



Treatment of Chronic Ovarian Vein Thrombosis

Huma Farid*

Instructor in Obstetrics and Gynecology, Harvard Medical School, USA

*Corresponding author: Huma Farid, MD, Instructor in Obstetrics and Gynecology, Harvard Medical School, Beth Israel Deaconess Medical Center, 330 Brookline Avenue, Boston, MA 02215, USA, Tel: 617-667-4600, E-mail: hfarid@bidmc.harvard.edu

Abstract

Background: Ovarian vein thrombosis is a rare condition, occurring most commonly in the postpartum or postoperative period, but has also been identified in cases of malignancy and infection. This report describes a case of chronic ovarian vein thrombosis that most likely developed postoperatively in a patient who was subsequently found to have a malignancy.

Case: The patient is a 34-year-old woman, gravida 8 para 6025, who had a supracervical hysterectomy 13 months prior and presented with one year of lower abdominal pain. An ultrasound was normal, but computed tomography demonstrated a right ovarian vein thrombus. Hypercoagulable workup was normal. Five months after initiating treatment with anticoagulation, the patient developed bright red bleeding per rectum and was diagnosed with colon cancer. After her bleeding resolved, the decision was made to continue her on anticoagulation for a total of six months of treatment as her pain improved significantly on anticoagulation.

Conclusion: This case demonstrates the challenges of treating a chronic thrombus. There are no clinical guidelines to recommend treatment of ovarian vein thrombus and typically duration of three months to six months of anticoagulation is recommended. Given the chronic appearing nature of the thrombus, it is most likely that a prolonged duration of anticoagulation was of more benefit to the patient.

Introduction

Ovarian vein thrombosis is a rare condition, and the first cases were recognized in postpartum patients. However, ovarian vein thrombosis has been identified in postoperative patients after gynecologic surgery, including total hysterectomy [1] and abortion [2], in women with tubo-ovarian abscesses [3] or Crohn's disease [4], and in patients with large fibroids [5], uterine prolapse [6] or malignancy [7]. Ovarian vein thrombosis can also occur idiopathically [8,9]. Ovarian vein thromboses are

diagnosed primarily on the basis of clinical signs such as abdominal pain and fever in conjunction with abnormal findings on imaging, including ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) [10]. In this case, we describe a patient with a one-year delay in the diagnosis of ovarian vein thrombosis and the challenges in treating a chronic thrombus complicated by a new diagnosis of malignancy.

Case

A 34-year-old woman, gravida 8 para 6025, was referred for evaluation of 12 months of chronic pelvic pain in the right lower quadrant. The pain was intermittent but occurred daily and could last for hours at a time. She denied fevers, nausea, or vomiting associated with the pain. She had been using over-the-counter anti-inflammatory and acetaminophen, but with minimal relief in her symptoms. She subsequently presented to the emergency department for evaluation of this pain when it became so severe that it was not relieved by over-the-counter medication.

Her obstetric history is notable for six full terms, uncomplicated vaginal deliveries. One of her infants died of SIDS. She had one termination and one spontaneous abortion. Her gynaecologic history is notable for severe dysmenorrhea, menorrhagia, and a history of endometriosis. She had no history of sexually transmitted infections, but had a LEEP for an abnormal pap smear. She underwent a supracervical laparoscopic hysterectomy 13 months prior to presentation for dysmenorrhea, menorrhagia and adenomyosis. The rest of her medical and surgical history was unremarkable. She was on no medications other than over-the-counter ibuprofen.

Citation: Farid H (2017) Treatment of Chronic Ovarian Vein Thrombosis. *Obstet Gynecol Cases Rev* 4:102. doi.org/10.23937/2377-9004/1410102

Received: September 21, 2016: **Accepted:** March 02, 2017: **Published:** March 06, 2017

Copyright: © 2017 Farid H. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

On physical examination, she was afebrile and normotensive. Body mass index was 33.7. Her abdominal exam was notable for diffuse tenderness to palpation in the lower quadrants, and a pelvic exam was notable for moderate tenderness to palpation in the bilateral adnexa, although no discrete adnexal masses were palpated. There was no abnormal discharge or bleeding noted in the vaginal vault.

