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Diagnostic utility of fine needle aspiration cytology in tumors of paediatric age group-a single institutional study

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Abstract

Introduction: Paediatric tumors differ markedly from adult tumors in their nature distribution and prognosis. Cancer in children is an emerging major childhood killer. FNA is increasingly being employed in diagnosis of paediatric tumors because of its high diagnostic yield, rapidity and safety**. Materials and methods:** The observational study conducted in tertiary care hospital in Kashmir in 5 years conducted from July 2012 to July 2017.This study was carried out in patients of paediatric age group (0-14years), presenting clinically and radiologically with any accessible swelling in body, attending outdoor and indoor facility of SKIMS and referred to the department of pathology for FNAC. **Results:** Our study included 126 cases, 70 (55.6%) were females and 56 (44.4%) were males. Maximum numbers of cases were seen in 10-14 years age group. Benign lesions comprised of 56 (44.4%) cases and malignant cases comprised of 70 (55.6%) cases. Most of the benign cases were from soft tissue (37) followed by breast (13) and the most common benign tumors were hemangiomas (13.5%) followed by fibroadenomas(9.5%). Most common site of malignant tumors was lymph node (34 cases) and most common malignant tumor was Hodgkins lymphoma (13.5%) followed by non-Hodgkins lymphoma (11.1%). Histopathological correlation could be done in 64 benign and 49 malignant cases. **Conclusion:** To conclude, FNAC is a safe, rapid, reliable, minimally invasive, and cost-effective procedure with no morbidity. It may not replace the biopsy but can be used as an effective initial screening tool in superficial and deep seated lesions in pediatric age group. Histopathological correlation shows high diagnostic accuracy establishing the role of FNAC as an efficient initial investigative procedure.

Keywords: Cytology, tumors, paediatric.

Introduction

The paediatric population constitutes 32.4% of the total population of India [1]. Paediatric patients represent a unique study population with regard to spectrum and frequency of disease. Paediatric tumors differ markedly from adult tumors in their nature distribution and prognosis [2]. Cancer in children is an emerging major childhood killer.

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Worldwide, approximately 215000 cancers are diagnosed per year in those younger than 15 years and about 85000 cancers in those aged 15–19 years. Childhood cancer is a public health problem in developing countries, and more resources should be provided to improve diagnosis, treatment, and infrastructure. Although childhood cancer survival rates are about 80% in high-income countries, they may be as low as 10% in some countries [3]. The proportion of childhood cancers in India relative to cancer in all age groups varied from 0.7% to 4.4% across the 29 reporting population based cancer registries (PBCRs). However, among boys, it varied from 0.7% to 5.4% whereas among girls, it was

somewhat lower at 0.5%–3.5% implying gender difference in childhood cancers [4]. Malignant neoplasms are the third commonest causes of death in the 1 to 4years age group and the second commonest causes of death in the 5 to 14 years age group[5].Fine needle aspiration (FNA) refers to a procedure that procures cellular material for diagnosis using suction or non-suction techniques. It is a minimally invasive, cost-effective technique with high diagnostic accuracy [6].FNA is increasingly being employed in diagnosis of paediatric tumors because of its high diagnostic yield, rapidity and safety. FNAC is an important and a non-invasive, investigational tool in children for identifying and planning the medical management of inflammatory and infectious conditions [7].

Material and Methods

The observational study conducted in tertiary care hospital in Kashmir in 5 years conducted from July 2012 to July 2017.This study was carried out in patients of paediatric age group (0-14years), presenting clinically and radiologically with any accessible swelling in body, attending outdoor and indoor facility of SKIMS and referred to the department of pathology for FNAC. All the relevant data regarding clinicopathological parameters including age, sex, site, size, histological type, recurrence was collected. FNA was done and slides were prepared in the cytology section. Material was obtained with a fine 25- 27guage needle fitted to a 10-20ml disposable syringe with Cameco syringe pistol. The wet fixed smears in 95% alcohol were stained with Papanicolaou (PAP) stain, Hematoxylin and Eosin (H & E) and the air dried smears were stained with May Grunwald Giemsa (MGG) stain. Histopathology study was done wherever samples were available. These samples were processed routinely. 3 to 5 micron thick sections were made from paraffin embedded blocks and stained with H & E.
Immunohistochemistry was done where ever needed. Final correlation was done between cytological and histopathological diagnosis.Statistical analysis of the recorded data was done by using Statistical Package for Social Sciences (SPSS Ver. 23.0) software.

