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Renal Artery Thrombosis in a Boy as First Manifestation of Juvenile Systemic Lupus Erythematosus

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Abstract

Introduction: Systemic Lupus Erythematosus (SLE) is a complex autoimmune disorder with a wide spectrum of clinical manifestations. Though Antiphospholipid Antibodies (APAs) in SLE increase thrombotic risks, renal artery thrombosis is uncommon, especially in younger patients.

Case report: A 15-year-old presented with fever, chest pain, arthritis, and discoloured skin scars. During his hospitalization, he suddenly developed severe acute abdominal pain. Imaging findings revealed renal artery thrombosis at the site of an anatomical variation involving the bifurcating right renal artery. Clinical manifestations and laboratory tests ultimately led to the diagnosis of APA-positive Systemic Lupus Erythematosus (SLE). Treatment with Low-Molecular-Weight Heparin (LMWH), intravenous methylprednisolone at a dosage of 30 mg/Kg/d for three consecutive days, followed by oral prednisolone at a dosage of 1mg/Kg/d, hydroxychloroquine, and methotrexate, resulting in significant improvement. However, arterial hypertension emerged in the seventh week, requiring lisinopril. Six months later, the patient remains in remission with stable blood pressure.

Conclusion: To our knowledge, this is the first documented case of renal artery thrombosis initiating paediatric-onset APA-positive SLE. Thrombotic events should prompt consideration of systemic vasculitis.

Keywords: Systemic lupus erythematosus • Renal artery thrombosis • Antiphospholipid antibodies

Introduction

Juvenile Systemic Lupus Erythematosus (jSLE) accounts for approximately 15-20% of all SLE cases. Compared to adult-onset SLE, jSLE is notably associated with a higher incidence of arthritis, nephritis, neurologic issues, and hematologic manifestations. In particular, adolescent-onset SLE tends to manifest as a more aggressive form of the disease [1]. It's worth noting that atypical, early-onset, or severe cases of SLE can be linked to mutations in single genes or multiple genomic variants [1]. While arterial and venous thrombosis have been observed in SLE patients with Antiphospholipid Antibodies (APAs) [2], the occurrence of renal artery thrombosis is an exceptionally rare event, even among SLE patients with APAs. To the best of our knowledge, this is the first documented report of renal artery thrombosis serving as the initial manifestation of paediatric-onset APA-positive SLE.

Methodology

Case report description according to CARE reporting guidelines [3].

Case Presentation

A 15-year-old Egyptian boy was referred to our Paediatric Department with a 4-day history of high fever, chest pain, and elevated serum levels of troponin (163 pg/ml, normal range: 0-58 pg/ml). The patient's medical history was notable for recurrent mouth ulcers, and his family history was unremarkable. On admission, his temperature was 39.0 , and he did not report experiencing chills. He was fully oriented and appeared well-nourished. Upon physical examination, we observed joint swelling in both ankles and identified multiple discoloured scarring lesions on the dorsal surface of the left hand and both legs. The remainder of the examination was unremarkable. The laboratory tests were as follow: White Blood Cells (WBC) count, 9.41*109/L; neutrophils, 7.62*109/L; lymphocytes, 1.22*109/L; hemoglobin level, 11.4 gr/dl; hematocrit, 35.4%; platelet count, 186 K/μL; Erythrocyte Sedimentation Rate (ESR), 113mm/h; C Reactive Protein (CRP), 23.57 mg/dl, normal <0.5 mg/dl. He has mildly affected coagulation pathway (PT: 18 sec, normal range: 10-13.5 sec, INR: 1.53, normal range: 0.85-1.15, fibrinogen: 504 mg/dl, normal range: 200-450 mg/dl) with no evidence of hemolysis (LDH 131U/L, negative direct Coombs test, normal reticulocyte count), and mild raised troponin levels (Trop: 42 pg/ml, normal <12 pg/ml). Renal and liver functions were within normal limits, and there were no significant abnormalities in the urinary sediment. PCR testing for SARS-CoV-2 returned negative results. Given the elevated troponin levels, an Electrocardiogram (ECG) and echocardiography were conducted, which did not show any evidence of endocarditis or other cardiac pathology. A chest X-ray also did not reveal any notable abnormalities. However, 36 hours later, the patient's condition suddenly deteriorated, and he experienced acute diffuse abdominal pain. An abdominal ultrasound was performed, revealing splenomegaly. Abdominal contrast-enhanced CT revealed a substantial non-enhancing area in the right kidney, which is consistent with infarction. This finding was accompanied by evidence of an abrupt occlusion in the cephalic branch of the proximally bifurcating right renal artery, indicative of arterial thrombosis (Figure 1). Following parental consent, ultrasonography with Contrast-Enhanced Ultrasound (CEUS) was conducted. The conventional B-mode ultrasonography did not reveal any significant abnormalities. However, when utilizing colour and power Doppler techniques, there was an inability to visualize blood flow signals within the renal parenchyma, which is consistent with the previously identified infarction. Despite the initial challenges related to motion artifacts potentially limiting the sensitivity of the technique, further diagnostic steps were taken. After the intravenous administration of 1.2 ml

