

# Pattern of Testicular Biopsies as Seen in a Tertiary Institution in Nnewi, Southeast Nigeria

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## ABSTRACT

**Background:** Testicular biopsy is an acknowledged method of examination of the testes for diagnostic and therapeutic purposes. We describe the pattern of testicular histologies in our environment. **Materials and Methods:** We carried out a retrospective review of testicular histology results from the Pathology Department of Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, over a 5-year period, January 2008 to December 2012. **Results:** During the period, 285 testicular histologies were reported. Eighty-one (28.4%) specimens were pathological specimens, while 204 (71.6%) were nonpathological specimens. Thirty-seven (13.0%) of the histology reports were for diagnostic purpose while 248 (87.0%) were for therapeutic purpose. Based on the results, indications could also be categorized into three, benign testicular pathology, malignant testicular pathology, and testicular biopsy for male factor infertility. Thirty-seven cases (13.0%) were due to male factor infertility with complete spermatogenic arrest as the most common histological finding in 21 (56.8%) of the cases. Malignant testicular diseases accounted for 16 (5.6%) of the indications for testicular biopsies. Benign testicular diseases accounted for 28 (9.8%) of the indications for testicular biopsies. Hemorrhagic infarction from testicular torsion represented the commonest histology in 12 (42.9%) cases, followed by inflammations of the testes. **Conclusion:** Indications for testicular biopsy can be diagnostic and therapeutic. They can also be categorized into benign testicular diseases, malignant testicular diseases, and male infertility. Investigation for male factor infertility was the only diagnostic indication for testicular biopsy. The high incidence of locally and metastatic prostate cancer in males explains why therapeutic removal of the testis is common.

**KEYWORDS:** Biopsy, histology, testis

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Tumors of the testis and para-testicular tissues are rare in men.<sup>[2]</sup> They constitute the most common solid malignancies in men aged between 15 and 34 years.<sup>[3]</sup> Whereas the incidence is rising in the Western and Asian countries, the incidence in the Black populations of Africa and West Indies is low.<sup>[4,5]</sup> The testes are a major source of testosterone in the male, contributing about 95% of total serum testosterone.<sup>[6]</sup> The standard of care for the initial treatment of metastatic prostate cancer is androgen deprivation therapy, which may be accomplished by surgical castration.<sup>[7]</sup> Metastatic carcinoma to the testis is very rare,<sup>[8]</sup> however, several cases of prostate cancer metastasizing to the testis have been documented in the literature.<sup>[8-11]</sup> Other primary tumor sites are the lungs, kidney, colon, stomach, bladder, and from lymphomas.<sup>[9]</sup>

The aim of this study is to characterize the common indications for testicular biopsy and determine the common histo-pathological pattern of testicular diseases in this environment.

## INTRODUCTION

Testicular biopsy is an acknowledged method of examination of the testes for diagnostic and therapeutic purposes. Aside from the known diagnostic and therapeutic indications, testicular biopsy can also be done for medico-legal reasons. More recently, testicular fine needle aspiration and percutaneous needle biopsies have become common procedures for the characterization as well as sperm retrieval in male factor infertility associated with oligospermia.<sup>[1]</sup> Sperms retrieved from this process can be used for intracytoplasmic sperm injection (ICSI) in artificial reproductive techniques (ART).<sup>[1]</sup>

## MATERIALS AND METHODS

The study is a retrospective review covering a 5-year period from January 2008 to December of 2012 at a tertiary institution in the south-eastern part of Nigeria. Patients who had testicular biopsy as part of their investigation for infertility or their testis removed for therapeutic reasons were analyzed. The specimens were preserved in 10% buffered formalin as fixative and read by a consultant pathologist after routine slide staining with hematoxylin and eosin stain.

The data collected from the records of the histo-pathology

department included age of the patients, indication for the biopsy and the final histology report as reported by the pathologist. Results were expressed in simple descriptive statistics using Microsoft Excel®.

## RESULTS

A total of 285 testicular tissues were submitted for histology within the period. Out of this number, 81 (28.4%) specimens were pathological specimens, while 204 (71.6%) were nonpathological specimens. Based on histological outcome, 37 (13.0%) of the histology reports were for diagnostic purpose while 248 (87.0%) were for therapeutic purpose.

As shown in Table 1, excision biopsy of the testis after surgical castration for advanced prostate cancer was the commonest therapeutic indication for testicular biopsy in 204 (71.6%) of the cases. This was followed by incision biopsy for male infertility, which accounted for 37 (13.0%), and the only diagnostic indication for testicular biopsy recorded. Benign conditions of the testes and malignancies of the testes accounted for 28 (9.8%) and 16 (5.6%) of the cases, respectively.

The mean age of patients with male infertility was  $40.1 \pm 7.5$  years (range 32-59) and the commonest histologic patterns in this group were complete spermatogenic arrest in 21 (56.8%) and sertoli cell only histology in 7 (18.9%) [Table 2]. Tubular hyalinization and hypo-spermatogenesis occurred less frequently in 5 (13.5%) and 4 (10.8%) of the cases, respectively. These results were reports of single testicular biopsies in 37 different patients.