Results

Our study included 126 cases, 70 (55.6%) were females and 56 (44.4%) were males. Maximum number of cases was seen in 10-14 years age group comprising of 67 (53.2%) cases followed by 0-5 years age group comprising of 31 (24.6%) cases in both genders. Both benign and malignant tumors were most common in 10-14 years age group followed by 5-10 years age group. Benign lesions comprised of 56 (44.4%) cases and malignant cases comprised of 70 (55.6%) cases. Out of 126 cases maximum number of cases i.e 49(38.9%) were from soft tissue followed by lymph node-34(27%) cases and from pancreas and bone-1(0.8%) each. Most of the benign cases were from soft tissue (37) followed by breast (13), skin (5) and bone (1). Among benign category maximum number of cases were hemangiomas (13.5%) followed by fibroadenomas (9.5%), lipomas (7.1%), benign spindle cell lesion and lymphangiomas (4.8% each), benign adnexal lesion (5%), gaint cell lesion (0.8%). Histopathological examination was available in only in 64 cases. In case of benign tumors HPE was done in 15 cases out of 56 cases and cytohistological correlation showed 14 (true negative) cases were benign on histopathological examination whereas 1(false negative) case was malignant. In benign cases with cytohistological correlation one case diagnosed benign spindle cell lesion turned out to be dermatofibrosarcoma protuberans (false negative) on HPE which was later confirmed by immune histochemistry (CD34+, SMA+, calponin-).It was misdiagnosed on FNAC because it showed moderate cellularity with mild anisokaryosis and scanty mitotic figures. On FNAC it is sometimes difficult to differentiate between benign and malignant lesions if cellularity is less and no mitotic figures are seen.

Table 1: Cytological spectrum of benign tumors as per age in study patients

Cytological Spectrum	Age (years)			Total
	0-5	5-10	10-14	
Benign adnexal lesion	0	1	4	5
Benign spindle cell lesion	1	1	4	6
Fibroadenoma	0	0	12	12
Gaint cell lesion	0	0	1	1
Lipoma	2	4	3	9
Lymphangioma	5	1	0	6
Total	15	9	32	56

Most common site of malignant tumors was lymph node (34 cases), followed by soft tissue (12 cases), thyroid (8 cases), parotid and kidney (5 cases each), skin (3 cases), liver (2 cases), pancreas (1 case). Among malignant tumors most common was Hodgkins lymphoma (13.5%), followed by non Hodgkins lymphoma (11.1%), small round cell tumor (7.9%), papillary carcinoma thyroid (8%).In case of malignant tumors HPE was done in 49 cases out of 70 cases Cytohistological correlation showed 48 (true positive) cases malignant on histopathological examination whereas 1(false positive) case turned out to be benign. One case diagnosed low grade mucoepidermoid carcinoma turned out to be myxoid schwannoma (false positive). It was misdiagnosed on FNAC because of site of the lesion (parotid), myxoid background and some vacuolated cells. Scanty spindle cells were also seen.

