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CASE REPORT

BEGINNER

CLINICAL CASE: CARDIONERDS' CORNER

A 27-Year-Old Woman With Postpartum Papillary Muscle Rupture

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ABSTRACT

Postpartum papillary muscle rupture (PMR) is extremely uncommon and tolerated poorly with limited management options other than emergency surgical intervention. This case demonstrates the challenges of postpartum PMR in a young woman with unrecognized vascular Ehlers-Danlos syndrome and highlights the importance of preconception screening of cardiovascular disease. (**Level of Difficulty: Beginner.**) (J Am Coll Cardiol Case Rep 2020;2:2191-5)

A 27-year-old primigravid woman presented to an outside hospital at 39 weeks of gestation with abdominal pain and vaginal bleeding. She was diagnosed with HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome, and admitted for labor induction. Labor was complicated by fetal bradycardia requiring emergency cesarean delivery (liveborn female), placental abruption, and right hepatic lobe laceration. On postoperative day 3, she developed acute pulmonary edema requiring intubation. Transthoracic echocardiogram revealed flail posterior mitral leaflet with severe mitral regurgitation (Video 1). Transesophageal echocardiogram confirmed posterior papillary muscle rupture (PMR) (Videos 2 and 3). Intra-aortic balloon pump (IABP) was placed and she was transferred to our center for surgical management.

LEARNING OBJECTIVES

- To establish a differential diagnosis of PMR.
- To recognize the clinical features of vEDS and the importance of genetic screening.
- To highlight the importance of preconception screening and subsequent counseling in young patients with known or suspected cardiovascular disease.
- To recognize the limitations and challenges of preventive cardiology in the young.

PAST MEDICAL HISTORY

The patient had balloon valvuloplasty at age 7 for pulmonary stenosis (PS). Family history was remarkable for fatal aortic rupture in her brother at age 15 and pneumothorax in her sister. Patient's mother reported that following her son's death, her children screened negative for Marfan syndrome. The patient last followed with her local cardiologist at age 18 years and was not aware of pregnancy contraindications. Pregnancy had been uncomplicated.

DIFFERENTIAL DIAGNOSIS

PMR is rare and most commonly results from acute myocardial infarction (AMI) (1). Postpartum PMR is even more uncommon with only 5 cases reported in

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ABBREVIATIONS AND ACRONYMS

AMI = acute myocardial infarction

IABP = intra-aortic balloon pump

MVR = mitral valve replacement

PA = pulmonary artery

PMR = papillary muscle rupture

PS = pulmonary stenosis

vEDS = vascular Ehlers-Danlos syndrome

the literature. Reported etiologies are limited to AMI with or without atherosclerosis and connective tissue disorders including systemic lupus erythematosus and vascular Ehlers-Danlos syndrome (vEDS) (1–3).

In a young patient with no risk factors for coronary artery disease, the differential diagnosis points more toward nonischemic causes, including myocarditis, infective endocarditis, Takotsubo cardiomyopathy, and unrecognized vEDS or systemic lupus erythematosus. In addition, despite no reports in the literature, spontaneous coronary artery dissection could result in ischemic PMR.

INVESTIGATIONS

Physical examination revealed a thin woman with no dysmorphic facies. Skin showed easy bruising, without thin or hyperextensible skin/joints. A loud holosystolic murmur was best heard at the apex. Blood pressure was 103/68 mm Hg, heart rate 118 beats/min, and saturation 90% on 100% oxygen.

Laboratory testing revealed normocytic anemia, neutrophilia, lactic acidosis, and elevated cardiac enzymes (troponin T 1.35 ng/ml, CK-MB 10 ng/ml). Electrocardiogram (**Figure 1A**) showed sinus tachycardia with anterior ST-segment depression consistent with posterior myocardial current of injury. Chest radiograph (**Figure 1B**) demonstrated pulmonary edema. Transthoracic echocardiogram and transesophageal echocardiogram did not reveal regional wall motion abnormalities. Left ventricular function was hyperdynamic, aortic root was 2.2 cm, and no vegetations were present. Her pulmonary valve appeared normal with no stenosis but her main pulmonary artery (PA) was dilated, with left PA larger than right PA, expected in congenital PS. Given her positive family history of aortic rupture and spontaneous pneumothorax, genetic consultation with testing was pursued.

