

Ovarian Varicose Veins may Provoke Premature Ovarian Failure?

Kennedy Gonçalves Pacheco^{1*} and Raquel Fortes²

¹Vascular Surgeon and Phlebologist, Brazil

²Full Member of the Brazilian College of Radiology, Brazil

***Corresponding Author:** Kennedy Gonçalves Pacheco, Vascular Surgeon and Phlebologist, Brasil, Mailing address: Rua Alcindo Guanabara, 25 – 1304, Centro da Cidade, Rio de Janeiro – RJ, Brasil.

Received: October 21, 2015; **Published:** October 28, 2015

Abstract

We will describe 2 cases of embolization of ovarian varicose veins in patients with confirmed diagnosis of premature ovarian failure that began menstruating again after the treatment.

Keywords: Premature ovarian failure; Ovarian varices; Varicocele; Embolization; Sclerotherapy

Primary ovarian insufficiency (POI), also known as premature ovarian failure (POF), may manifest itself through amenorrhea (for 4 or more months) before women reach the age of 40, as confirmed through hormonal exams. The level of FSH, usually above 50 IU/L, and estradiol, with levels lower than 50 pg/ml, suggesting hypoestrogenism [1].

Menopause can be characterized by the depletion of ovarian follicles and the ceasing of menstruation around 51 years of age [2].

The varicose veins beside the ovaries, the testicles and lower limbs result in venous reflux and oxidative stress and most of them are caused by valvular insufficiency [3-6].

We have reported two cases of women who had previous history of premature ovarian failure and infertility. We treated their ovarian varicose veins through embolization and sclerotherapy. After the treatment, both of them began menstruating again. With the informed consent of the patients, we decided to perform the phlebography and embolization of the ovarian varicose veins, as the pelvic varices could have led to venous thrombosis and/or pulmonary embolism [7].

Case Report 1

40 year old woman, with confirmed history of premature ovarian failure for 6 months, by FSH = 110.9 mIU/ml, LH = 54.3 mIU/ml and anti mullerian of 0.02 mg/ml. An ultrasound with colored doppler was carried out, which showed varicose veins in the right ovarian plexus (7.7 mm) and left ovarian plexus (5.4 mm) with reflux confirmed by the doppler, as shown in figures 1A and 1B.

On the 11th of May 2015, she decided to undergo intrauterine fertilization, aiming to become pregnant, but the procedure was not successful. I recommended the embolization of ovarian varicose veins, as she was presenting pain and heaviness in the pelvis and lower limbs. Also, there was a risk of venous thrombosis and pulmonary embolism [7]. On the 25th of July 2015, she was submitted to phlebography of pelvic veins (Figure 2A) and embolization and sclerotherapy of ovarian varicose veins with coils and 1% polydocanol (Figure 2B). On the 17th of August, on the 24th of September and on the 16th of October of 2015, the patient menstruated normally.



Figure 1A: Ultrasound highlights varicose veins in the broad ligament of the uterus – mode B.

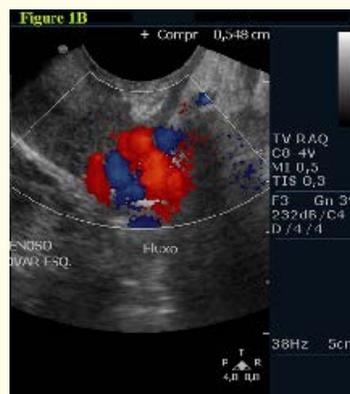


Figure 1B: Ultrasound confirms varicose veins beside the ovaries through the scale of colors.



Figure 2A: Ovarian Varicose veins confirmed by Pelvic Phlebography.



Figure 2B: Embolization of pelvic varicose veins with metallic coil and 1% povidone-iodine.

After this treatment, the patient reported an improvement in her menstrual flow that used to last for 8 to 10 days, with dark coloring and with disabling menstrual cramps. Now, it lasts only around 3 days, with brighter and red coloring and with no menstrual cramps. Also, she no longer had intestinal constipation.

