

## FEMALE VARICOCELE: A RAT MODEL<sup>+</sup>

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*Female varicocele is a subject of investigation. An animal model of female varicocele may be an option to detect pathologies associated with this phenomenon. For this purpose, a midline laparotomy was performed in female wistar rats. The left renal vein was identified and partially ligated to an external diameter of 0.85 mm. A consistent stenosis was achieved by using a 4-0 silk suture, which was ligated around both renal vein and a metal probe. The probe was removed and the vein was allowed to expand against the loop of suture. This model was macroscopically and microscopically investigated. Markedly dilated left ovarian vein and striking intraovarian venous congestion were observed. It was concluded that this model is an easy and cheap option to investigate female varicocele.*

**Key words:** Female varicocele, animal model, pelvic pain.

### **Dişilerde Varikosel: Rat Modeli**

*Kadınlarda varikosel şü anda araştırma konusudur. Geliştirilecek bir hayvan modeli bu konuyla ilgili patolojileri ortaya koymak için uygun bir seçenek oluşturabilir. Bu amaçla virjin dişi wistar ratlarda ortahat laparotomi yapılarak sol renal ven bulunup çapı 0.85 mm olacak şekilde kısmi daraltma yapıldı. Bu darlık, metal bir prob ve renal ven etrafına konan 4-0 ipek bir sütün sonrası metal prob alınarak sağlandı. Makroskopik ve mikroskopik olarak modelimizi araştırdık. Sol ovarian vende ve intraovarian damarlarda belirgin dilatasyon gözlemlendi. Bu modelin kadın varikoseli patolojik değişikliklerini araştırmak için kolay ve ucuz bir yöntem olduğu sonucuna varıldı.*

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The frequent association of varicocele with diminished male fertility has stimulated much clinical and scientific interest. However, the significance of varicocele in female patients is not well documented. This may be explained, in part, by the lack of obvious findings on clinical examination in women, compared with men. Data exist on the association of ovarian varices with the pelvic pain syndrome.<sup>1-7</sup> To be able to investigate

pathologies associated with female varicocele, an experimental varicocele was created in the adult rat. In this study, we discussed our animal model of female varicocele.

## MATERIALS AND METHODS

Virgin wistar rats (250-300g body weight) were obtained from the medical center vivarium. All animals were given free access to food and water. Control and experimental groups were matched for approximate age and weight.

Group 1 (control) consisted of 6 rats. They were sacrificed by injection of a saturated potassium chloride solution. Ovariectomy was performed for histopathologic examination.

Group 2 (experimental) included 8 rats. They were anesthetized with 15 mg. Ketamine (Ketalar, Parke-davis, morrisplains, NJ) and 2 mg. Xylazine (Gemini, Rugby Lab., Rockville Center, NY) for surgery. A previously described method in male rats was used.<sup>8</sup> In short, a midline laparotomy was performed. The left renal vein was identified and partially ligated to an external diameter of 0.85 mm. A consistent stenosis was achieved by using a 4-0 silk suture, which was ligated around both renal vein and a metal probe. The probe was removed and the vein was allowed to expand against the loop of suture. The suture was positioned medially to both the adrenal and ovarian veins. After recovery from anesthesia the rats were returned and maintained in the vivarium. Thirty days later, all animals were sacrificed as in control group and ovariectomy was performed.

Histopathologic examination: Tissues were fixed in 10% formaldehyde solution. After routine processing, 5  $\mu$ m sections were taken and hematoxylin-eosine staining was performed.

## RESULTS

The mean diameter (SD) of left ovarian veins before ligation of left renal vein was  $0.2\pm 0.1$  mm and after ligation, it became markedly

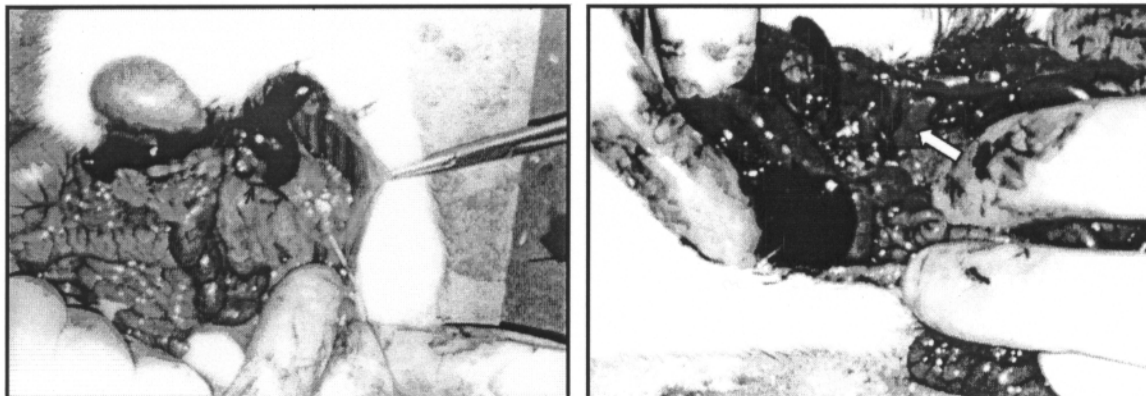
dilated to  $1.4\pm 0.3$  mm. This difference was significant ( $p<0.001$ ). Figure 1 shows left ovarian vein prior to partial ligation of left renal vein (A) and dilated ovarian vein thirty days after operation (B). Figure 2 shows histopathologic changes in ovarian tissues of control group (A) and study group (B). In control group, normal anatomic features were observed, namely follicles at various maturation cycle and corpora lutea and no venous congestion. In the experimental group, in addition to follicles and corpora lutea, dilated and congested blood vessels were prominent. No infarction or necrosis was observed. There was no arrest in follicular development.

