

## CASE REPORT

INTERMEDIATE

## CLINICAL CASE SERIES

# Ovulation Suppression to Prevent Hemoperitoneum and Surgical Menopause in Anticoagulated Women



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## ABSTRACT

Premenopausal women taking anticoagulation therapy are at risk of developing hemorrhagic ovarian cysts. This paper presents 3 cases of acute hemoperitoneum, with resultant surgical menopause, secondary to cystic hemorrhage in premenopausal women with repaired congenital heart disease (CHD). Adults with CHD taking long-term anticoagulation should be considered candidates for ovulation suppression with hormone-based contraception. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2019;1:50-4) © 2019 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Adults with congenital heart disease (CHD) represent a heterogeneous population with a high prevalence of thromboembolic events (1). Long-term, therapeutic anticoagulation has proven to be safe and effective in preventing thrombosis and provides an associated benefit of reduced mortality (2). Although major gynecological bleeding complications from anticoagulation therapy are rare, cases have been reported of hemorrhagic rupture of luteal cysts in premenopausal women in the absence of concurrent ovulation suppression (3). Hormone-based contraception can potentiate an already hypercoagulable state and is not routinely prescribed to women taking anticoagulation therapy (4). This paper presents 3 cases of hemorrhagic ovarian cyst rupture in premenopausal women with repaired CHD taking anticoagulation therapy. In each case, there had been no preceding formal recommendation for hormone-based ovulation suppression, and each patient required surgical management resulting in premature menopause.

## CASE #1

**PRESENTATION.** A 31-year-old G3P1021 patient on anticoagulation therapy for a history of Shone's complex, with prosthetic mitral and aortic valve replacement, presented with acute left lower quadrant pain. On examination, she was found to be hypotensive (blood pressure: 67 to 93/34 to 52 mm Hg), with poor distal perfusion. Her abdomen was rigid and diffusely tender, and there was visible blood within the vaginal vault.

**MEDICAL HISTORY.** Shone's complex, consisting of aortic coarctation, aortic valve stenosis, and mitral valve stenosis. Prior right hemorrhagic ovarian cyst, for which she had undergone oophorectomy at the age of 16.

**DIFFERENTIAL DIAGNOSIS.** Ruptured ovarian cyst, adnexal torsion, and ruptured ectopic pregnancy.

**INVESTIGATIONS.** The patient was acutely anemic (hemoglobin: 5.7 g/dl), with a supratherapeutic

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international normalized ratio (INR) of 5.3. Transvaginal ultrasonography revealed a large left adnexal mass of 13 cm.

**MANAGEMENT.** Given the patient's hemodynamic instability, she underwent an emergent, exploratory laparotomy. Preoperatively, she received human prothrombin complex concentrate (Kcentra) for anticoagulation reversal and 4 units of packed red blood cells (PRBCs). Intraoperatively, 800 ml of sanguineous fluid and a large hemorrhagic mass were visualized. A salpingo-oophorectomy was performed. Pathology confirmed a hemorrhagic corpus luteal cyst. Anticoagulation administration was resumed on postoperative day 2. However, on post-operative day 6, she experienced recurrent abdominal pain, with an acute drop in hemoglobin (9 to 7 g/dl). Subsequent

computed tomography (CT) demonstrated a 10-cm pelvic hematoma in the posterior cul-de-sac. The heparin drip was discontinued, and she was given a transfusion of 2 U of PRBCs, which stabilized her hemoglobin.

**FOLLOW-UP.** Therapy with coumadin and combined oral contraceptive pills was restarted prior to discharge on post-operative day 8.

## CASE #2

**PRESENTATION.** A 28-year-old gravid (G)0 patient on anticoagulation therapy for a history of a double-inlet left ventricle with Fontan repair presented with right lower quadrant pain. On presentation, she remained hemodynamically stable (blood pressure: 98/42 mm Hg), with lower quadrant fullness bilaterally on bimanual examination.