MANAGEMENT

The patient was managed with diuresis, sodium nitroprusside, and IABP for decongestion and afterload reduction given acute mitral regurgitation. Cardiac surgery took her for emergent mitral valve replacement (MVR).

Intraoperative findings were significant for posteromedial PMR with very friable tissues. After MVR and while coming off cardiopulmonary pump, she developed brisk bleeding secondary to spontaneous dehiscence of the left atrium, anterolateral papillary muscle, and ventricle below the mitral valve. The surgeon proceeded with redo MVR and reconstruction of the heart with bovine pericardium. She continued to bleed diffusely so was placed on venoarterial extracorporeal membrane oxygenation with IABP to decompress the heart.

Surgical pathology of the posteromedial papillary muscle revealed necrosis of the myocardium of approximately 72-h evolution. There was no evidence of myocarditis, infiltrative disease, or infection.

She remained in cardiogenic shock and was listed for heart transplant as United Network for Organ Sharing status 1 but her course was complicated by gastrointestinal and pulmonary hemorrhage contraindicating heart transplantation. Her family then expressed wishes to withdraw support and the patient died. An autopsy was requested.

Postmortem examination revealed an acute almost circumferential transverse aortic rupture in the suprarenal aorta and a 2.5-cm aneurysm in the infrarenal aorta (**Figure 2**). Histologic examination of the aorta and major vessels showed minimal medial degeneration. Coronary arteries were normal. Extensive hemorrhages were present in the myocardium, lung, and gastrointestinal tract. No hollow organ rupture was evident.

Genetic testing resulted shortly after the autopsy and confirmed a likely pathogenic variant, c.1897G>A (p. Gly633Arg), in gene COL3A1 consistent with vEDS.

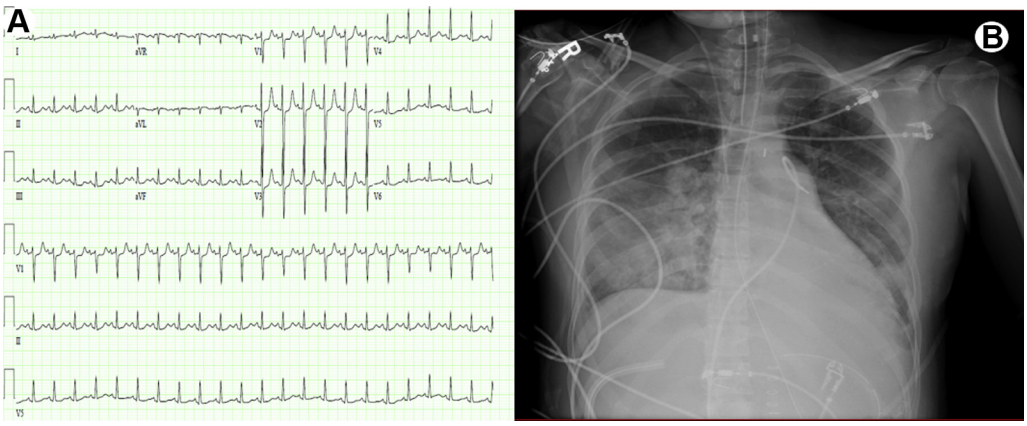
DISCUSSION

We report a case of a 27-year-old woman with postpartum PMR secondary to unrecognized vEDS. This patient's mechanism of PMR was likely secondary to HELLP-related thrombosis resulting in small nonatherosclerotic AMI.

