An Interinstitutional Review of the Value of FNAB in Pediatric Oncology in Resource-Limited Countries

Rubina Razack, M.D.,[1*] Pamela Michelow, M.D.,[2] Gladwyn Leiman, M.D., M.A.I.C.,[2] Anwari Harnekar, M.D.,[2] Janet Poole, M.D.,[3] Glynn Wessels, M.D.,[4] Peter Hesseling, M.D.,[4] Cristina Stefan, M.D.,[4] Mercia Louw, M.D.,[1] Pawel T. Schubert, M.D., F.I.A.C.,[1] Herchel Clarke, B.Sc. Hons.,[1] and Colleen A. Wright, M.D., M.A.I.C.[1]

Fine-needle aspiration biopsy (FNAB) has been widely accepted as a reliable diagnostic modality in the general pediatric population, but its role in pediatric oncology still remains elusive. With new treatment protocols subscribing to preoperative chemotherapy, the need for a quick, minimally invasive, and accurate diagnostic procedure has arisen. This study assesses the feasibility of FNAB in childhood malignancies to render a specific diagnosis on which treatment can be initiated. An 11-year retrospective study was done on FNABs in patients 19 years and under referred for clinically malignant mass lesions. Cases were confirmed with histology, immunocytochemistry, flow cytometry, or clinical follow-up. Of the 357 patients referred for FNABs, 36 patients were lost to follow-up and 31 FNABS were inadequate. A total of 290 cases were included in the study, of which 68 (23%) cases were benign and 222 (77%) were malignant. The most frequently occurring tumors were nephroblastoma (68), non-Hodgkin's lymphoma (39), rhabdomyosarcoma (22), Hodgkin's lymphoma (22), and neuroblastoma (22). The sensitivity of the procedure for neoplasia was 96.6%, the specificity 97.0%, positive predictive value 99.0%, and negative predictive value 90.1%, with a diagnostic accuracy of 96.7%. The ability of FNAB to enable a specific diagnosis to be made, that is correct and accurate subtyping of the tumor on which chemotherapy or radiotherapy could be commenced was 75.7%. This study shows that FNAB can be used with confidence to confirm malignancy in children. With clinicoradiological correlation and the aid of ancillary techniques, FNAB allows a rapid and accurate preoperative diagnosis for definitive therapy commencement in most cases. Diagn. Cytopathol. 2012;40:770–776.

Key Words: fine-needle aspiration biopsy; children; oncology; resource-limited countries

The utility of fine-needle aspiration biopsy (FNAB) in the general pediatric population has become an invaluable and cost-saving modality. However, primary pediatric tumor diagnosis by cytology remains slow to gain acceptance, despite increasing publications supporting this diagnostic procedure.[1–17] This may stem from the perceived rarity of childhood tumors and hence lack of exposure to diagnostic material, the diagnostic difficulty of these tumors, most of which are in the small round blue cell tumor category, as well as reliance on ancillary testing and clinicoradiological correlation. The scarcity of experienced cytopathologists willing to approach pediatric tumor aspirates contributes to the controversy.

The brunt of childhood malignancies is borne in developing countries, where more than 90% of the world's children reside.[18] Pediatric tumors are highly sensitive to treatment with a 70% response rate in developed countries; yet, 80% of children diagnosed with cancer in developing countries die of their disease.[18] This can be attributed to late presentation with advanced disease, as poverty, ignorance, and inaccessible healthcare are realities in poorly resourced countries.

