Chemotherapy induced Thrombotic Microangiopathy in a pediatric patient with single functioning kidney: A Case Report and Review of the Literature

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BACKGROUND

Thrombotic microangiopathy (TMA) presents with microangiopathic hemolytic anemia, thrombocytopenia, and organ dysfunction. In cancer patients, causes are often multifactorial, including chemotherapy, radiation, and malignancy. Plasma exchange, immunosuppression, and complement inhibition improve outcomes in Thrombotic Thrombocytopenic Purpura and complement-mediated TMA, while stopping the offending drug manages drug-induced TMA. Interrupting treatment may raise cancer progression risk. This report discusses a pediatric metastatic Wilm's tumor patient who developed biopsy-confirmed, nonimmune, chemotherapy-induced TMA following radiation nephritis.

CASE SUMMARY

An 8-year-old girl presented with gross hematuria, reduced appetite, and abdominal pain. After a left-sided nephrectomy in January 2024 for Wilms' tumor, she developed widespread metastatic disease involving lungs, liver, peritoneum, muscles, and skin by February 2024. She received multi-agent chemotherapy, including Actinomycin D, Doxorubicin, Vincristine, Cyclophosphamide, Carboplatin, and Etoposide, over one year (February 2024 - January 2025). In October 2024, she also underwent radiotherapy to the tumor bed, lungs, and whole abdomen.

By January 2025, the patient developed progressive renal insufficiency (baseline Creatinine 0.3mg/dL rising to 1.3 mg/dL), proteinuria (Protein/Creatinine ratio 3.975 g/g), and microscopic hematuria. Complications included new-onset heart failure and seizures. A renal biopsy confirmed acute TMA, showing focal fibrin thrombi in the peripheral capillary loops with mesangiolysis. Acute tubular injury was also noted. Given the temporal relationship and lack of response to steroids, non-immune, chemotherapy-induced TMA was suspected. Following the cessation of chemotherapy in March 2025, the patient's serum Creatinine improved to 0.8 mg/dL by April 2025 and multidisciplinary follow-up was advised.

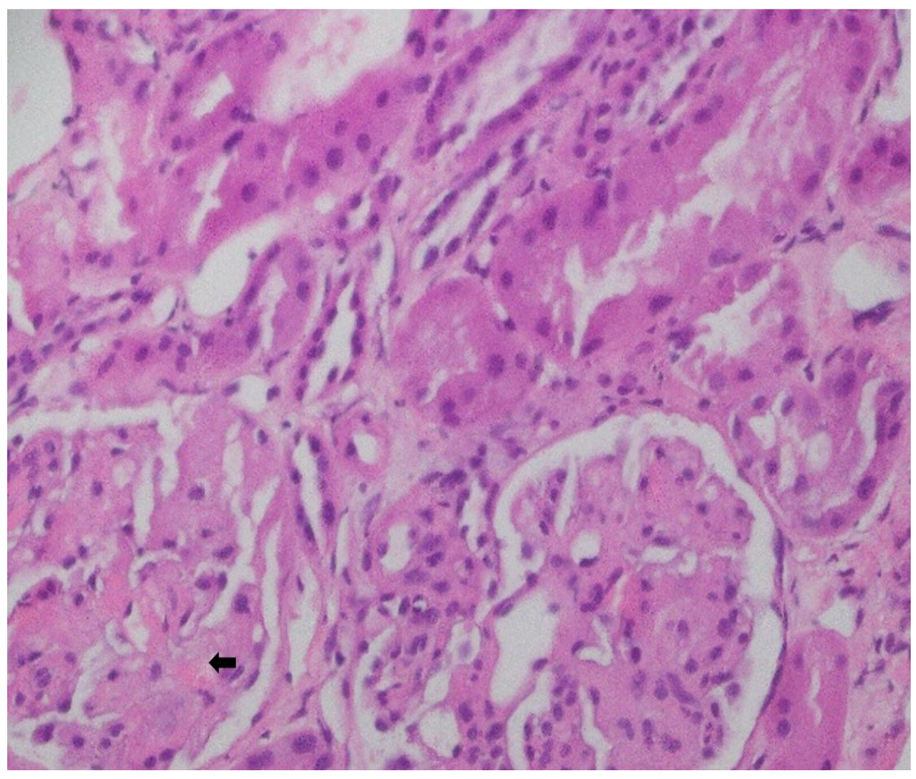

Fig 1: *Hematoxylin and Eosin stain, light microscopy, 40X. All glomeruli show features of acute thrombotic microangiopathy characterized by focal fibrin thrombi in the peripheral capillary loops(arrow) with mesangiolysis*

