

Case presentation

- 58-year-old woman with hypertension, increased intraocular pressure, cervical spinal cord compression from degenerative disc disease, with no prior ECG abnormalities.
- She was initially started on **amlodipine 5 mg daily**, which effectively normalized her BP. Three months later, she started **brimonidine/timolol ophthalmic solution**.
- No history of coronary disease, diabetes, or thyroid disorder. She reported minimal dietary sodium intake and daily caffeine consumption.

Presentation

- She presented to the emergency department with recurrent fatigue and lightheadedness.
- Vital signs:** BP 78/55 mmHg, HR 45 bpm.
- ECG:** Sinus bradycardia with **first-degree AV block (PR 248 ms)**.
- No chest pain, syncope, or dyspnea.

Investigation

- She was advised to stop amlodipine, and one week later, her BP rose to **174/95 mmHg**, HR 55 bpm prompting reinitiation of amlodipine.
- Four months later, she developed with recurrent dizziness several times per week, with her being BP **93/60 mmHg**, leading to a dose reduction to 2.5 mg daily.
- Despite dose reduction, she continued to experience fatigue and orthostatic dizziness, with **orthostatic vitals** dropping to **58/48 mmHg**.
- Repeat ECG:** Sinus bradycardia (49 bpm) with **Mobitz type I AV block**.
- Echocardiogram:** EF 63%, mild mitral/tricuspid regurgitation, no pericardial effusion or structural abnormalities.

- Workup ruled out** ischemic heart disease, infection, thyroid dysfunction, and electrolyte derangement.

Management

- Permanent discontinuation of amlodipine.**
- Counseling on limiting caffeine intake to avoid diuretic-induced dehydration, improving hydration and liberalizing sodium slightly.
- Continued brimonidine/timolol ophthalmic drops with monitoring.