Case Report 2

35 year old woman, with premature ovarian failure, confirmed by exams FSH = 114.0 mUI/ml, LH = 61.8 mUI/ml laboratory, was submitted to treatment with the hormone progesterone and became pregnant after 1 month of treatment. On the 1st of June 2013, six months into her pregnancy, she began having disabling pain in the supra pubic region. The delivery of the child was through a caesarean operation. The baby born was female. Six months after the gestation, an ultrasound of ovarian veins was carried out, which confirmed varicose veins in both ovarian plexus (Right = 5.0 mm) (Left = 3.0 mm), with reflux on the right ovarian plexus confirmed by the doppler as shown in Figures 3A and 3B.



Figure 3A: Ultrasound highlights varicose veins in the broad ligament of the uterus – mode B.



Figure 3B: Ultrasound confirms varicose veins beside the ovaries through the scale of colors.



Figure 4A: Ovarian Varicose veins confirmed by Pelvic Phlebography.



Figure 4B: Embolization of pelvic varicose veins with metallic coil and 1% povidone iodine.

Due to complaints of pelvic pain and the risk of thrombosis and/or pulmonary embolism (7), it was decisive to treat her with sclerotherapy and embolization of pelvic varicose veins on the 26th of April 2014. (Figures 4A and 4B).The patient began menstruating normally again in May 2014.

She stated that her menstruation used to be very painful, with increased menstrual flow. Nowadays, it is painless and lasts only for 3 days.

Discussion

POF may occur due to genetic, autoimmune, iatrogenic or metabolic problems, but the largest portion of cases are idiopathic, and may result in infertility [1].

There are reports of the correlation between POI and endocrine (thyroid, diabetes) and non-endocrine diseases (Lupus, autoimmune disorders [8, 9].

POI is present in 1% of women younger than 40 and in 0.1% of women younger than 30 [10].

Researchers show that this pathology may result in a deficiency of estrogen and in anovulation, causing vasomotor symptoms (hot flashes and increased sweating), atrophic vaginitis, dyspareunia, primary and secondary amenorrhea and infertility [11].

There is no cure for POF, but hormonal therapy is highly recommended in order to relieve the symptoms [12,13].

Varicose veins beside the testicles cause alterations in hormonal production, dysfunction in the Leydig cells and a decrease in the production and motility of sperms, which leads to decreased male fertility and the dysfunction of hypothalamic-pituitary-testes axis(14-17).

Varicocele in men can be associated with oxidative stress and sperm DNA fragmentation, possibly resulting in fibrosis and testicular atrophy [18,19] Researches have already evidenced that varicose veins in lower limbs can be associated with oxidative stress, ulcers and lesions in tissues in the leg [20, 21].

Oxidative stress causes dysfunction of organs, interferes with angiogenesis and in gene expression [22,23]. Two studies have shown that oxidative stress is greater in varicose veins with insufficient valves [5,6].

Studies have shown that there are several genes involved in biological functions, such as the regulation of the hypothalamic-pituitary-gonadal axis, the regulation of oncogenes and the coordination of germinating cells. They play an important role in the endocrinal system [24,25].

Although there aren't any studies relating ovarian varicose veins to oxidative stress, by analogy, we believe the same happens with the female germinating gland, causing depletion of the follicles, also lowering the ovarian reserve, provoking hormonal disorders and leading to alterations in the hypothalamic-pituitary-ovary axis.

Varicolectomy in men corrects oxidative stress, hormonal disorders and sperm production, making men more fertile [26]. By treating varicose veins in lower limbs through surgery or through the use of compression therapy with elastic stockings, there is a decrease in oxidative stress and consequent scarring of the ulcer [20,21].

In relation to ovarian varicose veins, Galkin., *et al.* reported in medical literature that by treating 19 women who were considered to be infertile by embolization, 14 became pregnant [27]. We have also identified 23 cases of pregnancies after treating pelvic varicose veins through the same process [27-33].

