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Spermatogenesis Disturbances of Infertile Patients with Bilateral Varicocele

Chalva Tchovelidze, Joseph Tritto, Thierry Guetta

Center Urology of Paris, France

ABSTRACT

Between 1990 and 2002, 179 varicocele patients, of which had bilateral varicocele, were consulted for infertility in the Urology and Andrology Department of the Saint Antoine and Tenon hospitals. The varicocele cases have been classified into four different grades. Its definition was based on the examination, palpation, the Valsalva procedure, Ultrasonography, color doppler examination and surgical operation data. In this article we describe the examination and the results obtained in 179 patients subjected to surgical intervention - microsurgical bilateral varicocele technique and systematic multiple and bilateral testicular biopsy at the scrotal examination. Mean patients age: 32,8 (range 19 to 60), primary infertility 154 cases and secondary infertility 25 cases. The results of testicular biopsies have been evaluated according to the biological group. In the group with azoospermia and the extreme oligozoospermia (77 patients) the TB has determined the degree of the spermatogenesis derangement (HYPO) in 35 (45,5%) cases, in the majority of cases-40 MA (maturation arrest)+SCOS(Sertoli Cell Only Syndrome)+TF(Tubular fibrosis). There are 126 cases (70,4%) of biopsies in our series HYPO (hypospermatogenesis). However in many cases HYPO is accompanied with MA, SCOS or TB. Among the MA there were 6 cases of early stage spermatocyte I, MA spermatocyte II in 8 patients and MA spermatide (late arrest) in 10 cases. SCOS was observed in 16 patients. Tubular and peritubular fibrose atrophy was observed in 5 cases. The common picture of spermatogenesis in varicocele cases as it demonstrates itself in our series of testicular biopsies is the disorganization of spermatogenesis accompanied by various disorders of intraluminal maturation in the somniferous tubule analysis in cases of varicocele.

KEYWORDS: *testicular biopsy, spermatogenesis, varicocele, male infertility*

The possibility of varicocele relation to infertility, even though it is still being discussed, seems to be established by now [4,8,10]. Whereas today the pathology of varicocele itself seems to be relatively well defined, the mechanism by which varicocele impairs spermatogenesis still remains under discussion, mostly when one must explain the bilateral effect of varicocele and its effect upon resulting infertility. Today there are four predominant hypothesis of the genesis to pathology: 1)effect of toxic metabolites carried by reflux; 2)thermoregulation troubles; 3)testicular hypoxia; 4)testicular androgen-regulation troubles.

Systematic study of biopsies allows to understand exactly the influence exerted on testicles by the infertility risk factors. The testicular biopsy was introduced more than 60 years ago in 1940 by Hotchkiss and Charny as an additional diagnostic tool for evaluation of infertility in the human male [2,3]. The testicular biopsy is to take more importance in the entire examination and consequently for the therapeutic decisions. Development in modern methods for assisted Reproductive Techniques (ART) give the testicular biopsy a second and very important role from the therapeutic point of view, i.e. TESE - Testicular Sperm Extraction for realization of ICSI - intracytoplasmatic sperm injection [1,7,9].

MATERIAL AND METHODS

Between 1990 and 2002, 362 varicocele patients, of which 179 had bilateral varicocele, were consulted for infertility in the Urology and Andrology department of the Saint Antoine, the Tenon Hospitals and Center Urology of Paris. The varicocele cases have been classified into four different grades. The basics of definition our classification was based on the examination, palpation, the Valsalva procedure, Ultrasonography, color doppler examination and surgical operation data. In this article we describe the examination and the results obtained in 179 patients subjected to surgical intervention - microsurgical bilateral technique and systematic multiple and bilateral testicular biopsy at the scrotal examination.

According to concentration of spermatozoa per milliliter of the sperm the patients were classified into 5 different biological groups (*Tab.1*).

Mean patients age: 32,8 (range 19 to 60), primary infertility 154 cases and secondary infertility 25 cases. In the protocol, the surgical intervention comprises the cure of varicocele using the microsurgery one and a systematic performing of multiple and bilateral testicular biopsies at the scrotal examination. Scrotal examination is indispensable since it allows: 1)To find out and ascertain anatomical and functional in-scrotum circumstances which can not be made apparent nor by conventional diagnostic techniques nor by biopsy made on the testicular surface through a small incision (for example, such as the presence of epididymis-testicular dysfunction). 2)To perform topometric and biometric testicular and epididymis measurements. 3)To supplement the varicocele classification with descriptions during operation. The semen analysis was

monitored three months later, then between the 6th and the 11th month and on the 12th month or later.

