antibody testing, underscoring the need for heightened clinical awareness. PIVKA-II demonstrated considerable diagnostic and monitoring utility in this case. Pediatric LAHPS predominantly manifests with bleeding, while thrombosis is uncommon. Early management may include factor replacement, with prompt discontinuation of prophylactic hemostatic agents after coagulation normalization to avoid thrombotic complications. Glucocorticoids are the cornerstone of definitive treatment, and non-SLE-associated LAHPS generally carries a favorable prognosis with timely intervention.

This study has certain limitations that warrant consideration. First, its conclusions are derived from a single case report; thus, the observed therapeutic responses and dynamic changes in laboratory parameters may not be fully representative of the broader pediatric LAHPS population. Second, current evidence supporting the association between PIVKA-II and LAHPS in children remains limited. Future studies should include larger pediatric LAHPS cohorts, systematically incorporate PIVKA-II testing, and further explore its potential value in treatment monitoring and prognosis evaluation. Such efforts will provide a more comprehensive scientific foundation for precise diagnosis, risk stratification, and individualized management of this disease.

Data Sharing Statement

The data that support the findings of the study are available from the corresponding author upon reasonable request.

Ethics Statement

Written informed consent was obtained from the patient's parents (his legal guardians) for the publication of this case report. All patient information has been de-identified to protect privacy. This study was approved by the Ethics Committee of Suzhou Hospital of Anhui Medical University (Approval No. KY-YJ-2025-013).

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Disclosure

All authors report no conflicts of interest in this work.

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