▪ *Original Article*

A correlative study on cytopathological and histopathological findings in male genital tract lesions

P Paudyal, AK Sinha[1], AK Karak[1], B Kumar[1], CS Agrawal[2]
[1]Department of Pathology, [2]Department of Surgery
BP Koirala Institute of Health Sciences, Dharan, Nepal

Abstract

Background: The incidence of male genital lesions has continuously increased during the last decades, especially in the developed countries. FNAC serves as an important tool to screen and diagnose all palpable lesions of the genital tract and provides sufficient information for the initiation of treatment without need for an open biopsy. This study compares the diagnostic outcome between FNAC and surgical biopsies in male genital tract lesions. **Objectives** To find out the correlative attributes of cytological findings with the histologic diagnosis in male genital tract lesions. **Methods:** This is a hospital based retrospective and prospective study spanning over a period of six years. A total of thirty seven male patients with genital tract lesions were subjected to both FNAC and biopsy. The age, site, duration of illness, onset of illness, history of pain, relevant past medical history, cytological and histological findings were recorded. Diagnostic contribution of FNAC was evaluated taking histologic diagnosis as gold standard. **Results:** The age range was 2-80 years. Mean age was 39.37 year. Commonest site involved was right testis (27.0%) followed by left epididymis (21.7%). Predominant lesion was benign which constituted 59.4%. Malignancies formed 18.9% of all cases. **Conclusion:** FNAC was observed to be capable of providing correct diagnosis in 78.4%. Taking histologic diagnosis as gold standard, FNAC was found to have a sensitivity of 81.48% and specificity of 42.85 %.

Keywords: fine needle aspiration cytology, male genital tract lesion, biopsy, testicular tumor

Introduction

The incidence of male genital lesions has continuously increased during the last decades, especially in the developed countries. Fine needle aspiration cytology (FNAC) is a rapid and relatively inexpensive technique which has been used extensively in the diagnosis of a large variety of neoplastic and nonneoplastic lesions in many organs. This study compares the diagnostic outcome between FNAC and surgical biopsies in male genital tract lesions. [1, 2] Biopsy by aspiration, also known as thin or fine needle aspiration biopsy, has become an important diagnostic technique, replacing to some extent and complementing tissue pathology in many clinical situations. Many clinicians feel that this remains the most important contribution of the technique from a practice point of view. The clinical value of FNAC is not limited to neoplastic conditions. It is also valuable in the diagnosis of inflammatory, infectious and degenerative conditions, in which sample can be used for microbiological and biochemical analysis in addition to cytological preparations.[3] The low risk of complications is an additional advantage which allows FNAC to be performed in an outpatient departments and in radiology theatres; it is also highly subtle in debilitated patients, readily repeatable and useful for multiple lesions.[3]

The simplicity of the technique and its relatively minor trauma to the patient along with the rapid response rate are some of the important advantages of this technique compared to surgical biopsies[4]. On the other hand interpreting biopsies is one of the most important duties of the surgical pathologist which is gold standard technique.[4] This study compares the diagnostic outcome between FNAC and surgical biopsies.

Address for Correspondence
Dr. Punam Poudyal
Department of Pathology BPKIHS, Nepal
Email: phopunamzpranju@hotmail.com

Methods

This is a hospital-based retrospective and prospective study spanning over a period of six years. For retrospective study, all the diagnosed cases of male

genital system over a period of five years from January 2002 to December 2006 were retrieved from the indexed histopathology files of the Pathology Department, BPKIHS, Dharan. Prospective study was conducted over a period of one year from January 2007 to January 2008. All the 37 patients with male genital tract lesions without any consideration for age were subjected to FNAC. The age, site, duration of involvement, onset of disease, history of pain, relevant past history, cytological diagnosis and histological diagnosis were studied in these cases. These patients were then subjected to biopsy for the evaluation of the accuracy of fine needle aspiration cytology in the diagnosis of male genital tract lesions and for comparison of cytological results with histopathology.

