**I pi limumab-induced Immune-related Renal Failure – A Case Report**

PATRICK M. FORDE¹, KATHY ROCK², GRAHAM WILSON³ and KENNETH J. O’BYRNE²

¹Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins Hospital, Baltimore, MD, U.S.A.; ²Department of Medical Oncology, St James Hospital, Dublin, Ireland; ³Department of Radiology, St James Hospital, Dublin, Ireland

*Correspondence to:* Dr. Patrick Forde, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins Hospital, 401 N. Broadway, Baltimore, MD, 21231, U.S.A. Tel: +1 4438313921, e-mail: pforde1@jhmi.edu

**Key Words:** Ipi limumab, renal failure, melanoma metastasis.

**Abstract.** Ipilimumab is a fully human monoclonal antibody targeting cytotoxic T-lymphocyte antigen-4 and has become the first immune checkpoint inhibitor to enter clinical practice, being recently approved for the treatment of metastatic melanoma. Immune toxicity due to ipilimumab causing colitis, hepatitis, dermatitis and hypophysitis is well-described. We report on a case of acute renal failure resolving rapidly with high-dose corticosteroid treatment highlighting the importance of vigilance for rarer immune-related toxicities as clinical experience with ipilimumab grows.

**Case Report**

A 59-year-old man with melanoma, metastatic to left supraclavicular and axillary lymph nodes received ipilimumab, 3 mg/kg every 21 days for 4 cycles. He had no significant co-morbidities and ECOG performance status 0. Baseline haematological/biochemical profiles were normal. He was on no concomitant medications. He had no significant toxicity during cycle 1 through 4.

Prior to restaging, the patient was admitted on cycle 4 day 17, unwell for the previous 12 hours with fatigue, dyspnoea and elevated serum creatinine of 1.66 mg/dL. He was otherwise asymptomatic. Septic screening was negative. Arterial blood gas measurement demonstrated mild metabolic acidosis. Blood pressure and cardiac output was maintained without pressors. Despite adequate fluid intake prior to and during admission, over the subsequent 72 hours, the patients serum creatinine level rose rapidly to reach a peak of 4.75 mg/dL, with declining urine output. Urine microscopy showed granular casts consistent with acute tubular necrosis.

CT scan of thorax, abdomen and pelvis demonstrated bilateral swelling of the renal cortices (Figure 1b, diameter R kidney 80.5 mm, L kidney 68.8 mm) when compared to baseline (Figure 1a diameter R kidney 64.4mm, L kidney 46.2 mm), however no precipitant of renal failure was noted. The patient was transferred to intensive care and dialysis was considered. High-dose steroid therapy with methylprednisolone 2 mg/kg was commenced 36 hours post-admission. Renal abnormalities rapidly improved with urine output recovery within 24 hours and complete restoration of baseline renal function within 1 week. Elevation of serum creatinine levels and rapid decline with steroid therapy is demonstrated in Figure 2. Dialysis was not required. Renal biopsy was not required due to the rapid response to immunosuppression. Repeat CT scan demonstrated a reduction in kidney size to baseline (Figure 1c, R kidney 64.3 mm, L kidney 53.3 mm).

Restaging PET/CT scan showed an almost complete metabolic response to treatment with only low-grade residual uptake in the left supra-clavicular lymph nodes.

To our knowledge this is the first described case of ipilimumab-induced acute renal failure in the literature. The absence of another precipitant of renal swelling and the rapid and complete response to steroid therapy is highly suggestive of an immune phenomenon as has been described previously to cause colitis and hepatotoxicity.

Ipilimumab is a fully-human IgG1 antibody to Cytotoxic T-lymphocyte Antigen 4 (CTLA-4). CTLA-4 is a co-inhibitory molecule on T-cells which reduces T-cell activation in response to an antigen, thereby, reducing immune reactivity. Ipilimumab inhibits CTLA-4 therefore increasing anti-tumor immunity (1). In a randomised phase III trial published in August 2010 ipilimumab became the first systemic therapy to show an overall survival benefit in treating metastatic melanoma, when compared to a vaccine therapy (2). The side-effects associated with ipilimumab are related to immune stimulation. The most common toxicities include colitis, skin toxicity and hepatotoxicity and resolve quickly with appropriate steroid therapy, as in this case (3).
The rapid recognition and protocol-driven management of immune-related toxicities is vital with early commencement of high dose steroid therapy averting serious complications such as GI perforation (4).

Conflicts of Interest

The Authors have declared no conflicts of interest.

References


Received July 25, 2012
Accepted August 24, 2012