Immune Checkpoint Inhibitor induced Sarcoid Like Reaction in The Kidney – A Case Report

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Abstract

Introduction:
The development of granulomatous/sarcoid-like lesions is recognized manifestation of immune related adverse events (irAEs) induced by immune checkpoint inhibitors (ICIs). It might involve various organs, however, kidney biopsy-proven sarcoid like granulomas in the context of sarcoidosis-like reaction induced by checkpoint inhibitors has not yet been described.

Case:
62-year-old male was admitted to the hospital for acute functional decline. He had recently been diagnosed with metastatic RCC and was undergoing treatment with nivolumab and ipilimumab. Eight days prior to admission he received his fourth cycle of treatment. His other comorbidities included hypertension and chronic kidney disease (CKD) stage 4 with baseline creatinine 2-2.4 mg/dL, thought to be related to hypertensive nephropathy, that had been stable for years. Laboratory workup showed worsening kidney function with creatinine of 5.32 mg/dL, hypercalcemia with total calcium 11.5 mg/dL, albumin 3.1 mg/dL, ionized calcium 6.6 mg/dL, and hyponatremia with sodium 123 mEq/L. He had suppressed TSH with low free T4 and low am cortisol with inappropriately normal ACTH. His other pituitary hormone elevations were concerning for ICI induced secondary hypophysitis that was also found on MRI. His hypercalcemia workup showed that PTH was appropriately suppressed < 6 pg/mL, PTHrP peptide was undetectable, and vitamin D was normal 48 ng/mL. However, there was significant increase of 1,25-dihydroxyvitamin D 100 pg/mL, from a previous normal level (57 pg/mL) just prior to starting therapy with ICIs. His CRP was elevated at 153.8 mg/L and urine retinol binding-to-creatinine ratio was elevated at 81,852 mcg/g Cr. Urinalysis showed sterile pyuria with 41-50 WBC/HPF, with urine protein-to-creatinine ratio 0.9 mg/mg and renal ultrasound showed mild right sided hydronephrosis. In order to evaluate the cause for worsening AKI patient underwent kidney biopsy that demonstrated interstitial granulomatosis nephrititis showing “sarcoid-like” noncaseating granulomatous lesions and mild acute tubular injury (Fig. 1). He was given one dose of 0.5 g of methylprednisone and was continued on treatment with prednisone 80
mg once a day for the first week. His kidney function initially stabilized and after two days serum creatinine started to decrease. His hypercalcemia was initially difficult to control, however after starting steroids it gradually improved and then normalized. He was discharged home in a stable condition. On the day of discharge creatinine was 3.4 mg/dL. During his follow up at onco-nephrology clinic after one week his creatinine was at his baseline and calcium was normal. He was continued on corticosteroid steroid taper, his serum creatinine continued to improve, and his last creatinine was 2 mg/dL.

Discussion:
This case illustrates that renal sarcoidosis can be induced by ICI treatment. Biopsy is the gold standard for evaluation of new lesions to guide management and to avoid premature discontinuation of agents with the potential to induce a durable response. As ICI has been increasingly used in cancer patients, clinicians should be aware of this potential complication associated with it for appropriate diagnostic and therapeutic approach.