**PAST MEDICAL HISTORY.** Double-inlet left ventricle; atrial tachycardia.

**DIFFERENTIAL DIAGNOSIS.** Ruptured ovarian cyst; adnexal torsion; ruptured ectopic pregnancy.

**INVESTIGATIONS.** The patient's hemoglobin remained stable at 13.1 g/dl with a therapeutic INR of 2.0. Pelvic ultrasonography demonstrated a right adnexal mass with complex fluid in the cul-de-sac.

**MANAGEMENT.** The patient underwent bilateral ovarian cystectomies, with pathological confirmation of endometriotic cysts. Enoxaparin sodium (Lovenox) therapy was resumed post-operatively. However, on post-operative day 2, she developed recurrent abdominal pain with related hemodynamic instability (blood pressure: 63 to 94/38 to 53 mm Hg) and acute anemia (hemoglobin: 8.8 g/dl). Transvaginal ultrasonography showed an 8-cm pelvic hematoma. She received 2 units of PRBCs and underwent a repeat exploratory laparotomy, with evidence of acute hemorrhage from the prior cystectomy sites. Hemostasis was achieved with a right oophorectomy.

**FOLLOW-UP.** Post-operatively, therapeutic anticoagulation was restarted without further complication. She ultimately declined hormone-based contraception.

## CASE #3

**PRESENTATION.** A 39-year-old G0 patient on anticoagulation therapy for a history of a partial atrioventricular septal defect, requiring mechanical mitral valve replacement, presented with left lower quadrant pain. On initial evaluation, her blood pressure

### LEARNING OBJECTIVES

- Women with CHD on long-term, therapeutic anticoagulation are at risk of developing hemorrhagic ovarian cysts, with the potential for significant morbidity and mortality from resultant hemoperitoneum.
- Hormone-based contraceptives can be used in the prevention of hemorrhagic ovarian cysts in adults with CHD. Selection of specific contraceptive agents, however, must be individualized, with consideration of both the thrombotic and bleeding risks imposed by each cardiac lesion, their related repairs, and a patient's comorbidities.
- Progestin-only based preparations, specifically desogestrel and DMPA, are preferred over estrogen-containing formulations due to their improved safety profile with regards to thromboembolism. However, limitations are imposed by their variable efficacy in ovulation suppression and potentially problematic side effects in patients with heart failure.
- It is important to discuss the indications for, available options, and potential side effects of hormone-based contraception with premenopausal women with CHD on anticoagulation. Shared decision making should be utilized, with early and repeated discussions occurring as part of routine clinical visits.
- Additional research is needed to better understand the risk factors for hemorrhagic ovarian cyst formulation and rupture, as well as to evaluate the safety and efficacy of hormone-based ovulation suppression in adults with CHD.

remained stable (95/62 mm Hg), although with notable peritoneal signs and appreciable fullness in the left lower quadrant on bimanual examination.

**MEDICAL HISTORY.** Partial atrioventricular septal defect; bicuspid aortic valve; endometrial atypia (hysterectomy at the age of 37 years).

**DIFFERENTIAL DIAGNOSIS.** Adnexal torsion; ruptured ovarian cyst; ruptured ectopic pregnancy; tubo-ovarian abscess.

**INVESTIGATIONS.** The patient's hemoglobin remained at baseline (10.8 g/dl), and her INR was therapeutic at 2.8. Transvaginal ultrasonography demonstrated an enlarged left ovary with a 2.3-cm hemorrhagic cyst and absent flow on color doppler, which was concerning for ovarian torsion.

**MANAGEMENT.** The patient received 3 U of fresh frozen plasma and underwent a left salpingo-oophorectomy. Pathology confirmed ovarian torsion due to a hemorrhagic ovarian cyst. Her anticoagulation therapy was restarted, and she was discharged the following day.

