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Testicular Biopsies of Azoospermic Men at The Lagos State University Teaching Hospital

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ABSTRACT

Objectives: This study was conducted to evaluate the histological findings from testicular biopsies in azoospermic men seen at the Lagos State University Teaching Hospital, Ikeja - Lagos, Nigeria.

Patients and Methods: A retrospective study of testicular biopsies of azoospermic men who presented to our institution from 2005 to 2006 was performed. The patient's age, type of infertility and histopathological diagnosis were evaluted. All biopsies were preserved in 10% formaldehyde solution.

Results: Of the 51 azoospermic men (mean age 30 years, range 25 – 46 years) 25 (49.0%) had primary infertility, 11 (21.6%) had secondary infertility and 15 (29.0%) were not specified. Five (9.8%) patients had normal spermatogenesis. Abnormal histological parameters occurred in 46 (90.2%) patients: testicular atrophy in 30 (58.8%), maturation arrest in 14 (27.5%) and hypospermatogenesis in 2 (3.9%) patients.

Conclusion: The presence of normal spermatogenesis in azoospermic men, which would suggest an obstructive lesion, is not common in our practice, in contrast to previous studies from our country. This may indicate a changing pattern in the aetiology of male infertility in our environment. Identification of the possible causes of testicular damage resulting in non-obstructive azoospermia in our environment may help to prevent male infertility.

Key Words: Azoospermia, etiology, diagnosis, testicular biopsies, histopathology, infertility, environment

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INTRODUCTION

Infertility remains a major public health problem despite recent developments in this field. About 15% of couples are unable to conceive after one year of unprotected sexual intercourse[1]. In about 20% of infertile couples, a male factor is solely responsible and in another 30–40% it is contributory[1-2].

Azoospermia, defined as complete absence of sperm from the ejaculate, is present in about 1% of all men and in 10-15% of infertile men[3]. The evaluation of a patient with azoospermia is performed to determine its aetiology. This allows the physician to determine whether a significant medical disorder is the underlying

cause of the azoospermia, to establish whether the cause of azoospermia is amenable to therapy and to identify appropriate treatment options[1].

The aetiologies for azoospermia fall into three categories: pre-testicular, testicular and post-testicular[1]. Pretesticular causes of azoospermia are endocrine abnormalities that adversely affect spermatogenesis (secondary testicular failure) and are relatively rare[1]. Testicular aetiologies (primary testicular failure) involve disorders of spermatogenesis intrinsic to the testes. Post-testicular aetiologies of azoospermia are due to either ejaculatory dysfunction or obstruction of sperm delivery to the urethral meatus, and are found in approximately 40% of patients[3]. The pretesticular and post-testicular abnormalities that cause azoospermia are frequently correctable[1]. Testicular disorders are generally irreversible, with the possible exception of impaired spermatogenesis associated with varicoceles[4]. However, with the current development in the field of infertility, men with irreversible testicular disorders may benefit from assisted reproductive techniques so as to be able to father children[5-7].

Azoospermic men with normal ejaculate volume may have obstruction of the reproductive system (obstructive azoospermia) or abnormalities of spermatogenesis (non-obstructive azoospermia). Diagnostic testicular biopsy is indicated in azoospermic men who have normal serum follicle stimulating hormone (FSH) and normal testicular size in order to differentiate the potentially correctible obstructive azoospermia from non-obstructive azoospermia[1].

The aim of this study was to review our experience with azoospemic men who had diagnostic testicular biopsy in our institution and to compare the findings with previous reports from other centers in Nigeria[8,9].

MATERIALS AND METHODS

A retrospective study of testicular biopsies of azoospermic men who presented to our institution during a 2-year period (2005 and 2006) was performed. These patients had the routine infertility evaluation in the Urology unit of our institution[1, 3]. The indications for testicular biopsy were azoospermia with normal testicular size and normal serum follicle stimulating hormone (FSH). Open testicular biopsy of the bigger testis was performed in all patients. All specimens were preserved in 10% formalin solution because of the non-availability of Bouin's and Zenker's solution. The patient's age, type of infertility and histopathological diagnosis were evaluted. The data were analyzed using SPSS 14.0 software for Windows. Statistical associations were determined using the Chi square test and p-values ≤ 0.05 were considered significant.