[1]Division of Anatomical Pathology, Stellenbosch University and NHLS Tygerberg, Tygerberg, South Africa
[2]Department of Pathology, University of the Witwatersrand and NHLS Johannesburg, Johannesburg, South Africa
[3]Department of Pediatrics and Child Health, University of the Witwatersrand, Johannesburg, South Africa
[4]Department of Pediatrics and Child Health, Stellenbosch University, Stellenbosch, South Africa
*Correspondence to: Rubina Razack, M.D., Anatomical Pathology, PO Box 19063, Tygerberg 7505, South Africa. E-mail: rubina@sun.ac.za
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South Africa reports an average of 600 childhood malignancies a year.[19] Hematological malignancies and brain tumors rank highest, followed by solid tumors. However, these figures are gross underestimates due to underreporting to the South African Cancer Registry, which is histologically based and does not record clinically or radiologically diagnosed malignancies cases.[18,19] In a resource-limited country such as South Africa, a cost-effective diagnostic modality with proven diagnostic accuracy is required. FNAB can expedite diagnoses and triage patients with malignant neoplasms to appropriate tertiary facilities, facilitating prompt initiation of treatment with improved patient outcome. The equipment and infrastructure required is inexpensive when compared with excisional biopsy.

This study involved patients from three major pediatric oncology centers in South Africa where cytology is frequently used to determine the nature of clinically suspicious mass lesions. The three centers, namely Chris Hani Baragwanath Hospital (CHB), Charlotte Maxeke Johannesburg Hospital (JBH), and Tygerberg Hospital (TBH) traditionally served patients from differing demographic backgrounds. CHB draws predominantly poor socioeconomic patients from a large semiurban area. JBH serves a mainly urban pediatric population from a middle socioeconomic class. The TBH is the tertiary referral center for patients from semiurban and farmland districts, who are also from middle to lower socioeconomic circumstances. Patients from these three institutions thus represent urban and semiurban pediatric populations using public healthcare services, and not private healthcare in South Africa.

It is in this multiinstitutional setting, where our study describes the prevalence and spectrum of pediatric tumors, with an assessment of the feasibility and reliability of FNA as a diagnostic modality in diagnosing childhood tumors.

Materials and Methods

A cross-sectional study of all cases referred by the respective oncology units for FNABs of clinically malignant cases was reviewed. The study cases comprised 132 from JBH between 1995 and 1999, 74 from CHB between 1997 and 1999, and 84 from TBH between 2001 and 2008. One of the reasons for the staggered time period is that one of the senior authors moved and introduced FNAB into one of these sites (TBH). Also, problems were encountered in retrieving data because of changes in the data capturing systems. A total of 290 were entered into the study. Inclusion criteria included all patients 19 years and under (the age group at which patients are managed as pediatric oncology patients at JBH), with confirmation of the cytological diagnosis in the form of histological correlation, ancillary techniques including immunocytochemistry and flow cytometry, as well as clinicoradiological follow-up. Inadequate smears were excluded.

Aspirates were performed using a 22- or 24-gauge needle attached to a 10-ml plastic syringe. Conventional slides were prepared, where a minimum of two passes was performed; alcohol-fixed slides were stained with the Papanicolaou method, whereas the air-dried slides were Diff-Quik stained. Palpable superficial lesions were performed by the cytopathologist under intravenous sedation with ketamine or midazolam (administered by the attending clinician) for children under the age of 8 years or for those 8 and older who were not able to cooperate. Occasionally, in patients in whom sedation was deemed dangerous, e.g., in cases with respiratory obstruction, superficial aspirates were performed without sedation. Palpable deep organ aspirates were performed by the cytopathologists, under general anesthesia with halothane, nitrous oxide, or intravenous sedation with ketamine. Nonpalpable lesions requiring ultrasound guidance were performed by radiologists, but prepared and assessed for adequacy by a cytopathologist on site.

Results

Of the 357 patients referred for FNABs, 36 (10.1%) patients were lost to follow-up with no confirmation, and 31 (8.7%) aspirates were inadequate. A total of 290 aspirates were included in the study, of which 68 (23.5%) cases were benign and 222 (76.5%) were malignant on final histological diagnosis.