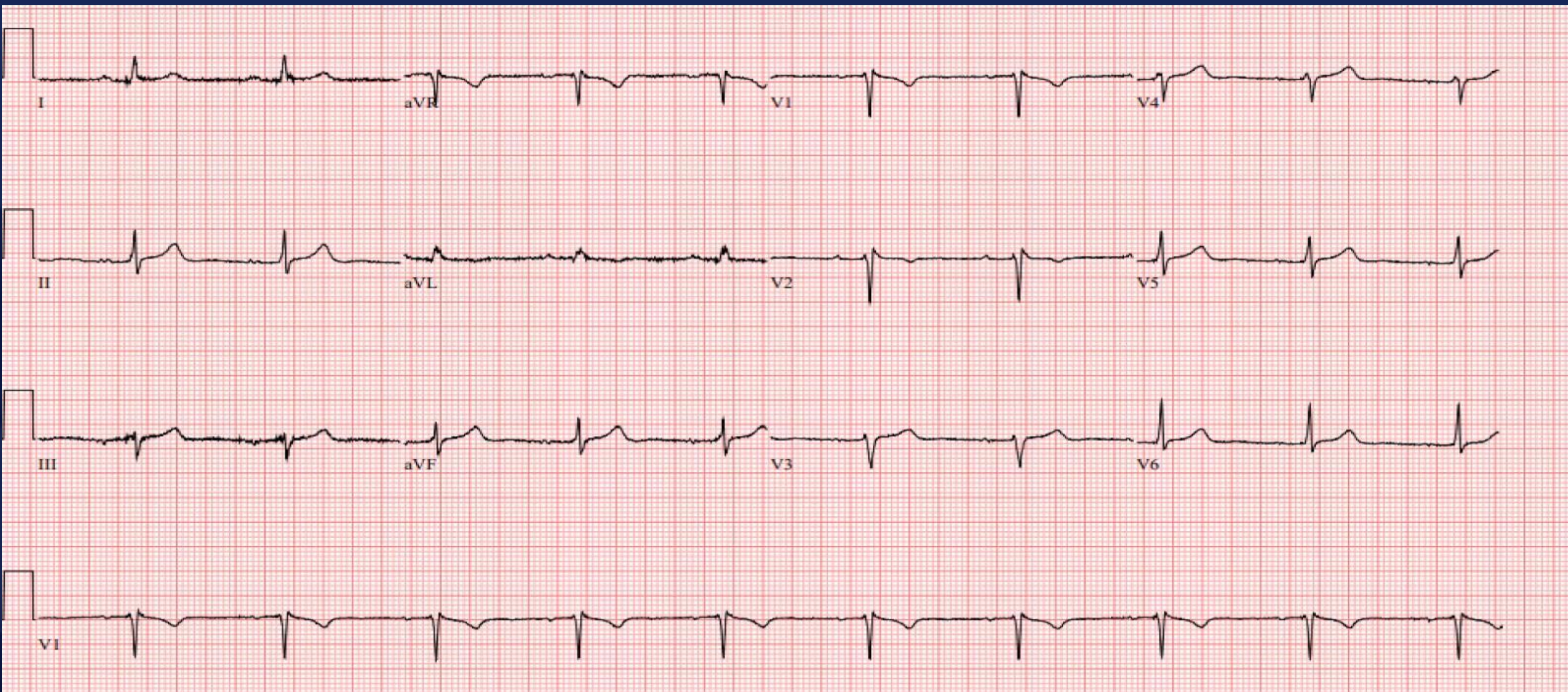


Figure 1: ECG displaying normal sinus rhythm, two months before the ED visit (HR: 60).