Collected data were entered in Microsoft Excel 2000 and converted it into SPSS PC$^+$ 10 Version for statistical analysis. The descriptive statistics were presented in percentage, proportion, tabular forms and mean and standard deviation were calculated. For inferential statistics odds ratio, chi square test with p-values were calculated at the level of significant at 95%, to find out the relationship between dependent variables and independent variables. Sensitivity, specificity, positive predictive value and negative predictive value were calculated.

Results

All the patients included in this study attended BPKIHS with genital tract swelling. The swelling were subjected to the FNAC and subsequent histopathology of excision biopsy for cyto-histopathological correlation was done in provided samples.

A total of 37 cases were studied with age range of 2-80 years. The mean age was 39.73 year. One case was under pediatric age group and 36 cases were in the adult age group. Majority 20 (54 percent) were in age group of 15-40 years. The commonest site of lesion in all age group was in the right testis (27.0 percent) followed by left epididymis (21.7 percent), right epididymis (18.9 percent) and left testis (13.5 percent).

When age was taken into account the most common site of lesion was right epididymis and left epididymis in equal frequency (13.5 %) which is among 15-40 year age of patient. The duration of the swelling ranges from 2 and 12 month. The predominant complaint in majority of the cases were painless swelling in various sites of genital tract (19\37, 51.4%), in 18 cases there was history of pain (18\37, 48.6%). Out of 37 cases majority 25 (67.6 percent) cases had insidious onset and 12 (32.4 percent) cases had acute onset of illness.

There were no significant correlation for the past history and family history in the cases. Only one case of tuberculous epididimytis had family history of pulmonary tuberculosis.

Table 1: Benign and malignant lesions

	Cytological diagnosis	Frequency (n)	Percentage (%)
Benign	Cystic lesion	4	10.8
	Adenomatoid tumor	3	8.1
	Tuberculous lesion	3	8.1
	Non specific chronic epididimytis	3	8.1
	Atrophic testis	3	8.1
	Granulomatous epididimytis	2	5.4
	Spermatic granuloma	2	5.4
	Spermatocele	1	2.7
	Hematoma	1	2.7
	Non-conclusive	8	21.7
Malignant	Seminoma	3	8.1
	Germ cell tumor	3	8.1
	Squamous cell carcinoma	1	2.7
Total		37	100.0

Cytologically the cases were divided into three groups i.e. Benign which constituted 59.4% (22 cases), Malignant constituted 18.9% (7 cases) and a third group where definite opinion was not possible on FNAC designated as non conclusive constituted 21.7 % (8 cases) (Table 1).

Benign lesions

There were 4 cases diagnosed as cystic lesion, aspirates of which on microscopy revealed sheets of mesothelial cells, few scattered macrophages and lymphocytes. On subsequent biopsy 2 of the cases were consistent with epididymal cyst (Figure 1).

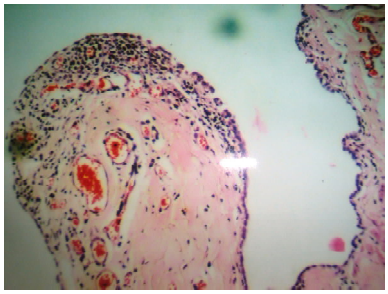

Figure 1: Cystic lesion of scrotum. Cystically dilated structure lined by flattened to cuboidal epithelium (H&E x 40)

Out of rest of the 2 cases 1 showed feature of necrotizing granulomatous lesion consistent with tuberculous orchitis with positive AFB (TB) and another showed chronic inflammatory cells, areas of hemorrhage and fibrosis.

There were 3 cases diagnosed as adenomatoid tumor, aspirates of which revealed mesothelial like cells in small clusters, sheets as well as forming glands (Figure 2).