Vascular EDS is inherited in an autosomal dominant pattern affecting 1 in 50,000 to 250,000 people and caused by defective collagen type III. It is characterized by large vessel and hollow organ rupture resulting in sudden death at a young age, with a median life expectancy of 40 to 50 years (4). The diagnosis requires molecular testing but clinical criteria aid in the decision to pursue testing (**Table 1**) (5). At the time of presentation, our patient had minimal criteria suggestive for vEDS with a positive family history. Interestingly, vEDS has also been associated with mitral valve prolapse but not with PS, like our patient had.

Patients with vEDS present a heterozygous mutation in *COL3A1,* which results in abnormal type III procollagen and tissue friability. Pathogenic mutations are a result of point glycine substitutions, most commonly Gly373Arg but more than 700 different

FIGURE 1 Initial Investigations

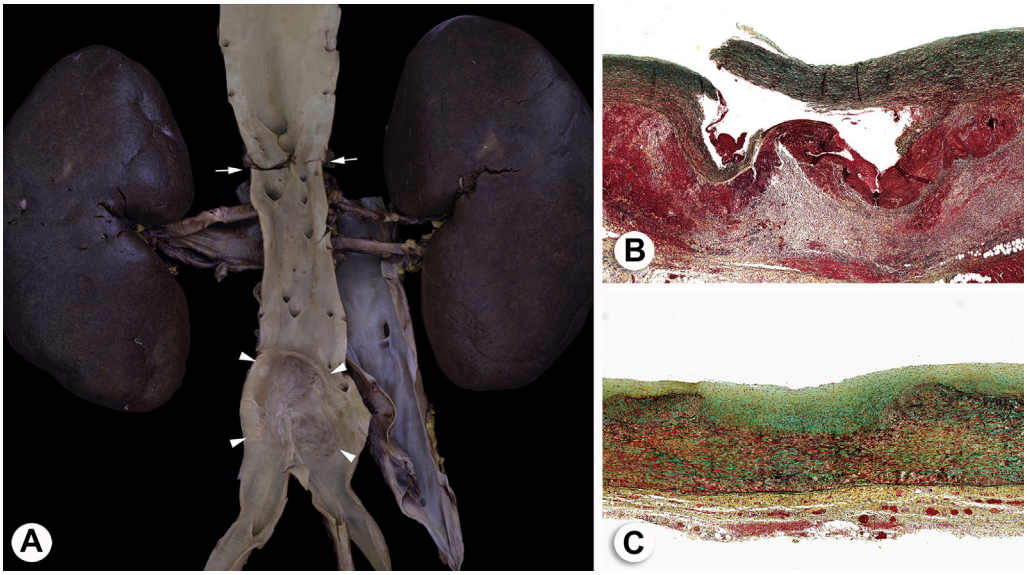


Admission electrocardiogram **(A)** and chest radiograph **(B)**.

mutations, including mutations in *COL1A1*, have been identified (4,6). Missense mutations located at the C-terminal end of the molecule result in the *acrogeric* (excessive wrinkling) form of vEDS associated with severe vascular problems and premature death (4).

This patient's family history pointed toward the presence of a hereditary connective tissue disorder, which provided the opportunity to identify this condition. Her case was prematurely closed after negative phenotypic screening for Marfan syndrome. Currently, molecular genetic testing includes a multigene panel for syndromic and nonsyndromic aortopathies. This facilitates the recognition of these entities that are otherwise difficult to identify based on clinical findings alone. In addition, despite the history of PS, she did not undergo transthoracic

FIGURE 2 Autopsy Findings



(A) Transverse aortic rupture **(arrows)** in the suprarenal aorta and aneurysm **(arrowheads)** in the distal aorta. **(B)** Rupture site showing transmural disruption of wall with periadventitial hemorrhage. **(C)** Aneurysm showing area of healed aortic tear with intimal hyperplasia **(green)** overlying partial disruption of the media.

