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Evaluation of Role of FNAC in Pediatric Kidney Tumors in a Tertiary Care Hospital

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ABSTRACT

Background: Fine Needle Aspiration Cytology (FNAC) is a very useful technique for morphological diagnosis of any tumors. It is useful in children as the chance of complication is very rare. Moreover, it is rapid, cost effective, and outpatient procedure. No anesthesia is required for this. Diagnosis can be available readily and suitable for giving preoperative chemotherapy. So FNAC plays important role in pediatric kidney tumor where neo adjuvant chemotherapy given before surgery. Guided FNAC is more reliable method than unguided FNAC. Core Needle Biopsy (CNB) is another investigation for preoperative diagnosis. Compared to core needle biopsy, FNAC is more easy to perform and it can be repeated in the same sitting, if necessary. Immunocytochemistry (ICC) can be done on Fine needle aspiration smear or Immunohistochemistry (IHC) can be carried out from the cell block.

Aims and Objectives: To find out the profile of kidney tumor, to help the clinicians to give neoadjuvant chemotherapy to the patients, and to evaluate the role of FNAC in pediatric kidney tumors.

Materials and Methods: The pediatric patients with clinical and radiological diagnosis of kidney tumors were advised for guided FNAC. After examining the patients CT/ USG guided FNAC was performed and Immunostains were applied on the smears and on cell block.

Result: FNAC was done in 96 cases of kidney tumors below 18 year of age over a period of 10 years. The commonest tumor was WILMS' tumor (86%) with male predominance . Majority patients were below 7 year of age. Mesoblastic Nephroma (5%), Clear Cell Sarcoma (2%), Rhabdoid tumor (1%), Ewing tumor (1%) and one case of Metanephric adenoma were identified. We had 91% accuracy rate. If we use Immunostain the accuracy becomes 96.9%.

Conclusion - Fine needle aspiration cytology is a safe and useful, rapid diagnostic tool in case of Pediatric Renal tumors.

ARTICLE DETAILS

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INTRODUCTION

Primary renal neoplasms are uncommon in children. They are the fourth most common tumor in pediatric age group. The renal tumor constitute 7-8% of all pediatric tumors [1]

Pediatric renal tumors are the second most frequent abdominal malignancy of children. The most common tumor in this group is Wilms' Tumor (WT). It is also known as Nephroblastoma It accounts for 90% of all renal tumors [1-3]. Fine Needle aspiration Cytology (FNAC) is a well - recognized method for diagnosis of tumor and tumor like conditions in patients of all age group. It is a simple , cost effective, minimally invasive technique for evaluation of any lesion.[4] By FNAC the renal tumors can be diagnosed . Immunostains can be used on the FNAC smears and also on the sections from the cell block for confirmation of the diagnosis.[5] Apart from WT several other tumors are also

seen in children. Among Non-Wilms tumors of kidney there are Mesoblastic Nephroma (MN) (5%). Clear cell sarcoma kidney (CCSK) (4%), malignant Rhabdoid Tumor Kidney (MRTK) (2%) and others (2-4%) [1, 6, 7].

The management of renal tumors includes preoperative diagnosis, preoperative chemotherapy followed by nephrectomy and postoperative therapy [6].

Several syndromes like WAGR syndrome (WT associated with aniridia and genital anomalies) and the Denys-Drash syndrome (pseudohermaphroditism, severe glomerulopathy, and WT) Beckwith–Wiedemann syndrome may be associated with Wilms Tumors [8].

Fernandez et al. showed that the specificity and sensitivity of FNAC for diagnosis of renal tumors are 95% and 83.3% respectively. The positive predictive value was 98.2% [9]. In other studies the preoperative diagnosis of renal tumors show sensitivity was 90.6%, and specificity was 100%. The chances of needle tract seedling were minimal [10]. So It is a safe procedure for early detection of tumors and to apply preoperative chemotherapy. The chances of complications are nil if the patients were tested for coagulation screening.

FNAC is more frequently used for diagnosis of renal tumors with or without core needle biopsy [11].

MATERIALS AND METHODS

The study was carried out over a period of 10 years. Approval was taken from the Institutional Ethics Committee. Informed consent was taken from the patients.

Inclusion criteria

The children below 18 years of age attending Pediatric Surgery Out Patient Department, diagnosed clinically and radiologically as renal tumor.

