Symptomatic Severe Bradycardia during Pazopanib Treatment

Pazopanib Tedavisi Sırasında Semptomatik Şiddetli Bradikardi

ABSTRACT

Pazopanib, a tyrosine kinase inhibitor that targets growth factor receptors, is associated with various side effects, including bradycardia. We report a severe case of symptomatic bradycardia, with a heart rate dropping to 28 beats per minute, in a patient with cardiac angiosarcoma treated with 800 mg/day of pazopanib. Reducing the dosage to 600 mg/day improved the heart rate to 53 beats per minute. This case highlights the risk of severe bradycardia associated with pazopanib, emphasizing the need for vigilant heart rate monitoring.

Keywords: Angiosarcoma, cardiotoxicity, pazopanib, permissive cardiotoxicity

CASE REPORT

Angiosarcomas are rare, highly vascular, and aggressive malignancies originating from endothelial cells lining the blood or lymphatic vessels. They are responsive to anti-angiogenic therapies.1 Pazopanib, a tyrosine kinase inhibitor, targets various growth factor receptors, including vascular endothelial growth factor receptors, platelet-derived growth factor receptors, and c-kit. By inhibiting vascular endothelial growth factor receptors, Pazopanib may restrict tumor growth by limiting blood supply, potentially making it a valuable therapeutic agent for diseases characterized by abnormal angiogenesis or cellular proliferation.1-3

Originally approved for renal cell carcinoma and certain soft tissue sarcomas, Pazopanib’s mechanism of inhibiting vascular endothelial growth factor receptor inhibition could make it a promising treatment for angiosarcomas. In rare cancers like angiosarcoma, where standard treatments may fail or be unsuitable, the consideration of Pazopanib for angiosarcoma treatment necessitates an understanding of its side effect profile, which includes hypertension, liver toxicity, and, less commonly, bradycardia. Ongoing monitoring and patient cooperation are essential for successful treatment with this drug.3-4

Case Report

A 25-year-old non-smoking, non-diabetic, normotensive female patient, previously diagnosed with Poland Syndrome, received a left breast implant for aesthetic purposes. She underwent heart surgery two years earlier at another hospital due to a sudden onset of shortness of breath caused by a pericardial effusion from primary angiosarcoma in the right atrium. Post-operation, she was administered three cycles of Adriamycin but did not achieve a sufficient clinical response. Consequently, she underwent six cycles of radiation therapy (RT) alongside Paclitaxel and Gemcitabine. She had contracted Coronavirus Disease 2019 (COVID–19) seven months prior to this diagnosis but was unvaccinated and received no treatment.
Approximately six months after the operation, when positron emission tomography–computed tomography (PET-CT) scans revealed recurrence and lung lesions, treatment with 800 mg/day of Pazopanib was initiated. Two electrocardiograms (ECGs) from her routine CardioOncology follow-ups showed sinus rhythm, with heart rates of 63 and 64 beats per minute (bpm), respectively (Figures 1–2). At about the third month, the patient was symptom-free, and her ECG showed sinus rhythm at 54 bpm (Figure 3).

After about eight months on Pazopanib, the patient presented to the cardio-oncology department with symptoms of lightheadedness and episodes of fatigue. Neither peripheral edema nor pulmonary rales were observed during the physical examination. The body mass index was 24.2 kg/m², blood pressure was 101/62 mmHg, and her resting heart rate was 36 bpm, as per ECG (Figure 4). The left ventricular ejection fraction was 51%, and no wall motion abnormalities were detected on transthoracic echocardiography. On the same day, a 24-hour Holter monitor was applied, detecting bradycardia that reached 28 bpm during sleep hours (Figure 5).

No other cause of bradycardia, such as medications and/or comorbidities, was identified in the patient. The relevant oncologist was consulted, and the Pazopanib dose was reduced to 600 mg/day. Subsequently, a control ECG showed the patient’s resting heart rate had normalized to 53 bpm (Figure 6),

**ABBREVIATIONS**

<table>
<thead>
<tr>
<th>Acronym</th>
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<tr>
<td>COVID-19</td>
<td>Coronavirus Disease 2019</td>
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<td>ECGs</td>
<td>Electrocardiograms</td>
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<td>PET-CT</td>
<td>Positron emission tomography–computed tomography</td>
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<td>RT</td>
<td>Radiation therapy</td>
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as low as 35 bpm. While the Poland Syndrome previously
bradycardia has been reported previously with rates reaching
primary angiosarcoma and its management. Pazopanib-induced
bradycardia that emerged during Pazopanib treatment for
this case report focuses solely on the severe symptomatic
published in conjunction with Poland Syndrome. However,
Several cases of primary angiosarcoma have been previously
Discussion
Several cases of primary angiosarcoma have been previously
in this instance, after detecting symptomatic bradycardia as
as low as 35 bpm. While the Poland Syndrome previously
identified in the patient is not the focus of this report, it is worth
noting that the patient’s cancer progressed even after surgery
and treatment with Adriamycin, Gemcitabine, Paclitaxel, and
radiotherapy. Given this progression, the oncologists deemed
Pazopanib an appropriate next step.
In conclusion, the use of Pazopanib for treating cardiac
angiosarcomas represents an intriguing area of exploration, given
its anti-angiogenic properties. While it may offer important
therapeutic benefits, more robust clinical studies are needed to
establish its efficacy and safety in this specific patient population.
Until then, its application should be considered on a case-by-
case basis, especially in settings where standard therapies have
failed or are unsuitable. This report exemplifies the concept of
“permissive cardiotoxicity,” where a dose reduction of Pazopanib
was chosen over discontinuing this life-saving treatment.
Effective implementation would require collaboration with a
multidisciplinary team and diligent patient monitoring.

**Informed Consent:** Written informed consent was obtained from the
patient.

**Peer-review:** Externally/Internally peer-reviewed.

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Critical Review – C.Z.

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**References**

**Figure 6. An ECG recorded four days after reducing the Pazopanib dose to 600 mg/day, showing a heart rate of 53 bpm and a QTcF of 456 ms.**