

# Fetal ductus arteriosus constriction associated with maternal metamizole use and excessive polyphenol consumption: Two case reports

Carolina Martins, João Seixas, Clara Vieira, Igor Mello, Ana Groetaers, Carolina Ferreira; *Centro de Ensino Superior de Valença, Faculdade de Medicina de Valença, Valença -RJ, Brazil*

## INTRODUCTION

The ductus arteriosus (DA) is a vital fetal vessel connecting the pulmonary artery to the aorta, bypassing the developing lungs. Patency is maintained by prostaglandins; inhibition leads to constriction.

### Risk Factors for Premature DA Constriction:

- Maternal exposure to NSAIDs or metamizole (prostaglandin synthesis inhibition).
- Excessive maternal polyphenol consumption (emerging cause).

### Clinical Consequences:

- Fetal pulmonary hypertension (PH)
- Right heart failure
- Fetal hydrops
- Intrauterine fetal death

## CASE 1: Polyphenol- Associated Constriction

**Patient:** 36-year-old, G5P2A2, with normal prenatal care until 38+2 weeks.

**Exposure:** Daily consumption of 6 oranges (~510.6 mg polyphenols).

**Ultrasound (38+2 weeks):** Reduced pulmonary artery (PA) flow, retrograde PA valve flow, absent DA flow, right ventricular (RV) and right atrial (RA) dilation, RV hypokinesia, RV hypertrophy, and holosystolic tricuspid regurgitation (HTR).

**Outcome:** Cesarean delivery at 39+1 weeks (Apgar 8/9).

**Postnatal Course:** Echocardiography showed patent foramen ovale, moderate RV dilation, RV hypertrophy, PH, and a small patent DA (1.8 mm). Newborn received oxygen support; subsequent DA closure and PH improvement observed. Discharged on day 11 for outpatient follow-up.

## CASE 2: Metamizole- Associated Constriction

**Patient:** 33-year-old, G2P1, with normal prenatal care until 35+6 weeks; history of gestational hypertension.

**Exposure:** Metamizole 1g every 8 hours for 4 days due to headache.

**Ultrasound (35+6 weeks):** Fetal cardiomegaly, RA/RV dilation, RV dysfunction, HTR, protodiastolic mitral regurgitation, dilated PA, reduced anterograde PA flow, diminished DA flow, and fetal skin edema.

**Outcome:** Emergency cesarean delivery at 36 weeks (Apgar 8/9).

**Postnatal Course:** Admitted to NICU, requiring mechanical ventilation and dobutamine for moderate/severe heart failure and PH.