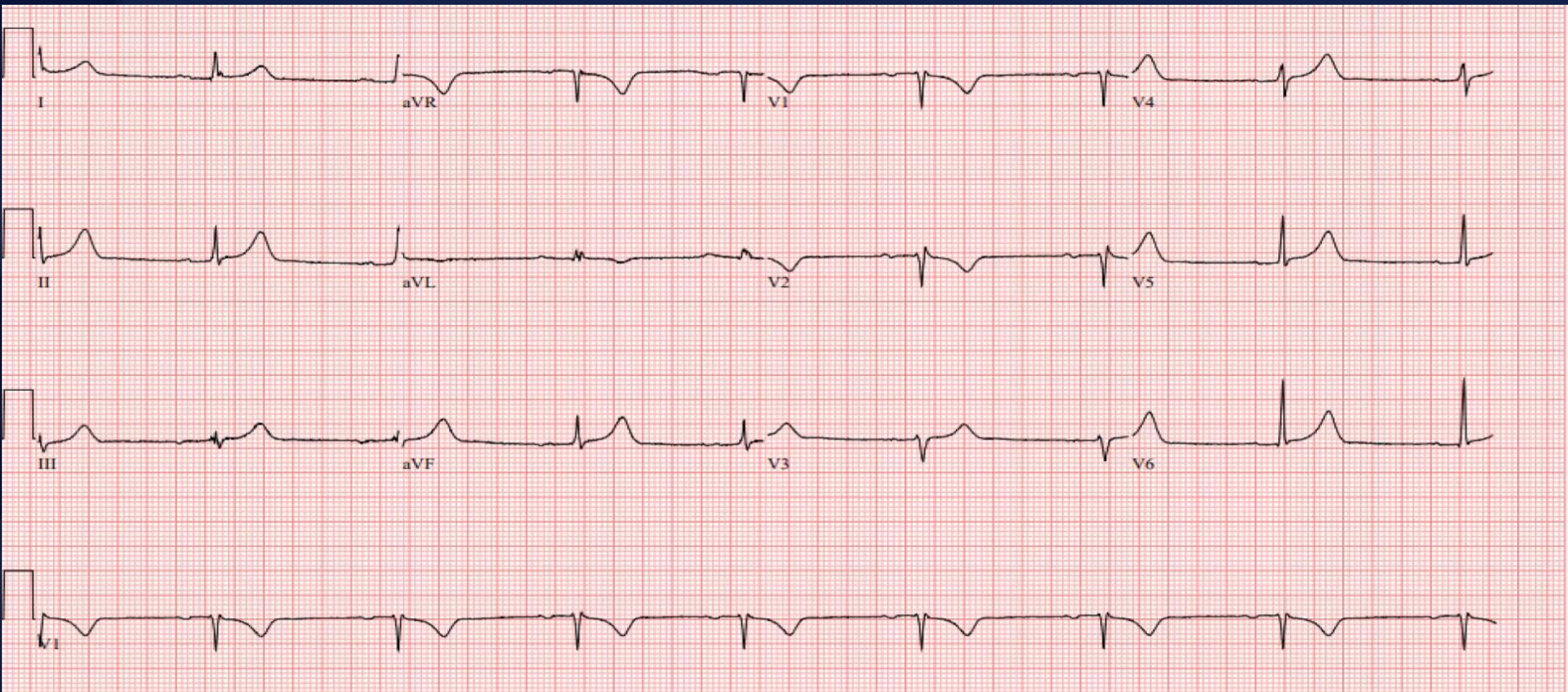


Figure 2: ECG displaying a first-degree AV block and sinus bradycardia, taken during her ED visit (HR: 49 bpm).