In another work, we have reported the disappearance of intestinal constipation as well as pregnancy after the embolization of pelvic varicose veins in a patient who had endometriosis and who was infertile [30]. Some studies have already shown the relationship

between varicocele and ovarian varicose veins with chronic intestinal constipation [34,35]. Research shows the correlation between endometriosis and infertility with ovarian varicose veins [36,37].

Conclusion

Varicose veins beside the testicles are associated with the dysfunction of this gland, semen abnormality and testicular atrophy. It is possible that ovarian varicose veins interfere with folliculogenesis and oogenesis, playing an important role in most cases of primary ovarian insufficiency. Still, more studies are required in order to confirm this association and solidify my theory.

Conflicts of interest

The authors declare that there are no conflicts of interest with respect to the authorship and/or publication of this paper.

Bibliography

1. Nelson L M. "Clinical practice. Primary ovarian insufficiency". *The New England Journal of Medicine: Research & Review* 360.6 (2009): 606-614.
2. Armstrong K., *et al.* "Hormone replacement therapy and life expectancy after prophylactic oophorectomy in women with BRCA1/2 mutations: a decision analysis". *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 22.6 (2004): 1045-1054.
3. Balasch J., *et al.* "Visible and non-visible endometriosis at laparoscopy in fertile and infertile women and in patients with chronic pelvic pain: a prospective study". *Human Reproduction* 11.2 (1996): 387-391.
4. Evans CJ., *et al.* "Prevalence of varicose veins and chronic venous insufficiency in men and women in the general population: Edinburgh vein study". *Journal of Epidemiology & Community Health* 53.3 (1999): 149-153.
5. Krzyściak W and Kózka M. "Generation of reactive oxygen species by a sufficient, insufficient and varicose vein wall". *Acta Biochimica Polonica* 58.1 (2011): 89-94.
6. Karatepe O., *et al.* "The impact of valvular oxidative stress on the development of venous stasis ulcer valvular oxidative stress and venous ulcers". *Angiology* 61.3 (2010): 283-288.
7. P. Everarts D., *et al.* "Pelvic Varicose Veins Thrombosis in a patient with pulmonar". *Read (JBR-BTR) - Belgian Society of Radiology* 91.5 (2008): 200-202.
8. Hoek A., *et al.* "Premature ovarian failure and ovarian autoimmunity". *Endocrine Reviews* 18.1 (1997): 107-134.
9. Doldi N., *et al.* "Premature ovarian failure: Steroid synthesis and autoimmunity". *Gynecological Endocrinology* 12.1 (1998): 23-28.
10. Skillern A and Rajkovic A. "Recent development in identifying genetic determinants of premature ovarian failure". *Sexual Development* 2.4-5 (2008): 228-243.
11. Bachelot A., *et al.* "Phenotyping and genetic studies of 357 consecutive patients presenting with premature ovarian failure". *European Journal of Endocrinology* 16.1 (2009): 179-187.
12. Nelson LM. "Clinical practice. Primary ovarian insufficiency". *The New England Journal of Medicine: Research & Review* 360.6 (2009): 606-614.
13. Pines A., *et al.* Board of the international Menopause Society. IMS updated recommendations on postmenopausal hormone therapy. *Climacteric* 10 (2007): 181-194.
14. Andò S., *et al.* "Physiopathologic aspects of Leydig cell function in varicocele patients". *Journal of Andrology* 5.3 (1984): 163-170.
15. Tanrikut C., *et al.* "Varicocele as a risk factor for androgen deficiency and effect of repair". *BJU International* 108.9 (2011): 1480-1404.
16. Swerdloff RS and Walsh PC. "Pituitary and gonadal hormones in patients with varicocele". *Fertility and Sterility* 26.10 (1975): 1006-1012.
17. Weiss DB., *et al.* "Leydig cell function in oligospermic men with varicocele". *Journal of Urology* 15.7 (1978): 427-430.
18. Wright EJ and Young GP. "Goldstein M. Reduction in testicular temperature after varicocelectomy in infertile men". *Urology* 50.2 (1997): 257-259.

