Case Report / Olgu Sunumu

High Dose Cytosine Arabinoside- Induced Asymptomatic Bradycardia

Yüksek Doz Sitozin Arabinozid İlişkili Asemptomatik Bradikardi

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Özet: Sitozin Arabinosid (Sitarabin), akut miyeloid lösemide (AML) yaygın olarak kullanılan ajanlardan biridir. Tedavi sırasında kardiyovasküler yan etkiler genellikle gözlenmez. Biz akut miyeloid lösemili bir hastada konsolidasyon tedavisi sırasında gelişen asemptomatik bradikardisi olan olguyu sunmayı amaçladık. 34 yaşındaki erkek hastaya Şubat ayında AML tanısı konuldu. İndüksiyon kemoterapisi sonrası konsolidasyon tedavisi için 2x1,5 gram/m² yüksek doz sitarabin tedavisine başlandı. Tedavinin 11. gününde (kemoterapi tedavisinin bitmesinden 6 gün sonra) nabzı 39 atım/dk'ya düştü. Yüksek doz sitozin arabinosid tedavisi başlandıktan sonraki 12. günde hastanın nabız sayısı 50/dk'nın üzerindeydi ve takip eden günlerde bradikardisi olmadı. Bradikardinin nedenlerinin diğer nedenleri dışlandı. Hastanın ejeksiyon fraksiyonunun %65 olduğu, sinüs bradikardisi olduğu ve kalp hızının ritmik olduğu saptandı. Literatürde akut miyeloid lösemili yedi hastada, akut lenfoblastik lösemili bir hastada, Hodgkin dışı lenfomalı bir hastada ve yüksek doz sitozin arabinozid ile ilişkili bradikardi bildiren Hodgkin lenfomalı bir hastada bradikardi saptanmıştır. Ayrıca akut miyeloid lösemili bir hastada düşük doz sitozin arabinosid ile bradikardi gelişti. Olgumuz literatürde sitarabin nedeniyle bradikardi gelişen 11. olgudur.
Anahtar Kelimeler: Kardiyovasküler Yan Etki, Akut Myeloid Lösemi, Bradikardi, Yüksek Doz Siterabin, Yan Etki.

Abstract: Cytosine Arabinoside (Cytarabine) is commonly used agents in acute myeloid leukemia (AML). Cardiovascular side effects are not common during treatment. We aimed to present asymptomatic bradycardia developed during the first consolidation treatment in a patient with acute myeloid leukemia. A 34-year-old male patient was diagnosed with AML in February. After induction chemotherapy, high dose cytarabine treatment was started at 2x1.5 grams/m² for consolidation treatment. On the 11th day of the treatment, his pulse decreased to 39 beats/min. On the 12th day after the initiation of high dose cytosine arabinoside treatment (6 days after chemotherapy treatment ends), the patient's pulse rate was above 50/min, and there was no bradycardia in the following days. Other causes of other causes of bradycardia were excluded. It was reported that the patient had sinus bradycardia with an ejection fraction of 65% and his heart rate was rhythmic. There are seven patients with acute myeloid leukemia, one patient with acute lymphoblastic leukemia, one patient with non-Hodgkin's lymphoma, and one patient with Hodgkin's lymphoma who reported high dose cytosine arabinoside associated bradycardia. In addition, one patient with acute myeloid leukemia developed bradycardia with low dose cytosine arabinoside. Our case is the 11th case in the literature that develops bradycardia due to cytarabine.
Keywords: Cardiovascular Side Effect, Acute Myeloid Leukemia, Bradycardia, High Dose Cytarabine, Side Effect.

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1. Introduction

Cytosine Arabinoside (Cytarabine) is one of the most commonly used agents for induction and consolidation in acute myeloid leukemia (AML). Myelosuppression, neurological, gastrointestinal, and liver toxicity are common and well-known side effects of high-dose cytarabine. However, cardiotoxic side effects are rare (1). Although pericarditis, pericardial effusion, and cardiac tamponade can be seen as cardiovascular side effects, conduction defects are very rare (2). We aimed to present asymptomatic bradycardia developed during the first consolidation treatment in a patient with acute myeloid leukemia.

