Microsurgical subinguinal varicocelectomy in "single testis" patients - a case series

S. Nedelea[1], S. Voinea[2], C. Gagiu[2], A. Ion[2], A. Preda[2], V. Jinga[3], I. Sinescu[2]

[1] *Department of Urology, "Prof. Dr. Agrippa Ionescu" Emergency Clinical Hospital, Bucharest, Romania*

[2] *Center for Uronephrology and Renal Transplantation, Fundeni Clinical Institute, Bucharest, Romania*

[3] *Department of Urology, "Prof. Dr. Theodor Burghele" Clinical Hospital, Bucharest, Romania*

Abstract

Introduction and Objectives. Varicocele affects one in ten adult men and one in four men with infertility. The exact mechanism through which it reduces male fertility is not known but surgical correction usually improves semen parameters. We consider the study of varicocele repair in single testis patients to be less biased by the presence of a healthy contralateral testicle and thus providing accurate results regarding the benefits of the procedure.

Materials and Methods. This is a retrospective, descriptive, single-center study, where we analyzed data from the clinical records of patients diagnosed with varicocele and a history of contralateral orchiectomy during a period of 4 years. All patients had varicocele surgery done by the same surgeon and the same surgical procedure of microsurgical subinguinal varicocelectomy was used. We follow their pathological history, clinical findings, hormonal work-up and semen analysis from before the surgery until the present day.

Results. There were six patients that corresponded to our criteria during the studied period. The patients were between 25 and 39 years old. All of them had right-sided orchiectomy for either benign or malignant disease and a left sided varicocele. Four of these patients presented for infertility of various lengths and two for clinical symptoms associated with the varicocele. Two patients that presented for infertility and were candidates for in-vitro-fertilization before varicocele repair managed to obtain natural pregnancies. All four patients that presented for infertility managed to obtain a pregnancy. The other two patients had their symptoms settled.

Conclusions. Microsurgical subinguinal varicocelectomy is a straightforward way to relieve clinical symptoms and upgrade the fertility status of single testis patients. Microsurgical treatment of a varicocele in single testis patients could result in the use of a safer, less invasive and less expensive artificial reproductive technique and a higher natural pregnancy rate.

Key-words: microsurgical, varicocelectomy, subinguinal, orchiectomy, single testis, TMSC

Correspondence to: Dr. Sebastian Voinea M.D., Ph.D.
Fundeni Clinical Institute, Uronephrology and Renal Transplantation Center
258 Fundeni Str., sector 2, code 022328, Bucharest, Romania
Tel/Fax: +40213007570
e-mail: voiniseb@yahoo.com

Introduction And Objectives

Varicocele repair, regardless of procedure, has been a subject of debate for several decades. A highly cited meta-analysis regarding the subject showed that varicocelectomy significantly improves semen parameters in men with abnormal semen, but only in men with a clinical varicocele[1]. Current research indicates that microsurgical varicocelectomy is the most effective method among the different varicocelectomy techniques[2]. This technique is also associated with the lowest rate of complications and reccurence[3]. It is still debatable whether varicocele is a unilateral or bilateral disease[4,5] and thus we consider the study of microsurgical subinguinal varicocelectomy in patients with a single testis highly relevant because it eliminates the possible bias of a healthy contralateral testicle.

Although there is an abundance of scientific literature on fertility potential after orchiectomy for either benign or malignant pathology we found none regarding the results of varicocele surgery, especially the microsurgical approach, on the remaining testicle.

A comprehensive search on both PubMed and Google Scholar search engines did not reveal any scientific article regarding varicocelectomy in adult patients with a single testis. Search terms included variations on: "orchiectomy", "single testes", "varicocele" and "infertility".

Materials And Methods

Study design is a descriptive and retrospective case-series.

These patients were admitted to the Center for Uronephrology and Renal Transplantation of Fundeni Clinical Institute and underwent microsurgical subinguinal varicocelectomy in the period between April 2013 and March 2017.

All patients had preoperative clinical examination, scrotal ultrasound, sexually transmitted diseases testing (urine culture, semen culture, urethral swab with real-time PCR testing for Mycoplasma/Ureaplasma), semen analysis and hormonal work-up (FSH (follicle stimulating hormone), LH (luteinizing hormone), Testosterone and Prolactin, Inhibin B and Anti Mullerian Hormone when necessary) preoperatively and reevaluation at every 3 months postoperative in the first year and every 6 months afterwards or until pregnancy. TMSC was obtained by multiplying the sample volume by the density and the percentage of A and B motility spermatozoa. We have collected data from the preoperative and postoperative clinical records, laboratory, ultrasound and surgical reports.