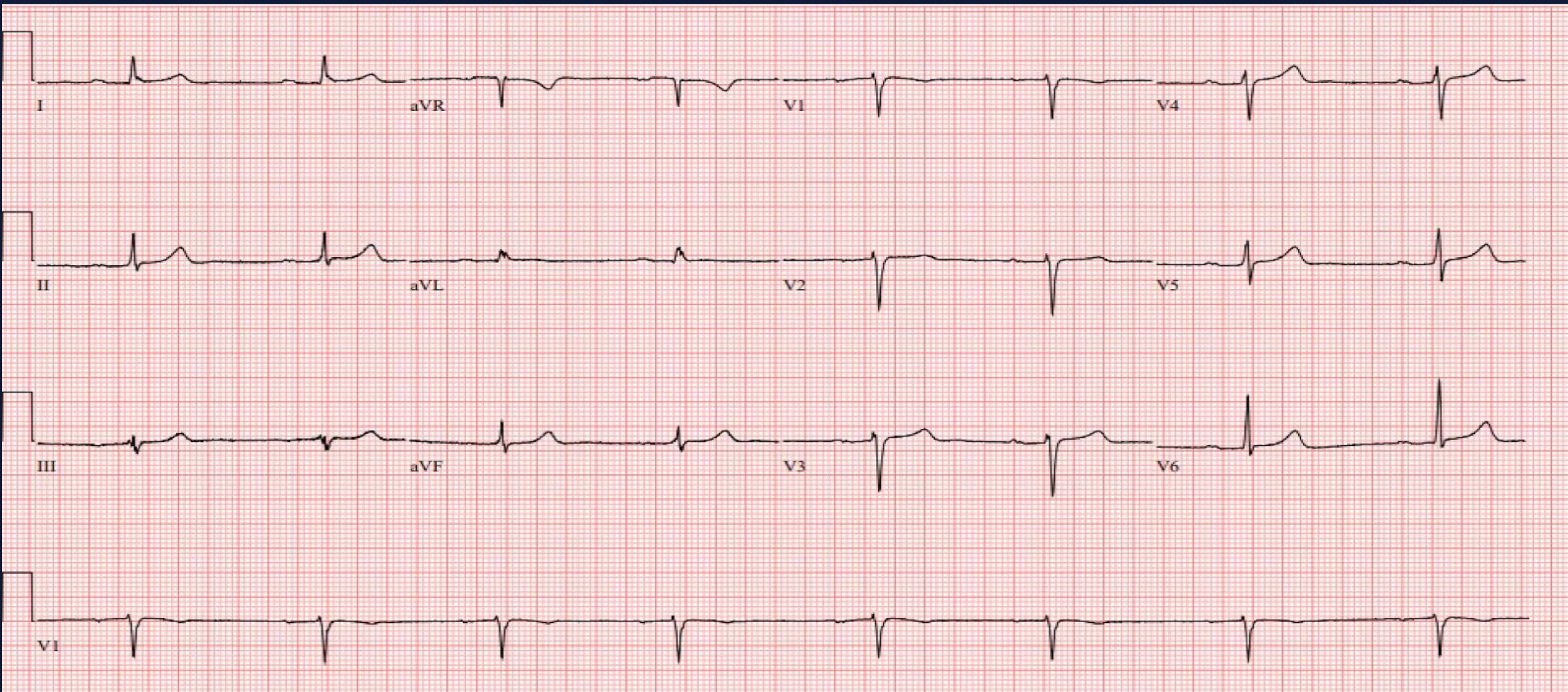


Figure 3: ECG displaying a first-degree AV block and sinus bradycardia, taken upon discontinuation of her amlodipine 2.5 mg (HR: 49 bpm).

Naranjo Adverse Drug Reaction Probability Scale				
Question	Yes	No	Do Not Know	Score
1. Are there previous <i>conclusive</i> reports on this reaction?	+1	0	0	1
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	2
3. Did the adverse reaction improve when the drug was discontinued or a <i>specific</i> antagonist was administered?	+1	0	0	1
4. Did the adverse event reappear when the drug was re-administered?	+2	-1	0	2
5. Are there alternative causes (other than the drug) that could <u>on</u> their <u>own</u> have caused the reaction?	-1	+2	0	-1
6. Did the reaction reappear when a placebo was given?	-1	+1	0	0
7. Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	+1	0	0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	1
9. Did the patient have a similar reaction to the same or similar drugs in <i>any</i> previous exposure?	+1	0	0	0
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	1
TOTAL SCORE: 7				

Table 1: Naranjo Adverse Drug Reaction Probability Scale for Amlodipine

Naranjo Adverse Drug Reaction Probability Scale				
Question	Yes	No	Do Not Know	Score
1. Are there previous <i>conclusive</i> reports on this reaction?	+1	0	0	1
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	2
3. Did the adverse reaction improve when the drug was discontinued or a <i>specific</i> antagonist was administered?	+1	0	0	0
4. Did the adverse event reappear when the drug was re-administered?	+2	-1	0	0
5. Are there alternative causes (other than the drug) that could <u>on</u> their <u>own</u> have caused the reaction?	-1	+2	0	-1
6. Did the reaction reappear when a placebo was given?	-1	+1	0	0
7. Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	+1	0	0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	0
9. Did the patient have a similar reaction to the same or similar drugs in <i>any</i> previous exposure?	+1	0	0	0
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	1
TOTAL SCORE: 1				

Table 2: Naranjo Adverse Drug Reaction Probability Scale for Brimonidine/Timolol

References
1. Amlodipine besylate and Bradycardia - a phase IV clinical study of FDA data. <https://www.ehealthme.com/ds/amlodipine-besylate/bradycardia/>

Outcome and Follow-up

- Within one week, she had complete symptom resolution.
- Home BP stable at **116–138 mmHg**, HR around 59 bpm.
- Clinic BP stabilized in the 130s/180s, HR was 50-60s
- Orthostatic vitals normalized.
- Close outpatient monitoring with no recurrent symptoms.
- Given symptom resolution and normal studies, tilt table testing was deferred after shared decision making.
- At one month follow-up she remained asymptomatic.

Discussion

- Dihydropyridine CCBs** like amlodipine are generally considered AV conduction neutral.
- Rare bradycardia cases (**0.9%**) have been reported, usually early and in older patients.¹ This case shows that chronic exposure can cause symptomatic bradycardia and AV block.
- Volume depletion, low sodium intake, and systemic absorption of topical beta blockers** likely contributed.
- Ophthalmic timolol** bypasses hepatic first-pass metabolism, causing systemic beta-blockade. **Brimonidine** may also contribute to bradycardia, especially in combination.
- The Naranjo Algorithm** confirmed amlodipine as the more likely cause.

Conclusion

- Amlodipine **can cause clinically significant bradyarrhythmias**, as the risk increases in the setting of **co-exposures** (e.g., topical beta blockers, dehydration)
- Early identification and drug withdrawal can fully reverse symptoms.
- Clinicians should consider amlodipine in the differential for bradycardia, especially when other causes are ruled out.