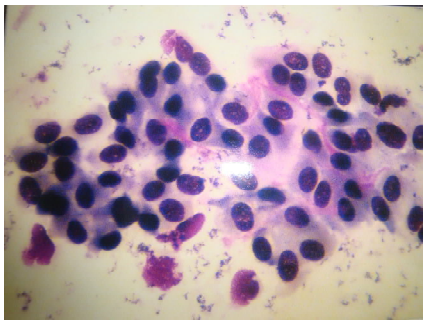

Figure 2: Adenomatoid tumor, testis. Clusters of plump spindle cells resembling mesothelial cells with mild nuclear atypia and well defined cytoplasm (MGG x 40)

These cells were round to oval with centrally placed vesicular nuclei and finely vacuolated cytoplasm. In the background lymphocytes were seen. On subsequent biopsy all the 3 cases revealed features of adenomatoid tumor. There were 3 cases diagnosed as tuberculous orchitis, aspirates of which revealed large areas of caseous necrosis, epithelioid cell granuloma and langhans giant cells against a dirty background with variable positivity for AFB (TB). Histopathological examination revealed features of tuberculous orchitis in all 3 cases (Figure 3).

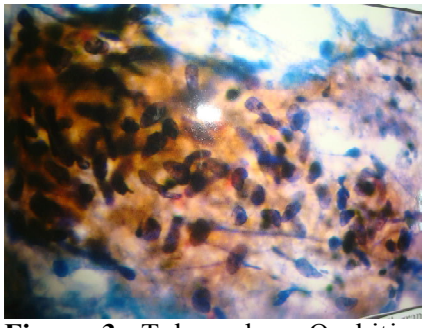

Figure 3: Tuberculous Orchitis. Epithelioid cell granuloma against a necrotic background (PAP x 40)

There were 3 cases diagnosed as Atrophic testis, aspirates of which revealed total absence of spermatogenesis. On subsequent biopsy all the 3 cases were consistent with testicular atrophy. There were 3 cases diagnosed as Non specific chronic epididimytis, smears of which revealed epididymal epithelial cells, scattered macrophages, lymphocytes and plasma cells. On subsequent histopathological examination all the 3 cases were consistent with Non specific chronic epididimytis.

There were 2 cases diagnosed as Granulomatous epididimytis, aspirates of which revealed epithelioid histiocytes, multinucleated histiocytic giant cells and chronic inflammatory cell infiltrates against a necrotic background with AFB (TB) negative. On subsequent histopathological examination one case showed features of pyocele and another case revealed ill defined granuloma only.

There were 2 cases diagnosed as Spermatic granuloma, smears of which revealed mixture of lymphocytes, degenerate sperm heads and debris intermingled in the epithelioid cell granuloma. On subsequent biopsy these 2 cases were consistent with Spermatic granuloma. There was 1 case diagnosed as spermatocele, aspirates of which revealed mature and degenerate spermatozoa with scattered histiocytes. Many of the histiocytes with engulfed spermatozoa were also seen. On histopathological examination this case was consistent with spermatocele. There was 1 case diagnosed as Hematoma, smear of which showed cholesterol crystals, few scattered macrophages, some were laden with hemosiderin against a hemorrhagic background. On subsequent histopathological examination it was consistent with Hematoma.

Malignant lesions

There were 3 cases diagnosed as seminoma, smears of which were cellular. Cells were seen in small clusters and scattered singly, having large, vesicular nuclei, prominent nucleoli and abundant amount of pale, vacuolated cytoplasm against a 'tigroid' background. Scattered lymphocytes were seen in the background (Figure 4).

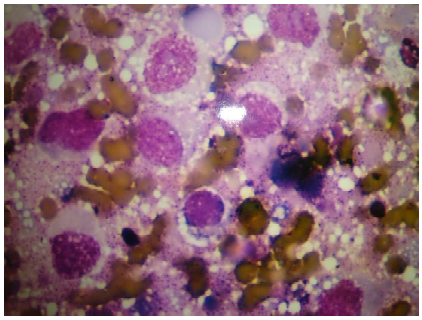

Figure 4: Seminoma, testis. Dispersed cells with large pale nuclei and poorly defined cytoplasm: note 'tigroid' background and lymphocytes (MGG x 40)

All the 3 cases were subjected for histopathological examination which confirmed the diagnosis of seminoma (Figure 5).

