Morphologic patterns of male infertility in Saudi patients

A University Hospital experience

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ABSTRACT

Objective: To determine the predominant histopathological patterns seen in the testicular biopsies taken during the investigation of male infertility and to compare the obtained histopathological findings with those seen in other similar studies.

Methods: This is a retrospective study performed on 230 testicular biopsies which were examined in the Department of Pathology at King Khalid University Hospital in Riyadh over a period of 10 years. The histopathological findings were grouped into 8 different morphologic categories. We have utilized a classification that is principally morphologic but that uses known or suspected clinical associations in the case of karyotypic abnormalities and excurrent duct obstruction.

Results: Of the total of 230 testicular biopsies studied, 72 cases showed normal spermatogenesis, of which 50 cases were suspected to be associated with excurrent duct obstruction. Germinal cell aplasia with and without focal spermatogenesis was found in about 90 cases. Thirty cases showed hypospermatogenesis, 25 cases showed maturation arrest and 12 cases showed end stage tubular sclerosis with interstitial fibrosis. Only one case was noted to show features associated with karyotypic abnormalities.

Conclusions: A higher percentage of germinal cell aplasia was noted in this study when compared with other similar investigations including one previous local study. Possible causes of these discrepancies may be related to several factors including environmental effects. The design of the different studies and the criteria used for patient selection or both could also explain the cause of these observed differences.

Keywords: Male infertility, biopsies, testis.

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Male infertility represents an important factor as the cause of infertility amongst infertile couples. Investigation of male infertility includes clinical history, physical examination, biochemical investigation, semen analysis, and testicular biopsy. Studies from various countries showed different morphologic patterns in the testicular biopsies. In this study, we retrospectively reviewed 230 testicular biopsies obtained from male patients with primary infertility, using a classical pathologic classification in their categorization. The results obtained are compared with those of other similar studies. A discussion of possible causes of the discrepancies noted is also included together with comments on the new trend of utilizing fine needle aspiration (FNA) for the assessment of male infertility.

Methods. The testicular biopsies from 230 infertile male patients were independently reviewed by two experienced pathologists (MR and ACR). The biopsies were performed at King Khalid

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Table 1 - Frequency of histological types of testicular lesions in infertile men.

Type	No of cases (%)
Normal spermatogenesis	72 (31)
No suspicion of obstruction	22 (10)
With suspicion of obstruction	50 (22)
Hypospermatogenesis	30 (13)
Maturation arrest	25 (11)
Germ cell aplasia	54 (23.5)
Germ cell aplasia with focal Spermatogenesis	36 (16)
Klinfelter like changes	1 (0.5)
Diffuse tubular atrophy and hyalinization	12 (5)
Total	**230 (100)**

University Hospital, a large teaching and tertiary referral hospital, over a period of 10 years (1987 to 1996). All biopsies were received fixed in Bouin's acid fixative, underwent the routine tissue processing, cut at about 5 micron thick sections and stained with hematoxilin and eosin. Cases with secondary infertility, cryptorchidism, and those with incomplete clinical data were excluded from the study. Classification of histologic patterns was based on the morphologic changes of the testicular tissue, which included the assessment of the presence of germinal cells and their maturation, size of seminiferous tubules and the presence or absence of associated fibrosis and Leydig cell hyperplasia or both.

The reported results were classified as follows: normal spermatogenesis, hypospermatogenesis, maturation arrest, germinal cell aplasia (Sertoli cell only syndrome), germinal cell aplasia with focal spermatogenesis, testicular changes associated with karyotypic abnormalities, and tubular sclerosis with interstitial fibrosis (end stage testis). Cases showing active spermatogenesis but with some features suggestive of obstruction were included under normal spermatogenesis. The criteria used in the above classification were discussed elsewhere.[1]

Results. The histopathology of 230 testicular biopsies was retrospectively reviewed. The age of patients ranged from 16 to 60. All came with the diagnosis of primary infertility and had oligo- or azospermia. The various pathological patterns of these biopsies were included in Table 1. Seventy-two cases showed normal spermatogenesis, of which 50 cases were suspected to be associated with duct obstruction. Germinal cell aplasia with and without focal spermatogenesis were found in about 90 cases. Thirty cases showed hypospermatogenesis, 25 cases showed maturation arrest, and 12 cases showed diffuse tubular sclerosis with interstitial fibrosis. Only 1 case was noted to show features associated with karyotypic abnormalities. Comparison between our findings and other studies is shown in Table 2.