Pelvic ultrasound was normal, demonstrating a surgically absent uterus and normal ovaries bilaterally, with normal arterial and venous waveforms on colour Doppler images. A computed tomography (CT) scan of the abdomen and pelvis was notable for a right ovarian vein thrombus. The abdominal aorta appeared normal. Her laboratory workup included complete blood count that was notable for hemoglobin of 11.1 g/dl with a hematocrit of 37%, and a white blood cell count of $13.2 \times 10^3/\text{mm}^3$. No differential was sent at that time. Coagulation studies, a full chemistry panel, liver function tests, and lipase were all normal. She had a complete thrombophilia workup, including Protein C, Protein S, antithrombin antigen, prothrombin 202010G mutation, Factor V Leiden, Cardiolipin antibodies, Beta-2-glycoprotein, and lupus anticoagulant that were all negative. Testing for gonorrhea and chlamydia was negative.

She was treated as an outpatient with therapeutic dosing of Lovenox, 80 mg subcutaneously twice daily, as she declined rivaroxaban. Initially, the patient reported minimal relief of her pain while on anticoagulation. A follow up CT scan was performed three months after initiation of anticoagulation, which demonstrated an unchanged, chronic appearing thrombus of the right ovarian vein. Given the unchanged appearance of the thrombus, the decision was made to discontinue her anticoagulation. Eleven days after discontinuing anticoagulation, the patient's pain became so severe that she presented to the emergency department for the second time in four months. A pelvic ultrasound was performed, which was again normal. A CT scan demonstrated a persistent right ovarian vein thrombus, which was unchanged from previous scans. The patient reported in hindsight that her pain had improved while she was on anticoagulation, because after discontinuing anticoagulation, the pain returned. She was started on warfarin for ease of administration as she declined further subcutaneous injections. The patient's pain improved once again on anticoagulation.

However, she then began to have bright red bleeding per rectum. A colonoscopy two weeks after initiating warfarin demonstrated a polyp in the cecum as well as a 3.5 cm polyp in the sigmoid colon. The polyp in the cecum was a benign adenoma, but the sigmoid colon polyp demonstrated an adenocarcinoma that was low grade in association with an adenoma with high grade dysplasia. There was some submucosal spread but clean margins and no lymphovascular spread. Carcinoembryonic

antigen (CEA) tumor marker was normal, and CT scan and magnetic resonance imaging was normal with no evidence of lymphadenopathy. The patient then had a significant episode of rectal bleeding requiring a hospital admission, presumed to be from the site of the polyp resection in the sigmoid colon, so her warfarin was held for eleven days. Her bleeding resolved and her hemoglobin and hematocrit remained stable. However, she reported recurrence of her abdominal pain, and the decision was made to continue her on a therapeutic dose of Lovenox for a treatment plan of six months.

Discussion

While thrombophlebitis was first described in 1721, the etiology of thrombophlebitis was not elucidated until Rudolf Virchow described his classic triad of susceptibility for thrombosis: stasis in the blood vessels, vascular endothelial injury and an inherited or acquired hypercoagulable state, such as malignancy, surgery or pregnancy [11].

Ovarian vein thrombosis was first described in the late 1800s [2]. In 1909, Dr. Williams performed a literature review and gathered 56 cases of puerperal thrombophlebitis, all of which were treated surgically with excision or ligation of the ovarian veins [12]. After the early 1900s, the condition was not described further until 1956 when Austin published a case report on a large ovarian vein thrombosis [13]. Ovarian vein thrombosis most often occurs postpartum, postoperatively, and in the setting of malignancy or pelvic infection [14], with a predilection for the right ovarian vein [15].