Chronic inflammations of the testes and hemorrhagic infarction from testicular torsion, as shown in Table 3, accounted for an equal proportion of the cases with benign testicular conditions 12 (42.9%). The mean age for the patients with hemorrhagic infarction from testicular torsion was  $19.9 \pm 6.8$  years (range 8-30 years). Of all the forms of inflammations of the testes, chronic granulomatous epididymo-orchitis was the commonest inflammatory condition that necessitated orchidectomy.

Malignant conditions of the testes accounted for 19.7% of the specimens submitted for histology. Primary tumors of the testes accounted for 13 (81.3%) of malignant conditions of the testes and the commonest primary tumor of the testis was seminoma occurring in 7 (43.7%) of the testes submitted for histopathologic study [Table 4]. Only three cases were due to secondary metastasis to the testis. Two (12.5%) were from secondary metastasis of prostate cancer to the testes. One (3.8%) was from secondary metastasis from Hodgkin's lymphoma.

## DISCUSSION

Cancer of the prostate is the most commonly diagnosed malignancy in males and has become a public health issue in some

**Table 1: Common indications for testicular biopsy**

Indications	Pathology	Number (n)	Percentage
Diagnostic	Male infertility	37	13.0
Therapeutic	Surgical castration for prostate cancer	204	71.6
	Benign testicular diseases	28	9.8
	Malignant testicular diseases	16	5.6
Total		285	100

**Table 2: Patterns of testicular histology for male infertility**

Age range (years)	Histology	Number of patients	Percentage
32-59 Mean 40.1	Complete spermatogenic arrest	21	56.8
	Tubular hyalinization	5	13.5
	Sertoli cell only	7	18.9
	Hypo-spermatogenesis	4	10.8
Total		37	100

**Table 3: Histological patterns for benign testicular diseases**

Primary diagnosis	Age range (years)	Histology	Number of patients	Percentage
Testicular torsion	8-30 Mean 19.9	Hemorrhagic infarction	12	42.9
	8-29 Mean 21.5	Testicular atrophy	4	14.3
Inflammatory conditions	28-74 Mean 51	Chronic nonspecific epididymo-orchitis	4	14.3
	7-45 Mean 30.8	Chronic granulomatous epididymo-orchitis	7	25.0
	41	Chronic fibrosing orchitis	1	3.6
Total			28	100

**Table 4: Histological patterns of malignant testicular diseases**

Tumor	Age range (years)	Histology	Number of patients	Percentage
Primary testicular tumor	15-30 Mean 24.3	Spindle cell sarcoma	2	12.5
		Seminoma	7	43.7
		Adenomatoid tumor of epididymis	1	6.3
		Sertoli cell tumor	3	18.7
Secondary testicular tumor	55-85 Mean 70.6	Metastatic adenocarcinoma of prostate	2	12.5
	15	Hodgkin's lymphoma	1	6.3
Total			16	100

parts of the world.<sup>[12,13]</sup> In patients suffering from prostate cancer, castration or the use of other mechanisms that lead to a decrease of testicular androgen production and of plasma testosterone levels usually results in a favorable response. After castration, serum testosterone decreases to 5-10% of the original values.<sup>[6]</sup> Endocrine treatment is often applied to either locally advanced or metastatic prostate cancer. Most reports from Sub-Saharan Africa have confirmed that patients with prostate cancer often present late.<sup>[14,15]</sup> This explains the high number of testicular tissues submitted for histology after therapy for advanced prostate cancer.

From our study, we conveniently categorized histological results of testicular biopsy into three groups [Tables 2-4]. These patterns can vary with geographical region.<sup>[16]</sup> Male factor infertility is a major cause of infertility among couples contributing to more than half of all cases of infertility.<sup>[17,18]</sup> Testicular biopsy may be required in the evaluation of azoospermic or severely oligospermic males with normal endocrine function.<sup>[19]</sup> Testicular histology in infertile men with azoospermia or oligospermia usually shows different patterns. In this study, a spectra of histological patterns were noted, with complete spermatogenic arrest occurring most frequently in 56.8% of 37 infertile male biopsy reports. Reports of testicular histology for male factor infertility differ significantly from one part of the country to another, due to several underlying etiological factors including social habits, genetic causes, and environmental conditions such as underlying infections, chemicals, radiation, and exposure to heat. Ahmed *et al.*,<sup>[20]</sup> in a review of 88 histology reports of men with infertility in Zaria, noted that 68.2% had hypo-spermatogenesis, while 11.4% had normal morphology. Granulomatous and nonspecific orchitis were uncommon. Thomas from Ibadan,<sup>[21]</sup> in a review of 58 testicular biopsies, observed that 38.2% had normal spermatogenic activity, suggesting a high incidence of obstructive azoospermia and 22.4% had extensive or marked diffuse tubular atrophy associated with peritubular hyalinization and interstitial fibrosis. Early and prompt treatment of known causes of infertility in the males is recommended to prevent progression to an irreversible histology.