Results

We identified six patients who addressed to the clinic for investigation and treatment of varicocele and had a history of orchiectomy in the past for either benign or malignant pathology. Orchiectomy had been performed for various pathological conditions like testicular torsion, testicular trauma, cryptorchidism or testicular cancer.

All patients were diagnosed with a palpable left sided varicocele and absent right testicle. Patients were 25 to 39 years old at the time of surgery. All patients had at least one semen parameter that was below the lower reference limit necessary for obtaining a natural pregnancy

Case 1 BA

A 35-year-old patient, non-smoker, with orchiectomy at 16 for right-sided cryptorchidism presented to the clinic for three-year long primary infertility. Patient had a history of urethritis (Ureaplasma) and had been diagnosed nine years previously with hepatitis B for which he underwent Interferon therapy. The couple also had a history of failed IUI (Intrauterine Insemination). Clinical examination and scrotal ultrasound revealed a hypotrophic left testicle (8 cm^3) with a spontaneous vein diameter of 2.6mm and up to 3.3mm during Valsalva maneuver.

Semen analysis revealed a sperm concentration of 12 million/ml with only 2% normal morphology. Sperm motility as well as all other semen parameters were above lower reference limit. TMSC (total motile sperm count) value was 11.8 million. There were no genetic abnormalities (karyotype analysis or Y-chromosome deletions). FSH, LH and testosterone had values within limits. Inhibin B value was well under the inferior limit 57.594 pg/ml (normal range: 120-400 pg/ml).

Patient had uneventful microsurgical subinguinal varicocelectomy and was discharged the following day. The follow-up at three months after the surgery revealed normal hormonal levels. Semen analysis was improved with 26 million/ml sperm concentration, normal motility and 3% normal morphology. Calculated TMSC was 37 million. The couple conceived spontaneously 8 months after the surgery.

Case 2 CI

A 25-year-old patient, non-smoker, with orchiectomy 10 months previously for testicular torsion and inguinal hernia surgery in the distant past was referred to the clinic for a clinical grade III left sided varicocele.

Clinical examination confirmed the diagnosis. Hormonal work-up revealed slightly higher levels of gonadotropins (FSH=16.1mUI/ml, LH=10.4mUI/ml) and normal testosterone. Patient had normal sperm volume and pH. Semen analysis showed cryptozoospermia. He underwent microsurgical subinguinal varicocelectomy and presented at 3 months post-op for follow-up. There was no clinical recurrence and semen analysis showed improvement but still oligo-teratozoospermia. Sperm concentration was 5.8 million/ml, 32% progressive motility and 3% normal morphology. Calculated TMSC was 4.45 million.

Case 3 DF

A 27-year-old male presented for visible left scrotal painful enlargement. The patient had a history of post-traumatic right sided testicular rupture at 26 for which he had orchiectomy and a left-sided microsurgical subinguinal varicocelectomy for grade III varicocele at 24. The patient had normal sperm volume, pH and oligo-astheno-teratozoospermia (OAT): sperm concentration= 2.2 million/ml, 20% progressive motility and 2% normal morphology. Calculated TMSC was 1.1 million. Hormonal levels (FSH, LH and testosterone) were within limits. Serum Anti-Mullerian Hormone (AMH) was 0.8ng/ml (reference interval: 1.18-9.16ng/ml) and Inhibin B was 57.6 pg/ml (reference interval: 120-400pg/ml). Both determinations were well below the inferior limits showing severely affected gonadal function. He underwent microsurgical subinguinal varicocelectomy and was discharged the following day. Semen analysis 3 month following surgery showed a sperm concentration of 67 million/ml with slight asthenospermia (31% progressive motility) and teratozoospermia with only 2% normal morphology. Calculated TMSC was 62.31 million. Hormonal levels (FSH, LH and testosterone) were within normal limits. The patient followed all indications regarding follow-up and life style after the surgery. He presented to regular follow-ups appointments and did multiple semen analysis. His sperm concentration was the first to be corrected after only 3 months. His further levels stabilized at around 25-55 million/ml. Motility was corrected 12 months after the surgery when he suddenly reached 40% progressive motility from repeated values of around 30%. Teratozoospermia was the last to be corrected 32 months after the surgery.