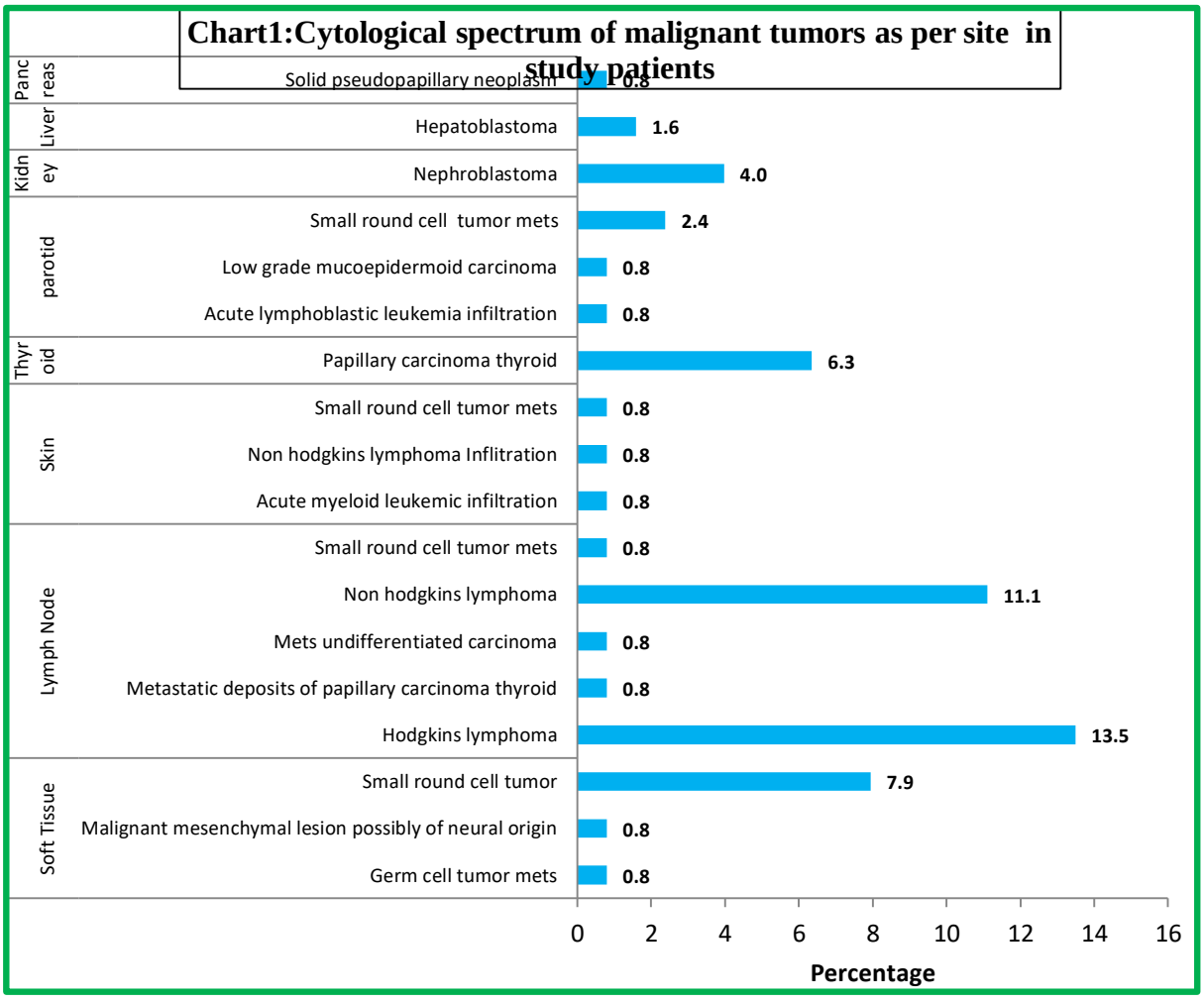
Table 2: Cytological spectrum of malignant tumors as per age in study patients