RESULTS

There were 51 azoospermic men with a mean age of 30 (range 25-46) years. Twenty-five patients (49.0%) had primary infertility, 11 (21.6%) had secondary infertility and 15 (29.4%) were not specified. No complications of testicular biopsy were recorded.

The findings on histological examination are shown in Table 1[1, 3]. We did not find any significant association between the testicular biopsy histology and the patient's age or the type of infertility ($p>0.05$).

The patients with normal spermatogenesis were further evaluated and managed for obstructive azoospermia while those with testicular hypofunction or failure were offered medical therapy and/or referred for assisted reproductive techniques.

DISCUSSION

Male factor infertility remains a major challenge in clinical practice. Approximately 20% of cases are caused entirely by a male factor, with an additional 30-40% involving both male and female factors. Therefore, a male factor is present in one half of infertile couples[1].

Testicular biopsy is important to differentiate potentially correctible obstructive

Table 1: Testicular histology in 51 azoospermic men

Diagnosis	N	%
Germinal aplasia	30	58.8
Normal spermatogenesis	5	9.8
Maturation arrest	14	27.5
Hypospermatogenesis	2	3.9

azoospermia from non-obstructive causes. It has been described that obstructive azoospermia occurs in 20-42 % of patients with azoospermia[1, 3, 7-12]. In our study, normal spermatogenesis (indicating obstructive azoospermia) was present in only 9.8% of patients. The majority of our patients (91.2%) had primary testicular failure. Comparing our findings with previous studies[8-9] from Nigeria, there was a higher incidence of primary testicular failure and a lower proportion of patients with obstructive azoospermia, who may benefit from corrective surgery.

It is possible that exposure to unknown environmental or industrial toxins that are hazardous to the testes, or some genetic factors may be contributory[12,13]. This may explain the apparent increased incidence of primary testicular failure in our environment. Other social factors peculiar to our environment may be responsible[12]. In addition, improved awareness and treatment of sexually transmitted diseases may be responsible for the lower proportion of cases with obstructive azoospermia.

Most azoospermic men in our environment require assisted reproductive techniques (ART) to father children. However, ART is still at a developmental stage in Nigeria and would not be affordable to most of our patients. Identifying environmental or genetic factors that impair spermatogenesis in our environment may help to reduce the incidence of testicular failure and improve male fertility. It is possible that smoking, atmospheric industrial pollutants and environmental waste containing cadmium may be contributory[13].

In this study all testicular biopsy specimens were preserved in 10% formalin, due to the non-availability of other testicular preservatives. Although formalin is often regarded as a poor fixative for testicular tissue, it has been demonstrated that 10% formalin can be satisfactorily used by pathologists experienced with testicular histology[14]. In our study, the pathologists found the specimens preserved in 10% formalin adequate for histopathological examination.

The main benefit of testicular biopsy is to identify normal spermatogenesis in azoospermic men, who may benefit from corrective surgery for obstructive azoospermia. Identification of the possible causes of testicular damage resulting in non-obstructive azoospermia in our environment may help to prevent male infertility. In addition, provision of accessible and affordable ART facilities is required in our environment to help the majority of patients with non-obstructive azoospermia.

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Editorial Comment

The The key question in this study is: are diagnostic biopsies still needed in men with azoospermia?

Serum markers (FSH, Inhibin B, Testosterone) together with clinical findings usually indicate if an obstruction of the seminal pathway is to be expected. Is microsurgery available in Nigeria, and can they correct obstructive azoospermia? In new guidelines it is advised to combine a testicular biopsy in infertile men always with cryopreservation of tissue for future ICS attempt, but this may not be applicable in Nigeria. Still, I would advise not to routinely perform testicular biopsies, since it will not have any clinical benefit to the patients in a developing country with limited health resources. Looking at the outcome of the biopsies it is surprising to see so many men with germ cell aplasia and maturation arrest: this probably reflects a genetic cause of infertility in these men. Environmental pollution will more likely result in hypospermatogenesis, unless there are pollutants in Nigeria that directly affect testicular development in early pregnancy and result in testicular dysgenesis. In addition, the review of Professor Skakkebaek from Denmark on TDS is to be considered. Is it likely that there are compounds in the Nigerian environment that act like estrogens or anti-androgens? Our guess would still be that there probably is a genetic cause of this increase in male infertility due to testicular failure and it would be of interest to further investigate the DNA of these men for potential genetic abnormalities. This could be done in collaboration with a European institute that focuses on genetic screening in infertile men.

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