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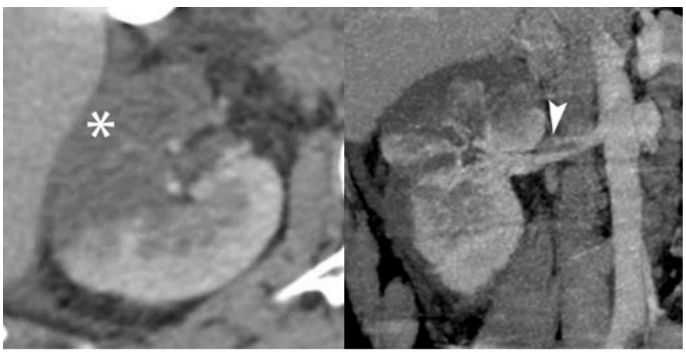
of SonoVueTM (Bracco SpA, Milan), followed by a 10 ml saline flush, half of the renal parenchyma displayed a complete absence of enhancement. This finding definitively established the diagnosis of parenchymal renal infarction (Figure 2). Additionally, a 99mTc-Dimercaptosuccinic Acid (DMSA) renal scan was performed, which revealed a small right kidney with an estimated residual relative renal function of 25%.

The patient was immediately initiated on subcutaneous Low-Molecular-Weight Heparin (LMWH) therapy as part of the treatment plan. Given the presentation of renal artery thrombosis and the positive findings in the laboratory tests, further investigations into prothrombotic risk factors were carried out. Notably, the results showed normal levels for Factor V Leiden, Protein C and S, antithrombin, prothrombin, low and high-density lipoproteins. However, the serum did test positive for anticardiolipin IgM and lupus anticoagulant, using the dilute Russell Viper Venom Time (dRVVT) test, while the remaining antiphospholipid antibodies were negative. Immunological examination also revealed positive antinuclear antibodies at a titer of 1:160 with a speckled pattern. Additionally, Rheumatoid factor, c-ANCA, p-ANCA, anti-ENA antibodies, anti-ds-DNA antibodies, C3 and C4 complement levels and immunoglobulin levels were within normal ranges. The patient's Glomerular Filtration Rate (GFR) was found to be within the normal range at 103 ml/min/1.73 m^2, indicating preserved kidney function. Further investigations were conducted to rule out various infectious causes, including respiratory pathogens, blood cultures, procalcitonin levels, tuberculosis spots, Epstein-Barr virus, cytomegalovirus antibodies, hepatitis B, hepatitis C, and HIV status. All of these tests returned negative results, excluding infectious etiologies. A skin biopsy was performed and revealed inflammatory lymphocytic infiltrates of a non-specific type, which is possibly indicative of a chronic systemic disease.

Based on the criteria established by the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) [4], the patient was diagnosed with Systemic Lupus Erythematosus (SLE) with positive antiphospholipid antibodies (APAs). This diagnosis was made considering the presence of fever, arthritis, skin lesions, oral ulcers, positive antinuclear antibodies (ANA), anticardiolipin IgM, and lupus anticoagulant.