Case 4 MC

A 35-year-old patient, smoker (36 pack-year), presented to the clinic for 24 months long primary infertility associated with alterations of the semen analysis (cryptozoospermia and necrospermia) and low Inhibin B (86.10pg/ml) (done for routine check-up). Patient had a history of orchiectomy at 17 for a suspicion of testicular malignancy that was not confirmed (histopathological examination revealed post-traumatic inflammation). Patient had uneventful microsurgical subinguinal varicocelectomy and was discharged the following day. At the 3-months post-op follow-up semen analysis showed normal volume and pH, a sperm concentration of 28 million/ml, 28% progressive motility, 3 % normal morphology and 62% viability. Calculated TMSC was 15.68 million. The couple obtained a natural pregnancy 17 months after the surgery.

Case 5 PV

A 39-year-old patient, non-smoker, presented to the clinic for left hemi-scrotal pain that had begun about 2 years previously and primary infertility of about 12 months. He had a history of right-sided orchiectomy for testicular seminoma and underwent postoperative chemotherapy and radiotherapy at 30. Clinical examination revealed a left sided grade III varicocele. Detailed anamnesis revealed a left hemi-scrotal venous swelling neglected for many years. Patient had azoospermia with normal semen volume and pH. Hormonal work-up revealed high levels of gonadotropins (FSH=17.1mUI/ml, LH=10.9mUI/ml) and normal testosterone and prolactin levels. The patient underwent microsurgical subinguinal varicocelectomy and was discharged 24 hours after. Patient neglected indications and only came back for follow up 14 months after the surgery with OAT. His semen analysis showed a sperm concentration of 3.8 million/ml, with 25 progressive motility and 2% normal pathology. Calculated TMSC was 4.75 million. FSH was still high at 13.9mUI/ml but lower than preoperatively. LH, testosterone and prolactin levels were within limits. The patient missed his follow-up appointments but the couple obtained a pregnancy through ICSI (Intra Cytoplasmic Sperm Injection) 48 months after the surgery.

Case 6 VM

A 25-year-old patient with a history of right-sided orchiectomy for testicular embryonal carcinoma (pT-1N0M0) presented for two-year long primary infertility. He had a left open inguinal hernia repair seven years before and was diagnosed with left renal lithiasis. Patient is a smoker (8 pack-year). Clinical examination revealed

a solitary left testicle with a grade III varicocele. Semen analysis showed severe OAT with a sperm concentration of 1.4 million/ml, 20% progressive motility and no normal morphology. Calculated TMSC was 0.84 million. Gonadotropins and testosterone were within limits. He underwent uneventful microsurgical subinguinal varicocelectomy and was discharged the next day. At the 3 months follow-up patient had no complaints and his semen analysis was improved but still OAT. (Sperm concentration = 6.4 million/ml, 30% progressive motility and still no sperm with normal morphology). Calculated TMSC was 7.68 million. Hormonal work up showed elevated gonadotropins (FSH=16.9mUI/ml and LH=15.6mUI/ml) and a testosterone level near the lower limit (13.32nmol/l). Patient repeated the test on his own will one month later and found the gonadotropins still high, although lower than 30 days earlier (FSH=14.6mUI/ml, LH=11.8mUI/ml) and a testosterone rise to 17.1nmols/l. Semen analysis also showed improvement with a sperm concentration of 12.8 million/ml, 60% progressive motility and still no normal morphology (oligo-teratozoospermia). The couple had a spontaneous pregnancy 28 months after the surgery.

Discussions

All orchiectomies were done for right-sided pathology and all patients were diagnosed with a left-sided clinical grade III varicocele. Laterality is in concordance with the general population where in 78% to 93% of cases varicocele is located on the left side[6]. Postponed medical examination is probably why all patients had grade III varicocele.

Four patients also presented for primary infertility of varying length (24 to 36 months) associated with the varicocele. A study by Dunphy et al[7] found no association between the length of involuntary infertility before presentation to a fertility clinic and subsequent chance of conception. Two of the patients were not interested in conceiving at the moment but intended to in the future.

Patients were discharged 24 hours after the surgery, same as patients without associated pathology. There were no immediate or late surgical or medical complications regarding the procedure. Microsurgical inguinal varicocelectomy is rarely associated[8] with post-operative complications like hydrocele, arterial injury or scrotal haematoma. It has a recurrence rate of 0.8 to 4%3 - one of our patients had a recurrent varicocele two years after the first surgery.