2. Case Report

A 34-year-old male patient was diagnosed with AML-M1 in February 2019 with a bone marrow biopsy. Flow cytometry showed a blast population with a myeloid phenotype, including greater than 80% of cells that expressed CD13, CD33, and CD117. He has no history of illness. He was given idarubicin 12 mg/m2 for 3 days and cytosine arabinoside 100 mg/m2 for 7 days in February 2019. After induction chemotherapy, the patient was re-performed bone marrow biopsy and aspiration. Bone marrow aspiration showed remission. In April 2019, high dose cytarabine treatment was started at 2x1.5 grams/m² for consolidation treatment. The patient had no history of cardiac disease, and his pulse rate was 84 beat/min before treatment (Picture-1). During the patient's follow-up, his pulse fell below 50 beats/min after the 7th day of treatment. On the 11th day of the treatment, his pulse decreased to 39 beats/min (Picture-2). Other causes of bradycardia were myocardial infarction (normal cardiac enzyme), electrolyte imbalance, structural heart disease (normal echocardiography), atrioventricular block, drugs and hypothyroidism were excluded. The patient did not describe any symptoms of bradycardia, such as dizziness, palpitations or chest pain. The patient was consulted to cardiology. It was reported that the patient had sinus bradycardia with an ejection fraction of 65% and his heart rate was rhythmic. Atropine treatment was recommended. Atropine was not given because the patient had no symptoms. On the 12th day after the initiation of high dose cytosine arabinoside treatment, the patient's pulse rate was above 50/min, and there was no bradycardia in the following days. The patient's cardiac enzymes were normal and there was no ST segment change. There was no ECG finding compatible with a-v block and there was sinus bradycardia. No structural heart disease was detected on electrocardiography. Thyroid function tests in the serum examined for hypothyroidism were found to be normal. Electrolytes of potassium, magnesium and calcium were found to be normal. There was no use of medications such as beta blockers, calcium channel blockers and antidepressants that cause bradycardia. When other causes of bradycardia were excluded, the patient was associated with high dose cytosine arabinoside.

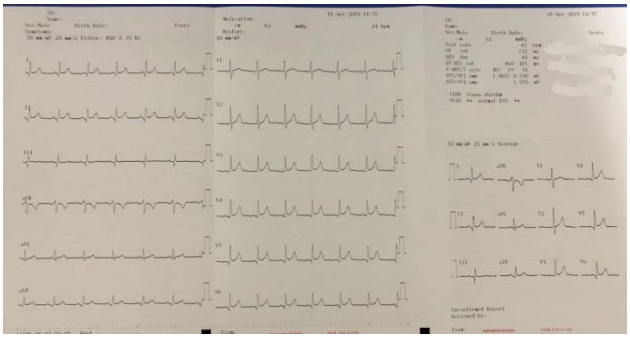

Figure 1. ECG in normal sinus rhythm.

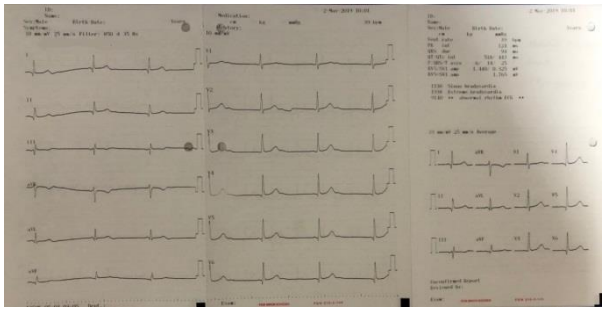

Figure 2. ECG showing sinus bradycardia

3. Discussion

Cardiac side effects due to high dose cytosine arabinoside are not very common. There are seven patients with acute myeloid leukemia, one patient with acute lymphoblastic leukemia, one patient with non-Hodgkin's lymphoma, and one patient with Hodgkin's lymphoma who reported high dose cytosine arabinoside associated bradycardia. In addition, one patient with acute myeloid leukemia developed bradycardia with low dose cytosine arabinoside.

In the literature review, some patients had bradycardia immediately after drug infusion, and some had bradycardia 3 days after the end of the treatment cycle (3-10). In our patient, bradycardia developed 7 days after the end of the treatment cycle.The mechanism of bradycardia due to high dose cytosine arabinoside is not fully understood. Although one case of low dose cytrabine has been reported in the literature, most of the reported cases have developed due to high dose. Since our patient was asymptomatic and hemodynamically stable, he was followed up in the clinic. When a patient had hemodynamic instability, treatment should be given under close observation in intensive care units (7). Bradycardia was not seen in the previous treatment of the our patient receiving low-dose cytarabine. The patient was asymptomatic when bradycardia developed with high dose cytrabine treatment, and bradycardia spontaneously improved 12 days after treatment.

4. Conclusion

Especially patients receiving high-dose cytosine arabinoside therapy should be closely monitored for bradycardia during the first days of the cycle and for the first week after the end of the cycle.

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Ethics

Informed Consent: The authors declared that informed consent form was signed by the patient.

Copyright Transfer Form: Copyright Transfer Form was signed by the authors.

Authorship Contributions: Concept: MŞ, AK, İA. Design: MŞ, AK. Data Collection or Processing: MŞ, AK, BÖ, MM, ÖB, İA. Analysis or Interpretation: MM, ÖB, İA. Literature Search: MŞ, AK, BÖ. Writing: MŞ, AK, BÖ.

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