Of the 290 cases, 156 (53.8%) patients were 5 years or less, 77 (26.6%) patients were aged between 6 and 10 years, and 54 (18.6%) patients were between 11 and 19 years. The ages of three patients were unknown. There were 133 (45.9%) males, 141 (48.6%) females, and in 16 (5.5%) the gender was not stated. There was no significant association between patient age ($x^2 = 0.16$, $P = 0.19$) or gender ($F = 1.7$, $P = 0.19$) and malignant versus benign diagnosis.

Most cases (208; 72%) had subsequent histology, usually postchemotherapy surgical excision. In 39 (13%) patients, the clinician confirmed the diagnosis by clinicoradiological follow-up. In 25 (9%) cases, the diagnosis was confirmed by flow cytometry, 11 (4%) with microbial culture and sensitivity, 4 (1%) with positive Ziehl-Neelsen staining, and 3 (1%) cases were confirmed with immunocytochemistry alone.

Table I shows tumor site distribution with 100 (34.5%) aspirates from lymph nodes, 67 (23.1%) from the kidney, 55 (19.0%) from the abdomen, 34 (11.7%) from the head and neck, 19 (4.5%) from soft tissue, 11 (6.5%) from the pelvis, and 2 each from the lung and mediastinum. Most benign aspirates were from lymph nodes, with the majority of malignant tumors from the kidney.

Two hundred and twenty-two cases were malignant. Of these, 125 (56.3%) patients were under 5 years of age and 56 (25.2%) between 5 and 10 years. This reflects the peak incidence of the spectrum of childhood tumors encountered in this series. The tumors encountered more frequently in this group were nephroblastoma, non-Hodgkin lymphoma (NHL), rhabdomyosarcoma, Hodgkin's lymphoma, neuroblastoma, and hepatoblastoma. Less frequently occurring tumors were Kaposi sarcoma (lymph node aspirates), germ-cell tumors, retinoblastoma, peripheral neuroectodermal tumor/Ewing's sarcoma, nasopharyngeal carcinoma, mucoepidermoid carcinoma, adenocarcinoma of the gastrointestinal tract, melanoma, and hepatocellular carcinoma. One case each of pleuropulmonary blastoma, renal cell carcinoma, Langerhans cell histiocytosis, dermatofibrosarcoma protuberans, desmoid tumor, primary clear cell sarcoma of the kidney, and acute myeloid leukemia were encountered. These tumors with their respective sensitivity values and ability to make a specific malignant diagnosis are tabulated in Table II.

Of 290 cases, 279 (96.2%) tumors were diagnosed as primary tumors, whereas 11 (3.8%) cases had a previous history of malignancy. Burkitt lymphoma was the most common NHL, and 14 (87.5%) of the 16 cases were accurately diagnosed by cytology. Acute lymphoblastic lymphomas totaled 15, six of which were subtyped accurately. The other nine cases were reported as NHL cytologically. One anaplastic large cell lymphoma was diagnosed cytologically. Figure 1 shows cytology performance in subtyping lymphomas.

Of the 132 JBH cases, 94 (71.2%) were malignant and 38 (28.8%) benign, compared to 64 (76.2%) malignant, 20 (23.8%) benign from TBH and 64 (86.5%) malignant with 10 (13.5%) benign at CHB. The specific tumor comparison is depicted in Table III. The proportion of cases seen was similar in all three institutions. A perceived higher percentage of nephroblastomas and rhabdomyosarcomas in JBH proved not to be significant ($x^2 = 15.7$, $P = 0.11$).

In 68 (23%) patients clinically suspected of having a potentially malignant mass lesion, a benign diagnosis was made on FNAB and cytology as shown in Table IV.

