Original Article

Use of Pretherapy Core Biopsy in the Diagnosis of Pediatric Renal Tumors

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ABSTRACT

**Background:** Pretreatment core biopsy of pediatric renal tumors has been advocated by United Kingdom Children’s Cancer Study Group to circumvent the disadvantage of International Society of Paediatric Oncology protocol, where neoadjuvant chemotherapy initiated without histopathological confirmation can result in over- or under-treatment.

**Aim:** This study aims (a) to assess if pretherapy core biopsy correlates with the nephrectomy biopsy; (b) to assess if neoadjuvant chemotherapy changes Wilms tumor (WT) histology, and (c) to assess the incidence of biopsy site recurrence.

**Materials and Methods:** Seventy-six children from 2005 to 2016 with renal tumors who underwent a pretherapy core biopsy were included in the study. The biopsy was performed through the posterior flank post-ultrasound marking of the renal mass, by administering intravenous anesthesia.

**Results:** Of the 62 children with WT, an accurate diagnosis was possible in 61. Accurate prediction of anaplasia was possible only in 25%. Reduction in blastemal elements was seen in 26 patients with 10 of them showing completely necrotic tumor. Eleven of the 14 children with non-WT were accurately diagnosed. Core biopsy corroborated with the nephrectomy biopsy in all but 4 patients. Two specimens were inadequate and two cases of congenital mesoblastic nephroma were inaccurately diagnosed, one as spindle cell neoplasm and the other as WT. Biopsy site recurrence was seen in 1 child.

**Conclusion:** Pretreatment posterior flank core biopsy in the diagnosis of pediatric renal tumors is safe, simple, and cost-effective with minimal complications.

**Keywords:** Core cut biopsy, non-Wilms renal tumors, Wilms tumor

INTRODUCTION

Pediatric renal tumors account for 7% of all childhood neoplasms with Wilms tumor (WT) being the most common. Advances in therapy from the two major treatment groups namely the American National Wilms Tumor Study (NWTS) and the European International Society of Paediatric Oncology (SIOP) have resulted in survival rates of over 80%. NWTS recommends primary nephrectomy followed by adjuvant therapy based on histology and stage. The advantage of this approach is that it enables accurate assessment of the extent, histology, and tumor biology as the tumor is untreated. Upfront resection of large tumors, however, may result in intraoperative tumor spillage, thereby upstaging the disease and increasing the risk of local relapse. The SIOP approach is to give neoadjuvant chemotherapy followed by surgery, postoperative staging, and further therapy based on histology. The preoperative chemotherapy helps in reducing the risk of intraoperative tumor spillage by downstaging the tumor. The disadvantage however is that treatment is initiated without histopathological confirmation of diagnosis. This

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can result both in overtreatment (benign tumors) as well as undertreatment (malignant rhabdoid tumor). To circumvent this problem, while preserving the advantages of the SIOP protocol, the United Kingdom Children’s Cancer Study Group (UKCCSG) recommended pretherapy tumor biopsy.[2,3]

In our center, we do a pretherapy core biopsy for all renal tumors with the exception of cystic tumors without any solid component and children <6 months of age. The aim of this study is to (a) to assess if pretherapy core biopsy correlates with the nephrectomy biopsy; (b) to assess if neoadjuvant chemotherapy changes tumor histology; and (c) to assess the incidence of biopsy site recurrence.

**MATERIALS AND METHODS**

A retrospective study was done on 76 children with renal tumors who underwent a pretherapy core biopsy followed by definitive treatment from 2005 to 2016. Data were obtained using hospital records, imaging, and pathology reports. Children who had surgery or biopsy elsewhere were excluded from the study.

**Method of biopsy**

The procedure was performed as an inpatient starting with an ultrasound assessment of the mass. The biopsy site was marked on the posterior flank after ascertaining the depth of the tumor from skin. The biopsy was performed using a No. 16 Fr core biopsy needle under intravenous anaesthesia (ketamine 2 mg/kg and midazolam 0.1 mg/kg) using a No 16 Fr. core biopsy needle. Two to three passes were routinely made. Oral paracetamol and ibuprofen were used for postprocedure analgesia, and all children were monitored overnight and discharged the next day.

**RESULTS**

Seventy-six children met the inclusion criteria. Of the 62 children with WT, an accurate diagnosis was possible in 61 (98.4%). However, accurate prediction of anaplasia was possible in only 25% (1 out of 4). Reduction in blastomal elements was seen in 26 patients with 10 of them showing completely necrotic tumor. Eleven of the 14 children with non-WT were accurately diagnosed by core cut biopsy (78.5%). While tumors such as malignant rhabdoid tumor and clear cell sarcoma had a 100% sensitivity and positive predictive value, congenital mesoblastic nephroma (CMN) had a sensitivity of only 33% (1 in 3).

