Fine needle aspiration cytology of non-hematological neoplasms in pediatric age group: Our experience

ABSTRACT

Background: The role of aspiration cytology has largely been ignored in pediatric population. The present study was undertaken to evaluate the role of fine needle aspiration cytology (FNAC) in non-hematological neoplasms in children in our institution, which is a rural tertiary care center.

Materials and Methods: A total of 88 cases of non-hematological pediatric mass lesions were studied in which cytopathological diagnosis could be corroborated with histopathology.

Results: Out of all the cases, 70 (80%) cases were benign tumors and 18 (20%) were malignant tumors. Fibroadenoma (37.9%) comprised the majority of cases in the benign category while small round cell tumors (SRCTs) (44.4%) comprised the majority of cases in the malignant category. Definite diagnosis could be offered based on the cytomorphology in 79.5% cases, while in 20.5% of cases only a broad cytological classification could be offered. Among the malignant lesions, FNAC showed 100% sensitivity while a specific diagnosis was made in 90% of cases.

Conclusion: FNAC proved to be a rapid and fairly accurate tool in diagnosing non-hematological tumors in the pediatric age group.

Key words: Fine needle aspiration cytology (FNAC), non-hematological neoplasms, pediatric

Introduction

Until recently, the application of fine needle aspiration cytology (FNAC) to the pediatric population was largely ignored in the world pediatric literature. Previous reports have studied its utility only among a small series of pediatric patients.[1-3] The cytopathologist forms a very important part of the clinical team in the management of pediatric neoplasms in giving a rapid and accurate diagnosis for these tumors thus eliminating the need for anesthesia and hospitalization.[4] Centers experienced in performing pediatric FNAC have shown excellent results with sensitivity and specificity rates approaching 93% and 100%, respectively, with outcomes comparable to those in the adult population.[5-7] Thus, FNAC is an invaluable tool in this regard when interpreted with clinicoradiological parameters. With this in mind, we decided to evaluate the role of FNAC in non-hematological neoplasms in children in our institution, which is a rural tertiary care center.

Materials and Methods

The study was undertaken after obtaining the requisite permission from the institutional review board. In our institution, a total of 137 FNACs were performed for non-hematological mass lesions in the pediatric age group.
(0-14 years) over a time period from January 2011 to July 2012. Out of these, in 88 cases the cytological diagnosis could be confirmed by subsequent histopathology. Cases in which histopathology was not done and those of hematological malignancies were excluded from this study.

Detailed clinicoradiological information was obtained for all these cases. A written informed consent was obtained from each patient. Ultrasound guidance was taken for deep-seated lesions. FNAC was performed using a 21-24 G needle fitted to a 10 mL syringe. Smears were fixed in 95% alcohol and were air-dried and stained with hematoxylin and eosin (H and E), Papanicolaou, and May–Grünwald–Giemsa (MGG) stains. Special stains, such as periodic acid-Schiff (PAS), were used when required. The histopathological specimens were processed routinely and were stained with H and E stain.

Results

The study included 88 cases of non-hematological pediatric mass lesions in which the cytological diagnoses were confirmed by subsequent histology. The age of the patients ranged 1 month-14 years. The majority of cases (68.18%) were seen in the 8-14 years age group. Females were predominant in the study population, accounting for 50 cases (56.8%). Out of a total of 88 cases, 70 (80%) of the tumors were benign and 18 (20%) were malignant. The majority of cases were of fibroadenoma (37.9%) [Figure 1C] in the benign category while small round cell tumors (SRCT) (44.4%) comprised the majority of the cases in the malignant category [Figure 2A].

Definite diagnosis could be offered on cytomorphology in 70 (79.5%) cases while in 18 (20.5%) cases only a broad cytological classification could be offered. The latter category included 14 cases of hemangioma diagnosed as benign vascular lesion, two cases of dermatofibroma and schwannoma each categorized as spindle cell tumors, and two cases of SRCT diagnosed as alveolar rhabdomyosarcoma and hepatoblastoma. Overall, soft tissue tumors were the most common category of tumors that occurred in 47 (53.0%) participants out of all the subjects, and benign tumors of vascular origin were the most common (15.9%), followed by lipoma (14.7%). All the benign vascular tumors were diagnosed as hemangioma on histopathology. Hemangiomas on aspiration mainly showed blood and few spindle cells without atypia. All cases of lipoma revealed mature adipocytes with clear cytoplasm and eccentric flattened nuclei. Smears from neurofibroma showed spindle-shaped cells with bland chromatin in a fibrillary background [Figure 1D]. A single case of giant cell tumor (GCT) of tendon sheath of left index finger yielded dispersed plump fibrohistiocytic cells with oval pale nuclei and a bland chromatin along with scattered osteoclast-like multinucleated giant cells. Smears from the single case of eosinophilic granuloma showed clusters of large histiocytes with pale nuclei having folded outline along with eosinophils and multinucleated giant cells [Figure 2B]. Two cases each of dermatofibroma and schwannoma were moderately cellular and showed cohesive fragments of monomorphic spindle cells with bland nuclear chromatin. These two cases were categorized as benign spindle cell tumor.