TABLE 1 Clinical Criteria for the Diagnosis of Vascular Ehlers-Danlos Syndrome

Major Criteria	Minor Criteria
1. Family history of vascular Ehlers-Danlos syndrome with documented causative variant in *COL3A1* 2. Arterial rupture at a young age 3. Spontaneous sigmoid colon perforation in the absence of known diverticular disease or other bowel pathology 4. Uterine rupture during the third trimester in the absence of previous cesarean delivery and/or severe peripartum perineum tears 5. Carotid-cavernous sinus fistula formation in the absence of trauma	1. Bruising unrelated to identified trauma and/or in unusual sites such as cheeks and back 2. Thin, translucent skin with increased venous visibility 3. Characteristic facial appearance 4. Spontaneous pneumothorax 5. Acrogeria 6. Talipes equinovarus 7. Congenital hip dislocation 8. Hypermobility of small joints 9. Tendon and muscle rupture 10. Keratoconus 11. Gingival recession and gingival fragility 12. Early-onset varicose veins (younger than 30 yrs and nulliparous if female)

In the presence of ≥1 major criteria OR several minor criteria, molecular testing is recommended. Minimal criteria: A family history of the disorder, arterial rupture or dissection in individuals younger than 40 years, unexplained sigmoid colon rupture, or spontaneous pneumothorax in the presence of other features consistent with vascular Ehlers-Danlos syndrome should all lead to diagnostic studies to determine if the individual has vascular Ehlers-Danlos syndrome. Adapted from Malfait et al. (7).

echocardiography before pregnancy. Data have shown that most maternal cardiovascular deaths occur in women not previously known to have disease (7). vEDS is associated with 5% to 12% maternal mortality risk but management is limited by the fact that many of these women and their providers learn of the diagnosis at the time of delivery or at the onset of complications (8,9).

Expert societies recommend pre-pregnancy risk stratification and preconception counseling for patients with *known* aortic disease (7,8); however, little guidance is offered to screen for these conditions before pregnancy. Pregnancy termination in patients with known vEDS is recommended by some, but a study suggested that pregnancy does not influence the life expectancy of these patients (9). Current guidelines suggest a risk-benefit discussion with the patient and family. In the event of pregnancy continuation, no guidelines dictate the mode of delivery but elective cesarean delivery before the onset of labor is increasingly recommended (4). Pregnancy follow-up and delivery should occur in a specialized center and include the presence of a vascular surgeon and potentially a general surgeon (4).

The management of vEDS is limited to prevention of vascular complications and genetic counseling. This includes avoidance of contact sports, antiplatelets/anticoagulation, arterial/intramuscular punctures, arteriography, routine colonoscopy, and pregnancy (4). Baseline arterial imaging is recommended for screening but frequency of follow-up imaging is not well established, as vascular catastrophe is unpredictable at any vessel diameter. Echocardiogram should be performed at least every 3 years if normal at baseline (4). Prophylactic blood pressure control is recommended to target systolic blood pressure <120 mm Hg with celiprolol, which showed reduction in major arterial events in a small trial (10). The use of mechanical support like IABP might have increased the risk of arterial trauma, but the characteristic of our patient's aortic rupture was felt to be spontaneous. Surgical and endovascular management of aortic disease in vEDS is particularly challenging given tissue friability and arterial site complications (4).

FOLLOW-UP

Her family was informed of the autopsy and genetic results. Genetic testing was recommended to her child and first-degree relatives.

CONCLUSIONS

This case demonstrates that vEDS can be complicated with postpartum PMR, which poses a unique surgical challenge due to extremely friable tissues and postoperative bleeding. This patient reminds us of the importance of preconception counseling and highlights the limitations of screening low prevalent but highly morbid conditions like vEDS. We propose creating mechanisms to identify these patients through a systematic family history during preconception and first pregnancy visit; and proper molecular genetic testing with counseling to prevent catastrophic complications.

AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS cardiovascular disease, mitral valve, papillary muscles, postoperative, pregnancy

APPENDIX For supplemental videos, please see the online version of this paper.