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ROLE OF THE PREOPERATIVE RETROPERITONEAL CORE NEEDLE BIOPSY (CNB) IN THE DIFFERENTIAL DIAGNOSIS OF SUSPECTED MALIGNANT RENAL TUMORS IN CHILDREN.

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Abstract-
Background: Childhood cancers represent a significant health concern worldwide, with malignant renal tumors accounting for approximately 7% of all childhood cancers. Differentiation of Wilms tumor (WT) from non-Wilms renal tumors(NWRT) is essential as the management of these two groups of tumors are very different, especially if we believe in the SIOP protocol of administering neo-adjuvant chemotherapy (NACT) in patients with WT.
Aims- This study done to evaluate role of the preoperative retroperitoneal core needle biopsy (CNB) in the differential diagnosis of suspected malignant renal tumors in children.
Material and methods: this is a prospective study done in NSCB medical college Jabalpur from January 2023 to January 2024. CNB was done in 20 patients (23 renal biopsies as 3 patients had bilateral tumors) with suspected malignant renal tumors. Thosediagnosed as WT on CNB received NACT followed by nephrectomy and adjuvant therapy.
Results: Out of the 23 renal biopsies, 21 were diagnosed as WT while the other 2 as malignant rhabdoid tumors of kidney (MRTK). One patient developed abdominal distension and respiratory distress after CNB. On HPE of the excised surgical specimen of those who received NACT for WT (diagnosed on CNB), 19 samples were confirmed as WT, while 2 were diagnosed as clear cell sarcoma of the kidney (CCSK). Of the 2 tumors that were diagnosed as MRTK on CNB, 1 wasconfirmed as MRTK and the other was diagnosed as CCSK on HPE of the excised specimen. The concordance between the HPE of CNB and the excised surgical specimen was 91%.
Conclusion: Pre-therapy CNB is a sensitive tool to differentiate WT from NWRT.The sensitivity, specificity, positive predictive value and negative predictive value of CNB in the diagnosis of renal tumors are 89%, 50%, 89% and 100% respectively.

KEYWORDS- core needle biopsy, wilms tumor, renal tumors.

Introduction- Wilms tumour (WT) is the most common paediatric renal tumour, accounting for over 85% of all cases in children. Childhood cancers represent a significant health concern worldwide, with malignant renal tumors accounting for approximately 7% of all childhood cancers.(1) Accurate diagnosis of renal tumors is crucial for selecting the most appropriate treatment and ensuring optimal outcomes for patients. It is not always possible to differentiate between different types of renal tumors by clinical examination and imaging alone.(2) Saula et al. noted approximately 13.6% of cases were NWRT in the developing countries, highlighting the importance of preoperative CNB in guiding treatment decisions.(3) Moreover, NWRT are far more commonly seen in Southeast Asian countries including India as compared to the Western world.(3) WT is treated according to the guidelines suggested by the National Wilms tumor study group (NWTSG) - recently renamed as Children's Oncology Group (COG) or the Inter- national Society of Pediatric Oncology (SIOP).(4) NWTSG/COG believes in up-front surgery followed by adjunct therapy, while SIOP believes in neo-adjuvant chemotherapy (NACT) followed by surgery and then adjuvant therapy.

During SIOP trials, it was noted that 5-10% of tumors initially suspected to be WT turned out to be either benign renal tumors or NWRT that do not respond to NACT.(5) COG approach has the advantage of studying tumor histology unaltered by prior chemotherapy and hence it makes sub-typing and staging of the tumor easier. Even in COG, NACT is administered to inoperable WT, WT in a solitary kidney, synchronous bilateral WT, tumor thrombus in inferior vena cava extending above the level of the hepatic veins and the tumor involving contiguous vital structure.

In India, pre-treatment CNB is not a popular practice, unlike in the United Kingdom where the Children's Cancer Study Group (UKCCSG) used to advocate preoperative CNB through the retroperitoneal route for all suspected WT to ascertain the histopathological diagnosis before administering neo-adjuvant chemotherapy.(5) As the management philosophy of WT and NWRT is very different, we intended to assess the role of the pre-therapy retroperitoneal CNB in the differential diagnosis of pediatric renal.

Aims- This study done to evaluate role of the preoperative retroperitoneal core needle biopsy (CNB) in the differential diagnosis of suspected malignant renal tumors in children.

Materials and methods- this is a prospective study done in NSCB medical college Jabalpur from January 2023 to January 2024**.** After obtaining the approval of the institute ethical committee study of 20 patients with suspected malignant renal tumors was done. Patients with recurrent disease and tumor rupture or hemorrhage necessitating emergency surgery were excluded. All the patients had routine bio- chemical investigations, ultrasonography (USG) abdomen with Doppler and contrast enhanced computed tomographic scan (CECT) of the chest and abdomen. All but one patient underwent USG-guided CNB through the retro-peritoneal route after administering adequate sedation and local anesthesia; one patient erroneously underwent transperitoneal CNB. At least 2-3 cores were taken and sent for HPE. Adverse events, either during or after the procedure, were recorded. HPE was reported within approximately 5-6 days. For patients with bilateral renal tumors, both tumors were biopsied as discordant pathologies are known to occur. Those who were diagnosed as WT were given NACT as per the Umbrella protocol of SIOP-RTSG(18) and those diagnosed as MRTK underwent upfront surgery. In CNB diagnosed WT, a re-evaluation was done by CECT of the abdomen before nephrectomy to assess the reduction in tumor volume due to NACT.