Table I. Tumor Site Distribution

Site	*Malignant*	*Benign*	*Total*
Lymph node	51	49	100
Kidney	65	2	67
Abdomen	54	1	55
Head and neck	26	8	34
Soft tissue	13	6	19
Pelvis	9	2	11
Lung	2	0	2
Mediastinum	2	0	2
Total	222	68	290

Table II. Cytological Accuracy in Making a Specific Diagnosis for Each Tumor

	Confirmed cases	*Tumor correctly specified on cytology*	*FN*	*Sensitivity (%)*	*SRBCT NOS*	*Error in specific maligancy*	*Deferred*	*Atypical or suspect*	*Accuracy in making a specific diagnosis (%)*
Nephroblastoma	68	60	0	100	5	1(RMS)	1	0	88.23
NHL	39	38	1	97.40	0	0	0	0	97.40
Neuroblastoma	22	18	1	94.70	3	0	0	0	81.20
Rhabdomyosarcoma	22	2	0	100	2	0	4	1	9.10
Hodgkin lymphoma	22	15	3	83.33	0	0	0	4	68.20
Hepatoblastoma	8	7	0	100	1	0	0	0	87.50
Kaposi sarcoma	5	5	0	100.00	0	0	0	0	100
Germ cell tumor	5	5	0	100	0	0	0	0	100
Retinoblastoma	5	3	0	100	2	0	0	0	60
PNET/ES	4	3	0	100	1	0	0	0	75.00
NPCA	3	2	1	66.66	0	0	0	0	66.66
Melanoma	2	2	0	100	0	0	0	0	100
HCC	2	2	0	100	0	0	0	0	100
Sarcoma	1	1	0	100	0	0	0	0	100
Neuroendocrine	1	1	0	100	0	0	0	0	100
MECA	3	1	0	100	0	1(NPCA)	0	1	33.33
Malignant	1	1	0	100	0	0	0	0	100
Adenocarcinoma	2	1	0	100	0	1(GCT)	0	0	50
PPB	1	1	0	100	0	0	0	0	100
RCC	1	0	0	100	0	0	0	1	0
LCH	1	0	0	100	0	0	0	1	0
DFSP	1	0	0	100	0	0	1	0	0
Desmoid tumor	1	0	0	100	0	0	1	0	0
Clear cell sarcoma	1	0	0	100	0	0	1	0	0
ALL/AML	1	0	1	50	0	0	0	0	50
Total	222	168	7	96 (ave)	14	3	8	8	75.70

FN, false negatives; PNET/ES, primitive neuroectodermal tumor/Ewings sarcoma; NPCA, nasopharyngeal carcinoma; HCC, hepatocellular carcinoma; MECA, mucoepidermoid carcinoma; PPB, pteuropulmonary blastoma; RCC, renal cell carcinoma; LCH, Langerhans cell histiocytosis; DFSP, dermatofibrosarcoma protuberans; ALL/AM, acute lymphoid/myeloid leukaemia.

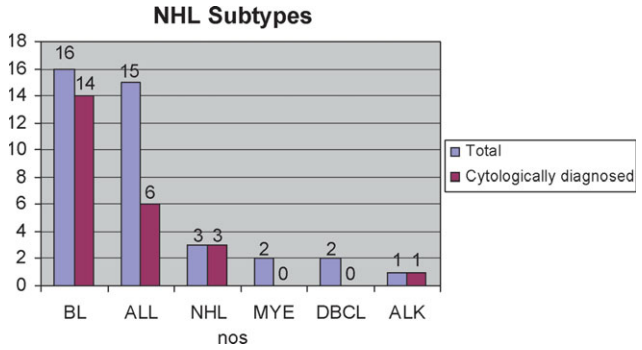

Fig. 1. NHL subtypes (BL, Burkitt lymphoma; ALL, acute lymphoblastic lymphoma, NHL nos, not otherwise specified; MYE, multiple myeloma; DBCL, diffuse B-cell lymphoma; ALK, anaplastic large cell lymphoma). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

The overall sensitivity of cytology for detecting malignancy in this pediatric oncology population was 96.6%, with a specificity of 97.0%. The positive predictive value was 99.0%, with a negative predictive value of 90.1%. Overall diagnostic accuracy was 96.7%. The ability to make a specific malignant diagnosis, that is correct and accurate subtyping of the tumor on which chemotherapy or radiotherapy could be commenced was 75.7%. A specific diagnosis in nephroblastoma (Fig. 2), Burkitt lymphoma (Fig. 3) and neuroblastoma was highly accurate, whereas a specific diagnosis for rhabdomyosarcoma (Fig. 4) was poor.

