Open Journal of
Clinical & Medical
Case Reports

Volume 7 (2021)
Issue 03

ISSN: 2379-1039

The first report of acute tubular necrosis in the setting of enasidenib use

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Abstract

Enasidenib was approved for treatment of acute myeloid leukemia. There are literatures describing acute renal failure in these patients secondary to differentiation syndrome. We present a case of acute tubular necrosis in a patient on Enasidenib that has not been described previously.

Keywords

Enasidenib; leukemia; renal failure; acute kidney injury.

Abbreviations

IDH2: Isocitrate dehydrogenase 2; AML: Acute myeloid leukemia; DS: Differentiation syndrome; AKI: Acute kidney injury; ATN: Acute tubular necrosis.

Introduction

Enasidenib is a mutant IDH2 protein inhibitor that was approved by the US Food and Drug Administration in 2017 for use in mutant IDH2 AML [1]. This drug is known to cause DS and subsequently AKI in approximately 12% of patients [2]. The mechanism of AKI secondary to DS remains poorly understood, but it is believed that an excessive inflammatory response is the main phenomenon involved [3,4].

Case Presentation

An 83 year-old female with past medical history of AML, diabetes mellitus, and hypertension presented with worsening edema and weight gain for 4 days. Her home medications included Enasidenib (started 20 days prior the admission), acyclovir, and pantoprazole. Her physical exam was significant for bilateral lower extremity edema. Laboratory work revealed pancytopenia, AKI with serum creatinine of

2.06 (up from her baseline of 0.6 mg/dL prior to initiation of Enasidenib), hyperuricemia of 8.8, and normal urinalysis. Chest x-ray showed a new right pleural effusion. Differential diagnosis included DS in the setting of Enasidenib use, pantoprazole-induced interstitial nephritis, and crystal-induced nephropathy secondary to acyclovir. Dexamethasone was started for suspected DS. Enasidenib was continued as there is no proven benefit of withholding this medication due to its prolonged half-life. Pantoprazole and acyclovir were discontinued. After her uric acid increased up to 10.2, she received rasburicase due to possibility of acute uric acid nephropathy. Further work-up, which included antinuclear antibody, complement levels, serum and urine protein electrophoresis, serum and urine immunofixation, anti-glomerular basement membrane antibody, human immunodeficiency virus, and renal ultrasound, was unremarkable. Renal biopsy revealed ATN. There were no signs of cell infiltrate, interstitial nephritis, crystal deposition, or glomerulonephritis. The patient was treated with dexamethasone and her renal function slowly improved.

Discussion

Our case highlights challenges with managing AKI in patients on Enasidenib due to a multitude of potential etiologies. These patients are at risk of DS or tumor lysis syndrome while they receive chemotherapy [5,6]. They could also be on medications that increase the risk of interstitial nephritis. An early and accurate diagnosis defining the type of AKI are essential as it would guide management. In our case, the patient had ATN without evidence of tissue infiltration by inflammatory cells. We hypothesize she developed ATN secondary to renal hypoperfusion related to increased vascular permeability and endothelial damage secondary to release of inflammatory vasoactive cytokines caused by Enasidenib [7].

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Manuscript Information: Received: January 12, 2021; Accepted: March 25, 2021; Published: March 30, 2021

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Citation: Shin YI, Perdomo W, Barbery M, Recinos AR. The first report of acute tubular necrosis in the setting of enasidenib use. Open J Clin Med Case Rep. 2021; 1737.

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