Ultrasound guided Core Biopsy with on-site cytology – immediate diagnosis in pediatric oncology

boris Sokolovski[1], michal scolnik[1], Leonid Malkin[2], sergey Postovski[1], shifra ash[1], and Anat Ilivitzki[1]

[1]Rambam Health Care Campus
[2]Rambam Medical Center

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Abstract

Background: Accurate and swift tissue diagnosis is extremely important for the timely initiation of treatment in pediatric oncology. In our department, ultrasound guided core needle biopsy (US guided CNB) is used for tissue diagnosis. In 2016, we added on-site cytology, allowing for an immediate primary diagnosis. We retrospectively reviewed our performance in terms of safety and accuracy for CNBs and on-site cytology Procedure: All pediatric biopsies performed in our hospital between February 2016, and December 2019 were included. Patient clinical, procedural and follow up data were collected. CNB pathology and cytology results were compared to final pathologic diagnosis. Results: We included 185 patients for which 210 biopsies were performed; Median latency time to biopsy was one day. Altogether, we had 164 tumors, (148 malignant,16 benign) and 46 other lesions. 159 tumors were correctly diagnosed by CNB; five malignant tumors were misdiagnosed as benign. The sensitivity of our US guided CNB is 96.7%, specificity 100%, and accuracy 97.6%. On-site cytology was performed in 41 cases; 36 malignant tumors, 2 benign tumors and 3 reactive lymph nodes. The cytologist correctly differentiated tumor from inflammation in all cases, and diagnosed the precise tumor type in 38 cases, with accuracy of 93% for final diagnosis. We had no complications related to the procedure or sedation. Conclusions: US guided CNB with on-site TI cytology for suspected malignancy in the pediatric population highly available, safe and accurate, with real time diagnosis in most cases. The accelerated diagnostic root has huge impact on patient care.

Introduction

The incidence of pediatric cancer has increased in recent decades (1). Only 2% of cancers occur in the pediatric population, yet it is the second most common cause of death in children, second only to accidents (2) Diagnosis of pediatric tumors often requires the integration of histopathologic examination with histochemical, immunocytochemical, ultrastructural, cytogenetic, and diagnostic molecular pathology techniques (2). Prompt diagnosis is essential for oncologic patients in order to begin treatment as soon as possible (2).

In recent years, image-guided percutaneous core needle biopsy (CNB) proved to be a prompt, safe and accurate diagnostic tool in pediatric oncologic patients (3). Along with other minimally invasive procedures, CNB is gaining ever more acceptance as the primary technique for diagnosis of tissue samples for suspected pediatric malignancy, with high accuracy and low complication rates (4). Despite the many advantages of CNB, there is the risk of inadequate tissue for diagnosis, due to sampling error or extensive tumor necrosis (5).

In our department, ultrasound (US) guided CNB is the first choice for tissue diagnosis in the paediatric population. In the last 4 years, we added an on-site cytological evaluation to our procedure in order to reduce sampling error and adjust the ancillary testing according to the primary diagnosis provided by the cytologist.

In this retrospective study, we summarized our 4 years of experience with on-site, touch imprint (TI) cytology during core needle biopsies. We will discuss the efficiency and accuracy of on-site smear cytology in comparison to the final histological diagnosis, as well as the benefits of this procedure for patient management.

Material and Methods

We retrospectively studied US guided CNB performed on paediatric patients in our institution between February 2016, and December 2019. All biopsies performed for suspected malignancy were included. Altogether 218 biopsies were performed on 185 patients, and on-site cytology was performed in 41 of these biopsies.

The institutional Helsinki committee, approved this research. Before each procedure, the parents were provided with the needed information about the procedure including risks and benefits , and they signed an informed consent for both the procedure and sedation.

Patient data was collected and analysed, including demographics, clinical data, anatomic site and availability of the biopsy, diagnosis from the on-site cytology, and the final pathologic diagnosis. Availability of the biopsy was assessed as the time lag between the request for the biopsy and the procedure itself, the immediate and delayed complications related to the biopsy, and the sedation. The biopsies were performed under sonographic guidance in the paediatric US unit, most of them under deep sedation. The team included a radiologist, US technician, oncologist, a nurse, and an anesthesiologist.

