TESTICULAR BIOPSY IN AZOOSPERMIA

(A Review of 81 cases of Male Infertility)

by

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Testicular biopsy has got its place in the management of cases of male sterility, for diagnosis, prognosis and evaluation of results in surgery in obstructive azoospermia. Charny *et al* in 1948, were the first to report on the use of testicular biopsy in human fertility. In the same report, they gave credit to Hotchkiss (1944) as the first to use this method. Since then it has been extensively employed, notably by Engle (1947), Nelson (1953), Heller and Clemont (1964), Amelar (1966), Etriby *et al*, (1967), and Girgis *et al*, (1969).

The present study concerns the testicular biopsy reports of 81 men who had reported with infertility problems due to azoospermia. The various histological pattern are described in detail, and their role in the proper management of these cases are discussed.

Material and Methods

In this report, the case material of 81 azoospermic patients is considered. All these men were subjected to thorough physical examination, and diagnosis of azoospermia was confirmed by repeated seminal analysis. The age range of these patients varied from 25 to 45 years, most patients being between 30 to 39 years. Biopsies were taken from all these patients for diagnostic purpose. The incidence of different testicular pathologies associated with azoospermia is reviewed. No attempt is made to correlate the clinical picture with the testicular histology.

Observations

Of the 81 men biopsied, 24 (about 30%) showed normal testicular pattern with active spermatogenesis, thus denoting their obstructive nature, while the remaining 57 (about 70%) showed various types and grades of hypofunction (functional azoospermia).

Obstructive Azoospermia: In the 24 patients with obstructive azoospermia the seminiferous tubules were normal in size and shape and contained germinal epithelium showing active spermatogenesis. There was no thickening of the basement membrane or lamina propria. Lying on the basement membrane were the Sertoli cells, resting and dividing spermatogonia. Closer to the lumen were found the other types of cells in the spermatogenic series showing a sequential, orderly arrangement, with axis perpendicular to the basement membrane. In some cases, the tubular lumen contained immature cells showing signs of degeneration. The interstitial tissue was not prominent. (Fig. 1 a and b).

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Functional Azoospermia: (Table I)

TABLE I

Functional Azoospermia: Distribution by type

	Patients	
	Number	%
Sertoli-cell-only syndrome	21	36.8%
Tubular Hyalinization	15	26.3%
Spermatogenic Arrest	9	15.8%
Klinefelter's Syndrome	9	15.8%
Multiple Lesions	3	5.3%
Total	57	100.0%

Of the 57 cases with functional azoospermia, the most frequent type (21 cases) was that of "Sertoli-cell-only syndrome" (SCOS), with seminiferous tubules populated only by Sertoli cells, while spermatogenic cells were absent. In most of the patients there was no evidence of degenerative changes, so that tubular walls were thin and the Leydig-cell component was normal (Fig. 2 a and b). In a few patients, however, there was peritubular thickening of variable degree (Fig. 3 a and b).

The second cause of functional azoospermia in 15 cases was hyalinization of the seminiferous tubules with thickening of their walls and basement membranes (26.3%). The condition was not always uniform, the degenerative process was incomplete, with residual spermatogenic elements. Leydig cells, in most of the patients, showed compensatory diffuse hyperplasia (Fig. 4 a and b).

Spermatogenic arrest was seen in 9 patients (15.8%) with arrested spermatogenesis at the stage of primary spermatocyte being predominant. Arrest at the primary spermatocyte stage was often incomplete, so that few secondary spermatocytes and sometimes spermatids were observed; in addition primary spermatocytes often showed abnormal mitosis and sloughing into the lumen (Fig. 5 a and b).

The Klinefelter syndrome, hyalinization of small-diameter tubules associated with Leydig-cell hyperplasia in clumps (Fig. 6 a and b) was noticed in 9 cases (15.8%). Leydig-cell hyperplasia was so marked in many of the cases that only sheets of Leydig cells were observed. In few cases tubules containing Sertoli cells alone were present with marked hyperplasia of the Leydig-cells (Fig. 7 a and b).

The remaining 3 cases (5.3%) could not be included in any of the foregoing classification, since more than one main type of changes were present. In all these cases, however, focal necrosis was present, as denoted by areas of tubular hyalinization, while the associated tubular changes were spermatogenic arrest, SCOS tubules, sloughing and disorganization.