Cytological spectrum	Age(years)			Total
	0-5	5-10	10-14	
Acute lymphoblastic leukemia infiltration	0	1	0	1
Acute myeloid leukemic infiltration	0	0	1	1
Germ cell tumor	1	0	0	1
Hepatoblastoma	2	0	0	2
Hodgkins lymphoma	1	8	8	17
Malignant mesenchymal lesion possibly of neural origin	0	1	0	1
Metastatic deposits of papillary carcinoma thyroid	0	0	1	1
Mets undifferentiated carcinoma	0	0	1	1
Mucoepidermoid carcinoma	0	0	1	1
Nephroblastoma	4	1	0	5
Non hodgkins lymphoma	2	2	10	14
Non hodgkins lymphoma infiltration	0	1	0	1
Papillary carcinoma thyroid	1	1	6	8
Small round cell tumor	3	2	5	10
Small round cell tumor mets	2	2	1	5
Solid Pseudopapillary neoplasm	0	0	1	1
Total	16	19	35	70

Table 3: Cyto-histological correlation of malignant tumors

FNAC	**Histopathological Diagnosis**	**IHC**
Papillary carcinoma thyroid (8)	Papillary carcinoma thyroid(4)	
	Papillary carcinoma thyroid solid variant(2)	
	Papillary carcinoma thyroid mixed variant(1)	
	Papillary carcinoma thyroid oxyphill variant(1)	
Small round cell tumor (9)	PNET/Ewings sarcoma (8)	CD99+,FLI1+,SYN+,CD56+, CD45-,Desmin-,panCK-(8)
	Embryonal Rhabdomyosarcoma (1)	Desmin+, Myogenin+(1)
Hodgkins Lymphoma (14)	Hodgkins Lymphoma mixed cellularity (11)	CD15+,CD30+(7)
	Hodgkins Lymphoma-lymphocyte predominant (2)	CD15+,CD30+(1)
	Hodgkins Lymphoma-nodular sclerosis (1)	
non Hodgkinslympoma (10)	non Hodgkins lymphoma(1)	CD45+(1)

	Burkitts lymphoma(3)	CD10+,CD20+,ki67>95% (3)
	NHL- T lymphoblastic lymphoma(2)	CD3+,tdt+, CD20-(2)
	Diffuse large cell lymphoma(2)	CD10, bcl2+(2)
	High grade B cell NHL(2)	CD10+,CD20+,bcl6+,ki67100%
Benign spindle cell lesion (1)	Dermatofibrosarcoma protuberans (1)	CD34+,SMA+, calponin –(1)
Germ cell tumormets(non Seminomatous) (1)	Germ cell tumormets (non Seminomatous) (1)	
Wilms tumor (4)	Wilms tumor (4)	
Mets undifferentiated carcinoma (1)	Mets poorly differentiated squamous cell carcinoma non- keratinizing (1)	
Hepatoblastoma (1)	Hepatoblastoma (1)	



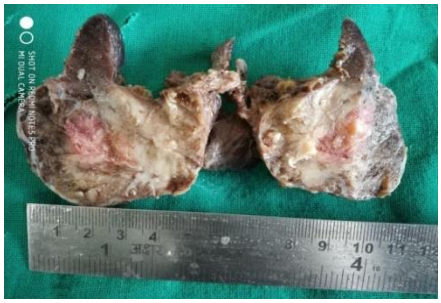


Fig 1: Gross morphology of Papillary carcinoma thyroid showing greyish white area with irregular margins.

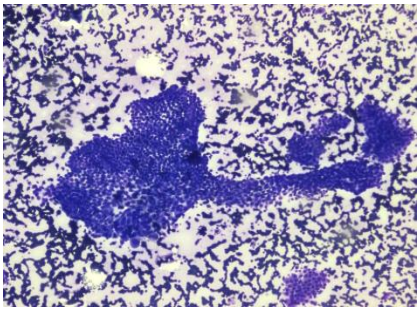


Fig 2: Photomicrograph of Papillary carcinoma thyroid on FNAC showing cells arranged in papillae and clusters with distinct anatomical border and nuclear overcrowding and overlapping

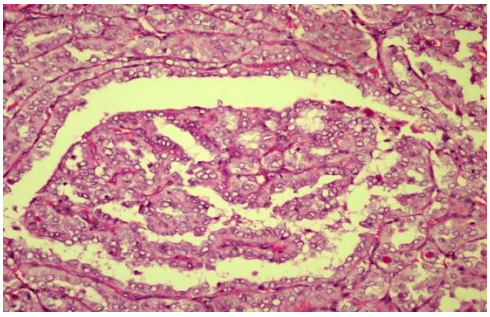


Fig 3: Photomicrograph of Papillary carcinoma thyroid on HPE showing well formed papillae with fibrovascular core lined by cells with Orphan Annie eye nuclei.

