

Recurrent Bradycardia Episodes Induced by Cisplatin Infusion

Sisplatin İnfüzyonuna Bağlı Tekrarlayan Bradikardi Atakları

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Abstract

Chemotherapy may induce entire spectrum of cardiac pathology. Cisplatin has been used in oncology practice for a long time, but no sufficient clinical evidence exists about arrhythmogenic potential of this drug. We report a rarely diagnosed case of asymptomatic bradycardia probably induced by cisplatin infusion.

In December 2010, a 28 years of woman was diagnosed with Sertoli-Leydig cell tumor. Three courses of BEP (bleomycine, etoposide, and cisplatin) chemotherapy was planned because of the poor prognostic factors. During the third course of chemotherapy, she had bradycardia during cisplatin infusion on routine vital sign assesments. Her physical examination including blood pressure was within normal limits. Electrocardiogram (ECG) revealed sinus bradycardia (40 beats/min). The patient had no clinical symptoms consistent with vagal stimulation. Blood pressure remained normal during and after the bradycardia episode. Concomitant serum concentrations of urea, creatinine, and electrolites (sodium, potassium, calcium, chloride, and magnesium) were within normal ranges. Her chemotherapy was terminated and 24-hour holter ECG was performed to reveal the bradycardia episodes. She had asymptomatic bradycardia during the records of holter ECG. After a few days of follow up her bradycardia episodes resolved.

It was worthwhile for this case presentation because the patient presented with asymptomatic bradycardia after cisplatin infusion. Cisplatin-induced sinus bradycardia is an unusual adverse effect with underlying mechanisms that remain to be clarified.

Keywords: Hemihyperplasia, Beckwith-Wiedemann syndrome

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Introduction

Several antineoplastic drugs are known to have cardiac toxic effects which range over a wide spectrum of cardiac pathology, including cardiomyopathy, ischemia and arrhythmia¹⁻³.

Cisplatin is widely used in the treatment of many neoplastic diseases. Its main side effects include nephrotoxicity, myelotoxicity, neurotoxicity, ototoxicity and

gastrointestinal toxicity⁴. Although cisplatin has been used in the treatment of common cancers, there is no enough clinical evidence regarding the cardiotoxicity of this drug. There are some case reports of arrhythmia including supraventricular tachycardia, bradycardia and conduction abnormalities caused by cisplatin infusion in the literature⁵⁻¹⁰.

In this paper, we report a case of asymptomatic bradycardia probably induced by cisplatin infusion.

Case Report

In December 2010, a 28 years of woman was diagnosed with Sertoli-Leydig cell tumor. The pathology revealed stage I undifferentiated sertoli-leydig cell tumor with a high proliferation index. Because of the poor prognostic factors three courses of BEP chemotherapy was planned. Chemotherapy was started with intravenous (IV) Cisplatin 20mg/m² on days 1-5 plus IV Etoposide 100mg/m² on days 1-5 and bleomycine 30MÜ on days 2,9 and 16. There was no significant feature in her medical and family history. Her previous cardiac history was unremarkable and her baseline heart rate prior to chemotherapy was within normal ranges. She had grade 1 neusea and astenia during the two courses of chemotherapy, she had no other side effects. However, during the third course of chemotherapy on day 4, she had bradycardia during cisplatin infusion on routine vital sign assesments. The patient experienced no neusea, vomiting, or other clinical symptoms consistent with vagal stimulation, and her physical examination including blood pressure was within normal limits. Electrocardiogram (ECG) revealed sinus bradycardia (40 beats/min).

Cisplatin infusion and the other chemotherapy agents planned were terminated. Blood pressure remained normal during and after the bradycardia episode. Concomitant serum concentrations of urea, creatinine, and electrolites (sodium, potassium, calcium, chloride, and magnesium) were within normal ranges. She had no symptoms during bradycardia episode. Cisplatin infusion was started again on the fifth day of the therapy but bradycardia developed soon after cisplatin infusion. 24-hour holter ECG was performed to reveal the bradycardia episodes after cardiology consultation. She had asyptomatic bradycardia during the records of holter ECG. The mean heart rate was 56 beats/min and the minimum recorded heart rate was 35 beats/min. Although the episodes were asymptomatic it was her last chemotherapy course and the therapy was terminated. After a few days of follow up her bradycardia episodes resolved. She continues her oncologic follow up visits every three months.

Discussion

Cardiac toxicity is a well known side effect of many antineoplastic drugs and most commonly described with anthracyclines. Toxic effects may be acute or chronic, and a wide spectrum ranging from myocardial damage leading to heart failure, ischemia, or dysrhythmias have been described^{1, 2}. Arrhythmias, in general, frequently have an acute onset, and in some cases may be fatal. Many chemotherapeutic agents have been reported to induce rhythm disturbances, through direct and indirect pathogenetic mechanisms.

Arrhythmias have also rarely been described with cisplatin. There is not enough data about the pathogenesis of arrhythmia caused by cisplatin infusion. Entire spectrum of arrhythmia, including supraventricular tachycardia, bradycardia and block in any degree may be observed during or shortly after cisplatin administration, some of them being clinically important and may cause death⁵⁻¹⁰.

Arrhythmias caused by anticancer drugs may occur during and shortly after drug administration by different possible mechanisms such as direct effects of drug on heart, coronary artery spasm, electrolyte imbalance and autonomic cardioneuropathy. There is no known toxic effect of cisplatin on myocardial cells directly, but a possible side effect on coronary arteries has been reported (10). The other possible mechanisms for cisplatin related arrhythmias include electrolyte imbalance that might occur after cisplatin administration¹¹. Cisplatin frequently induces electrolyte changes primarily associated with decreases in intracellular and extracellular potassium as well as magnesium concentrations^{12, 13}.

Our patient has not a history of cardiac disease or cardiac abnormality or neoplastic pericardial involvement. Sinus bradycardia occurred immediately after infusion of the cisplatin. There were no alterations in the serum electrolyte concentrations in our patient. Hypomagnesemia has been suggested as a contributing mechanism of cisplatin induced tachyarrhythmias¹³. However, our patient was not hypomagnesemic during any of these bradycardia episodes.

The contribution of bleomycine and etoposide to the observed cardiac events could be excluded, as bleomycine infusion was given on day 2 and bradycardia occurred before the start of etoposide. Also there is no reported arrhythmias associated with bleomycine or etoposide in the literature. The episodes of bradycardia after cisplatin infusions suggest an association with cisplatin. After cessation of cisplatin infusion the bradycardia episodes improved gradually over several days. Cisplatin has a half-life elimination up to 73 hours (range 44-73 hours). The effect of cisplatin may continue for several days¹³. Thus, our patients' bradycardia episodes resolved after approximately three days.

Cisplatin-induced sinus bradycardia is an unusual adverse effect with underlying mechanisms that remain to be clarified. As patients receiving cisplatin are not routinely monitored, this adverse effect may not be detected in clinical practice. It is usually recognized on routine vital sign assessments for other reasons. Since the bradycardia episodes are asymptomatic and reversible in nature, no dosage adjustment or cessation of cisplatin therapy seems to be necessary. But particular attention should be given to patients who already have bradycardia or those using medications known to cause cardiac arrhythmias.

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