RESULTS AND DISCUSSION

The results of testicular biopsies have been evaluated according to the biological group. In the group with azoospermia and the extreme oligozoospermia the TB has determined the degree of the spermatogenesis derangement (HYPO) in 35 cases, in the majority of cases – 35 (45,5%) MA+SCOS+TF. The spermatogenesis disturbance according to the biological group is presented in more detail in the *Tab.2.*

In the group biologic (I-V) of our patients the results were the following: of 179 patients 98 (54,8%) improved the spermogram, 39 (21,8%) worsened the spermogram, the spermogram was not changed in 42 (23,4%). In the first biological group of 77 patients 35 (45,5%) improved the spermogram, what enables using several methods for this difficult group (ICSI, IVF- in vitro fertilization) for Assisted Reproductive Techniques - ART. As for the III, IV and V biological groups the observed spermogram improvements sharply increase the patients liability to spontaneous pregnancy and makes them intrauterine insemination candidates.

The double bilateral biopsy is to be of particular importance in the cases where varicocele is accompanied by a grave masculine infertility, especially by severe azoospermia and oligospermia. The testicular biopsy as a diagnostic tool in varicocele cases was described by many authors [5,6,8,9] and fundamentally it shows different degrees of maturation arrest and hypospermatogenesis accompanied by the peritubular fibrosis. The recent works [7,8,10] have well show, in concordance with all the pictures obtained with biopsy, the augmentation of different pathologies of spermatozoa, in particular the described intraluminal somniferous teratospermia, to be compatible with all the pathologies found in the semen analysis in cases of varicocele.

In our series, according to the biological group, the spermatogenesis disorder is most profound in the groups with a severe azoospermia and oligoterato-asthenospermia. In this biological group in varicocele cases there are often found SCOS initiated irreversible testicular lesions, to the point of severe atrophy or absence of germinal cells. However in various publications it is still under discussion whether varicocele is responsible for all profound testicular lesions since varicocele often goes together with various other hormonal abnormalities and testicular disorders [1,4,9].

The aim is to restore the normal semen analysis with possibility of eventual natural fecundation or to improve sufficiently the semen analysis for ART or, if the spermatozoa number in the ejaculate is insufficient, to allow the technique of ICSI starting with MESA (Micro Epididymal Sperm Aspiration) or with TESE (Testicular Sperm Extraction).

BIOLOGICAL GROUP	**CONCENTRATION** m/ml	**NOMBER OF PATIENTS**
I. Azoospermia or extreme oligozoospermia	0-1	77 (43,1%)
II. Severe oligozoospermia	1,1–5	35 (19,5%)
III. Moderate oligozoospermia	5,1–10	20 (11,5%)
IV. Relative oligozoospermia	10,1–20	19 (10,6%)
V. Normozoospermia	>20	28 (15,4%)
TOTAL		179

Tab.1 *Biological groups of semen analysis.*

BIOLOGICAL GROUP **SPERMOGENESIS**	No Patients	**I** (m/ml) 0-1	**II** (m/ml) 1,1–5	**III** (m/ml) 5,1–10	**IV** (m/ml) 10,1–20	**V** (m/ml) >20
Normal	8	1	_	_		7
Hypospermatogenesis	126	36	31	19	19	21
MA Spermatocyte I	6	5	1	_	_	_
MA Spermatocyte II	8	7	1	_	_	_
MA Spermatide	10	7	2	1	_	_
S.C.O.S Sertoly cell only Syndrome	16	16	_	_	_	_
Tubular Fibrosis	5	5	_	_	_	_

Tab.2 *Spermatogenesis biologic group.*

REFERENCES:

1. Cayan S, Edmemir F, Ozbey I, et al Can Varicocelectomy significantly change the way couples use assisted reproductive tecnologies?//Journal of Urology - Vol. 167 - April 2002 - pp. 1749-1752
2. Charny CW : Testicular biopsy in the study of male infertility(Its currentusefulness, histological techniques and prospects for the future) .// Hum. Pathol 10: 569-584, 1979
3. Hotchkiss RS. Testicular biopsy in the diagnosis and treatment of sterility in the male.//Bull. NY Acad. Med. 18: 600-605, 1942.
4. Kass E J.Adolescent varicocele.//Pediatric Clin. North America - Dec.2001 - 48(1) pp 1559-69
5. Kim E.D, Lin W.W, Abrams J; Lipshultz L.Testis Biopsy image analysis effectively quantifies spermatogenix cell types.//J. of Urology - vol 157. January 1997, pp 147-150
6. Magid M.S., Cash K.L, Goldstein M.The testicular biopsy in the evaluation of infertility. //Seminars in Urology - Vol. III n° 1 (february) 1990, pp51-64.
7. Pasqualotto FF, Lucon AM, hallak J, Goes PM, Saldanha LB, Araj.Introduction of spermatogenesis in azzospermic men after varicocele repair. //Hum Reprod 2003 Jan ;18(1) :108-12
8. Schoor RA, Elhanbly S, Niederberger CS, Ross LS.The role of testicular biopsy in the modern management of male infertility.// Jour; of Urology2002. jan. vol.167 pp.197-200.
9. Tchovelidze Ch., Guetta Th., Sibony M., Kirsch-Noir F., Arvis G. Bilateral microsurgical inguinal varicocelectomy with bilateral testicular biopsy of infertile men - spermatogenesis and altered semen quality. Georgian Medical News. Tbilisi-New-York. February. N2 (95) 2003. pp.31-37.
10. Tritto J. Giarga E. Erdei E, Morlier D. The role of testicular biopsy in microsurgical correction of bilateral varicocele. Amber 95 Paris . Proceedings 274-278. 1995.

Нарушения сперматогенеза у бесплодных мужчин с двусторонним варикоцеле

Шалва Човелидзе, Жозеф Тритто, Тьеры Гетта

Парижский урологический центр, Франция

Р Е З Ю М Е

С 1993 по 2002 г.г. у 179 больных с двусторонним варикоцеле проведена двусторонняя микрохирургическая коррекция варикоцеле с одновременной двойной двусторонней биопсией яичек. Средний возраст больных - 32,8 (от 19 до 60 лет). Первичное бесплодие отмечалось у 154 больных, а вторичное - у 25. На основе осмотра, пальпации, манёвра Valsalva, допплерографии и дооперационного состояния варикоцеле было классифицированно по 4 стадиям. В зависимости от концентрации сперматозоидов, выраженных в миллионах на миллилитр (млн/мл) спермы, пациенты были классифицированы в 5 различных биологических групп. Результаты биопсии яичка изучены соовествеснно биологическим группам. На основании биопсии яичек выделенны следующие группы сперматогенеза: нормосперматогенез (Normospermatogenesis - N) 8 больных (4,5%), гипосперматогенез (Hypospermatogenesis - HYPO) - 126 больных (70,4%), задержка созревания на ранней и поздней стадиях (Maturation Arest - AM) - 24 больных (13,4%), синдром сертолевых клеток (Sertoli Cell Only Syndrime - SCOS) - 16 больных (8,9%), атрофия яичка и канальцевый фиброз (Sclerose – Hyaline - TF) - 5 больных (2,8%). По данным послеоперационных контрольных спермограмм у 98 (54,8%) больных улучшилась спермограмма, спермограмма осталась без изменений у 42 больных (23,4%), а у 39 больных (21,8%) ухудшилась спермограмма. Лечение варикоцеле желательно сочетать с двойной двусторонней биопсией яичек и эксплорацией мошонки, чтобы всегда иметь возможность проверки состояния сперматогенеза. Кроме диагностики биопсия имеет терапевтическое направление. Она применяется с целью MESA (Microsurgical Epididymis Sperm Aspiration) или TESE (Testicular Sperm extraction) с последующей ICSI (Intracytoplasmatic sperm injection). Применение ассистированной репродуктивной техники (APT - Assisted Reproductive Technic) расширяет терапевтические возможности лечения бесплодия мужчин.

КЛЮЧЕВЫЕ СЛОВА: *биопсия яички, сперматогенез, варикоцеле, мужское бесплодие*