Discussion. Testicular biopsy is an important tool in the investigation and the assessment of male infertility. It may shed some light on the etiology as well as providing essential prognostic information.[2]

Table 2 - Comparison of distribution of histological pattern of testicular biopsies in infertile males.

	KKUH series (%)	Wong et al[1] (%)	Branner & Roth[3] (%)	Thomas[4] (%)	Colgan et al[12] (%)
Normal spermatogenesis	31	25	35	38	20
Hypospermatogenesis	13	23	27	19	49
Maturation arrest	11	32	12.5	5	11
Germ cell aplasia	39	8	12.5	9	12
Klinfelter's-like	0.4	5	12.5	5	3
Diffuse tubular atrophy and hyalinization	5	--	--	23	--
Mumps orchitis	--	1	--	--	--
Cryptorchidism	--	4	--	--	--
Irradiation damage	--	2	--	--	--
Inadequate sample	--	--	--	--	6

The histologic patterns in the testicular biopsies are classified according to the presence and amount of spermatogenesis, maturation of germinal cells and presence of associated tubular atrophy, interstitial fibrosis and Leydig cell hyperplasia or both.[1] Previous reports showed different pattern of testicular morphologic changes. The studies carried out in the western world[1,3] showed a higher incidence of hypospermatogenesis combined with maturation arrest, while on the contrary, the one study from an African country, Nigeria,[4] showed much higher incidence of tubular atrophy and fibrosis. The reason for these discrepancies was attributed to environmental factors such as toxic fumes, lead or other polluting chemicals, which may play an important role in the development of hypospermatogenesis and maturation arrest in the industrial countries. In addition there is the possible effect of wearing tight insulating clothing, in these cold climates, which increases scrotal temperature and thus reducing spermatogenesis.[1] In Nigeria, Ibadan, neither significant pollution, nor tight clothing is present. The higher percentage of diffuse tubular atrophy with interstitial fibrosis was attributed to the possible increased incidence of testicular infections such as mumps orchitis. Our study showed similar incidence of hypospermatogenesis combined with maturation arrest to that seen in Nigeria, however, there was no increase in the percentage of cases with diffuse tubular atrophy with interstitial fibrosis. The striking difference between our study and the other studies was the presence of a much higher percentage of germinal cell aplasia among our cases. The etiology of germinal cell aplasia is not well defined. Several factors may, however, lead to this morphologic pattern, including varicocele, prepubertal gonadotropin deficiency, estrogen treatment, irradiation, alkylating agents, cryptorchidism, and in del Castello's syndrome.[1,2] A previous study carried out on a local Saudi population showed a higher percentage of testicular fibrosis and atrophy and it was found that the most associated diseases with primary infertility included infections, mainly viral and sometimes bacterial or parasitical, maldescent testis, varicocele, and diabetes.[5] One possible explanation for the discrepancy between the two Saudi studies is the criteria used in selecting patients for biopsies. Patients with azospermia, small testes and high FSH were not considered for testicular biopsies in many centers. This is due to the fact that many investigations have showed that this type of patients is most probably going to show germinal cell aplasia or diffuse testicular atrophy, thus there is no indication for testicular biopsy.[2] Recent advances in intracytoplasmic sperm insemination (ICSI) would still try to get a biopsy from these patients in order to get at least a few sperms to do the insemination.[6] FNA biopsy was introduced in the past 10 years as an alternative for testicular biopsy in assessing male infertility.[7-10] Studies have also showed FNA to be highly sensitive in detecting active spermatogenesis, and that it gives a fairly accurate idea about the histologic patterns. This type of procedure is however, still not very popular, possibly, because it is a new technique, and the fact that there are not many people who are expert in performing or interpreting its results. In addition there may be as much as 50% discrepancy in the classification based on FNA between different centers.[11] Despite that, FNA biopsy would still be recommended in assessing male infertility because of its higher sensitivity in detecting spermatogenesis, which is most important now in the management of infertility through the use of ICSI.

In summary, we have shown in this retrospective study the different histopathologic patterns of male infertility, which are encountered in our local population. These changes appear to be different from those described in other similar studies. The possible causes of these differences are not clearly understood but could include environmental factors. The explanation of the high incidence of germinal cell aplasia (Sertoli cell only syndrome) in our population is not clear, but could be related to the high incidence of undetected cryptorchidism and orchitis or both in this community. In addition, as mentioned earlier, the criteria used in patient selection for testicular biopsy may also represent an important factor that influences the outcome results of the different studies.

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