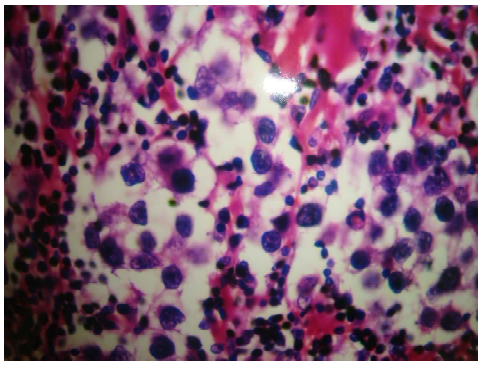

Figure 5: Seminoma, testis. Note the large nuclei, prominent nucleoli, abundant clear cytoplasm, sharply outlined cell membranes and inflammatory infiltrate in the stroma (H & E x 40)

There were 3 cases diagnosed as Germ cell tumor. On subsequent histological examination first case was diagnosed as Germ cell tumor with teratomatous and Yolk sac component. Second case was diagnosed as mixed germ cell tumor – predominance of Yolk sac component with minor seminomatous component and third case was diagnosed as Yolk sac tumor. There was 1 case diagnosed as squamous cell carcinoma, penis, smears of which revealed atypical squamous cells having bizarre shaped cells, large irregular hyperchromatic nuclei and prominent nucleoli with abundant amount of dense cytoplasm against a hemorrhagic and necrotic background (Figure 6). This case was subjected for histopathological examination and confirmed the diagnosis of squamous cell carcinoma.

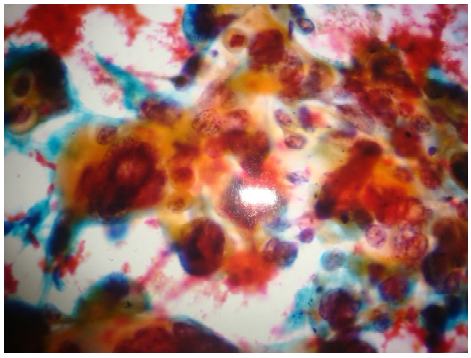

Figure 6: Squamous cell carcinoma, penis. Atypical squamous cells having large, irregular, hyperchomatic nuclei and prominent nucleoli with abundant dense cytoplasm (PAP x 40)

Nonconclusive cases

There were 8 nonconclusive cases, out of which 2 cases revealed blood and its elements only and rest of the 6 cases were inadequate for definite diagnosis. On subsequent biopsy, out of 2 former cases one was histologically unremarkable and another revealed fibro vascular and fibro adipose tissue only.

All the 6 nonconclusive cases were subjected for histopathological examination. Out of 6 cases 4 were diagnosed as granulomatous epididimytis, atrophic testis, chronic nonspecific epididymoorchitis and spermatic granuloma respectively. Rest of the 2 cases remained unconclusive even after subsequent biopsy.

Table 2: Comparison of cytological and histological diagnosis

CD	Histological Diagnosis														
	CL	AD T	AT	TB O	NSCE	SG	GE	S	H	SEM	GCT	SCC	NC	P	UR
CL	2			1									1		
ADT		3													
AT			3												
TBL				3											
NSCE					2								1		
SG						2									
GLE													1	1	
S								1							
H									1						
SEM										3					
GCT											3				
SCC												1			
NC			1		1	1	1						3		1
Total	2	3	4	4	3	3	1	1	1	3	3	1	6	1	1

CL - Cystic lesion SCC- Squamous cell carcinoma
ADT- Adenomatoid Tumor P- Pyocele
AT- Atrophic testis TBL- Tuberculous lesion
GCT- Germ cell tumor SG- Spermatic granuloma
SEM- Seminoma GE- Granulomatous epididimytis
S- Spermatocele H- Hematoma UR- Unremarkable
NSCE- Non specific chronic epididimytis T B O - Tuberculous orchitis

In this study it was found that FNAC was observed to be capable of providing correct diagnosis In 78.4%. The histopathology is highly significant to diagnose male genital system lesions ($p < 0.001$). Histopathology is 2.33 (Odds ratio with 0.99-5.49 confidence interval) times better than cytopathology to diagnose male genital system lesions.