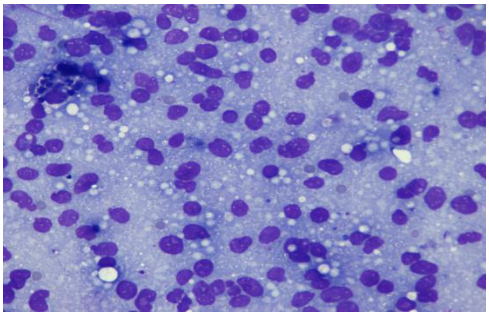


Fig 4:Photomicrograph of NHL on FNAC showing atypical lymphoid cells with round nuclei, granular chromatin and scanty cytoplasm. Tingible body macrophage is also seen.

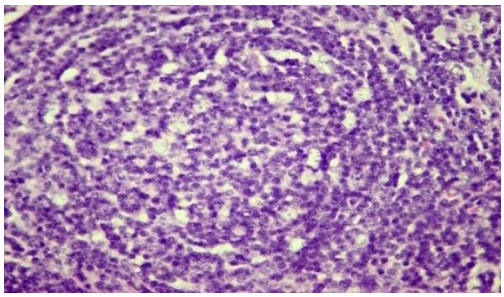


Fig 5: Photomicrograph of NHL on HPE showing monotonous population of atypical lymphoid cells with round nuclei, increased nuclear to cytoplasmic ratio and scant cytoplasm.

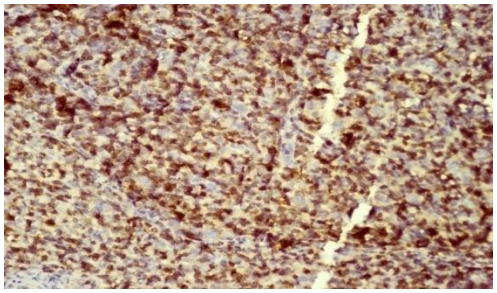


Fig 6: Photomicrograph of NHL showing CD19 positivity

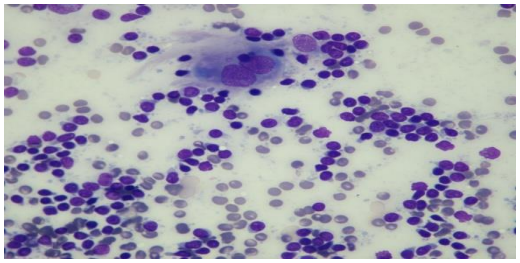


Fig 7: Photomicrograph of Hodgkins lymphoma showing characteristic Reed Sternberg (RS) cell in a background of lymphocytes

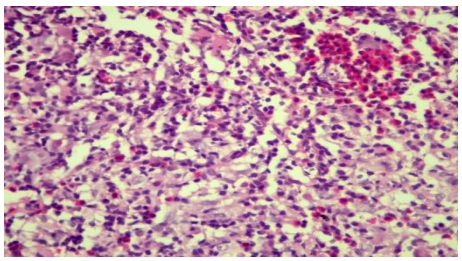


Fig 8: Photomicrograph of HL showing atypical mononuclear cells in a background of small lymphocytes, eosinophils and plasma cells

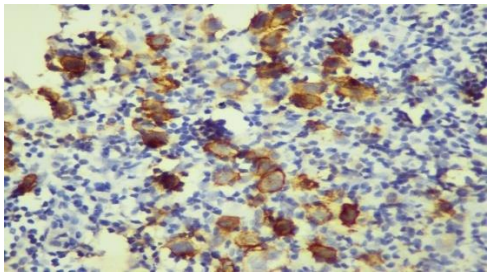


Fig 9: Photomicrograph of HL showing CD30 positivity.