Discussion

With sensitivity and specificity of 96.6 and 97.0%, respectively, this series supports previous studies showing sensitivities from 76 to 100% and specificities of 92–100%.[1,3,4,9–12,15] FNAB has again been shown to be a reliable tool in distinguishing benign from malignant pediatric lesions. The purpose of this study was to investigate the feasibility of using FNAB in oncology patients to make a specific diagnosis on which treatment may be commenced. FNAB has been shown to be accurate for treatment initiation in the majority (75.7%) of cases. With new treatment protocols requiring preoperative chemotherapy for small round cell tumors of childhood, the need for a quick, low risk, and accurate procedure has expanded. The accuracy of the initial diagnosis is also essential as chemotherapy/radiotherapy can cause considerable alterations to morphology if and when the residual neoplasm is excised. The procedure is not infallible and does have pitfalls which must be heeded. The 75.7% accuracy for making a specific diagnosis is a reflection of the average of all malignant tumors diagnosed. Tumors in which cytological diagnoses were of higher accuracy are thus masked, and those in which cytology performed poorly, disguised. The strengths and weakness of this diagnostic ability are elucidated in Table II and discussed further below.

Table III. Tumor Type per Hospital

Diagnosis	*JHB*	*TBH*	*CHB*
Nephroblastoma	36	15	17
NHL	12	12	15
Neuroblastoma	7	6	9
Rhabdomyosarcoma	13	3	6
Hodgkin lymphoma	7	10	5
Hepatoblastoma	2	6	0
Other	17	12	12
Total malignancies	94	64	64

Table IV. Results of Benign Aspirates

Diagnosis	*Final*	*Correctly diagnosed by cytology*
Tuberculosis	28	25
Reactive node	20	19
Inflammation	6	5
Abscess	2	2
Ganglioneuroma	2	0
Schwannoma	2	1
Cyst	1	1
Fibromatosis colli	1	1
GCT (mature teratoma)	1	1
Hemangioma	1	0
Lipoblastoma	1	1
Multicystic dysplastic kidney	1	1
Mesoblastic nephroma	1	1
Salivary gland tissue	1	1
Total	68	59

Considering the five dominant malignancies in this series, FNAB showed sensitivities (detected malignancy) of 83.33–100%. The ability to make a specific diagnosis on which treatment could be commenced was best in NHL (97.4%) and nephroblastoma (89%), followed by neuroblastoma (81.2%). Less impressive were Hodgkin's lymphoma (68.2%) and rhabdomyosarcoma (9.1%).

In the nephroblastoma group, six tumors could not be subtyped, five were signed out as malignant, small round blue cell tumors, and one uncertain for malignancy. The latter was called a spindle cell tumor and deferred for histology, as immunocytochemistry for WT1 was negative. Histology showed a triphasic and stromal-rich nephroblastoma. Most (98.5%) of the nephroblastomas in this series were that of the classic triphasic type. There was one case of anaplastic nephroblastoma reported on histological evaluation, which was missed on cytology.

In the NHL group, one case of Burkitt lymphoma reported as a reactive lymph node accounted for the only false negative in this tumor group. On review of the cytomorphology and flow cytometry performed, no evidence of a lymphoproliferative disorder was found. This was thus attributed to a sampling error. Flow cytometry was done in 19 (48.7%) of 21 cases where further classification was attempted. In cases where subtyping was not done, a diagnosis of NHL sufficed and biopsy for further classification was performed. The current WHO classification emphasizes morphology and immunophenotype as well as geno-