Core cut biopsy corroborated with the nephrectomy biopsy in all but 4 patients. Of these 4 patients, the core biopsy specimen was found to be inadequate in 2 children. The final biopsy showed renal cell carcinoma in one and WT in the other. Two cases of CMN were inaccurately diagnosed, one as spindle cell neoplasm and the other as WT. The sensitivity and positive predictive values of pretherapy core biopsy for the different pediatric renal tumors are summarized in Table 1.

Oral analgesics were adequate for pain relief, and there was no significant fall in hematocrit (assessed indirectly as tachycardia). All children could be discharged as planned the next morning. One child with bilateral WT presented 4-month post partial nephrectomy while on chemoradiation with tumor at the biopsy site. He was found to have local recurrence with tumor tracking to the biopsy site with lung metastases.

**DISCUSSION**

Although neoadjuvant chemotherapy as per the SIOP protocol helps in reducing intraoperative tumor rupture rates, the diagnosis is based on imaging. Initially, pretherapy tumor biopsy was thought to upstage the disease to Stage 3 thereby increasing the risk of local relapse.[1] However, even though the recent SIOP guidelines have stated that biopsy per se does not upstage disease,[4,5] it still does not enjoy patronage among those who follow the SIOP protocol. Despite the advances in imaging technology, studies have shown that around 10% of cases that are clinically and radiologically diagnosed as WT have been proven to be other tumors on histopathological examination.[6,7] This rate was found to be higher in our study where 18.6% of all pediatric renal tumors were non-Wilms. Thus, the disadvantage of a purely

| Pediatric renal tumor       | Core cut diagnosis | Nephrectomy diagnosis | Sensitivity (%) | Positive predictive value (%) |
|-----------------------------|--------------------|-----------------------|----------------|-----------------------------|
| Wilms tumor*                | 61                 | 62                    | 98.4           | 98.4                        |
| Clear cell sarcoma          | 6                  | 6                     | 100            | 100                         |
| RCC*                        | 3                  | 4                     | 75             | 100                         |
| CMN*                        | 1                  | 3                     | 33.3           | 100                         |
| Malignant rhabdoid tumor    | 1                  | 1                     | 100            | 100                         |

*One child each with Wilms tumor and RCC had inadequate core cut biopsy specimens, 2 cases of CMN were inaccurately diagnosed – one as Wilms tumor and the other as spindle cell neoplasm. RCC: Renal cell carcinoma, CMN: Congenital mesoblastic nephroma
imaging-based diagnosis is that it can result in both undertreatment as well as overtreatment. In our cohort, core biopsy was especially useful for the 2 cases of CMN (one diagnosed as CMN and the other as spindle cell neoplasm) and the 3 cases of RCC where surgery was performed primarily without administering neoadjuvant chemotherapy.

Performing a posterior flank core biopsy as described earlier, decreases the chance of upstaging the disease by possible transperitoneal tumor contamination and also reduces morbidity. A screening ultrasonogram before the biopsy ensured that the passes would be made only through the solid components of the tumor, thereby preventing tumor rupture/bleeding. None of the children had any post procedure complications as evidenced by absence of pain requiring prolonged admission, tachycardia, pallor, or paralytic ileus. Biopsy site tumor recurrence was seen in 1 child with bilateral Wilms with this being the third instance of the same in literature.[1,8]

Our results confirm that a posterior flank core biopsy is extremely useful in diagnosing pediatric renal tumors. Specimen inadequacy and inconclusive diagnosis were seen only in 5.4%, which was similar to the UKCCSG study[1] and better than previous studies where the rates ranged from 8.3% to 24%.[9,10] A diagnosis of non-WTs could be established in 11 of the 14 patients, thus leading to appropriate treatment. Concordance of core biopsy with the nephrectomy biopsy was high in all tumors except for CMN where only 1 of the 3 cases could be diagnosed. This high concordance rate for non-Wilms renal tumor except for CMN is better than other published studies but lesser than the UKCCSG study. Further, concordance rates for Wilms were similar to other published studies.[1,9-11]

Neoadjuvant chemotherapy causing alterations to the WT histology is considered as one other disadvantage of the SIOP protocol. In our study, alteration in the tumor histology in the form of reduction in blastemal elements was seen in 34.4% and a complete disappearance in 8.1% of children. This is due to the fact that of the three cell lines, blastemal ones are the most susceptible to chemotherapy.[12] Concordance rates for anaplasia were found to be only 25% and were similar to other published studies.

Recent studies have shown fine-needle aspiration cytology to be almost equal to biopsy in differentiating the different renal tumors with advantages being lesser morbidity and complications.[13] However, we have not employed this at present as accuracy rates have differed depending on the experience of the pathologist.[14] In our experience, the core cut biopsy is a safe and effective diagnostic tool for renal neoplasms in children.

**Conclusion**

Pretreatment posterior flank core biopsy is an excellent method for diagnosing pediatric renal neoplasms in centers following the SIOP protocol. The procedure is safe, simple, and cost-effective with minimal complications and with the advantage that appropriate therapy can be instituted at the earliest.

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**Conflicts of interest**

There are no conflicts of interest.

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