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Systemic Inflammatory Response Syndrome (SIRS) Induced By Bendamustine – A Case Series

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INTRODUCTION

Bendamustine is an alkylating agent classified into the group of nitrogen mustard analogs, that displays a unique pattern of cytotoxicity compared with conventional alkylating agents. In 2008, the US Food and Drug Administration approved it for treating indolent B-cell non-Hodgkin lymphoma and chronic lymphocytic leukemia. Later, studies confirmed the efficacy of bendamustine in heavily pretreated patients with Hodgkin lymphoma. Despite bendamustine is well-tolerated, it can provoke allergic reactions as well as drug fever or hypersensitivity reactions. In one case series, Bendamustine was reported to cause hypersensitivity in two patients who developed general erythema and had positive allergological studies.

AIM

We noticed that some patients developed systemic inflammatory response syndrome (SIRS) a few hours after administering bendamustine. Three patients with a similar clinical presentation are described here.

CASE 1

A-60-year old woman with advanced Hodgkin lymphoma, was treated with bendamustine as a fourth-line treatment. A few hours after the second dose, she had a fever of 38.5 Celcius, vomiting and diarrhea. On the day after she was admitted to our hospital with signs of shock - her blood pressure was (77/54 mmHg) with mild tachycardia (110 BMP). Blood tests showed new leukocytosis (14.87 K/micl) and neutrophilia, acute kidney injury (Creatinine elevated from normal value to 3.02 mg/dl) and a combined elevation of liver enzymes. Her CRP level was extremely high – 24 mg/dl. In the initial 36 hours, we used hydration and dopamine to maintain her blood pressure. Additionally, we administered a broad spectrum of antibiotics and a high dose of steroids. We fulfilled a wide investigation that included and was normal: three sets of blood culture, urine culture, chest X-ray, abdominal ultrasounds and echocardiography. After four days she was discharged with normal blood-pressure and an improvement in her blood tests. A PET/CT scan after two courses of bendamustine and one month later showed complete remission. Due to her severe reaction to bendamustine and excellent response to treatment, she was referred to alloHCT.

CASE 2

A-70-year old woman with advanced Hodgkin lymphoma, was treated with bendamustine as a fifth-line treatment. A few hours after the second dose, she complained of weakness and measured low blood pressure. On the day after she was admitted to our hospital with signs of high fever and shock - she had high temperature, low blood pressure and moderate tachycardia. Blood tests showed new leukocytosis (18.3 K/micl) with profound neutrophilia (17.1 K/micl), acute kidney injury (Creatinine elevated from normal value to 2.8 mg/dl) and a combined elevation of liver enzymes. In the first 48 hours, we administered hydration and dopamine to stable her blood pressure. Additionally, we administered a broad spectrum of antibiotics. All the additional tests including three sets of blood cultures were normal. After four days she was discharged with normal blood-pressure and an improvement in her blood tests. A PET/CT scan after two courses of bendamustine and two weeks later showed partial remission. The treatment was halted because of her severe reaction to bendamustine, and now she is a candidate for gemcitiabine based chemotherapy regimen.

CASE 3

A-58-year-old man with marginal zone lymphoma, that treated with bendamustine and rituximab as a second-line treatment. A few hours after the second dose, he had a fever and vomiting. He was admitted to our hospital with signs of high fever and shock. Blood tests showed new leukocytosis (17.65 K/micl) with profound neutrophilia (17.1 K/micl), acute kidney injury (Creatinine elevated from normal value to 1.46 mg/dl) and hypophosphatemia (1.3mg/dL).
In the initial 48 hours, dopamine was used to maintain his blood pressure. All additional tests were normal, and three sets of blood cultures were negative. After four days he was discharged with normal blood-pressure and an improvement in her blood tests. The treatment was halted because of his severe reaction to bendamustine, and the patient treated with DHAP protocol and autologous stem cell transplantation.

CONCLUSIONS

We herein report three cases of severe SIRS after bendamustine. Interestingly, it was after the second course in all three. All our patients had fever, low blood pressure, tachycardia and signs of shock in their blood tests including significant kidney failure. All of them have been treated with hydration, dopamine and a broad spectrum of antibiotics, and after 36-48 weaned from amines. All of them had negative blood cultures. The exact component responsible for the quick improvement is still unknown, but all the patients were given amines and extensive hydration. They were all investigated thoroughly, including negative blood cultures, but only given antibiotic treatment for three days. Bendamustine has been previously associated with infections, but severe cases of SIRS like in our patients have not been reported