Additionally, there has been some suggestion that varicose veins are also a risk factor for venous thromboembolism, both superficial and deep. One study demonstrated a nearly 7-fold increased risk for deep venous thromboembolism in patients with varicose veins [16]. Interestingly, there is a connection between endometriosis, chronic pelvic pain, and ovarian vein varices. Ovarian vein varices were found in 80% of patients with endometriosis [17]. Our patient, who had a history of endometriosis, could have had ovarian varicose veins, thereby predisposing her to a thromboembolus.

Symptoms of ovarian vein thrombosis most commonly include lower abdominal pain (often unilateral), fever, and elevated white blood cell count [14]. There has also been description of pulmonary embolism in the context of ovarian vein thromboses [18]. The differential diagnosis is broad, given the nonspecific symptoms, including gastrointestinal etiologies such as appendicitis or diverticulitis, infectious etiologies such as tubo-ovarian abscesses, pyelonephritis or pelvic inflammatory disease, and ovarian torsion. Imaging studies can therefore be crucial in confirming the diagnosis.

While ultrasound is often chosen as the first imaging modality, it has a poor sensitivity. Even with colour Doppler's, ultrasound has only 55.6% sensitivity

and 46.2% accuracy in identifying an ovarian vein thrombosis. CT has a sensitivity of 78% in detecting ovarian vein thrombosis, while MRI is the most sensitive radiologic test in confirming the diagnosis, with 100% sensitivity and specificity [10]. However, CT is often the preferred imaging method, given its lower cost and easier accessibility when compared to MRI [10,19]. Therefore, even in cases where the initial ultrasound is normal but the clinical suspicion for ovarian vein thrombosis is high, a CT or MRI should be considered.

There are no clinical guidelines to recommend duration of treatment of ovarian vein thrombus. The recurrence rate of ovarian vein thrombosis appears to be low, with only 3 recurrent venous thrombi per 100 patient-years in one study [20]. If there is no underlying inherited coagulopathy, lifelong treatment with anticoagulation is not recommended, but duration of at least three to six months of treatment with anticoagulation is recommended [21].

While postoperative ovarian vein thrombosis has been described in the literature, such a delayed diagnosis as in our case has not been described previously. This patient likely had developed the ovarian vein thrombus in the context of her surgery, as her pain developed within four weeks postoperatively; however, given her later diagnosis of malignancy, the timeline of the thrombus is unclear. Regardless, the postoperative state has been recognized to be a hypercoagulable state. The American Congress of Obstetricians and Gynecologists (ACOG) recommend perioperative venous thrombosis prophylaxis with unfractionated heparin, low molecular weight heparin, or intermittent pneumatic compression devices for the majority of surgeries (with the exception of a surgery lasting less than 30 minutes in a woman younger than age 40 with no risk factors). In patients undergoing surgery who have a malignancy, the recommendation is for both mechanical and medical prophylaxis, and the consideration of medical prophylaxis with low molecular weight heparin or unfractionated heparin for two to four weeks postoperatively [22]. General surgery guidelines also emphasize the need for perioperative venous thromboembolism prophylaxis with either mechanical or pharmacological prophylaxis for the vast majority of patients with the exception of very, very low risk patients who have a less than 0.5% risk of venous thromboembolism. Orthopedic surgery guidelines are even more stringent, recommending both mechanical and pharmacological prophylaxis for major surgery and pharmacological prophylaxis for up to 35 days postoperatively [23]. Despite these guidelines and endorsement from ACOG, the rates of VTE prophylaxis range from 39-59% [24].

By the time the patient presented for evaluation, the thrombus appeared to be chronic. Interestingly, the diagnosis in this case would have been missed had a computed tomography (CT) scan not been performed, as the pelvic ultrasound, including Doppler ultrasonography, was completely normal in this patient.