**FOLLOW-UP.** One year later, the patient developed acute right lower quadrant pain. Transvaginal ultrasonography revealed an enlarged right ovary with a 3-cm hemorrhagic cyst. She received 4 units of fresh frozen plasma and underwent an emergent laparoscopy and right salpingo-oophorectomy, with intraoperative findings of acute hemoperitoneum. Pathology confirmed a hemorrhagic ovarian cyst. She was bridged back to warfarin (Coumadin) and was discharged post-operative day 3. Hormone-replacement therapy with transdermal estrogen was initiated on follow-up.

## DISCUSSION

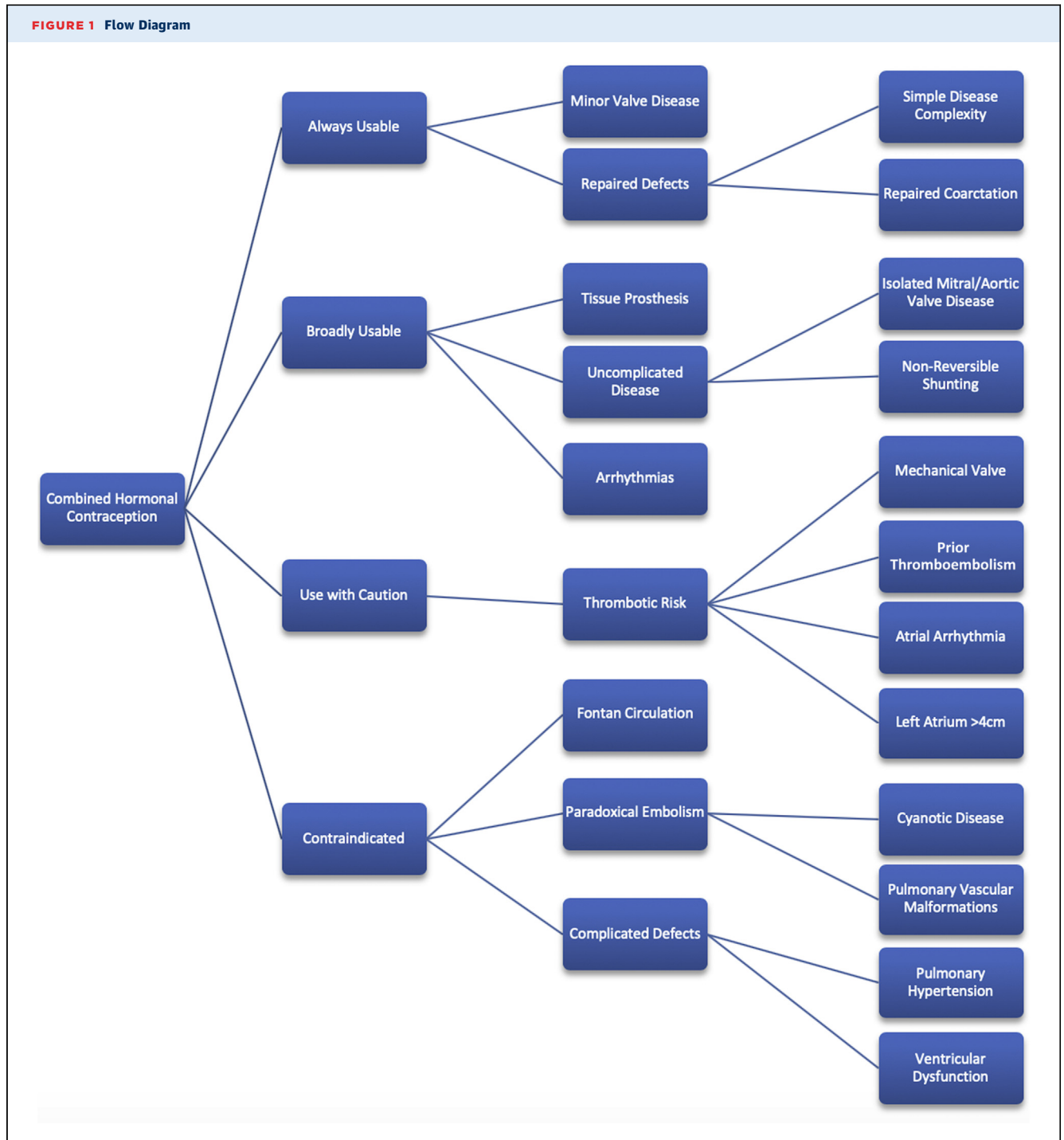
Ovarian cysts commonly occur in reproductive age females, with the cyclical development and subsequent rupture of corpus luteal cysts occurring with normal ovulation. Although this physiologic event is often asymptomatic, serious and even life-threatening bleeding can occur with cystic hemorrhage from rupture, with an associated mortality rate from resultant hemoperitoneum of more than 11% (5). As this complication is inherent to ovulation, a higher prevalence is observed with concurrent use of ovulation induction agents and is additionally further potentiated by anticoagulation (5).