Taking histologic diagnosis as gold standard, FNAC was found to have a sensitivity and specificity of 78.37 % and 42.85 % respectively.

The positive predictive value and negative predictive value were 84.6 % and 37.5 % respectively.

Discussion

FNAC has a well defined role in the diagnosis of various neoplastic and non-neoplastic lesions. As an initial step, FNA can yield information which assists greatly in planning subsequent steps in management and treatment. FNAC may also be used as a very useful alternative to excision biopsy in the diagnostic work up of male genital tract lesions. [4, 5, 6, 7]

In view of sparse research in this and the related field of male genital system lesions, it is pertinent here to discuss findings of this study and the findings obtained from various other studies.

Age

In the present study the age range was between 2-80 years. Similarly, in the retrospective study conducted by Fukatsu et al the patients ranged in age from 1 to 76 years old (average: 27.8 year old).[8] In our study mean age was 39.73 years. This is closer to the study done by Vishwaroop et al in which the median age was 32 years where as the median age of patients was 28 year in the study conducted by Spiess et al. [9, 10] In our study the highest number of cases is in the age group between 15-40 years which includes 20 (54%) cases. Similarly, in the study conducted by Fukatsu et al, maximum number of cases of genital tract lesions were diagnosed in 19-32 years and in the study done by Shafiq et al most of the tumors were diagnosed in the third and fourth decade of life. [8, 11] It is proven by several authors that, adenomatoid tumor is the most common epididymal tumor and typically occur in the third and fourth decade of life, which is consistent with our study. [12, 13]

In this study among malignant conditions the age group was between 2 - 60 years.

When age was taken into account considering the malignant lesions, seminoma (4.5%) was the predominant tumor among 25-45 years of patient in this study. Fukatsu et al [8] described seminoma in the age between 25-44 years and Damjanov[14] described it in the age group between 30-50 years.

Site

The commonest site of lesion in all age groups was in the right testis (27.0 percent) followed by left epididymis (21.7 percent), right epididymis (18.9 percent) and left testis (13.5 percent).

This finding is consistent with the study done by Shafiq et al [11] and Talerman et al.[15]

Encountered lesions

The commonest lesion encountered in our study was benign lesion which is similar to the study conducted by Verma et al.[16]

Irrespective of age and site the most common benign lesion encountered was epididymal cyst (10.8%) in this study. Similarly, in the study done by Perez-Guillermo et al where he studied 89 palpable lesions of the scrotum, testicle and epididymis using fine needle aspiration, cystic lesions and inflammatory pathology were the most frequent findings. [17]

Adenomatoid tumor, tuberculous orchitis, non specific chronic epididimytis and atrophic testis (8.1% each) were the second most common lesions encountered in our study.

In the study, where Viswaroop et al compared the efficacy of FNAC with that of open biopsy in the evaluation of chronic epididymal lesions, tuberculous epididimytis was found to be the commonest cause of chronic epididymal lesions, followed by non-specific epididimytis, sperm granuloma, epididymal cyst and normal epididymis. [9]

Similarly, in the study conducted by Gupta et al [12] where he retrieved and studied a total of 228 cases, tuberculous

epididimytis was the predominant lesion.

In the study done by Handa et al, the predominant lesions among inflammatory conditions were non-specific inflammation and granulomatous epididymoorchitis. [18]

When age and site was not taken into account the most common malignant lesion encountered in this study was seminoma and germ cell tumor (8.1% each).