Primary testicular tumor is a disease of the young and the incidence is low in Nigeria.<sup>[5,22]</sup> Most testicular tumors occur in infancy, late adolescence, and young adults. Primary testicular tumors represent the most common malignancy in males in the 15- to 35-year-old age group and have become one of the most curable solid neoplasms.<sup>[23]</sup> Seminoma, embryonal carcinoma, and teratoma are mainly childhood tumors with better prognosis than the corresponding tumors in adults.<sup>[24]</sup> Germ cell tumors, mainly seminomas accounts for the most common histology.<sup>[25]</sup> Results from our study are in tandem with results from Port Harcourt, where seminomas accounted for 75% of the total testicular tumors.<sup>[26]</sup>

Secondary metastases to the testis are even rarer. Approximately 200 cases of metastatic carcinoma to the testis have been reported.<sup>[23]</sup> In the vast majority, it is discovered incidentally at autopsy in patients dying of widespread metastatic disease. In

rare circumstances, a metastatic focus in the testis maybe the presenting feature of an occult neoplasm or the first evidence of a recurrent, previously diagnosed or treated neoplasm.<sup>[23]</sup> In our series, three (18.8%) were positive for secondary metastasis to the testes. None of these cases were diagnosed at autopsy. The common primary sources in decreasing order of frequency are prostate, lung, gastrointestinal tract, melanoma, and kidney.<sup>[23]</sup> From our study, only two (12.5%) were metastatic from prostate cancer and one (6.3%) from Hodgkin's lymphoma. This relative high incidence of prostatic lesions reflects in part the frequency with which carcinoma of the prostate occurs and the use of orchidectomy in its treatment. With only 80 cases of prostate cancer metastasizing to the testis, documented in the literature,<sup>[10]</sup> this study also confirms that secondary metastasis of tumors especially of prostate cancer to the testis is an uncommon phenomenon, even though most cases of bilateral orchidectomy in prostate cancer are done for advanced disease. Metastatic carcinoma of the prostate to the testes represents an advanced disease and is usually accompanied by multiple metastases to other organs.<sup>[11]</sup> However, the prognostic significance of testicular localization of prostate carcinoma is still unknown.<sup>[11]</sup> Significantly, almost all cases of secondary metastases to the testes are commonly detected incidentally in orchidectomy specimens, and they may sometimes mimic primary testicular tumors. These characteristics of secondary metastases to the testes may pose diagnostic challenges to the pathologist.

Excision biopsy of the testis can often be indicated therapeutically for some benign conditions of the testis, such as testicular infarction from testicular torsion, testicular atrophy from cryptorchidism, or in some forms of chronic epididymo-orchitis recalcitrant to conventional treatment. This is indicated to document testicular damage and to prevent sympathetic injury to the normal contralateral testis. Testicular torsion is the commonest cause of acute scrotum in the pubertal and postpubertal ages.<sup>[27]</sup> Since it was first reported in the literature in 1840, the clinical features and mode of treatment has remained unchanged.<sup>[28]</sup> Emphasis should be placed on correct diagnosis and excluding other causes of acute scrotum such as epididymo-orchitis and epididymitis with which this condition can be confused. Time is of great importance in the surgical management of testicular torsion. After 4 h of testicular ischemia, sufficient damage is inflicted on the affected testis enough to result in hemorrhagic infarction and atrophy.<sup>[29]</sup> With prolonged testicular torsion, there is germinal cell ischemia and necrosis.<sup>[29]</sup> Early diagnosis and prompt effective treatment will improve testicular salvage.

In our study, all testicular tissues were preserved using 10% buffered formalin as preservative. Zenker's, Bouin's, or buffered glutaraldehyde fixatives are preferred over formalin for fixation of testicular biopsies.<sup>[30]</sup> Of the many fixatives that have been proposed, 10% buffered formalin remains the best compromise under most circumstances. It is inexpensive, the tissue can remain in it for prolonged periods without deterioration, and it is compatible with most special stains, including immunohistochemical techniques, as long as the tissue is placed

in the fixative shortly (<30 min) after surgical removal, and over fixation (>24-48 h) is avoided.<sup>[31]</sup> However, for testicular biopsies, formalin can introduce distortion artifacts, making histologic analysis less accurate. Zenker's fixative (which incorporates mercuric chloride) is an excellent fixative, but it is expensive, requires careful disposal of the mercury, and necessitates meticulous attention to fixation times and washing procedures to remove the precipitates of mercury. Bouin's fixative (which contains picric acid – a strong toxic yellow crystalline acid) has been especially recommended for testicular biopsies.<sup>[31]</sup> However, Bouin's and Zenker's fixatives are not readily available in low to medium income countries like ours and they (Bouin and Zenker fixatives) have serious potential public health issues, hence formalin is a suitable compromise.

## CONCLUSION

Indications for testicular biopsies can be diagnostic or therapeutic. The only diagnostic indication for testicular biopsy was for investigation of male factor infertility. Based on histological results, the indications for testicular biopsies can be categorized into benign testicular diseases, malignant testicular diseases, and male infertility. The high incidence of locally and metastatic prostate cancer in males explains why therapeutic removal of the testis is common.

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