Depending on their underlying cardiac condition, adults with CHD can be at an increased risk of thromboembolic events, necessitating long-term, therapeutic anticoagulation (1). This unique

predisposition is multifactorial in the setting of endothelial dysfunction, an increased predisposition to tachyarrhythmias, and prior surgical repair with prothrombotic substrates (1). Furthermore, abnormal anatomical connections often persist and allow for residual shunting, which further increases the patient's risk for potentially fatal thromboembolic events (2). When combined with this population's simultaneously increased risk of bleeding, predominantly due to abnormalities in platelet function and procoagulant factors, these patients pose a unique challenge for primary thromboprophylaxis.

Due to the heterogeneous nature of their underlying lesions and surgical repairs, recommendations for anticoagulation in adults with CHD are often variable, with the most common indications being mechanical heart valves and episodes of atrial arrhythmia (6). Although the major bleeding complications of therapeutic anticoagulation, including intracranial and gastrointestinal hemorrhage, similarly apply to this population, there have been relatively few documented reports of gynecologic bleeding events. As described in the current series, however, events are often life-threatening and recurrent in nature and heralded only by acute abdominal or pelvic pain, requiring a high index of clinical suspicion among providers (3).

Hormone contraception can be used in the prevention of ovarian cysts, with a resultant potential decrease in the related morbidity and mortality of cystic hemorrhage while on anticoagulation. Implementing safe and efficacious ovulation suppression in adults with CHD remains challenging, given their underlying hypercoagulable state and difficulties in predicting risk for hemorrhagic cyst formation and rupture. Although the inherent risk of thromboembolism with low-dose estrogen-containing preparations remains controversial (4), the European Society of Cardiology currently recommends against the use of combined oral contraceptives, given their limited safety data (6). Specifically, caution should be used with estrogen-containing preparations in patients with unrepaired defects; those with surgically repaired defects with associated mechanical prostheses; and those with defects complicated by cyanosis, ventricular dysfunction, atrial fibrillation, or Eisenmenger physiology (Figure 1) (4). On the other hand, progestin-only-based preparations, including depot medroxyprogesterone acetate (DMPA) and desogestrel, can be safely used in adults with CHD receiving anticoagulation therapy, although with variable efficacy in suppressing ovulation (7).



Although the adequacy of ovulation suppression can be assessed with gonadotropin hormone monitoring (8), there are no recommendations for routine clinical monitoring while on progestin-based contraceptives, with rates of ovulation remaining approximately 50% (7).

**CONCLUSIONS**

This case series highlights the significant morbidity associated with hemoperitoneum secondary to ruptured ovarian cysts, which can largely be prevented with hormone-based ovulation suppression.

Although the risks of specific hormonal contraceptives in this patient population still warrant further investigation, with shared decision making, hormonal contraception can be safe and efficacious in adults with CHD taking long-term anticoagulation therapy for ovulation suppression.

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**KEY WORDS** anticoagulation, congenital heart defect, hemorrhage, hemorrhagic ovarian cysts, ovulatory suppression