PATIENT PROFILE

TP (the patient), a 65 year old Caucasian male, presented to the emergency department (ED) on 6/3 with 4 days of right flank pain with radiation to his right groin. His pain was variable in severity with no associated nausea, vomiting, constipation, or diarrhea. In the ED, TP was also found to have thrombocytopenia and anemia, with platelet count of 6,000/uL, Hgb 12.9/gdL, and Hct 35.9%. TP displayed no signs of overt bleeding. Elevated transaminases were also found. Past medical history: imatinib-resistant CML, platelet transfusion dependent thrombocytopenia, polycythemia vera, and myelodysplastic syndrome. At presentation, he was also noted to have a 40 lb weight loss over the past 2 months.

Medications at presentation:
- Tramadol 50 mg PO TID for pain
- Ondansetron 4 mg PO BID
- Methylprednisolone 125mg IV BID for pain
- Hydrocortisone 50mg IV prn pain
- Amiodapine 5 mg PO daily
- Dronabinol 5 mg PO BID ac
- Hydrocodone/APAP 5/500 mg PO Q6H prn pain
- Ammonium Lactate 12% lotion to skin
- Sinus Rinse 1 packet nasally BID
- Fluticasone 50 mcg in each nostril
- PEG 3350 1 TBSP daily mixed in 8 oz water, juice, soda or coffee
- Ondansetron 4 mg IV x 3 doses
- Pantoprazole 40mg PO x 2 doses
- Tramadol 50 mg PO x 4 doses
- Hydrocodone/APAP 5/500 mg PO Q6H prn pain

The adverse events were severe. The patient was admitted due to pain, thrombocytopenia and elevated transaminases. He required daily monitoring for blood transfusion, fever and pain. He required daily platelet transfusion due to a low platelet count in ERCP, if ERCP could be performed. Due to the need for an ERCP procedure, the patient spent 2 additional days in the hospital.

OUTCOMES

After ponatinib discontinuation, and the administration of fluid replacement and blood transfusions, transaminases, platelets and symptoms of pancreatitis normalized. Following hospital admission, the patient was restarted on a decreased dose of 15 mg daily which was increased after a week to 30 mg. After re-initiation, there were no signs of platelets or elevated transaminases. Due to low platelet count (33,000 platelets/uL), ponatinib therapy was again discontinued the following month. When platelet count increased again, the patient was restarted on 15 mg daily. Ponatinib was eventually discontinued due to lack of efficacy and bosutinib was initiated.

DISCUSSION

For patients who are resistant or intolerant to imatinib, dasatinib, or nilotinib, physicians could initiate ponatinib. Patients started on CML treatment are routinely monitored for thrombocytopenia and myelosuppression. Myelosuppression typically occurs within the first 4 weeks of therapy and is more common in patients with advanced disease.4 In the 43 patients with chronic phase CML treatment-related thrombocytopenia of grade 3 or more occurred in 12 patients (28%).5 Ponatinib can also cause acute pancreatitis and liver dysfunction. Dose-limiting toxic effects included pancreatic events, with pancreatitis observed in 14% of patients. Patients should be educated about symptoms and complications of ponatinib. Cortes et al. discussed that thrombocytopenia and pancreatic are self-limiting once the drug is discontinued.2 Discontinuation of ponatinib should resolve pancreatic symptoms within 2 weeks.6 There is no research evaluating restarting the medication. However, it is recommended to decrease the dose and serum lipase levels should be checked every 2 weeks for the first 2 months of initiation, and then monthly thereafter.7 For patients with history of alcohol abuse, additional serum monitoring should be considered.8 This case showed that discontinuation of ponatinib allowed the patient’s labs to normalize. Due to lack of an available alternative agent, the patient’s disease was restarted on ponatinib.

On October 31st, Aria Pharmaceuticals suspended production of ponatinib due to case reports of life-threatening blood clots and severe narrowing of blood vessels linking the drug to fatal heart attacks and strokes within two weeks of initiating Ponatinib. Patients can only be requested for compassionate use. In U.S., however, the Pharmacovigilance Risk Assessment Committee of the European Medicines Agency have decided to keep ponatinib on the market with a stronger warning precautions.9

REFERENCES & DISCLOSURES


Saba Hasan, Crystal Fedorkiv and Naba Rahman - nothing to disclose

Jennifer Andres – nothing to disclose