Assi et al performed FNAC on 17 patients with testicular lesions where the predominant cytological diagnosis was seminoma in 7 cases. [19] Similarly, in the study done by Shafiq Germ cell tumors constituted higher percentage of all malignant testicular neoplasms. Amongst this seminoma was the most common tumor followed by mixed germ cell tumors. [11]

In a series of 834 germ cell tumors by Mastofi et al (1973) also classified predominant tumor as seminoma and the second most common tumor as germ cell tumors which were with combinations. [20]

In the study conducted by Fukatsu et al germinal tumors accounted the predominant lesion. [8] Similarly, in the study done by Mukada et al the highest percentage of tumors were germ cell tumors including seminoma and also Weinstein et al noted the commonest malignant tumors as germ cell tumors. [20, 21] The commonest swellings encountered in our study were painless swelling which is similar to the study done by Talerman et al where the commonest presenting symptom was painless testicular enlargement.[13] Similarly, Paula et al described the manifestation of testicular neoplasia, the most common manifestation being a painless scrotal mass. [22]

Other lesions in this study that did not contribute to a significant proportion of cases were spermatocele, hematoma and squamous cell carcinoma of penis.

Squamous cell carcinoma constituted 2.7 percent in our study and was seen in 60 year of age group. Similarly several authors described that this tumor constituted less than 0.5 percent of all cancers in male and age group was sixth decade of life. [22, 23, 24]

FNAC has an overall sensitivity and specificity of 90%, respectively, for diagnosing chronic epididymal lesions, with a positive predictive value of 87.5%.[16] Similarly, high accuracy was observed in our study.

Non-conclusive smears were observed in eight (21.6%) cases in our study, similarly in the study done by Verma et al where he performed FNAC in 380 patients, there were 109 (28.68%) unsatisfactory aspirates. [6] In a retrospective study done by Handa et al over a 5-year period, 164 cases of FNAC of testicular and scrotal nonneoplastic lesions were retrieved. Of 164 cases, 27 (16%) remained inconclusive.[17]

FNAC has become an important diagnostic procedure in the evaluation of male genital tract lesions. However, it has not widely been used because of concern about its diagnostic accuracy.

The difficulties arise in exact typing and diagnosis of germ cell tumors, but it gives fairly accurate results regarding the nature of lesion, especially when supported by appropriate clinical findings and other diagnostic data.[11]

However reporting high rates of diagnostic accuracy and minimal risk of complications, these limited numbers of studies have served FNAC to gain more interest and to encourage its use for diagnosing male genital system lesions.

Conclusion

This is a small study conducted on a hospital-based sample at BPKIHS, Dharan, eastern part of Nepal, but it may be pertinent to summarize the important findings as follows.

1. FNAC is a useful first choice of investigation as it provides a successful diagnosis in the male genital tract lesions.
2. It is minimally invasive outpatient procedure, not requiring any incision or sutures, and thus is more accept-able to the patients; it provides a more repre-sentative sample of the testis as compared to biopsy.
3. The cytodiagnosis of male genital tract lesions is a reliable method in the initial management of the patients as its results show high sensitivity and specificity.
4. FNAC gives an accuracy of 78.37% in the diagnosis of male genital tract lesions.

Therefore, FNAC has an established role in the diagnosis of male genital tract lesions as it can detect malignancy and benign conditions.