## DISCUSSION

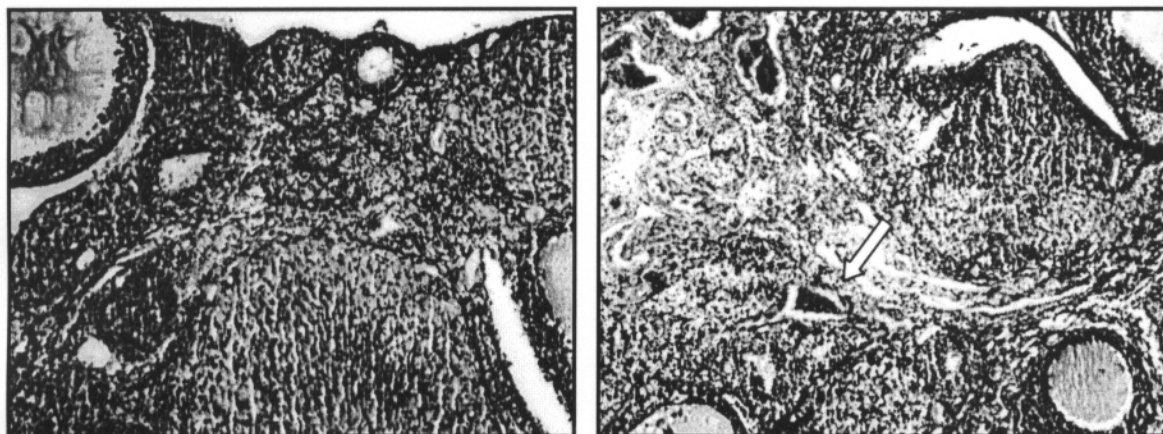
Varicocele is a well-recognized disorder occurring in up to 10% of men.<sup>9</sup> In women, an analogous varicosity of the salpingo-ovarian plexus is rare. The reason for this is that the diagnosis of varicocele in female patients is difficult clinically and the absence of an adequate animal model of female varicocele. In this study, we have applied a previously described animal model of male varicocele<sup>8</sup> to female rats. The most striking histologic findings were marked dilatation of left ovarian veins and congestion in vessels within ovarian tissue on the varicocele side. This model may be used as an adequate animal model of female varicocele.

The knowledge on pathophysiology of female varicocele and its clinical reflection is still far from known. Some studies were performed on this matter. At autopsy, ovarian venous valves were absent in 15% of women on the left side and in 6% on the right side.<sup>10</sup> Cross-communications between left and right ovarian veins were observed in 55% of women at autopsy.<sup>11</sup> Heavy physical work and disturbance of renal outflow (as in stenosis of the renal vein and the nutcracker phenomenon) may increase ovarian varicosity.<sup>2,3</sup> Pregnancy has also important contribution to the incidence of ovarian varicocele.<sup>12</sup> The association of pelvic

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**Figure 1.** Normal left ovarian vein before (A) and thirty days after ligation of left renal vein (B). (→) shows left ovarian vein before and after ligation.



**Figure 2.** Histopathologic changes in normal left ovary (A) and the ovary on varicocele side thirty days after ligation of renal vein (B). (→) shows dilated intraovarian venous structures.

congestion with ovarian varicosities has been recognized for many years.<sup>1-7</sup> Until recently, invasive venographic methods were used to confirm the diagnosis of ovarian varicosities in patients who usually complained chronic pelvic pain. Abdominal and transvaginal US, angioscintigraphy<sup>13</sup> and selective ovarian venography<sup>3-5</sup> are among imaging techniques to document pelvic varicocele in women. Since there is difficulty in clinical diagnosis of female varicocele, and need for invasive imaging techniques to diagnose, an animal model should be a logical option. It may be possible to investigate the effect of ovarian varicocele in various clinical situations, including pelvic congestion syndrome, infertility, and molecular and cellular changes associated with follicular

growth.

In conclusion, our female model of varicocele is an easy and cheap option for the investigation of female varicocele and was described for the first time. Further studies should be performed to detect basic molecular and cellular changes to detect the important clinical aspects of female varicocele.

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