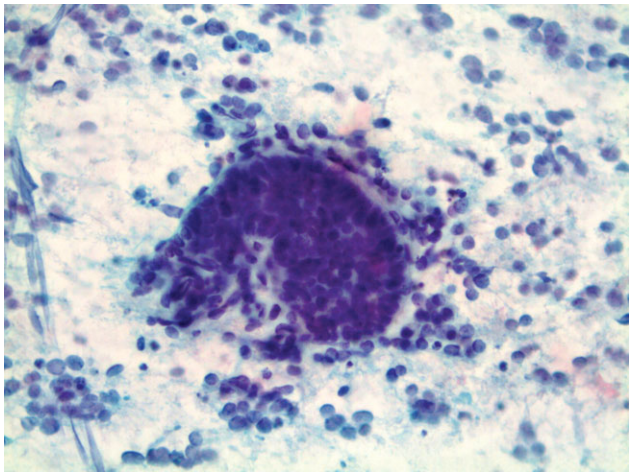

Fig. 2. Glomeruloid body in a nephroblastoma (Papanicolaou, ×400). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

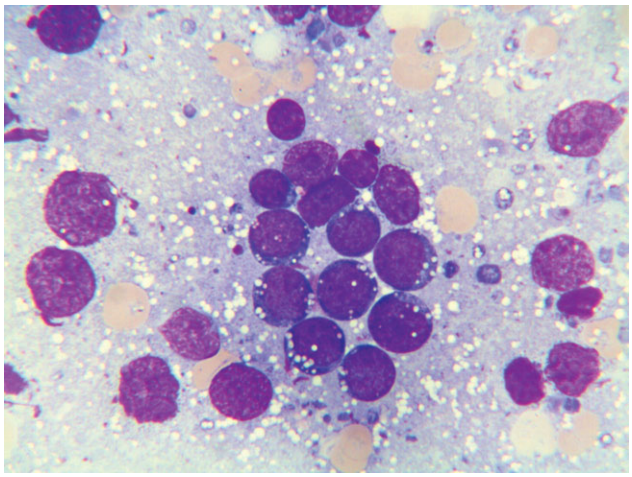

Fig. 3. Burkitt lymphoma. Monomorphic cells with basophilic cytoplasm containing lipid vacuoles (Giemsa, ×1,000). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

type and clinical presentation for diagnosing lymphomas.[20] This implies that architecture is no longer considered essential in some, but not all NHL subtypes. Studies have shown that cytology, coupled with flow cytometry, results in high diagnostic yields for NHL subtypes.[21–27] Had the unclassified NHL cases been submitted for flow cytometry, an improved diagnostic accuracy for subtyping NHL with cytology would have been attained.

One neuroblastoma was misdiagnosed as a cyst with no malignancy. On review of the cytological material, no evidence of malignancy was found. This was attributed to sampling error and emphasizes the importance of clinicopathological correlation as persistent clinical and radiological concern prompted further investigation. Histology revealed a differentiating neuroblastoma undergoing cystic degeneration.

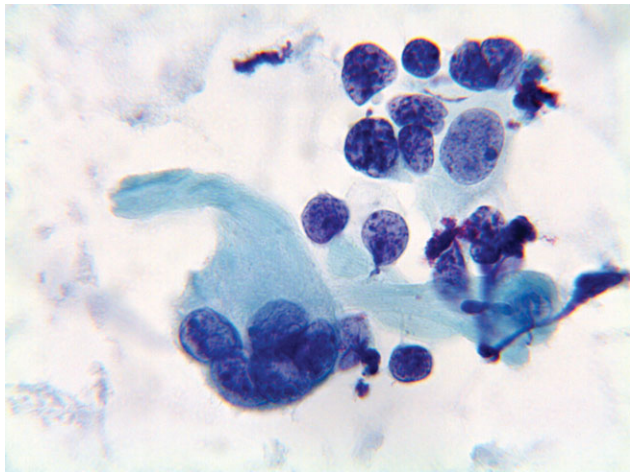

Fig. 4. Round, polygonal cells and a multinucleated tumor giant cell in an alveolar rhabdomyosarcoma (Papanicolaou, ×1,000). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Three false-negative Hodgkin's lymphoma cases did not yield any tumor cells (histologically subtyped as syncitial and mixed cellularity Hodgkin's lymphoma). Two were signed out as reactive lymph nodes and the other as acute inflammatory changes. On review, misdiagnosis was attributed to sampling error. The cytological diagnosis of Hodgkin's lymphoma in the absence of classic Reed Sternberg cells has been acknowledged and still remains a challenge.[2]

