TESTIS BIOPSY IN VARICOCELE AS RELATED TO FERTILITY

by

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Eventhough testicular biopsy has been part of the diagnostic armamentarium in the investigation of male infertility for over 30 years (Hotchkiss, 1956; Heller and Clemont, 1964; Amelar, 1966), testicular morphology in varicocele as related to fertility has not been fully evaluated. In 1963, Charny referred to "incompletely (Etriby *et al* 1967) matured spermatogenic elements" in testicular biopsies of men with varicocele. More recently Etriby *et al* (1967) described a state of maturation arrest, and (Dubin and Hotchkiss 1969) demonstrated germinal cell hypoplasia and premature sloughing of immature germinal cells as features of varicocele.

According to the earlier report, 26.67% of subfertile men who attended the infertility clinic had associated varicocele and next to testicular failure it was the common cause of infertility in man. (Rajan, 1977). Following semen analysis and female evaluation, when indication existed for correction of varicocele, bilateral testicular biopsy was performed either preliminary to or at the time of varicocelectomy.

This report deals with the study of testicular morphology in a series of subfertile men with varicocele, as determined by bilateral testicular biopsy. An attempt is made to find out as to how far the varicocele is responsible for the underlying pathology in the testes and the manifested infertility.

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Materials and Methods

Fifty-five subfertile men with varicocele, none of whom had ever fathered a child, underwent detalied investigation at this centre during the period, August 1975 to September 1976. The female partners were completely evaluated and infertility problems in them were either ruled out or when existed were corrected. In the male evaluation special attention was paid to the nature of varicocele and size and consistency of the testicles. Seminal samples were collected by masturbation after abstaining from intercourse for 5 days. In all patients semen analysis was done by the authors, and different samples were studied before arriving at a conclusion. Cases of oligospermia were further investigated with post-coital test (PCT) in the mid-cycle phase. PCT was found to be either negative or poor (less than 5 sperms/HP field, and majority nonmotile).

Biopsies were taken from either testicle of the 55 subfertile men at the time of varicocelectomy in 17 instances and only as an investigative procedure in the remaining 38 cases. The tissue was fixed in Bouin's solution, which yielded

satisfactory nuclear details by preventing the shrinkage of the tissue.

Observations

The age ranges of the 55 men studied are shown in Fig. 1, with the highest con-

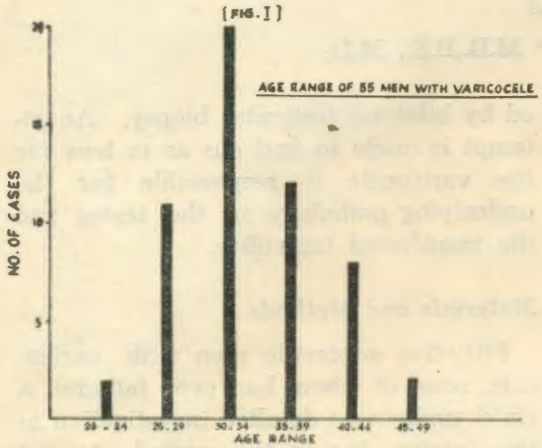

Fig. 1

centration in 30-40 yrs. Duration of sterility in them ranged from 1 year to 20 years with a mean of 5.4 years.

Semen analysis revealed marked oligospermia in 38 instances and azoospermia in the remaining 17 cases. Twenty men in the oligospermia group demonstrated the typical stress pattern of sperm morphology (tapering and amorphous cells and the exfoliation of immature cells of the germinal line into the ejaculate), described by (Macleod 1965).

Except for the 3 cases where the anatomical defect was bilateral, varicocele was invariably unilateral and left sided. But the testicular changes were of the same type on both sides, though of more advanced degree on the side of varicocele. In 4 cases there was a significant difference in the histology seen in the contralateral testicle which would have been missed if bilateral biopsy was not taken. The findings are summarised in Fig. 2.

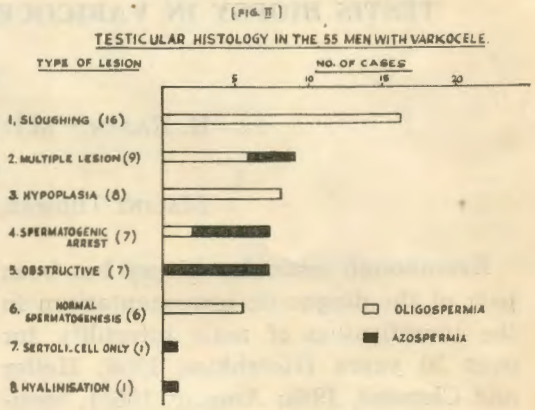

Fig. 2

Histology in Oligospermia: The most prominent pattern of testicular morphology noted in 16 cases was that of germinal cell hypoplasia with premature sloughing of immature cells into the lumen of the tubules. There was also apparently an increase in the amount of active interstitial tissue. (Fig. 3).