![Figure 1A](image1a.png)  
Figure 1A: Microphotographs showing benign pediatric tumors. (a) Pleomorphic salivary adenoma [MGG, x100] with the inset showing chondromyxoid material admixed with myoepithelial cells (MGG, x400). (b) Aspirate from benign cystic teratoma of ovary showing mature squamous cells (MGG, x400). (c) Epitheliosis in juvenile fibroadenoma with the inset showing stromal fragments [H and E, x100]. (d) Cytological features of neurofibroma (MGG, x100)

![Figure 1B](image1b.png)  
![Figure 1C](image1c.png)  
![Figure 1D](image1d.png)  

![Figure 2A](image2a.png)  
![Figure 2B](image2b.png)  
![Figure 2C](image2c.png)  
![Figure 2D](image2d.png)  

Figure 2: Microphotographs showing malignant pediatric tumors. (a) Small round cell tumor with mitotic figure (white arrow) [MGG, x400]. (b) Langerhans cells and eosinophils in eosinophilic granuloma. The inset shows multinucleated cells with eosinophils (MGG, x400). (c) Pleomorphic osteoblasts lining osteoid in osteosarcoma (MGG, x400). (d) Embryonal rhabdomyosarcoma with rhabdomyoblasts (MGG, x400)
A single case of neuroblastoma revealed scattered small cells with scanty cytoplasm and hyperchromatic nuclei along with nuclear molding in a fibrillary background. A few rosette-like structures were also noted.

Two cases of embryonal rhabdomyosarcoma revealed pleomorphic population of round-to-spindle-shaped cells, with elongated hyperchromatic nuclei having high nucleocytoplasmic ratios [Figure 2D].

Three cases of Ewing’s sarcoma/primary neuroectodermal tumors (PNETs) revealed a dual cell population, consisting of large pale cells with abundant PAS-positive cytoplasmic granules and small round cells with scanty cytoplasm and condensed nuclear chromatin [Figure 3C]. A single case of pleomorphic adenoma of salivary gland showed predominantly plasmacytoid cells against a background of fibrillary chondromyxoid ground substance [Figure 1A].

Smears from cases of Wilms’ tumor (WT) showed varying combinations of blastemal, epithelial, and stromal elements along with necrosis, inflammatory cells, and occasional rosettes [Figure 3D].

Tall columnar cells with basally placed nuclei against a background of highly viscous mucus were seen in a single case of mucinous cystadenoma of ovary while dermoid cyst showed mature squamous cells as well as anucleate squames [Figure 1B]. Granulosa cell tumor was diagnosed on the basis of monomorphic nuclei with longitudinal grooves arranged in follicular groupings. Single case of yolk sac tumor showed vaguely glandular clusters of malignant cells with vacuolated cytoplasm and intracytoplasmic hyaline globules. The only case of ovarian dysgerminoma revealed poorly cohesive malignant cells with fragile cytoplasm, vesicular nuclei, and prominent nucleoli along with lymphocytes and nuclear smudging. The papillary carcinoma of thyroid [Figure 3A] showed classical papillae with characteristic nuclear features. The medullary carcinoma of thyroid showed mostly dispersed and few clusters of plasmacytoid cells with sudden anisonucleosis and presence of amorphous amyloid-like material [Figure 3B].

In bone tumors, multinucleated giant cells, attached to the periphery of sheets of spindle-shaped stromal cells, were seen in all the cases of GCTs. Smears from cases of osteosarcoma showed pleomorphic plump spindle cells with multinucleated tumor giant cells and amorphous eosinophilic osteoid material [Figure 2C]. Clinicoradiologic correlation was of much help in the cytological diagnosis of bone tumors.

Discussion

The sites of non-hematological pediatric neoplasms were varied and encompassed a spectrum of diagnosis ranging from benign to malignant. Our study confirms the conclusion reached by previous investigators in other pediatric series on FNAC.

Overall, FNAC could specifically diagnose 79.5% of cases while the remaining cases were included under a broad cytological group. FNAC could distinguish between all cases of malignant and benign lesions. Among the malignant lesions, FNAC showed 100% sensitivity while a specific diagnosis was made in 90% of the cases.

FNAC of hemangiomas of any morphologic type yields plenty of venous blood[8] and so was in our case hence a specific diagnosis could not be made. These tumors fall into the broad category of benign vascular lesions.