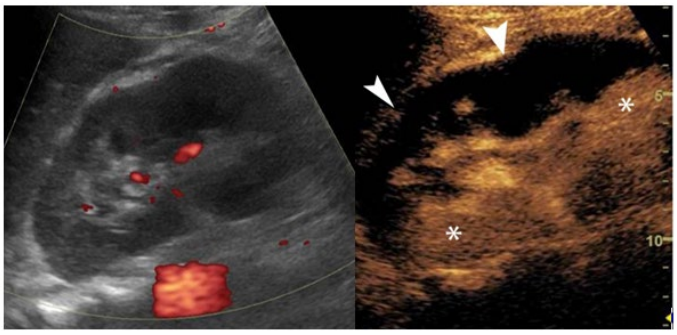
The patient received intravenous methylprednisolone at a dose of 30 mg/kg per day for three consecutive days, followed by oral prednisolone at a dose of 1mg/kg per day. Hydroxychloroquine and methotrexate were also introduced into the treatment regimen. The patient experienced significant clinical improvement, and their laboratory markers of inflammation, such as Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP), returned to normal levels.

By week 7 of the treatment course, the patient developed arterial hypertension, although the rest of the physical examination remained unremarkable. Baseline B-mode imaging demonstrated the presence of a focal cortical scar in the area corresponding to the previous renal infarction. Lisinopril dihydrate was added, resulting in a favorable response in managing the hypertension. By week 12, the lupus anticoagulant remained positive,



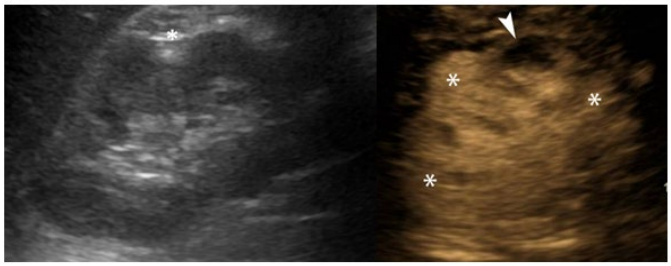
(A) (B)

Figure 1. Contrast-enhanced CT on admission showing a large renal infarction. **A)** Axial image showing the non-enhancing part of the parenchyma (asterisk) and **B)** Coronal thick-slice Maximum Intensity Projection (MIP) reformatted image showing the abrupt occlusion of renal artery branch (arrowhead).



(A) (B)

Figure 2. US and CEUS examination on admission. **A)** Long-axis power Doppler technique image showing no significant echogenicity abnormality but complete absence of blood flow signals and **B)** Long axis CEUS image confirmed the complete absence of enhancement in the lateral half of the renal parenchyma, establishing the diagnosis of infarction (arrowheads). Note the normally perfused parenchyma (asterisks), not detected with conventional power Doppler technique.



(A) (B)

Figure 3. Follow-up US and CEUS examination 40 days after conservative treatment. **A)** Long axis B-mode image showing a focal cortical echogenic scar (asterisk) and **B)** Long-axis CEUS showing the significant decrease of the infarcted area (arrowhead), while the majority of renal parenchyma was now seen normally enhancing (asterisks).

indicating ongoing autoimmune activity. A follow-up Contrast-Enhanced Ultrasound (CEUS) at this time revealed a significant improvement in renal perfusion. The previously non-enhancing portion of the renal parenchyma had notably decreased, with a larger proportion of the parenchyma now displaying enhancement (Figure 3). As of the 6-month follow-up, the patient is in remission, and their arterial pressure is well controlled.

Results and Discussion

We present a case of renal artery thrombosis as the initial manifestation of juvenile Systemic Lupus Erythematosus (jSLE). It is widely recognized that SLE patients with positive Antiphospholipid Antibodies (APAs) have a heightened risk of thrombotic events; however, it's important to note that not all APA-positive SLE patients necessarily experience thrombotic complications [2]. Additionally, children and adolescents diagnosed with SLE carry a higher burden of risk factors compared to adult SLE patients [5]. The epidemiology of Antiphospholipid Syndrome (APS) in the pediatric population remains largely undefined. It is often considered a rare diagnosis, but it is possible that pediatric APS is underdiagnosed, particularly due to the absence of pediatric-specific classification or diagnostic criteria. In terms of gender distribution among affected children, there is a slight predominance in females at a ratio of 1:1.2. An intriguing finding is that only 2% of children diagnosed with APS demonstrated a combination of arterial and venous thrombosis. Around 6% of children experienced small-vessel thrombosis, presenting as digital ischemia or renal thrombotic microangiopathy. The limited available data suggests an annual risk of thrombosis in the range of 2 to 6% among children who test positive for antiphospholipid antibodies (aPL) and have lupus. Furthermore, the presence of aPL appears to signify more aggressive forms of lupus and is associated with an increased risk of developing lupus-related damage over time [6].