The lymphomas presenting in the pediatric age group are limited when compared with adults. Lymphoblastic lymphoma and Burkitt lymphoma are readily diagnosed using flow cytometry, although Hodgkin's lymphoma may necessitate excision biopsy (addressed).

Two other false-negative diagnoses, one a nasopharyngeal carcinoma and the other acute lymphoblastic lymphoma/leukemia, were both due to sampling error as no malignancy was detected on review of the lymph node FNABs. Two false positives were reported as atypical lymphocytes from lymph node aspirates, and histology confirmed one node to be a reactive node and the other noncaseating granulomatous inflammation (Table IV).

FNAB proved 100% sensitive for detecting malignancy in the rhabdomyosarcoma group, but in only 68.2% of these cases was the initial cytology diagnosis issued as rhabdomyosarcoma. In the remaining 31.8% of cases, the diagnosis was malignant, suspicious of rhabdomyosarcomas pending a surgical biopsy. The ability to differentiate alveolar from embryonal rhabdomyosarcoma was only done in two cases (9.1%). As the treatment regimes for the two subtypes are quite distinct, the value cytology adds in this category of tumors is to identify the lesion as rhabdomyosarcoma and to request subsequent biopsy for further subtyping.

All deferred cases represented spindle cell lesions where cytology was of limited diagnostic value. Caution is warranted in these cases, as cytology is acknowledged to distinguish poorly between spindle cell lesions[2] (Table II).

Factors affecting the ability to make a specific diagnosis included (1) sampling error in cystic lesions or partially involved lymph nodes, (2) tumor composition in which heterologous components exist, (3) predominance of an unusual element and (4) overwhelming necrosis, (5) equivocal or erroneous immunocytochemistry, and (6) spindle cell lesions.

The lack of immunocytochemical specificity in small round blue cell tumors is a drawback shared equally by cytology and surgical pathology.[27] Tumors are either so poorly differentiated that they lack antigen specificity or show cross reactivity with other antigens. Lack of standardization of immunocytochemistry protocols also raises questions about the reliability of the ancillary technique.[27] This requires particular attention if immunochemistry is performed on smeared slides as opposed to cell block preparations in which an inbuilt control can provide quality assurance. Caution must be exercised when making definitive diagnoses based solely on this ancillary technique. Results should be interpreted in close correlation with cytomorphology and clinical and radiological findings.

If immunocytochemistry is equivocal or doubtful, cytogenetics can be performed on FNAB material, provided that enough material is available. Genetic analysis of FNAB material has shown to aid diagnoses of Ewing's sarcoma and PNET, alveolar rhabdomyosarcomas, synovial sarcoma, desmoplastic small round cell tumor, neuroblastoma, mesoblastic nephroma, and renal cell carcinoma.[28] Cytogenetics studies are, however, time consuming, costly, and not always available, which limits their use in the South African public health sector, already severely constrained in terms of available staff and funds.

Several study limitations were encountered in this retrospective cross-sectional study. First, ancillary techniques were not always requested by clinicians. In some cases, a diagnosis of small round blue cell tumor or NHL sufficed. These cases are thus difficult to equate with aspirates in which ancillary techniques were used. Also, when ancillary techniques were used, there was no standardization of protocols. With flow cytometry in JBH and CHB cases, samples were not necessarily processed on the same day, as opposed to TBH, where they were processed on receipt. This may have lead to noncontributory flow cytometry and compromised further subtyping of NHL cases. Clearly documented evidence (especially in the false-negative cases) that the lesion aspirated was the lesion eventually excised for histological evaluation was not readily available.