Exclusion criteria

Very serious patients and who did not give the consent for this study.

The radiological imaging helps to locate the tumor and guides the needle to choose the site of aspiration from the tumor (Fig.1)

CT guided or ultrasound guided Fine needle aspiration was performed by standard technique with strict aseptic technique using a 22-G spinal disposable needle attached to a 10-ml disposable syringe fitted into a Cameco syringe handle. Two to three passes were taken to obtain adequate material and 3 to 6 slides were prepared. The procedure was carried out by the Pathologist in presence of the radiologist. The smears were prepared, air dried and stained with May Grunwald Giemsa (MGG) stain. Wet smears were stained with Hematoxylin and Eosin (H&E), and Papanicolaou (PAP) stains. Extra slides were preserved for immunostains and preserved at 4 degree Celsius. Cell blocks were prepared from each case for future Immunostain.

Using light microscopy, cytopathological findings were reported.

Tru-Cut biopsy from the tumors of the clinically stable and willing patients were done using 18 gauge needle and sent for histopathological examinaton. ImmunoCytoChemistry (ICC) was done from the smears and cell blocks.

After Neoadjuvant chemotherapy surgical resection, the specimens (Fig.2) were sent to the department of Pathology for histopathological examination. WT1 IHC was done in all cases. This antibody is a monoclonal antibody. Following dewaxing and antigen retrieval, blocking it was incubated with anti WT1 antibody. Then secondary antibody, chromogen and counterstain by hematoxylin were applied. The IHC slides were checked by two independent Pathologists.

RESULTS

Among total 96 cases , 83 cases (86%) were Wilms Tumor, 5 cases (5%) were Mesoblastic Nephroma, 4 cases (4.2%) were Clear Cell Sarcoma, 2 cases (2%) were Malignant Rhabdoid Tumor Kidney, 1 case(1%) was Ewing Tumor and another one (1%) was Metanephric adenoma. All cases were undergone guided FNAC. Out of 83 cases of Wilms tumor 81 cases were diagnosed as Wilms tumor. FNAC smears as well as cell blocks were used for the diagnosis.

The FNAC of WT showed small round to oval cells in clusters, a few epithelial cells and occasional spindle shaped stromal cells (Fig.3,4,5).

We carried out WT1 IHC in all cases. WT1 shows nuclear positivity on FNAC smears and on cell blocks of WT (Fig.6 & 7). Normal fetal kidney was the positive control. In negative control the primary antibody was omitted. If the percentage of positive cells were more than 10% the specimens were taken as positive [8].

The patients of Wilms tumor were of different age group, starting from 3 Months to 8 years. There was no predilection for the side of the kidney. Both right and left kidneys were involved. Only one case there was bilateral kidney involvement.

All the WTs were diagnosed as Wilms Tumor by FNAC except 2. In one case it was diagnosed as round cell tumor where blastemal cells were predominant and the other was spindle cell tumor where stromal cells were more frequent.

All the cases of CCSK the patients were between 2 to 6 years of age We came across 4 cases. 3 were male and 1 was female. All of them had involvement of Left sided kidney. We could diagnose 2 CCSK cases by FNAC. The other 2 cases were diagnosed as spindle cell tumor and the other was round cell tumor.

The smears from CCSK showed spindle cells and round cells arranged in the myxoid background (Fig.8 & 9).

Among 5 cases of Mesoblastic Nephroma, four cases could be diagnosed as Mesoblastic Nephroma showing spindle shaped cells in FNAC. One case of MN with insufficient material could not be diagnosed. It was diagnosed as benign tumor. It also showed heterogeneous soft tissue mass in the right kidney (Fig.10). After resection of this tumor the specimen showed a well circumscribed greyish white mass (Fig.11). The histopathology showed spindle cells

arranged in sheet and presence of cartilage. It was a case of Mesoblastc nephroma.

FNAC from Ewing Tumor shows round cells arranged in clusters and also in the form of acini (Fig.14). The Ewing Tumor was diagnosed as Round cell tumor on aspiration.

In 2 cases of Rhabdoid tumor one baby aged 3 months and the other 6 months. One was male and the other was female. In both these cases right kidney was involved. By FNAC we could not diagnose both the cases. The smears show large cells having eosinophilic cytoplasm, vesicular nuclei and prominent nucleoli. The cells are poorly cohesive. (Fig.15) One was diagnosed as Round Cell Tumor and other was diagnosed as Wilms Tumor with diffuse anaplasia. After histopathology the correct diagnosis was made.