Further complicating her treatment course was the new diagnosis of colon cancer which was discovered five months after her diagnosis of ovarian vein thrombosis. The patient was initially started on a three month treatment course with Lovenox, but the decision to continue anticoagulation for a total of six months was made after the patient's pain recurred with discontinuation of anticoagulation and a CT scan demonstrated persistence of the thrombus. Given the chronic nature of the thrombus, a longer course of anticoagulation was thought to be of more therapeutic benefit. In this case, the contribution of the underlying malignancy to the persistence of the thrombus should be considered. Patients with cancer have a known hypercoagulable state due to increased procoagulant activity [25]. 20% of patients with malignancy will develop a deep venous thrombosis, and in fact, in a small number of patients, a venous thromboembolism will be the initial manifestation of malignancy, as it was with our patient [26]. Armand Trousseau first described this association between venous thromboembolism and malignancy in patients with gastric cancer, and in an ironic twist of fate, diagnosed his own gastric cancer after developing a venous thromboembolism [27]. However, the 5-year mortality for patients with ovarian vein thrombosis in the setting of malignancy was 43%, but the elevated mortality rate was thought to be due to the underlying malignancy [20].

Interestingly, the patient's pain improved on anticoagulation despite imaging findings demonstrating no change in the size of the thrombus. There is evidence that heparin has anti-inflammatory properties that exist apart from its role in anticoagulation [28,29]. The action of mechanism is thought to involve the inhibition of mediators involved in inflammation [30]. Specifically, heparin binds to growth factors, adhesion molecules, cytotoxic peptides, and tissue destructive enzymes that are involved in inflammation. It then inhibits their activation and prevents the accumulation of inflammatory cells in tissues, thus limiting tissue destruction [31].

This patient's chronic thrombus in the context of a new diagnosis of colon cancer was difficult to treat, and this case illustrates the need for an interdisciplinary approach to anticoagulation in complex patients.

Funding and Financial Support

I received no financial support or funding for this case report.

Acknowledgements

I would like to acknowledge my colleagues in the department who were so generous with their advice and time, in particular Dr. Hye-Chen Hur.

References

1. Tanaka Y, Kato H, Hosoi A, Isobe M, Koyama S, et al. (2012) Ovarian ven thrombosis following total laparoscopic hysterectomy. Asian J of Endosc Surg 5: 179-182.