The next frequent findings were that of pronounced hypoplasia in 8 cases, and relatively normal testicular structure with thinning of germinal epithelium in 6 cases. (Figs. 4 a and b).

A rather interesting finding was that of mixed pattern with multiple lesions (6 cases), tubules showing complete agenesis side by side with others showing active though partially arrested spermatogenesis. The least common type of testicular lesion was that of spermatogenic arrest, demonstrated in 2 cases. (Figs. 5 and 6).

Histology in Azoospermia: Analysis of 17 cases of azoospermia showed that 7 had ductal obstruction as denoted by a picture of normal spermatogenesis except for moderate sloughing. In another 8 cases, 5 specimens showed spermatogenic

arrest and 3 mixed pattern with varying degrees of spermatogenic maturation. The remaining 2 cases showed a picture of irreversible testicular damage, Sertoli-cell-only syndrome and tubular hyalinisation for which the associated varicocele could not be responsible.

Testicular Size and Consistency: The size of the testicles clearly reflected their spermatogenic function. In cases of oligospermia, they were moderate in size, with the affected side soft and sometimes smaller than the opposite side. In case of azoospermia, small testicles were associated with irreversible degree of testicular changes, while those with normal size were associated with obstructive lesions or other reversible lesions like arrest, or rarely sertoli-cell-only type also.

Discussion

That varicocele has an adverse effect on testicular function has become an accepted concept. Numerous confirmations of the beneficial effects of varicocelectomy have followed the 1952 report by Tulloch of a successful outcome after varicocelectomy in an instance of azoospermia. Davidson (1954), Tulloch (1955), Young (1956), Scott (1961). Charny (1962), MacLeod (1965), Dubin and Hotchkiss (1969) and Dubin and Amelar (1971) have reported improve ment in semen quality in 70 to 80% of cases, while a conception rate of 40 to 48% has been observed by (Zorgniotti and MacLeod 1966; and Dubin and Amelar 1971).

The seminal findings of oligospermia, hypokinesis, and an increase in abnormal immature forms associated with varicocele have been well elucidated by MacLeod (1965). The mechanisms of retrograde flow down the internal spermatic vein associated with cross-collateral circulation have been studied by Brown *et al* (1967).

Varicocele may affect the testicular spermatogenic function at least in two ways. The first is that of chronic venous congestion and hypoxia ending in atrophy of the testis. This is proportional to the size of the associated varicocele and its duration. This vascular effect is strictly unilateral. However, recovery in many cases after varicocelectomy indicates another bilateral inhibitory mechanism. This may be an increased intrascrotal temperature or an abnormal testicular hormonal environment induced by venous regurgitation. This inhibitory effect is transmitted to the contralateral testicle.

Whatever the underlying inhibitory mechanism may be, the urgent question is the proper choice of patients for operation, as varicocele may be an associated condition that has nothing to do with the manifested sterility. This is well documented in the present study, specially in the 17 cases of azoospermia among which in only 8 patients could varicocele be implicated. Of the remaining 9 cases, 7 patients had normal spermatogenesis indicating ductal obstruction and 2 patients had irreversible testicular changes, SCOS and tubular hyalinisation. Varicocelectomy will be indicated and be beneficial only in the former group of 8 patients, and in the latter group of 9 patients it will be unnecessary procedure. Hence it may be reasonable to conclude that prior testicular biopsy for diagnosing the testicular morphology is a must before correcting the associated varicocele in azoospermic men.

Concentrating on the 8 patients with azoospermia and 38 patients with oligospermia all of whom showed a reversible testicular lesion—we found that the com-

monest change was that of germinal cell hypoplasia with premature sloughing of immature forms into the lumina of the seminiferous tubules, in 16 cases (34.8%). Many of these patients showed a relative hyperplasia of the interstitial tissue. According to (Dubin and Hotchkiss 1969), this is the commonest type of testicular change associated with more than 50% of their patients with oligospermia and varicocele. But Etriby *et al* (1967) hold that the predominant finding is that of spermatogenic arrest, in 66% of men with reversible testicular lesions. In our study only 15% of cases (7 patients) showed a picture of spermatogenic arrest and this condition was as common as germinal cell hypoplasia (8 patients) and normal spermatogenesis (6 patients) associated with varicocele. Mixed pattern with multiple lesions ranging from germinal cell aplasia to poor spermatogenesis, probably a progressive degenerative condition, was demonstrated in 9 of our cases.

