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Case Presentation

Unmasking Renal Complications of Immunotherapy: A Case of Nivolumab-induced FSGS

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Abstract

Immune Checkpoint Inhibitors (ICPIs), while revolutionizing cancer therapy through potentiation of anti-tumour responses via targeted blockade of T-lymphocyte inhibitory receptors, are associated with immune-related adverse events (irAEs), including diverse renal manifestations. This report presents a case of a 69-year-old male with urothelial carcinoma who developed Acute Kidney Injury (AKI) and nephrotic-range proteinuria following initiation of nivolumab, an anti-PD1 antibody, necessitating renal biopsy to clarify the aetiology. The biopsy revealed Focal Segmental Glomerulosclerosis (FSGS) with endotheliopathy, suggesting a direct ICPI-induced glomerular injury. This case underscores the need for heightened awareness of ICPI-associated glomerular disease, alongside more common renal adverse events such as Acute Interstitial Nephritis (AIN), and for the need for renal biopsy in such cases. While the incidence of ICPI-associated AKI is approximately 17%, and AIN is a more frequent finding, FSGS and other glomerular pathologies should also be considered. Current treatment for such renal events involves discontinuation of the ICPI agent and initiation of immunosuppression with glucocorticoids. The management of these cases requires prompt detection, timely diagnosis, and often interdisciplinary collaboration, thus highlighting the need for more case reports, research, and better treatment strategies.

Introduction

Immune Checkpoint Inhibitors (ICPIs), a class of monoclonal antibodies targeting inhibitory receptors on T cells and tumor cells (e.g., CTLA-4, PD-1, PD-L1), have revolutionized oncology by enabling a robust antitumor immune response. While they offer significant survival advantages, these therapies are also associated with immune-related adverse events (irAEs), including diverse renal manifestations such as Acute Kidney Injury (AKI), Acute Interstitial Nephritis (AIN), and glomerular lesions. This review explores the renal complications of ICPIs, highlighting their unique diagnostic and management challenges.

Case presentation

A 69-year-old male with urothelial carcinoma developed hypertension and Acute Kidney Injury (AKI) three months after initiating nivolumab, an anti-PD1 antibody. Urine analysis revealed nephrotic-range proteinuria, confirmed by a 24-hour urine protein-creatinine ratio, and worsening serum creatinine (Figure 1). A renal biopsy was performed, revealing global glomerulosclerosis in five out of six glomeruli, along with focal subcapsular collagen, periglomerular fibrosis, and one segmentally sclerosed tuft. Immunofluorescence showed negative results for IgA, IgG, C1q, kappa, and lambda light chains, while IgM and C3 were segmentally positive (2+ and 1+, respectively). Electron microscopy identified effacement of visceral epithelial cell foot processes (60%), severe active and chronic endothelial injury, prominent, diffuse GBM

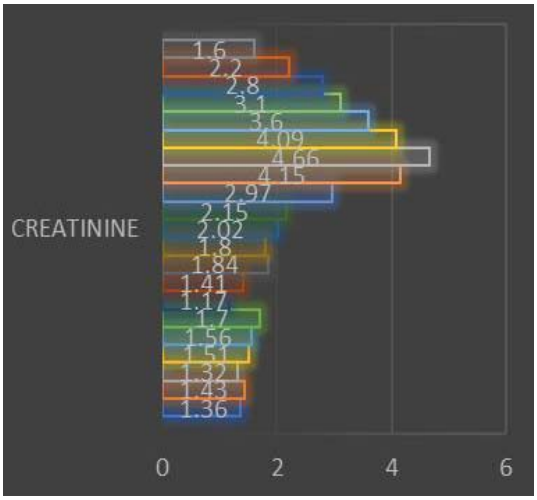

Figure 1: Laboratory data showing worsening creatinine.

subendothelial widening, and no immune complex type electron-dense deposits (Figures 2,3). The diagnosis was Focal Segmental Glomerulosclerosis (FSGS) secondary to vascular endothelial disorder and podocyte damage, likely induced by nivolumab. Despite discontinuing nivolumab, his renal function remained compromised [1-5].