2. Allan TR, Miller II GC, Wabrek AJ, Burchell RC (1976) Postpartum and Postabortal Ovarian Vein Thrombophlebitis. *Obstet and Gynecol* 47: 525-528.
3. Maldjian PD, Zurlow J (1997) Ovarian vein thrombosis associated with a tubo-ovarian abscess. *Arch Gynecol Obstet* 261: 55-58.
4. Marcovici I, Goldberg E (2000) Ovarian vein thrombosis associated with Crohn's disease: A case report. *Am J Obstet Gynecol* 182: 743-744.
5. Haynes MC, Lu BY, Winkel AF (2014) Ovarian Vein Thrombophlebitis Related to Large Uterine Myoma. *Obstet Gynecol* 123: 450-453.
6. Lenihan JP, Kovanda C (2009) Bilateral Ovarian Vein Thromboses in a Postmenopausal Woman with Uterine Prolapse. *J of Min Inv Gynecol* 17: 280-281.
7. Verde F, Johnson PT (2012) One Not to Miss: Ovarian Vein Thrombosis Causing Pulmonary Embolism with Literature Review. *J Radiol Case Rep* 6: 23-28.
8. Harris K, Mehta S, Iskhakov E, Chalhoub M, Maiatis T, et al. (2012) Ovarian vein thrombosis in the nonpregnant woman: an overlooked diagnosis. *Ther Adv Hematol* 3: 325-328.
9. Doherty K, New M (2015) Idiopathic Ovarian Vein Thrombosis in a Nonperipartum Patient. *Obstet Gynecol* 125: 1468-1470.
10. Virmani V, Kaza R, Sadaf A, Fasih N, Fraser-Hill M (2012) Ultrasound, Computed Tomography, and Magnetic Resonance Imaging of Ovarian Vein Thrombosis in Obstetrical and Nonobstetrical Patients. *Can Assoc Radiol J* 63: 109-118.
11. Bagot CN, Arya R (2008) Virchow and his triad: a question of attribution. *Br J Haematol* 143: 180-190.
12. Williams JW (1909) Ligation or excision of thrombosed veins in the treatment of puerperalpyemia. *Am J Obstet* 59: 758-789.
13. Austin OG (1956) Massive thrombophlebitis of the ovarian vein. *Am J Obstet Gynecol* 72: 428-429.
14. Sharma P, Abdi S (2012) Ovarian vein thrombosis. *Clinical Radiology* 67: 893-898.
15. Heavrin BS, Wrenn K (2008) Ovarian vein thrombosis: a rare case of abdominal pain outside the peripartum period. *J Emerg Med* 34: 67-69.
16. Muller-Buhl U, Leutgeb R, Engeser P, Achankeng EN, Szescenyi J, et al. (2012) Varicose veins are a risk factor for deep venous thrombosis in general practice patients. *Vasa* 41: 360-365.
17. Pacheco KG, Fortes de Oliveira MR (2016) The Prevalence of Ovarian Varices in Patients with Endometriosis. *Ann Vasc Surg* 34: 135-143.
18. Benfayed WH, Torreggiani WC, Hamilton S (2003) Detection of pulmonary emboli resulting from ovarian vein thrombosis. *Am J Roentgenol* 181: 1430-1431.
19. Gayer G (2001) Ovarian Vein Thrombosis-Computerized Tomography Diagnosis. *Isr Med Assoc J* 3: 627-628.
20. Wykosinska EM, Hodge D, McBane II RD (2006) Ovarian vein thrombosis: Incidence of recurrent venous thromboembolism and survival. *Thromb Haemost* 96: 126-131.
21. Cook RM, Rondina MT, Horton DJ (2014) Rivaroxaban for the Long-term Treatment of Spontaneous Ovarian Vein Thrombosis Caused by Factor V Leiden Homozygosity. *Annals of Pharmacotherapy* 48: 1055-1060.
22. American College of Obstetricians and Gynecologists (2007) ACOG Practice Bulletin No. 84: Prevention of Deep Vein Thrombosis and Pulmonary Embolism. *Obstet Gynecol* 110: 429-440.
23. Guyatt GH, Aki EA, Crowther M, Guterman DD, Schuunemann HJ, et al. (2012) Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 141: 7S-47S.
24. Corr BR, Winter AM, Sammel MD, Chu CS, Gage BF, et al. (2015) Effectiveness and safety of expanded perioperative thromboprophylaxis in complex gynecologic surgery. *Gynecol Oncol* 138: 501-506.
25. Heit JA, Fallon WM, Petterson TM, Lonse SM, Silverstein MD, et al. (2002) Relative impact of risk factors for deep venous thrombosis and pulmonary embolism: a population-based study. *Arch Inter Med* 162: 1245-1248.
26. Bauer KA (2000) Venous thromboembolism in malignancy. *J Clin Oncol* 18: 3065-3067.
27. Carrier M, Le Gal G, Wells B, Fergusson D, Ramsay T, et al. (2008) Systematic Review: The Trousseau Syndrome Revisited: Should We Screen Extensively for Cancer in the Patients With Venous Thromboembolism? *Ann Intern Med* 149: 323-333.
28. Lever R, Page CP (2012) Non-anticoagulant effects of heparin: an overview. *Handb Exp Pharmacol* 207: 281-305.
29. Terrell DJ, Horne AP, Holme KR, Preuss JM, Page CP (1999) Heparin in inflammation: potential therapeutic applications beyond anticoagulation. *Adv Pharmacol* 46: 151-208.
30. Cassinelli G, Naggi A (2016) Old and new applications of non-anticoagulant heparin. *Int J Cardiol* 212: S14-S21.
31. Day JRS, Landis RC, Taylor KM (2004) Heparin is much more than just an anticoagulant. *J Cardiothorac Vasc Anesth* 18: 93-100.