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Leukopenia associated with long-term colchicine administration

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Abstract

Purpose A case of leukopenia in a patient receiving colchicine for calcium pyrophosphate dihydrate deposition disease, or pseudogout, is reported.

Summary An 85-year-old man experienced leukopenia likely due to colchicine. His medical history included chronic lymphocytic leukemia (CLL), pseudogout, osteoarthritis, and hypertension. In February 2011, his white blood cell (WBC) count was 2700 cells/ μ L, and his absolute neutrophil count (ANC) was 2200 cells/ μ L. Colchicine 0.6 mg orally daily was initiated in March for the prophylaxis of pseudogout. His WBC count decreased, and his colchicine dosage was reduced to 0.6 mg every other day. Despite this decreased dosage, his WBC count and ANC were 600 and 100 cells/ μ L, respectively, in September. In October, the patient received chemotherapy for presumed worsening of his CLL. One month later, his WBC count and ANC were 400 and 200 cells/ μ L, respectively. Subcutaneous filgrastim was administered, and colchicine was discontinued. At the end of November, he received another cycle of chemotherapy followed by pegfilgrastim. On the day of pegfilgrastim administration, the patient's WBC count and ANC were 2000 and 1300 cells/ μ L, respectively. Two weeks later, his WBC count was 8800 cells/ μ L, and his ANC was 8300 cells/ μ L. Daily colchicine was restarted at the end of December. Two months later, his WBC count and ANC were 800 and 500 cells/ μ L, respectively. Given the symptomatic relief with colchicine, therapy was continued with close monitoring.

Conclusion A patient with CLL developed leukopenia in association with colchicine administration for pseudogout.

Colchicine is widely used for both the treatment and prophylaxis of gout. Gastrointestinal effects typically precede severe colchicine toxicity; therefore, treatment is usually discontinued before significant toxicity develops.¹ Colchicine inhibits leukocyte chemotaxis and phagocytosis, urate crystal disposition, and microtubule assembly via inhibition of β -tubulin polymerization in cells (including leukocytes). These actions prevent the neutrophil activation, degranulation, and migration associated with mediating gout symptoms without producing any inherent analgesic or antihyperuricemic effects. A rare adverse effect related to colchicine is leukopenia, which may be caused by the drug's inhibition of leukocyte migration into tissues and its antimitotic effects.² The occurrence of leukopenia secondary to colchicine use at low-to-normal dosages has not adequately been characterized in the literature. We describe a case of leukopenia in a patient receiving colchicine for calcium pyrophosphate dihydrate deposition disease, or pseudogout.

Case report

An 85-year-old Caucasian man (84 kg, 68 in) with a normal serum creatinine concentration (1 mg/dL at baseline) developed leukopenia after receiving treatment with colchicine for pseudogout. His medical history included chronic lymphocytic leukemia (CLL), pseudogout, osteoarthritis, and hypertension. His medications included acetaminophen 500–1000 mg orally every four to six hours as needed for pain, doxazosin 2 mg orally daily at bedtime, polysaccharide–iron complex 150 mg (of iron) orally daily, omeprazole 20 mg orally daily, and testosterone enanthate 200 mg intramuscularly once monthly.

In February 2011, his white blood cell (WBC) count was 2700 cells/ μ L, and his absolute neutrophil count (ANC) was 2200 cells/ μ L. Colchicine 0.6 mg orally daily was initiated in March for the prophylaxis of pseudogout. In June 2011, his WBC count was 1200 cells/ μ L, and his ANC was 800 cells/ μ L. His WBC count continued to decrease to 800 cells/ μ L in July, with an ANC of 400 cells/ μ L. In August, the patient's colchicine dosage was reduced to 0.6 mg every other day. Despite this decreased dosage, his WBC count and ANC were 600 and 100 cells/ μ L, respectively, in September.