Semen analysis was performed in the same laboratory for all patients, with value references from the "WHO laboratory manual for the examination and processing of human semen"[9] Semen analysis revealed normal semen volume (2.4ml to 5ml) and pH (7.8 to 8) in all patients. Sperm concentration was severely low: azoospermia in one patient, cryptozoospermia in two patients and oligospermia for the other three: 1.4, 2.2 and 12 million/ml. None of these values alone were consistent with the lower reference limit for sperm concentration of 15 million/ml. Only one of the 6 patients had a progressive motility rate higher than the lower reference limit of 32% and none had a normal morphology rate higher than 4%.

Hormonal work-up was done in the same laboratory, with the same instruments, units and reference limits. Although we consider patients in this case series highly heterogeneous regarding age, initial pathology, age of orchiectomy and fertility potential, all of them had improved postoperative semen parameters.

All semen parameters improved following surgery with sperm concentration being the first to improve, even after only 3 months. Highest rise in sperm concentration was from 2.2million to 68 million/ml. Repeated sperm analysis revealed slower improvement in motility and morphology.

There are studies10 that use TMSC values in counseling couples regarding their pregnancy options: men with TMSC <5 millions are considered candidates for in-vitro-fertilization (IVF), 5–9 million for IUI, and >9 million for natural pregnancy. Using this classification, preoperatively, we had 5 patients suited for IVF, with TMSC <5 million and one patient suited for natural pregnancy. Using TMSC 3 months postoperative we had 3 patients suited for natural pregnancy, one for IUI and two at the upper limit for IVF.

By treating these patients we aimed to improve the sperm quality in order for them to ideally obtain a spontaneous pregnancy or to increase their chances of IVF. Regarding ICSI it is known that fertilization rates, embryo development and pregnancy rates are lower in men with severe OAT or non-obstructive azoospermia[11], so the better the semen parameters the higher the pregnancy odds. Regarding the patient with initial non-obstructive azoospermia, studies show that only one out of seven men embarking on ICSI with testicular sperm extraction eventually father their genetically own child[12]. Our patient succeeded in obtaining a pregnancy through an ICSI procedure using ejaculated sperm.

Cryptozoospermic patients are suggested to use

only (ICSI) as infertility treatment[13]. Surgically extracted sperm of these patients will do better than ejaculated sperm in ICSI and improve pregnancy outcomes[13]. Both patients with cryptozoospermia had semen parameters improvement after the surgery making them better candidates for ICSI or even IUI. With these improvements in mind they may be spared a surgically sperm retrieval, as in OAT (as they have become after surgery) spermatozoa retrieved either from ejaculate or testicular biopsies have nearly identical chances in achieving pregnancies[14].

Taking into consideration TMSC as a better predictor of spontaneous pregnancy15, intrauterine insemination[16,17] and ICSI[18] there are 3 predictive groups. The first group has TMSC<5, the second one has TMSC between 5 and 20 and a third one has TMSC>20 million. The higher the TMSC value, the higher the chances of obtaining a pregnancy are.

Patients in our case series not only had a better postoperative TMSC but also, moved up at least one TMSC group. Patients with preoperative azoospermia and cryptozoospermia had postoperative TMSC close to 5 million.

All 4 patients that presented for infertility managed to conceive, 3 of them spontaneously and one of them through ICSI. Spontaneous pregnancy occurred at 8, 17 and 28 months intervals after the surgery. Chemotherapy, radiotherapy, orchiectomy and cancer itself all have negative effects on spermatogenesis.19 Both patients who had testicular cancer, one of them with adjuvant chemotherapy and radiotherapy managed to obtain a pregnancy. Patients that presented for pain and discomfort had their symptoms relieved. The patient with recurrent varicocele achieved normospermia after 32 months. Patients with cryptozoospermia achieved mild asthenotheratozoospermia and OAT.

Conclusions

We conclude that left microsurgical subinguinal varicocelectomy is a safe procedure for single testis patients as we had no intra or post-operative complications. The type of previous conditions that required orchiectomy do not seem to influence surgery results. There is important improvement in patient fertility following surgery. Diagnosis and microsurgical treatment of a varicocele in single testis patients could result in a less invasive, less expensive artificial reproductive technique and in a higher natural pregnancy rate.

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