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References

1. Rozanski TA, Bloom D. The undescended testis: Theory and management. Urol Clin North Am 22: 107, 1995.
2. Nistal M, Paniagua R: Testicular biopsy: contemporary interpretation. Urol clin N am 26:255, 1999.
3. Koss LG, Zajicek J. Aspiration biopsy. In: Koss LG. Diagnostic cytology and its histopathologic bases. 4th ed. Philadelphia; Pennsylvania; 1992:1234-1324.
4. Smith R, Melcher D, Ashton-key M. Cytology of testis and scrotum in: Gray W, Mckee G, editors. Diagnostic cytopathology. 2nd ed. Elsevier; London; 2003:629-639.
5. Orell SR, Sterrett GF, Whitaker D. Atlas of fine needle aspiration cytology. 4th edition. Churchill Livingstone, 2005; 2-5.
6. Verma K, Ram TR, Kapila K. Value of fine needle aspiration in the diagnosis of testicular neoplasms. Acta cytol 1989; 33: 631-634.
7. Garcia-Solano J, sanchez-sanchez C, Montalban-Romero S. Fine needle aspiration of testicular germ cell tumors; a 10 year experience in a community hospital. Cytopathol 1998; 9: 248-262.
8. Fukatsu H, Waki M, Hatano Y, Hirajwa S, Kikuchi T, Muramatsu T et al. A clinical study on testicular tumor. 1985 Apr; 31(4):633-8.
9. Shafiq GM, Shah SH, Soomro IN, Kayani N, Hasan SH. Morphological pattern of testicular tumors: Journal of Pakistan medical association. 2000, vol. 50, pp. 110-113.
10. Gupta N, Rajwanshi A, Srinivasan R, Nijhawan R. Fine needle aspiration of epididymal nodules in Chandigarh, north India: an audit of 228 cases. Cytopathology. 2006 Aug; 17(4):195-8
11. Manjunath GV, Nandini NM, Sunila. Fine needle aspiration cytology of adenomatoid tumour-a case report with review of literature. Indian J Pathol Microbiol. 2005 Oct; 48(4):503-4.
12. Damjanov I, SM Katz, and MA Jewett. Leydig cell tumors of the testis. Annals of Clinical and Laboratory Science, Vol 9, Issue 2, 157-163
13. Talerman A. Spermatocytic seminoma: clinicopathological study of 22 cases. Cancer. 1980 ; 45(8):2169-76.
14. Shah VB, Shet TM, Lad SK. Fine needle aspiration cytology of epididymal nodules. J Cytol. 2012; 28:103-7.
15. Perez-Guillermo M, Thora A, Lowhagen T. Paratesticular adenomatoid tumors. The cytologic presentations in fine needle aspiration biopsies. Acta Cytol. 1989; 33: 6-10.
16. Vishwaroop BS, Kehre N, Gopalakrishnan G. Isolated tuberculous epididymitis: a review of forty cases. J Postgrad Med. 2005; 51:109-11.
17. Handa U, Bhutani A, Mohan H, Bawa AS. Role of fine needle aspiration cytology in nonneoplastic testicular and scrotal lesions and male infertility. Acta Cytol. 2006 Sep-Oct; 50(5): 513-7.
18. Assi A, Patetta R, Fava C, Berti GL, Bacchioni AM, Cozzi L. Fine-needle aspiration of testicular lesions: report of 17 cases. Diagn Cytopathol. 2000 Dec; 23(6):388-92.
19. Mastofi, F.K. (1973) testicular tumors. Epidemiologic, etiologic and pathologic features. Cancer, 32, 1186.
20. Mukada T, Andoh N, Sasano N. Tumor of the testis: An attempt of Histological classification according to WHO guide line. The Tohoku journal of experimental medicine. Vol 134;4:367-373.
21. Weinstein MH, Hirsch MS, Kantoff PW, Oh WK. Anatomy and pathology of testicular tumors. 2008; 1-5.
22. Paula J. Woodward, Sohaey R, Michael J. O'Donoghue, Douglas E. Green. Tumors and Tumorlike lesions of the testis. Radiologic Pathologic Correlation. January 2002; 22(1): 189-216. 23. Lucia MS, Miller GJ. Histopathlogy of malignant lesions of the penis. Urol Clin North Am 1992, 19: 227-246.
24. Harish K, Alka NK, Arun Kumar SP, Manga Gouri SR. Cytological diagnosis of nonulcerative penile neoplasms: report of two cases: Diagn Cytopathol. 2003 Dec; 29(6): 358-9.