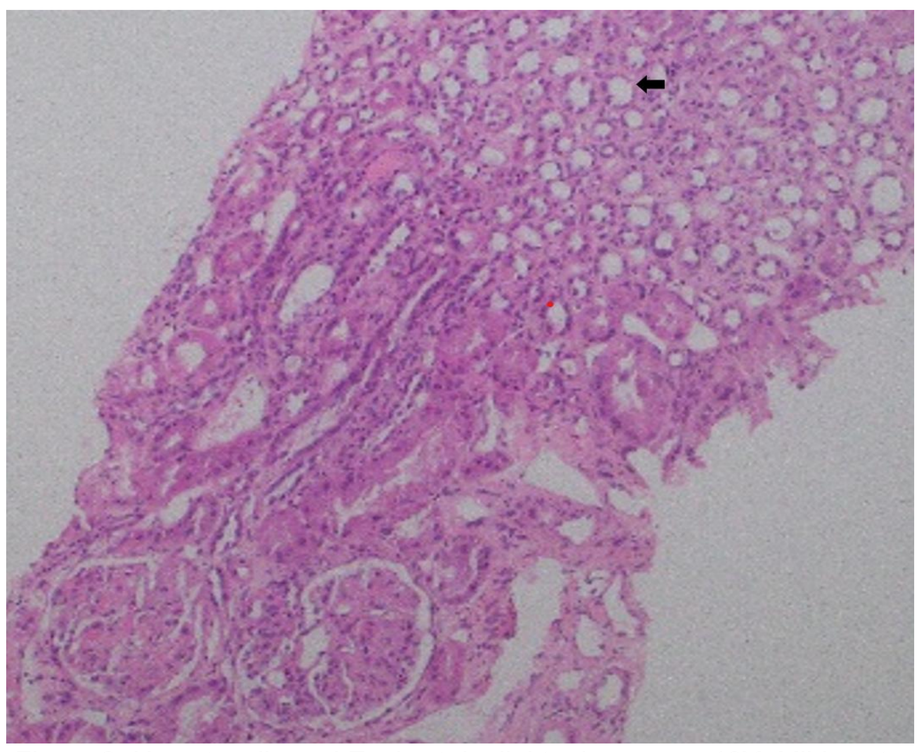

Figure 2: Hematoxylin and Eosin stain, light microscopy, 10X. Mild acute tubular injury with dilatation of tubules with loss of brush border and hyperchromasia of nuclei (arrow).

DISCUSSION

This case highlights the diagnostic complexity of thrombotic microangiopathy (TMA) in oncology patients with concurrent chemotherapy and radiation exposures.This clinical course is most consistent with a non-immune drug-induced TMA (DI-TMA), supported by the patient's clinical improvement after chemotherapy cessation. Non-immune DI-TMA is characterized by a delayed, dose-dependent onset, aligning with the patient's progressive renal decline after multiple cycles [1-2]. A comprehensive diagnostic workup is essential to exclude other primary etiologies, such as Thrombotic Thrombocytopenia Purpura or complement-mediated TMA [3]. While radiation nephritis is a critical differential, as ionizing radiation directly damages the renal microvasculature and leads to TMA pathology [4], the rapid onset of renal dysfunction three months post-radiotherapy is less characteristic of its typical insidious course. However, prior radiation may have predisposed the patient's kidney to further chemotoxic insult. Management in a patient with a single functioning kidney is particularly critical, as the loss of nephron reserve places them at an elevated risk for end-stage renal disease [5]. Treatment centers on immediate cessation of the suspected drug and vigilant supportive care, including strict blood pressure management. The case underscores the significance of early recognition, intervention, and long-term nephrology follow-up to mitigate permanent renal dysfunction in this vulnerable population.

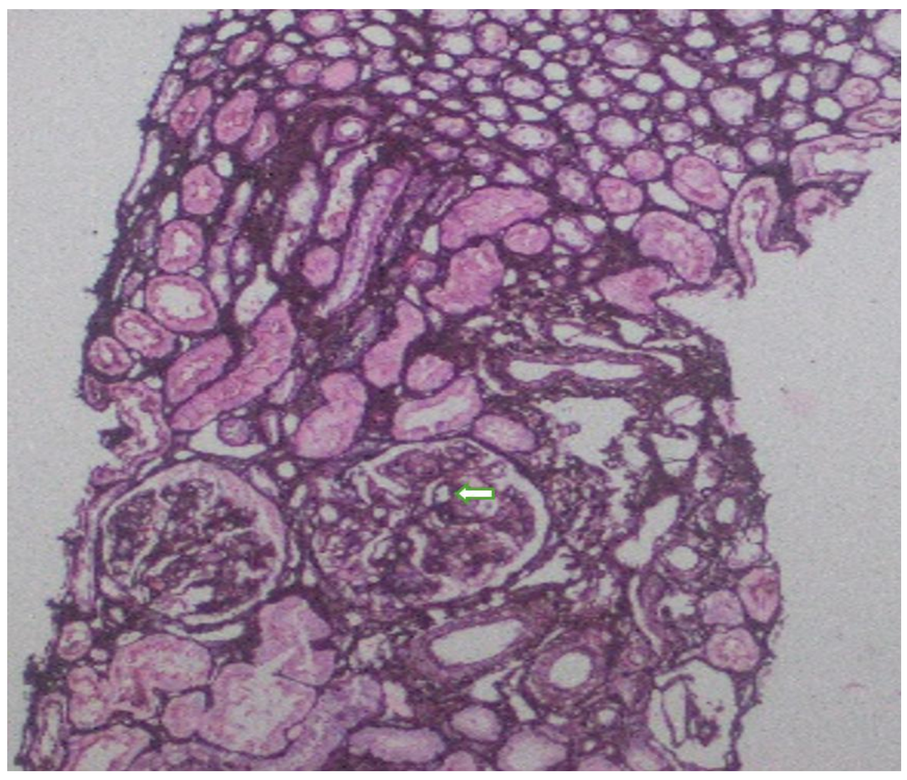

Figure 4: Renal biopsy with Jones methenamine silver (JMS) staining, 10X. There is prominence of endothelial cells(arrow) No proliferative changes are seen. The basement membranes do not show any double contouring

CONCLUSION

This case shows that Vincristine may cause DI-TMA through a non-immune, dose-dependent process, as indicated by the timing of kidney injury after exposure. Radiation nephritis was considered but was unlikely due to standard radiotherapy dosing and its gradual effect on renal function. Because of the high risk of lasting kidney damage, rapid recognition, early treatment, and close nephrology monitoring are essential for paediatric patients with a single kidney.

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