For core biopsy, we used a spring-loaded core biopsy needle (Super Core Biopsy Instrument; Angiotech), 14 to 18-G calibre. The 14-G calibre was mostly used in musculoskeletal biopsies, and for lymph biopsies we usually used 18-G needle. Core biopsies, 3 cores in most cases, were sent for pathologic evaluation, molecular biology, and genetic studies as needed. The first core was used for on-site cytology. The first core was taken and gently placed and squashed on a slide to preserve the material. The slides were air-dried and immediately stained with H&E and reviewed by a board-certified cytologist for adequacy of the tissue preliminary diagnosis of tissue type and final diagnosis of cancer type when indicated. For inadequate tissue, either due to necrosis or sampling error, a second core was taken from a different location and the on–site TI cytological evaluation was repeated. Once adequate, the cytologist gave a preliminary diagnosis. Additional cores were then taken from the same location and sent for pathology and relevant ancillary testing. When indicated, following our CNB, the oncologist performed bone marrow biopsy.

We compared the diagnosis obtained from our on-site TI cytology to the final diagnosis from any other pathology procedure, including additional biopsy, incisional biopsy, or resection of tumor. The additional pathologic evaluations were used as the gold standard for which to measure the true positive, true negative, false positive and false negative of the cytology results. A false-negative was defined as a failure to identify a tumor in the on-site cytological evaluation of a percutaneous biopsy, that was later identified as tumor tissue by other means. We calculated the sensitivity, specificity, and accuracy rate of the on-site cytological evaluation of CNBs.

The correlation between the on-site cytological diagnosis and the final pathological diagnosis was assessed for the accuracy of three distinct diagnostic assessments in the cytological analysis. The first was the primary distinction between tumour and non-tumour lesions, the second was identification of the main type of tumour cell (for example, small round blue cell), and the third was the precise diagnosis. Based on the three diagnostic assessments the cytological evaluation could be diagnostically accurate (positive correlation of all three assessments with the final diagnosis), partially accurate (positive correlation of assessments one and two), able to distinguish between benign and tumour lesions only (positive correlation of the first assessment), or inaccurate. We calculated the sensitivity and specificity for the third assessment (precise diagnosis), and the accuracy of the procedure for the different diagnostic assessments.

Results210 biopsies were performed on 185 patients: 32 known oncologic patients and 153 to establish diagnosis. Patient demographics are shown in table 1. The median lag time between the request for biopsy

and the procedure itself was one day, and lag times included less than one day and up to 44 days. Altogether, we had 164 tumors, (148 malignant and 16 benign) and 46 other lesions (table 2). 159 tumors were correctly diagnosed by US guided CNB, five tumors were misdiagnosed as benign lesions, and 46 biopsies were correctly diagnosed as non-tumor tissue. The sensitivity of our US guided CNB is 96.7%, specificity 100%, and accuracy 97.6%.

Smear cytology was performed in 41 cases with the following diagnoses: 36 malignant tumors, 2 benign tumors and 3 reactive lymph nodes (table2). The cytologist correctly differentiated tumor from inflammation in all cases, and diagnosed the precise type of tumor in 38 of the cases. Accuracy of smear pathology was 100% for differentiating tumor from non-tumor tissue (diagnostic assessment one) and for delineating groups of tumor cells (diagnostic assessment two). For the diagnosis of the exact type of tumor (diagnostic assessment three), on–site TI cytology showed a sensitivity of 91.6%, specificity of 100% and accuracy of 93%. There were no complications related to the procedure or the sedation.

Discussion

The diagnosis of pediatric tumors is constantly evolving, and the introduction of CNB followed by on-site cytology has vastly improved patient care in pediatric oncology, allowing for both timely diagnosis and more immediate initiation of treatment (2). Recent publication from our institution, summarizing 16 years of experience with 597 US guided CNBs in pediatric oncology patients, showed high accuracy rate of 98% for the technique, yet highlighted some limitations (3). Diagnosis was established in the first biopsy in the vast majority of our patients. In 12 patients, 2% of the sample, the tissue was inadequate for diagnosis, and an additional procedure was needed for diagnosis; half required a second CNB and half an operational biopsy

The 12 cases that required a second biopsy for diagnosis shed light on the main drawbacks of CNB, which are sampling error and inadequate tissue for diagnosis, seen mainly in cases of extensive necrosis within the tumor or in small masses. The need for repeated biopsy delayed the initiation of treatment and prolonged the stressful period of uncertainty for the child and family (6). In order to minimize such cases, we added on-site TI cytology to the CNB procedure.

Our results show that in all the procedures that combined CNB with on-cite cytology a final diagnosis was reached, with no need for a second diagnostic procedure. The cytologist correctly differentiated benign from malignant tissues in all cases, and in 93% correctly diagnosed the type of tumor (Fig. 1,2). The additional information from the on-site TI cytological evaluation improved the efficiency of the CNB procedure, guiding decisions to complete all the relevant ancillary testing, with minimal number of cores. The time to diagnosis and start of treatment were considerately shortened.