Fig 10: Gross morphology of Fibroadenoma showing rubbery, white, well circumscribed mass.

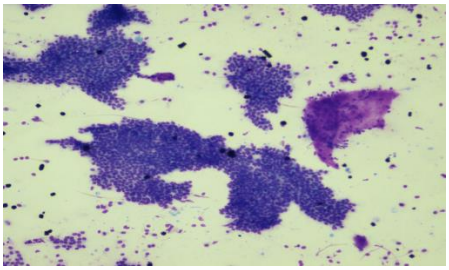


Fig 11:Photomicrograph of Fibroadenoma on FNAC showing cellular smears arranged in sheets containing bimodal cell population of epithelial and myoepithelial cells. Numerous bare bipolar nuclei and fibromyxoid stroma are also seen.

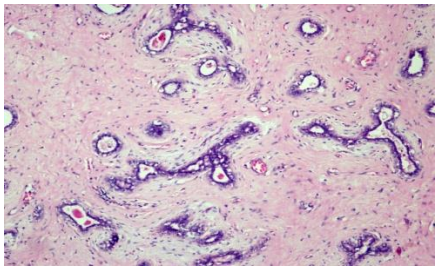


Fig 12: Photomicrograph of Fibroadenoma on HPE showing intracanalicular and pericanalicular patterns of epithelium and stromal proliferation

Discussion

Fine Needle Aspiration Cytology (FNAC) is a simple and a rapid diagnostic technique. In recent years it has attained the stature of an indispensable diagnostic tool for a pathologist because of its simplicity, economic viability and early availability of results. The procedure even though involves a needle and considered to be invasive is feasible in paediatric age group because of minimal trauma it is associated with[8].The single vital advantage of FNAC is lack of anaesthesia which is of important concern in paediatric population[9]. No complications were observed after FNAC in this study. A few complications following FNA mentioned in literature like haemorrhage, edema, needle tract tumor seeding etc are rare and do not prevent this technique from being routinely used[10]

Fine needle aspiration cytology (FNAC) has become an important modality of diagnosis of malignant small round cell tumors. The technique yields adequate numbers of dissociated, viable cells and making it ideally suitable for ancillary techniques. Malignant small round cell tumors are characterised by small, round, relatively undifferentiated cells. They generally include Ewing's sarcoma, peripheral neuroectodermal tumor, rhabdomyosarcoma, synovial sarcoma, non-Hodgkin's lymphoma, retinoblastoma, neuroblastoma, hepatoblastoma, and nephroblastoma or Wilms' tumor. Other differential diagnoses of small round cell tumors include small cell osteogenic sarcoma, undifferentiated hepatoblastoma, granulocytic sarcoma, and intraabdominal desmoplastic small round cell tumor. Differential diagnosis of small round cell tumors is particularly difficult due to their undifferentiated or primitive character. Tumors that show good differentiation are generally easy to diagnose, but when a tumor is poorly differentiated, identification of the diagnostic, morphological features is difficult and therefore, no definitive diagnosis may be possible[11]. In our study small round cell tumors constitute a good proportion of malignancies, accounting for 7.9% of cases and were most common in the age group of 0-5 years.

In our study out of 126 cases cytological diagnosis of benign tumor was given in 56(44.4%) cases and malignant tumor diagnosis was given in 70(55.6%) cases. Our findings were comparable with the study conducted by Shakoor KA (1989) in which they found 47/81(58.02%) cases were malignant and 34/81 (41.98%) were benign.