**Evolution:** Rapid improvement; extubated on day 5 and discharged on day 9 with no clinical repercussions.

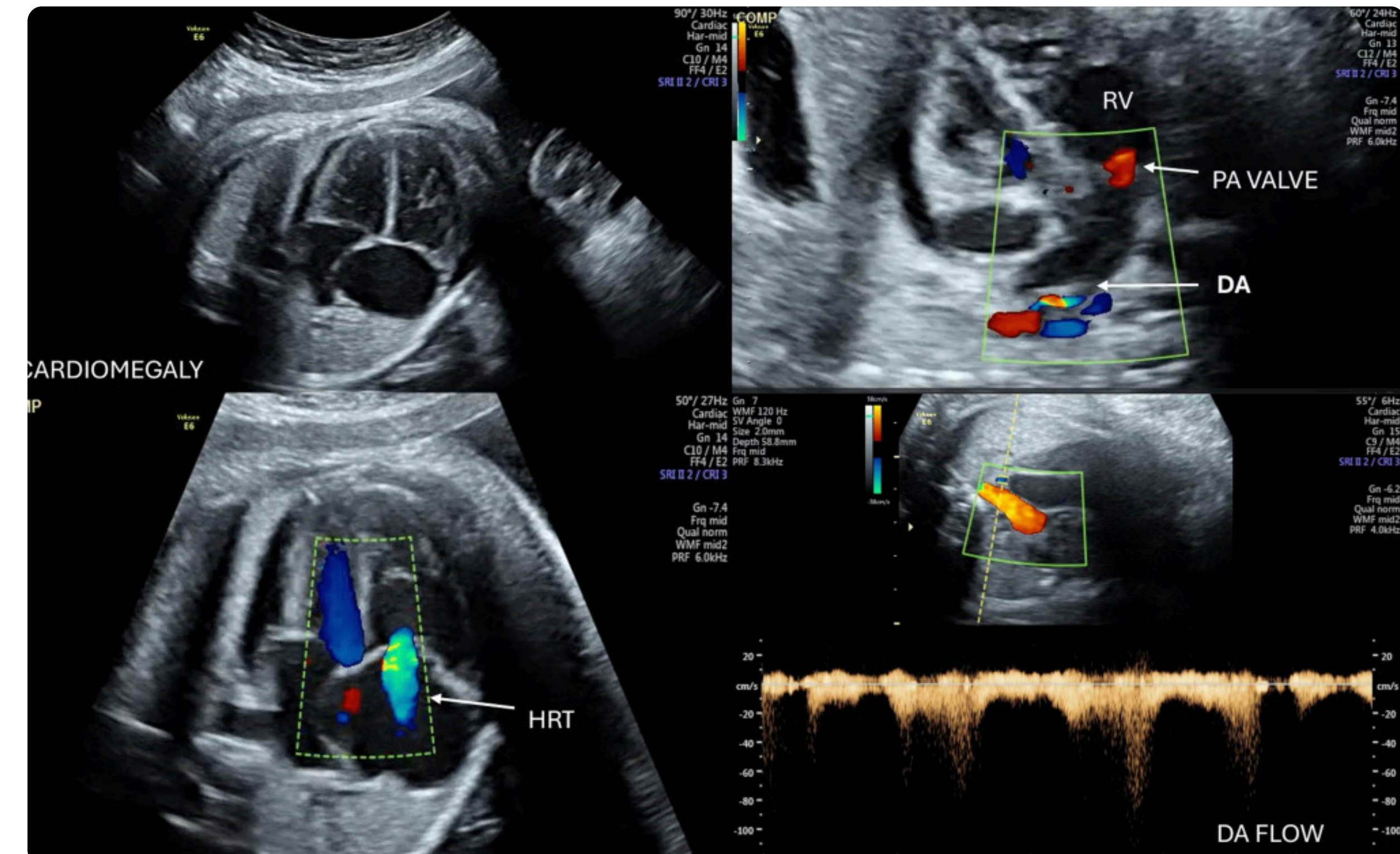


Figure 1. Case 2: Illustrates cardiomegaly, DA constriction, PA valve flow abnormalities, and holosystolic tricuspid regurgitation.

## DISCUSSION

Metamizole and polyphenols can induce premature DA constriction by inhibiting prostaglandin synthesis, similar to NSAIDs.

### Literature Insights:

- Polyphenol intake >1089 mg/day linked to increased ductal velocities (Zielinsky et al., 2009).
- Dietary restriction reversed constriction in >90% of cases (Zielinsky et al., 2011, 2013).
- Third-trimester NSAID/metamizole use increases fetal cardiac risks (Dathe et al., 2022).

### Key Findings:

- **Case 1:** Lower polyphenol intake (510.6 mg) suggests individual susceptibility to polyphenol-induced constriction.
- **Case 2:** Brief metamizole exposure (4 days) caused severe effects, emphasizing third-trimester vulnerability.

**Both cases demonstrated complete resolution upon cessation of the implicated substance.**

## CONCLUSION

- **Maternal metamizole and excessive polyphenol consumption can induce fetal ductal constriction.**
- **Maintain high clinical suspicion and obtain detailed maternal exposure history.**
- **Immediate cessation of causative substances**
- **generally leads to favorable fetal outcomes.**
- **Regular ultrasound monitoring and interdisciplinary**
- **care are essential for affected cases.**
- **Consider individual patient susceptibility to these**
- **agents.**