The least frequent type lesion, namely, developmental arrest was not encountered in this series.

It is observed that the incidence of obstructive azoospermia is less (30%) when compared with that of functional azoospermia (70%). In the series reported by Girgis *et al* (1969) the incidence of obstructive azoospermia is more (55%) than functional azoospermia. (45%). Their figures for functional azoospermia are as follows: SCOS 38.73% (commonest) spermatogenic arrest (26.26%), tubular hyalinization (14.85%), Klinefelter's Syndrome (11.4%), developmental arrest (2.39%) and multiple lesions (6.37%).

Discussion

The differential diagnosis of male infertility ultimately rests on testicular biopsy. In azoospermia the findings of normally functioning seminiferous

tubules eliminate the testes as the cause of the semen deffect and points to an obstructive lesion of the seminal tract as the seat of trouble. However, testicular biopsy has a wider scope than that. The histologic appearance of spermatogenic elements gives an insight into the nature of the lesion, if one be present, and this has both diagnostic and prognostic usefulness. Occasionally, lesions are observed that lead to specific therapy, as in some instances of hypopituitarism. More often one encounters end-stage lesions pointing out the hopelessness of the problem, thus sparing the patient and avoiding months of useless treatment.

Considering the aetiological aspect of the subject, one is impressed by the prevalence of a congenital factor. In functional azoospermia cases, SCOS constitute the commonest type, 21 cases (26.1%) and are explained on the basis of failure of primary spermatogenic cells to migrate from the cloacal entoderm to the genital ridge. In obstructive lesions (30% of the total cases), over two-thirds are congenital. Thus, in azoospermia, at least 46% are of congenital origin.

Chromosomal aberrations is another eatiologic factor. These are accepted as the underlying cause in sex chromatin-positive cases of Klinefelter's syndrome due to an error in the transmission of sex chromosomes during the stage of meiotic non-dysjunction, or in mosaics, mitotic non-dysjunction. De L Balze *et al* (1967) also believe that in some patients multiple lesions in testicular biopsy specimens are due to underlying chromosomal defects. But, Girgis *et al* (1969) are of opinion that the condition is one of degeneration to tubular hyalinization rather than a separate entity.

Tubular hyalinization which was seen in 15 cases (19% of the total), was quite often idiopathic, though it may be associated with mumps orchitis, other inflammatory scrotal swellings or varicocele.

The hormonal factor is difficult to assay. It is apparent only in patients with developmental arrest who show hypogonadotropic hypogonadism. Another possible hormonal factor is adrenal hyperfunction due to enzymatic block in cortisol synthesis.

Selection of proper line of treatment can be based on the findings of testicular biopsy. According to Girgis (1969), the subject of azoospermia as a whole is not so hopeless as many would think. As per this study, in about 30% of cases, the cause is obstructive, and in more than one-half, epididymo-vasostomy can prove beneficial. In the present series 15.8% of cases (21 patients) had spermatogenic arrest, who could be benefited by treatment, with more hope now-a-days, since the introduction of human gonadotropin, clomiphene citrate and also by varicocelectomy in selected cases of varicocele. Thus, in azoospermia at least 30% can be hopefully treated.

Conclusion

In spite of some views to the contrary, testicular biopsy has got a definite place in the diagnosis of male sterility problems presenting with azoospermia. Of the 81 men biopsied, 24 had normal spermatogenesis, indicating the obstructive nature of the condition (30%), 21 had SCOS (26.1%), 15 had tubular hyalinization (19%), 9 had spermatogenic arrest (11.2%), another 9 had Klinefelter's Syndrome (11.2%) and 3 biopsies showed multiple lesion (3.8%).

Testicular biopsy is also essential for the proper management of cases of male infertility. Admittedly, in some of the

functional cases, such as those of SCOS, tubular hyalinization or Klinefelter's syndrome with total hyalinization, it is of little help to the patient, but it saves him from unnecessary operations or expensive hormonal treatment (56% of the reported cases). Since the lesion is irreversible, the couple may be given sound advice regarding adoption or artifical insemination. In 30% of cases of obstructive azoospermia, where biopsy suggests spermatogenesis, further investigations will locate the site of block and at least 50% may be benefited by surgical correction of the block. Spermatogenic arrest (15.8%) are cases suitable for gonadotropin therapy, or varicocelectomy is associated with varicocele.

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