Discussion

The incidence of Acute Kidney Injury (AKI) with ICPIs is approximately 17%, with Acute Interstitial Nephritis (AIN) being the most common histopathological finding (80%-90%) [1]. However, glomerular pathologies like Focal Segmental Glomerulosclerosis (FSGS) account for approximately 24% of ICPI-induced kidney injuries. Diagnosis often relies on non-invasive biomarkers, such as urine tests and imaging studies, but renal biopsies may be warranted for definitive diagnosis [2-5]. Current treatment for ICPI-induced AKI includes discontinuation of the offending agent and slow tapering doses of glucocorticoids, often combined with PNEUMOCYSTIS JIROVECII PNEUMONIA (PJP) prophylaxis and gastrointestinal protection with Proton Pump Inhibitors (PPI) or H2 blockers [1,2]. This case highlights the importance of considering ICPI-induced glomerular injury [3-5].

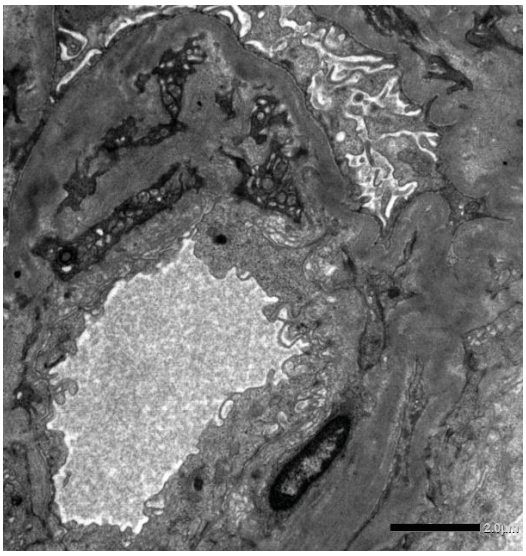

Figure 2: Electron microscopy (EM) illustrating podocyte effacement.

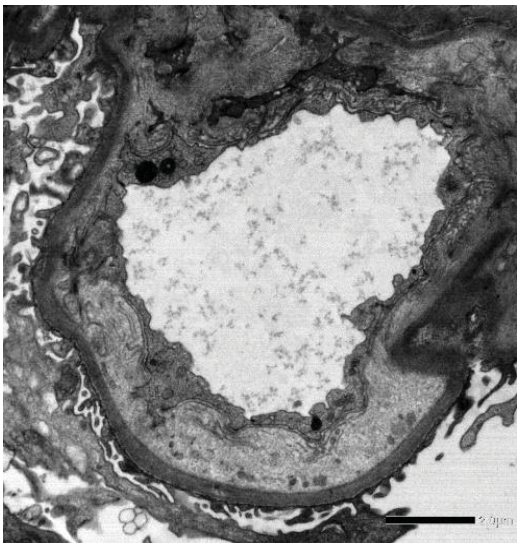

Figure 3: Electron microscopy (EM) showing GBM subendothelial widening.

Conclusion

Anti-PD1 antibodies are frequently used ICPIs. The diverse renal manifestations associated with ICPIs underscore the need to understand their complex mechanisms thoroughly. Regular monitoring of urine and creatinine levels is essential for early detection of potential renal complications. Renal biopsy should be considered for definitive diagnosis of ICPI-induced kidney disease. Discontinuation of ICPIs and initiation of glucocorticoid therapy are shown to improve renal outcomes in many patients. Therefore, a vigilant and proactive approach to managing ICPI-related renal adverse events is necessary for better patient care and treatment success. A detailed analysis and reporting of all such events should be encouraged.

Ethical considerations

Informed patient consent was obtained for the publication of this case report.

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