This type of classification of testicular histology is based on the predominant changes noticed, though often other changes are associated. For example, in cases of sloughing, although most of the tubules are clogged with sloughed premature cells, some of the adjoining tubules show spermatogenic arrest and hypospermatogenesis. It is thus probable that the sloughed cells are ultimately transmitted to the epididymis. This would explain the character of semen in cases of varicocele that reveal an abundance of immature spermatogenic cells (Davidson, 1954). Similarly, in cases of spermatogenic arrest, hypospermatogenesis is commonly associated which explains the few spermatozoa seen in the ejaculate.

Bilateral testicular changes, though of the same type, differed in degree—being more advanced on the side of varicocele. In 4 cases there were significant differences in the histology seen in the contralateral side. These observations signify the need for bilateral rather than unilateral testicular biopsies in these subfertile men.

Effect of varicocele corrections are summarised by Etriby *et al* (1967). Cases with sloughing of immature cells have the best chances of improvement, followed by those with incomplete spermatogenic arrest. Any peritubular fibrosis seems to diminish the chance of recovery markedly. The larger the size of the testicles, the less the associated testicular derangement and the more the chance of recovery. According to Dubin and Hotchkiss (1969), over 50% of the patients who improved after varicocelectomy exhibited sloughing and germinal layer hypoplasia; however, those patients who did not improve showed no specific histologic pattern which would differentiate them from the improved group, thus rendering testicular biopsy of limited value for prognostication.

In our study, since the number of patients operated upon is limited (17 cases) and the follow-up is not yet completed, no attempt at present, is made to assess the prognosis for varicocelectomy on the basis of testicular morphology.

Summary

1. Bilateral testicular biopsies of 55 subfertile men with varicocele were studied.

2. All the 38 patients with oligospermia showed a possibly reversible testicular picture of varying type, with germinal cell hypoplasia and sloughing predominating in 16 cases.

3. Of the 17 cases of azoospermia, only in 8 cases could varicocele be implicated.

Predominant picture in 5 out of the 8 cases was that of spermatogenic arrest.

4. Testicular changes were of the same type on both sides, though of more advanced degree on the side of varicocele. However, in 4 instances the contralateral testicle showed a different morphology.

5. In cases of azoospermia, a preoperative biopsy was essential to exclude obstructive cases and those with irreversible tubular lesions.

6. The probable prognostic value of testicular biopsy in operative correction of varicocele is discussed.

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References

1. Amelar, R.: Infertility in men. Davis, Philadelphia. 5: 1966.
2. Brown, J. S., Dubin, L. and Hotchkiss, R. S.: Fertil. & Steril. 18: 46, 1967.
3. Charny, W. C.: Fertil. & Steril. 13: 47, 1962.
4. Charny, W. C.: Fertil. & Steril. 14: 610, 1963.
5. Davidson, H. P.: Practitioner. 173: 703, 1954.
6. Dubin, L. and Hotchkiss, R. S.: Fertil. & Steril. 20: 50, 1969.
7. Dubin, L. and Amelar, R.: Fertil. & Steril. 22: 469, 1971.
8. Etriby, A., Girgis, S. M., Hefnawy, H. and Ibrahim, A. A.: Fertil. & Steril. 18: 666, 1967.
9. Heller, C. G. and Clemont, Y.: Rec Progr Hormone Res. 20: 545, 1964.
10. Hotchkiss, R. S.: Fertil. & Steril. 7: 284, 1956.
11. MacLeod, J.: Fertil. & Steril. 16: 735, 1965.
12. Rajan, R.: J. Obst. & Gynec. India. 1977 (accepted for publication).
13. Scott, L. S.: Brit. J. Med. 1: 788, 1961.
14. Tulloch, W. S.: Subfertility in male., Trans Edin Obstet. Soc., 1951-52, p. 29.
15. Tulloch, W. S.: Brit. Med. J. 2: 356, 1955.
16. Young, D.: Brit. J. Urol. 28: 426, 1956.
17. Zorgniotti, A. W. and MacLeod, J.: Treatment and results of varicocelectomy in the subfertile male. Presented at the American Fertility Society, Chicago, Ill., April, 1966.

See Figs. on Art Paper I-II