We could not diagnose one case of Metanephric Adenoma on cytology. It was diagnosed as Wilms Tumor.

FNAC was done in all 96 cases. Out of all the cases we could diagnose 89 cases by cytology. We could not diagnose 7 cases by FNAC. Those 7 cases were diagnosed by histopathology. Some cases also confirmed by FNAC and core needle biopsy. Ultimately all the cases were undergone histopathological examination after nephrectomy. One MN we diagnosed only after Histopathology. It revealed presence of spindle cells with bland nuclei (Fig.12&13). One Metanephric Adenoma was diagnosed as WT. In our series the result was as follows:

True positive – 89. False positive – 1(One case of Metanephric adenoma was diagnosed as Wilms Tumor). False negative – 8 (those could not be correctly diagnosed). True Negative – 6 (5 Mesoblastic Nephroma and 1 Metanephric adenoma).

Sensitivity -91.75%, specificity – 85.71%, accuracy – 91.35%

All cell blocks of 96 tumors were stained for WT1 immunostain. 81 cases of Wilms Tumor show WT1 positivity. 2 cases of WT did not show WT1 positivity. Mesoblastic nephroma, CCSK , one Rhabdoid Tumor ,Ewing sarcoma did not show WT1 positivity. The Metanephric adenoma showed WT1 positivity. So True positive was 84, False positive 1. False negative was 2 and 12 cases were True negative

A case of Rhabdoid tumor showed WT1 positivity. WT1 sensitivity was 97.67%, specificity 92.3% and accuracy 96.97%.