Written consent for surgery was obtained from caregivers. All patients underwent tumor excision by a single senior surgeon (YKS). Sixteen patients underwent total nephroureterectomy; these include 2 children diagnosed to have MRTK on CNB. Four patients underwent nephron-sparing surgery; 3 of them had bilateral WT. Intra- operative and post-operative adverse events, if any, were recorded. The excised surgical specimen was sent for HPE to study tumor staging and risk-stratification. Concordance between the pre-therapy CNB report and that of post-nephrectomy HPE was recorded.

NACT-induced changes in histopathology were noted. In the case of bilateral tumors, adjuvant therapy was based on the tumor having the higher risk stratification.

Results-

This is a prospective study done in NSCB medical college Jabalpur from January 2023 to January 2024. CNB was performed for 23 renal tumors in 20 patients; 3 had bilateral renal tumors. In one patient, the CNB was done trans-peritoneally by mistake. She developed abdominal distension, respiratory distress and a fall in hemoglobin due to intra-abdominal bleeding. She was upstaged to stage-3 and was treated accordingly. CNB-related hemorrhage, tumor rupture or tumor seeding was not noted in any other patient.

Eighteen patients including 3 having bilateral WT (21 renal CNB) were diagnosed to have WT. They received NACT as per SIOP protocol. The other 2 patients diagnosed as MRTK on CNB underwent upfront nephrectomy. More than half of the WT (57.1%) patients were reported to have biphasic WT on CNB.

The interpretation of monophasic WT withblastemal component alone (n=2) on CNB was easy to interpret. However, interpreting monophasic WT with stromal component (n=2) neededconsiderable expertise. In 19% (4/21) rhabdomyoblastic changes were seen. None of the WT showed anaplasia. The mean reduction of tumour volume after NACT was 41.8$\pm$ 2%. No change in the tumor volume after NACT was noted in 13/21 (61.9%) tumors. None of the bilateral tumors (n=6) or the 2 tumors that later turned out to be CCSK showed any change in tumor volume. Only 3 patients with unilateral WT on CNB showed considerable (>50%) reduction in tumor volume following NACT. Heterologous elements like cartilage and bone were found in 2 specimens, while rhabdo-myoblastic changes were seen in 5 specimens.

On histopathology of the excised specimens, 17 (73.9%) patients had intermediate-risk tumors and 6 (26%) had high-risk tumors as per working SIOP classification; none was of 'low-risk' category (completely necrotic).

In 2 out of the 21 WT and one out of the 2 MRTK diagnosed on CNB, the diagnosis was revised as CSSK on the final histology of nephrectomy specimen. The concordance betweenCNB and histology of resected specimen was 91%. The sensitivity, specificity, positive predictive value and negative predictive value of CNB in the diagnosis of pediatric renal tumors were 89%, 50%, 89% and 100% respectively.

Three-fourths of the 19 excised surgical specimens had <33% viable tumor cells reported as the blastemal component, thus proving that the blastemal component is chemo-sensitive. Only 2 specimens had shown blastemal component of >66% thus designating it as a high-risk tumor with a poor prognosis.

DISCUSSION

In the field of pediatric oncology, obtaining an accurate diagnosis in the shortest period of time with minimal morbidity is of utmost importance. (17) Of all childhood cancers, malignant renal tumors comprise 7% of all cancers. Among them, WT is the most common renal tumor which is commonly presented in the age group from 1-4 years. (1,2,6) The differentiation between WT and NWRT can be challenging as they share many radiological features. Therefore, CNB is necessary for accurate diagnosis. UKCCSG WT Study 3 adopted pre-NACT CNB for histological diagnosis to address these issues [13].

The diagnosis of WT and other renal tumors istypically made by imaging studies, including USG (including Doppler), computed tomography and magnetic resonance imaging. These studies can provide detailed information about the size, location and characteristics of the tumor, which are

invaluable in therapeutic decision making. In some cases, a CNB may be performed to confirm the diagnosis, but this is not always necessary, especially when the imaging studies are highly suggestive of a specific type of tumor. (5) According to Umbrella protocol, CNB is now considered only in cases with unusual clinical presentation like age >6 years, urinary infection or septicemia, psoas infiltration, pulmonary metastasis in <2 years, and extra-hepatic or extra-pulmonary metastasis, unusual radiological findings like numerous calcifications, voluminous lymphadenopathy, non-visualization of renal parenchyma, extra-renal projections and biological findings like hypercalcemia or LDH level >4 x ULN (upper limit of normal).(18) It is our institutional policy to do CNB in every patient suspected to have a malignant renal tumor.

Skoldenberg's study showed that the sensitivity of CNB was 76%. (14) Taskinen et al. reported a sensitivity of 100% for CNB in diagnosing WT; however, only two out of five NWRT cases in their series were diagnosed with CNB.(4) Jackson et al. showed that the sensitivity and specificity of CNB were 86% and 99.6%, respectively. In 25 out of 518 cases, CNB changed the management, thereby demonstrating the value of this procedure. (15) Mitchell et al.(16) reported that approximately 12% of cases were diagnosed as NWRT due to CNB and were treated accordingly, even though they had features suggestive of WT in radiological studies.

CONCLUSION

We conclude that in our experience CNB is an effective tool in diagnosing WT and differentiating it from NWRT. Inappropriate NACT has been avoided in 2 patients who were diagnosed with NWRT on CNB. In 3 bilateral WT, NACT prescribedby SIOP Umbrella protocol didn't reduce any tumour volume, which indicates that we shouldconsider administering 3-drug NACT as suggested in COG.

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