In our study male to female ratio was 1:1.25 [12]. Our study results were comparable with the study done by Sanjay M, Sarvesh B M (2015)[13], Sadegh S et al (2016)[14], Paul E W, Thomas F et al (1988)[15], Shakoor K A (1989)[12]

In our study maximum number of cases i.e 49 (38.9%) were seen in soft tissue. Our study results were

comparable with the study done by Veena M et al (2008) in which soft tissue tumors were the most common category consisting of 259 (44.1%) cases out of 588 (100%) cases[16]

Malignant tumors were mostly seen in lymph node (34/70) and our results were comparable with studies conducted by Paul EW, Thomas F et al (1988)[15], Savita M. Sonawane et al (2017)[17], Syed FH et al (2013)[18], Cole CD, Howard HW (2014)[19], Shakoor KA (19890[12], Sanjay M, Sarvesh BM (2015)[13] and Suzanne R Taylor et al (1984)[20]

In our study most common benign tumor was hemangioma consisting of 17/56 (13.5%) cases followed by fibroadenoma 12/56 (9.5%) cases, lipoma 9/56 (7.1%) cases and benign spindle cell lesion 6/56 (48%). Our study results were comparable with studies conducted by Paul E W, Thomas F et al (1988)15 and Veena M et al (2008) [16]

We found in our results Hodgkins lymphoma17/70 (13.5%) and non Hodgkins lymphomas 14/70 (11.1%) were the most common malignant lesion followed by small round cell tumor 10/70 (7.9%) and papillary carcinoma thyroid 8/70 (6.3%). Our results were comparable with studies conducted by Neha S, Abhishek S et al (2016) and Purnima M, Rajni B et al (2013)[21,22]

14 cases of Hodgkins lymphoma on FNAC were in concordance with histopathology and were further classified as Hodgkins lymphoma mixed cellularity(11 cases), Hodgkins lymphoma lymphocyte predominant(2 cases), hodgkins lymphoma nodular sclerosis type(1 case). In 8 cases diagnosis was further confirmed by immunohistochemistry and all of these 8 cases were positive for CD15 and CD30.

Non-Hodgkins lymphoma (10 cases) diagnosed on FNAC were in concordance with histopathology and which was further confirmed by immune histochemistry.

3 cases were found to be burkitts lymphoma (CD10+,CD20+,ki67>95%), 2 were NHL- T cell lymphoblastic lymphoma (CD3+,tdt+, CD20-),2 were Diffuse large cell lymphoma(CD10, bcl2+), 2 were high grade B cell NHL(CD10+,CD20+,bcl6+, ki67100%) , and 1 was simply given the diagnosis of NHL(CD 45+).Small round cell tumors (9 cases) diagnosed on FNAC were in concordance with histopathology which was further confirmed by immunohistochemistry. 8 cases were found out to be PNET/ Ewings sarcoma (CD99+, FLI1+, SYN+, CD56+ , CD45-,Desmin-, panCK-), 1 case was Embryonal Rhabdomyosarcoma (Desmin+, Myogenin+). 8 cases of Papillary carcinoma thyroid, diagnosed on FNAC were confirmed by histopathology and included Papillary carcinoma thyroid (4cases), Papillary carcinoma thyroid solid variant (2 cases), Papillary carcinoma thyroid mixed variant (1 case), Papillary carcinoma thyroid oxyphill variant (1 case). Rest of the malignant tumors that were confirmed by histopathology included Wilms tumor (4 cases), Metastatic poorly differentiated squamous cell carcinoma non keratinizing (1case), Hepatoblastoma (1 case), Germ cell tumor mets (non Seminomatous) (1 case)In our study we found that FNAC can be useful in diagnosing suspected malignant tumors with sensitivity and specificity rates being 97.9% and 93.3% respectively and our results were in correlation with the studies conducted by Paul E W, Thomas F et al (1988),Cohen MB, Bottles K, et al (1989) and Cole C D, Howard H W (2014).

Conclusion

To conclude, FNAC is a safe, rapid, reliable, minimally invasive, and cost-effective procedure with no morbidity. It may not replace the biopsy but can be used as an effective initial screening tool in superficial and deep seated lesions in pediatric age group. Histopathological correlation shows high diagnostic accuracy establishing the role of FNAC as an efficient initial investigative procedure.

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