FNAC is considered a productive diagnostic tool, especially when used by a skilled cytopathologist for documenting primary and recurrent SRCTs in pediatric patients.[9] During the past decade, a number of articles highlighting the role of FNAC in the diagnosis of SRCT have been published. Cytologic diagnosis is possible only in those SRCTs that show good differentiation. However, poorly differentiated tumors cannot be exactly categorized at the level of light microscopy. In fact, a definite diagnosis based on clinical and cytomorphological criteria was possible in 57% of the cases in one study[10] and
in 68% of the cases in another study,\[11\] while it was possible in 75% of the cases reported in our study.

Histopathology and other ancillary techniques, such as immunohistochemistry, were performed subsequently in all the cases to confirm the cytologic diagnosis. A clinically relevant classification is thus possible on the basis of FNAC in pediatric SRCTs when interpreted in correlation with clinicoradiological parameters. This obviates the need for a more time-consuming biopsy procedure in critical situations.

In cases of Ewing’s sarcoma, we found that a useful technique to confirm the diagnosis is a strongly positive PAS stain that is sensitive to diastase treatment. Cytological examination was diagnostic in all cases, and here the relevant clinical and radiological background also helped. Similar views have been expressed by other authors as well.\[11,12\] McGhaey\[et al\].\[11\] have emphasized that although FNAC is successful as a diagnostic tool in the pediatric population, confirmatory ancillary studies are essential for proper diagnosis of SRCTs due to the extensive cytomorphological overlap. An important precaution to be taken especially in intra-abdominal tumors is to have an ultrasonography (USG) report, or preferably to perform a USG-guided FNAC, which reveals the exact organ of origin of the tumor; since even an inadvertent FNAC from normal spleen may be interpreted as a SRCT. Abdominal masses are a common presenting complaint in pediatric surgery, and many of them are diagnosed as WT. It was the only renal tumor (three cases) observed in our study, and revealed varying combinations of blastemal, stromal, and epithelial elements. Similar findings have been observed by Beckwith.\[13\] FNAC is a relative contraindication in primary resectable WTs because of the risk of tumor seeding and rupture of the renal capsule.

However, a study by the International Society of Pediatric Oncology\[14\] found that diagnostic needle biopsy, followed by preoperative chemotherapy, resulted in a decreased rate of intraoperative tumor rupture and other complications, especially in case of massive and advanced tumors. Cytomorphology alone is enough for the diagnosis of two-thirds of aspirates while immunocytochemistry can resolve the remaining one-third as well. Therefore, FNAC is a useful and less invasive alternative to biopsy. Now, WT-1 immunocytochemistry is available, which is always positive in the blastemal cells of WT, except in rare cases where both copies of the WT-1 gene are mutated. Even poor aspires with very few tumor cells are positive for WT-1 immunocytochemical stain.\[15\] The high specificity of cytologic diagnosis of ovarian cystic masses found in our study is similar to those reported by others in adult population. Zardawi,\[15\] for example, in a study of 100 FNAC cases from multiple anatomic sites with concurrent histological evaluation of tissue obtained from surgical intervention, reported FNAC to have an accuracy of 94% and a positive predictive value for malignant disease of almost 100% when practiced in a multidisciplinary setting involving pathologists, radiologists, and clinicians. An area of concern is the potential risk of seeding an early stage ovarian cancer via the aspiration procedure. This complication is mentioned in several recent cytopathology textbooks\[16-18\] yet only one main reference is cited—a report published 17 years ago detailing two cases that had tumor spread thought to be related to FNAC.\[19\]

Breast lesions in adolescent females are a relatively common concern. Study by Neinstein\[20\] involving adolescent subjects with breast lesions diagnosed since 1960 reviewed a total of 1,797 cases retrospectively. In our study, the most common lesions found were fibroadenomas (68.3%) and fibrocystic changes (18.5%). Malignant lesions were uncommon (0.8%).\[20\]

Fibroadenomas are benign neoplasms that constitute 50-76% of breast masses in children and adolescents.\[21\] Fibroadenomas have high cellularity and a biphasic pattern consisting of epithelial and stromal components. The cause of fibroadenoma is uncertain, but hormonal influences probably play an important role because a significant proportion of fibroadenomas change in size with changes in hormonal environment.\[22,23\]

Ancillary studies including immunohistochemistry, electron microscopy, cytogenetic studies, flow cytometry, and microbiological culture can be performed on aspirated material. This would enable a more specific diagnosis and provide additional information on some difficult cases, especially PNET of the thorax; abdominal tumors; and retroperitoneal SRCTs,\[4\] lymphomas, and undifferentiated sarcomas. These were not done in our study due to the lack of proper infrastructure as ours is a rural hospital.

FNAC is thus an effective method for evaluation of masses in pediatric patients. It need not replace the open surgical biopsy, but can be a valuable tool used for screening of palpable as well as non-palpable masses and to follow up the patients with a history of malignancy. To realize the diagnostic potential of this procedure, the clinician must understand its strengths and weaknesses along with its technical limitations.

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Conflicts of interest
There are no conflicts of interest.

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