19. Sirvent JJ, et al. "Leydig cell in idiopathic varicocele". *European Urology* 17.3 (1990): 257-261.
20. Murphy MA, et al. "A reduction in serum cytokine levels parallels healing of venous ulcers in patients undergoing compression therapy". *European Journal of Vascular and Endovascular Surgery* 23.4 (2002): 349-352.
21. Flore R, et al. "Long saphenous vein stripping reduces local level of reactive oxygen metabolites in patients with varicose disease of the lower limbs". *World Journal of Surgery* 27.4 (2003): 473-475.
22. Martins PS, et al. "Upregulation of reactive oxygen species generation and phagocytosis, and increased apoptosis in human neutrophils during severe sepsis and septic shock". *Shock* 20.3 (2003): 208-212.
23. Ohura N, et al. "Global analysis of shear stress-responsive genes in vascular endothelial cells". *Journal of Atherosclerosis and Thrombosis* 10.5 (2003): 304-313.
24. Simpson J L. "Genetic and phenotypic heterogeneity in ovarian failure: overview of selected candidate genes". *Annals of the New York Academy of Sciences* 1135 (2008): 146-154.
25. Dixit H, et al. "Genes governing premature ovarian failure". *Reproductive BioMedicine Online* 20.6 (2010): 724-740.
26. Chen SS, et al. "Attenuation of oxidative stress after varicocelectomy in subfertile patients with varicocele". *Journal of Urology* 179.2 (2008): 639-642.
27. Galkin EV, et al. "[Roentgeno-endovascular surgery of hypofunctional ovaries in varicosities of the ovarian veins]". *Vestn Rentgenol Radiol journal* 5 (1991): 51-59.
28. Kim HS, et al. "Embolotherapy for pelvic congestion syndrome: long-term results". *Journal of Vascular and Interventional Radiology* 17.2 (2006): 289-297.
29. Ghosh A, et al. "Laparoscopic sclerotherapy in a case of pelvic congestion syndrome". *BJOG: An International Journal of Obstetrics & Gynaecology* 113.5 (2006): 610-611.
30. Pacheco KG and Fortes R. "Pregnancy after sclerotherapy and embolization of ovarian varicose veins in a patient with infertility and deep endometriosis". *Gynecologic and Obstetrics* 4 (2014): 2161-2932.
31. Tarazov P, et al. "Pregnancy after embolization of an ovarian varicocele associated with infertility: report of two cases". *Diagnostic and Interventional Radiology* 17.2 (2011): 174-176.
32. Venbrux AC, et al. "Pelvic congestion syndrome (pelvic venous incompetence): impact of ovarian and internal iliac vein embolotherapy on menstrual cycle and chronic pelvic pain". *Journal of Vascular and Interventional Radiology* 13.2 (2002): 171-178.
33. Bachar GN, et al. "Initial experience with ovarian vein embolization for the treatment of chronic pelvic pain syndrome". *The Israel Medical Association* 5.12 (2003): 843-846.
34. Turgut AT, et al. "Chronic constipation as a causative factor for development of varicocele in men: a prospective ultrasonographic study". *Journal of Ultrasound in Medicine* 26.1 (2007): 5-10.
35. Bachar GN, et al. "Initial experience with ovarian vein embolization for the treatment of chronic pelvic pain syndrome". *IMAJ / The Israel Medical Association Journal* 5.12 (2003): 843-846.
36. Matalliotakis IM, et al. "Arguments for a left lateral predisposition of endometrioma". *Fertility and Sterility* 91.4 (2009): 975-978.
37. Wassong C, et al. "Radiologic findings of pelvic venous congestion in an adolescent girl with angiographic confirmation and interventional treatment". *Pediatric Radiology* 42.5 (2012): 636-640.

Volume 2 Issue 2 October 2015

© All rights are reserved by Kennedy Gonçalves Pacheco and Raquel Fortes.