In October 2011, the patient received chemotherapy for presumed worsening of his CLL. The regimen consisted of rituximab i.v. on day 1 and bendamustine i.v. on days 1 and 2. Pegfilgrastim was administered subcutaneously on day 3. One month later, his WBC count and ANC were 400 and 200 cells/ μ L, respectively. Subcutaneous filgrastim was administered, and the colchicine was discontinued.

Two weeks later, the patient's WBC count and ANC increased to 1800 and 1400 cells/ μ L, respectively. These counts were maintained for two weeks, with a WBC count of 1900 cells/ μ L at the end of November; his ANC remained the same. At the end of November, he received another cycle of chemotherapy followed by pegfilgrastim. On the day of the pegfilgrastim administration, the patient's WBC count and ANC were 2000 and 1300 cells/ μ L, respectively. Two weeks later, his WBC count was 8800 cells/ μ L, and his ANC was 8300 cells/ μ L.

Daily colchicine was restarted at the end of December. Two months later, his WBC count was decreased to 800 cells/ μ L, and his ANC was 500 cells/ μ L. Colchicine controlled the painful joints related to the patient's pseudogout. Cessation of colchicine treatment was consistently followed by a flare-up of pseudogout symptoms. Given the symptomatic relief with colchicine, therapy was continued with close monitoring.

Due to the association between the patient's WBC and ANC values with initiation and repeated challenge of colchicine, the patient was believed to have developed leukopenia secondary to colchicine.

Discussion

To our knowledge, colchicine-associated leukopenia in a patient being treated for pseudogout has not previously been reported. With a score of 6 on the Naranjo et al.³ scale, this event was deemed a probable adverse reaction associated with colchicine.

A confounding variable is the intermittent treatment of CLL with rituximab and bendamustine. Although this treatment may be considered a possible cause of the patient's leukopenia, the initial occurrence and recurrence of leukopenia was closely associated with the timing of the colchicine therapy and occurred before the patient received his first cycle of chemotherapy and again when chemotherapy was not being administered. Further, the patient was treated with a colony-stimulating factor (CSF) to stimulate neutrophil growth during the first cycle of chemotherapy. Despite CSF therapy, resolution of neutropenia did not occur until colchicine was discontinued. During cycle 2, when colchicine was not given, CSF administration resulted in full resolution of any hematologic toxicity associated with the chemotherapy. Lastly, hepatic impairment leading to impaired colchicine metabolism was not likely, as (1) the patient's aspartate transaminase and alanine transaminase concentrations remained normal during this time frame, (2) acetaminophen was used only occasionally, and (3) the patient reported no alcohol consumption.

Reports describing leukopenia in adult patients receiving varying dosages and durations of colchicine have been published.^{1,4,5} In one report, a 68-year-old man experiencing an acute gout attack received colchicine therapy, and his WBC count decreased from 16,700 to 2,000 cells/ μ L over the course of nine days.¹ The colchicine dosage was reduced, and the drug was subsequently discontinued, followed by treatment with filgrastim. The patient's cell counts recovered after colchicine discontinuation. Ben-Chetrit and Navon⁴ described the case of a 19-year-old woman receiving colchicine for familial Mediterranean fever. The patient developed leukopenia, and colchicine was discontinued, after which time her cell counts recovered. Lastly, Lee and colleagues⁵ described the cases of two adults with Behçet's disease whose WBC counts dropped during treatment with colchicine. In both cases, colchicine was discontinued, patients were treated with granulocyte CSFs, and their cell counts recovered thereafter. Our patient received lower colchicine dosages than in these previously reported cases yet continued to experience hematologic effects, indicating that this effect may not have been dosage related.

Colchicine was a likely cause of leukopenia in our patient. Monitoring of WBCs and neutrophils may be warranted in patients receiving long-term colchicine therapy, even at low-to-normal dosages.

Conclusion

A patient with CLL developed leukopenia in association with colchicine administration for pseudogout.

Footnotes

The authors have declared no potential conflicts of interest.

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