In addition to being positive for Antiphospholipid Antibodies (APAs), several other factors have been considered in the context of thrombotic events in jSLE. These factors include: hypertension, hyperlipidemia, vasculitis, hypercoagulability, corticosteroid therapy, hypoalbuminemia, proteinuria, low levels of antithrombin III, decreased functional activity of protein C and S, high fibrinogen levels, high hematocrit and platelet counts, increased platelet aggregation and reduced plasma volume [7,8]. Furthermore, genetic factors have been associated with an increased risk of thrombotic events in jSLE, such as the presence of factor V Leiden and MTHFR gene mutations [2]. In the adult population, it's noteworthy that female sex and African-American origin appear to have a somewhat protective effect against thrombosis [2]. Additionally, Rajagopalan S, et al. have reported that increased apoptosis of endothelial cells could be a significant factor contributing to atherothrombosis [8]. In the case of our patient, the presence of an anatomical anomaly in the renal artery with invariance could indeed be a significant predisposing factor for thrombosis.

Driest KD, et al. conducted a study involving 974 pediatric patients with Systemic Lupus Erythematosus (SLE) and reported that 2.5% of the patients experienced arterial thrombosis, 3.36% venous thrombosis, 0.9% cerebral vascular accident and 0.2% coronary heart disease [2]. Furthermore, it was observed that 8.8% of patients with positive Antiphospholipid Antibodies (APA) had experienced a thrombotic episode [7]. In the context of pediatric SLE patients with nephrotic syndrome, renal venous thrombosis was found to occur in approximately 40% of cases, whereas arterial thrombosis, especially in the renal artery, is exceedingly rare and typically affects smaller branches [9]. This rarity of arterial thrombosis in the renal artery may be attributed to the substantial production of nitric oxide and prostacyclin (PGI2) by mesangial cells. These molecules play a role in regulating platelet activation and help to prevent thrombotic events within the glomerular capillaries [10].

Regarding the initial high troponin levels observed in our patient, it is possible that systemic inflammation played a role. Studies conducted among patients treated in intensive care units for conditions such as sepsis or Systemic Inflammatory Response Syndrome (SIRS) have indicated a significant association between the release of cardiac Troponin T (cTnT) and interleukin-6 (IL-6) levels. Importantly, this association appears to be independent of factors such as age, gender, renal function, and the presence of cardiovascular risk factors [11]. This suggests that systemic inflammation can contribute to elevated troponin levels, even in the absence of primary cardiac pathology.

Several guidelines have been published regarding the management of thrombotic events in the pediatric population, depending on the underlying cause of the thrombosis, whether it is related to thrombophilia, cancer, systemic diseases, or other factors [9]. The treatment is typically divided into three distinct phases: a) Acute phase b) Recovery phase c) Chronic phase. Throughout these phases, the mainstay of treatment involves the use of antithrombotic agents, which can include anticoagulants such as heparin or warfarin, antiplatelet agents like aspirin, and revascularization procedures when feasible [12].

In the case of our patient, treatment with enoxaparin yielded a favorable response. While the disease activity had been effectively controlled with a combination of steroids, hydroxychloroquine, and methotrexate, the patient developed hypertension. This hypertension can be attributed to a combination of factors, with renal infarction and subsequent renal scarring being the most prominent explanation. Other contributing factors may include vasculitis, hypercoagulability, and the use of corticosteroids. Managing these complications alongside the underlying condition is crucial for the overall well-being of the patient.

Conclusion

In conclusion, this case report emphasizes that renal artery thrombosis can serve as the initial manifestation of Antiphospholipid Antibody (APA) positive pediatric Systemic Lupus Erythematosus (SLE) patients. Therefore, it is imperative to consider systemic vasculitis as a potential underlying cause in any patient presenting with a thrombotic event.

Declaration of Conflicting Interests

All the authors have declared no competing interests.

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Informed consent

Informed consent was obtained from the patient's guardian for the purpose of publishing this case report.

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