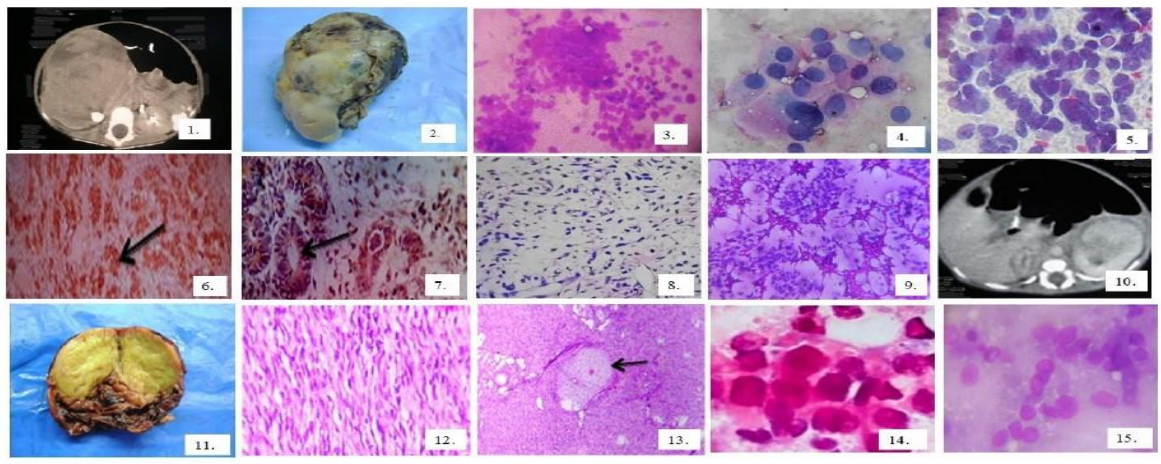

Figure 1. CT abdomen shows heterogenous soft tissue mass on right sided kidney (Wilms tumor).
Figure 2. Gross specimen of Wilms tumor measuring (7x5x3) cm.
Figure 3. LG (100X) Wilms tumor demonstrating epithelial component with cells arranged in complex patterns.
Figure 4. LG (400X) Round cells arranged in the form of acini.
Figure 5. LG (400X) Small round cells with scant cytoplasm.
Figure 6. IHC (100X) Wilms tumor with WT1 positive blastemal cells.
Figure 7. IHC (400X) Wilms tumor with WT1 positive epithelial component.
Figure 8. LG (40X) Clear cell sarcoma with loosely cohesive spindle shaped cells.
Figure 9. LG (100X) Clear cell sarcoma with loosely cohesive large oval and spindle shaped cells with prominent nucleoli and abundant cytoplasm.
Figure 10. CT abdomen shows heterogenous soft tissue mass on right sided kidney (Mesoblastic nephroma).
Figure 11. Mesoblastic nephroma. Gross appearance demonstrates a well circumscribed tumor with greyish white cut surface.
Figure 12. H&E (400X) Mesoblastic nephroma with monomorphic spindle cells having bland nuclei.
Figure 13. H&E (40X) Mesoblastic nephroma demonstrating highly cellular smear.
Figure 14. LG (400X) Ewing's sarcoma with a mixture of small cells with dark nuclei and large cells with pale nuclei and cytoplasmic vacuoles.
Figure 15. LG (400X) Rhabdoid tumor demonstrating cells with perinuclear cytoplasmic inclusions.

DISCUSSION

FNAC is a simple method which can be applied in any set up. If core needle biopsy is applied along with FNAC the accuracy rate is increased. Chi Shun Yang et al. demonstrated that the chance of risk is very little during guided FNAC or core biopsy. Moreover, the DNA and RNA that can be obtained from the aspirates for the application of molecular technique. Subsequently targeted therapy can be planned [11]. Use of IHC WT1 is helpful in many cases. It can be done directly on the smears and on the sections from the cell block. This was also supported by V. Iyer, who also discussed about usefulness of WT1 in his paper [12]. We also used WT1 IHC in all cases. Still we could not diagnose 2 cases (2%) of Wilms tumor.

Percutaneous Needle biopsy in pediatric kidney tumors before administering preoperative chemotherapy sometimes associated with morbidity of the patients [13]. With the help of FNAC such complications can be avoided. The Fine needle aspiration has been used for renal tumors in childhood population with high diagnostic accuracy . The diagnostic sensitivity of 76-95% and a specificity of 80-100% [14]. Sometimes problem with diagnosis occurs in case of cystic lesions such as Cystic Nephroma and Cystic Partially Differentiated Nephroblastoma, where the aspirate material is fluid [14]. In these cases aspiration from different sites and correlation with clinical and radiological findings may be helpful. We also missed the diagnosis of MN where the material was insufficient.

The advantage of FNAC is that aspiration can be can be done in different areas of the tumor and a diagnosis can be made. In a series of renal tumors they showed that malignancy could be diagnosed in 72% of cases. FNAC can be used as a primary diagnostic technique in the pediatric tumors. It can be used for both superficial and deep tumors [15] Jain et al. showed that only 6% cases had unsatisfactory in FNAC in a series of 748 children [16]. According to Prathima S. et al ,FNAC is a good, safe, simple, inexpensive procedure for the children . It can be repeated and chance of complication is also rare [17]. In developing countries like India this FNAC is suitable for diagnosis of pediatric tumor because it is simple and economic and can be used in remote areas where other facilities are not available [18, 19]. According to Chi shun Yang et al. the diagnostic accuracy of FNAC is 94% and in case of core needle biopsy it is 92% [11].

In our cases also no complications were noted. The accuracy rate of our series was 91%. This technique is particularly helpful in places like primary health center where all the facilities of Tertiary Care Hospital are not available. But initial diagnosis is necessary before referring the cases to another center.

For many years pediatric renal FNAC has been used for giving Neoadjuvant chemotherapy by many Cytologists [19,20]. Now some like to do Tru cut biopsy, but there is always some risk specially in case of children. With the help of FNAC the chance of risk is minimal. So we usually Fine needle aspiration before giving preoperative chemotherapy. In stable patients we also did tru cut biopsy in addition to FNAC. There is always some risk and it also needs the availability of disposable guns in the treating centers. In Tertiary Care Centers it is not a problem but in case of small set up this is not always available. It also needs the expertise of the Pathologists in all these centers.

CONCLUSION

FNAC is a simple OPD procedure. It is safe, cost effective and can be applied on children for diagnosis of renal tumors before giving Neoadjuvant therapy. Immunostain can be applied directly on the smears or on the cell blocks prepared from the aspirated material. It is also suitable for health centers where trucut guns are not available. No special equipment is required for this. Report can be available on the same day. FNAC when combined with core needle biopsy gives high specificity, sensitivity and high accuracy rate.

CONFLICT OF INTEREST

None.

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None declared.

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