The impact on patient care was considerable. The oncologist was able to inform the parents at the end of the biopsy, with a high level of certainty, whether their child had a benign or malignant tumor. The period of uncertainty was shortened, and for benign lesions it offered immediate relief.

Fine needle aspiration, which is less invasive than CNB, is a well-established cytological procedure. FNA is widely used as a primary tool for tissue diagnosis in a variety of tumors (for e.g. thyroid, breast, lung, pancreas), and on-site cytological evaluation offers an improved diagnostic rate (7, 8). However, in many tumors, FNA is not sufficient for accurate diagnosis due to several limitations. Inadequate material to prepare a cellblock is a problem that limits the ability to perform diagnostic ancillary studies. Other issues with FNA are a lack of tissue architecture, an inability to evaluate the relationship between the tumor and surrounding tissues, and an inability to distinguish between a benign or borderline lesion, a problem seen more often in lymphoid diseases and soft tissue lesions. Additionally, certain types of lymphomas need tissue sampling (9).

Indeed, in our series, in three cases the cytology was partially correct. The cytologist diagnosed malignant small round blue cells in two cases, and the final diagnoses were rhabdomyosarcoma in the first case and osteosarcoma in the second. In the third case the cytologist diagnosed lymphoma and the final diagnosis was Hodgkin's lymphoma. As concluded in Joudeh et al, cytology cannot always be a substitute for tissue

biopsy (9).

The role of cytopathology has evolved over the years from a purely diagnostic technique to an adjuvant method that guides decisions for other sampling procedures (9-12). On-site cytology followed by CNB in the adult population improves diagnostic success compared to CNB alone, and it is becoming generally accepted that the two procedures together are synergistic (9-13). Additionally, the cytological technique was first used with FNA only, and has evolved to include touch imprint (TI) from core biopsies (14).

The two methods are different; FNA is an active process and yields a cellular reach sample with minimal stroma, while TI from CNB is a passive process that provides both cells and stroma, better in fibrotic tissues. There are several techniques for preparation of TI, from gentle touching of the core onto a slide, to rolling it on the slide and even crushing the tissue between two slides (14). A vigorous technique might deplete the core of the cells with a subsequent decrease in DNA content. A light touch might produce a poor cellular specimen and an incorrect interpretation (14).

Li et al. showed that in the adult population the accuracy rates of on-site TI in various tissues are as high as 88.5-97% (12). Kubik et al. found that by adding on-site TI cytology to CNB in the setting of adult lesions, adequate tissue was obtained in over 98% of cases (10). In Li et al., the overall correlation rate between the preliminary interpretations of on-site cytology and the final histological diagnosis was 91%, with 100% for benign lesions and 89% for malignant lesions. Adequacy rate was lowest in cases of sarcoma (12). Moghadamfalahi et al. showed that on-site TI for Computed Tomography (CT) guided CNB in the adult population, minimized the number of biopsies required for obtaining adequate diagnostic material and sufficient specimens to guide ancillary studies (15).

The literature in the pediatric population is sparse. Patel et al. showed an increase in the diagnostic rate of pediatric CNB in bone lesions from 79% to 97% when on-site FNA and cytology was added (11). Our results for a variety of tumors in the pediatric population was very promising, yet the cohort was small. Larger cohorts of pediatric patients are needed to further validate the added value of on-site TI cytopathology in the pediatric population.

The impact of on-site TI cytology on patient care is huge, both time and money are saved by this quick and efficient procedure. On-site cytology shortens the time to diagnosis, allowing for both a swift discharge of patients without malignancy and earlier imaging and treatments for patients diagnosed with a new or recurrent tumor. In our cohort, on-site cytology was an excellent, real-time tool for identifying tumor tissue, and in most cases allowed for an early correct diagnosis.

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Figure legends:

Figure 1:

Forehead mass in 14 years old girl. A. On-site touch imprint shows lasts with scant cytoplasm and cleaved nuclei or irregular contours, diagnosed as Lymphoma. B. Pathologic slide H&E stained confirmed the diagnosis of Lymphoma.

Figure 2:

Retroperitoneal mass in 2 years old child .A. On-site touch imprint shows small round blue cells with eosinophilic fibrillary cytoplasm, and vague rosettes consistant with Neuroblastoma. B. Pathologic slide H&E stained confirm the diagnosis of Neuroblastoma

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`Tables 1-2 cytology 25 aug for PED BLOOD CANCER.docx` available at https://authorea.com/users/359534/articles/481454-ultrasound-guided-core-biopsy-with-on-site-cytology-immediate-diagnosis-in-pediatric-oncology