361

Ixazomib Associated Thrombotic Microangiopathy (TMA) in a Myeloma Patient

Dr Heidy Hendra[1], Dr Lauren Heptinstall[2], Dr Stephen B Walsh[1]
[1]UCL Centre for Nephrology, Department of Renal Medicine, Royal Free London NHS Foundation Trust, London, United Kingdom, [2]Department of Cellular Pathology, Royal Free London NHS Foundation Trust, London, United Kingdom

Introduction

Proteasome Inhibitors (PIs) are now a cornerstone in myeloma treatment. Ixazomib increases median time of progression-free survival when used in treatment of refractory/ relapsing multiple myeloma (MM). Drug-induced TMA (DITMA) is increasingly recognised as an adverse effect of PI treatment with most cases linked to Bortezomib and Carfilzomib. TMA, characterised by microangiopathic haemolytic anaemia and thrombocytopenia, can result in organ failure, including acute kidney injury (AKI).

Case study

A 75-year-old female was diagnosed with IgG kappa MM 4 years previously and had a relapse with serum kappa light chain of 309.6 mg/L. She was started on treatment with Ixazomib, Lenalidomide and Dexamethasone. Four days later she was admitted with AKI (creatinine of 278 µmol/L) and was oliguric with urine output of 300 mL/ 24 hours, vomiting and diarrhoea. No other new medication was taken. Ultrasound showed no urinary tract obstruction. Urinalysis showed 2+ blood and 2+ protein, urine protein: creatinine ratio (uPCR) was 57 mg/mmol. Stool culture was negative. A full blood count showed thrombocytopenia and anaemia (Table 1). Despite intravenous rehydration, her renal function continued to deteriorate reaching a creatinine peak of 406 µmol/L.

Renal biopsy revealed the presence of TMA in light microscopy (LM), subsequently the electron microscopy (EM) reported myeloma casts (Figure 1). Results of haemolytic screen can be found in the table below. Following drug discontinuation her renal function stabilised, then partially. She remains in CKD stage 4 and currently under regular follow-up in the low clearance clinic.

Discussion

TMA remains a rare cause of kidney disease in MM patients. Although MM alone is a potential underlying cause of TMA, the timing of AKI coincides with initiation of the new drug makes DITMA a likely diagnosis. So far there are only 3 case reports of association between Ixazomib and TMA. The patient was treated with steroids, Rituximab and plasma exchange in the first report1, FFP and plasma exchange in the second one2 and Eculizumab in the latest one3. By comparison, our patient's renal function was improving following discontinuation of treatment and no plasma exchange was initiated. Out of the two main mechanisms of DITMA that have been described (immune-mediated and dose-dependent toxicity), there is a possibility that it is an immune response as she developed AKI within 21 days after treatment initiation.

This case highlights the importance of recognising DITMA as a potential cause of renal impairment in patients treated with Ixazomib as early recognition can influence their outcome significantly. It also underlines the importance of histological diagnosis for AKI in MM patients. The most important step is to discontinue the implicated drug and refrain from its further use in the future.

Conclusion

To our knowledge, this is the first report of drug-induced TMA due to Ixazomib where improvement in renal function is achieved solely with drug discontinuation.