This interinstitutional study revealed that FNAB is applicable to resource-limited countries. Compared with small caliber core biopsy needles, the tools used for aspirating are more accessible, less costly, and in addition to providing on-site diagnoses, take less time in the processing of the material. FNABs have the added advantage of sampling more fields within a tumor compared with core biopsies where only one field is sampled. Thus, in the setting of limited healthcare resources, FNAB is a reliable first-line diagnostic tool for assessing mass lesions in pediatric patients. It aids in triaging patients to appropriate levels of care, thus avoiding unnecessary surgery in benign lesions and expediting management in malignant cases. It provides material for culture for infections, especially tuberculosis, otherwise difficult to prove in children.

In pediatric oncology, cytological diagnoses of nephroblastoma, NHL (particularly Burkitt lymphoma), and neuroblastoma are highly reliable. FNAB can thus provide rapid on-site diagnoses in life-threatening presentations, particularly airway obstruction, when definitive treatment can be commenced. It can complement the SIOP protocols of preoperative therapy for tumor reduction. On-site adequacy assessment can guide formal biopsy in cases of cystic or necrotic lesions, even in lesions where cytology may not be of definitive value, e.g., rhabdomyosarcomas.

In conclusion, FNAB can be used with confidence to confirm clinically suspected malignancy in children. This minimally invasive, safe and cost-effective procedure with its negligible complication rate is ideal in resource-limited settings. With appropriate clinical and radiological correlation and judicious use of ancillary techniques, it is a valuable diagnostic modality in pediatric oncology, allowing a rapid and accurate preoperative diagnosis with commencement of definitive therapy in the majority of cases.

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References

1. Rapkiewicz A, Thuy Le B, Simsir A, Cangiarella J, Levin P. Spectrum of head and neck lesions diagnosed by fine-needle aspiration cytology in the pediatric population. Cancer Cytopathol 2007;111: 242–251.
2. Kocjan G, editor. Fine needle aspiration cytology, diagnostic principles and dilemmas. Springer; Heidelberg, New York. 2006.
3. Orrel S, Sterret G, Whitaker D. Fine needle aspiration cytology. Elsevier Churchill Livingstone; Philadelphia, 2005.
4. Drut R, Drut RM, Pollono D, et al. Fine-needle aspiration biopsy in pediatric oncology patients. A review of experience with 829 patients. Paediatr Haematol Oncol 2005;27:370–376.
5. Pohar-Marinsek Z, Anzic J, Jereb B. Value of fine needle aspiration biopsy in childhood rhabdomyosarcoma: Twenty six years experience in Slovenia. Med Pediatr Oncol 2002;38:416–420.

6. Frostad B, Tani E, Brosjo O, Skoog L. Fine needle aspiration cytology in the diagnosis and management of children and adolescents with Ewing sarcoma and peripheral primitive neuroectodermal tumour. Med Pediatr Oncol 2002;38:33–40.
7. Smith MB, Katz RL, Black CT, Cangir A, Andrassay RJ. A rational approach to the use of fine-needle aspiration biopsy in the evaluation of primary and recurrent neoplasms in children. J Pediatr Surg 1993;28:1245–1247.
8. Akhtar M, Bedrossian W, Ashraf M, Bakry M. Fine needle aspiration biopsy of pediatric neoplasms: Correlation between electron microscopy and immunocytochemistry in diagnosis and classification. Diagn Cytopathol 1992;8:258–265.
9. Gorczyca W, Bedner E, Juszkiewicz P, Chosia M. Aspiration cytology in the diagnosis of malignant tumors in children. Am J Pediatr Hematol/Oncol 1992;14:129–135.
10. McGahey B, Moriarty A, Nelson W, Hull M. Fine needle aspiration biopsy of small round blue cell tumors of childhood. Cancer 1992;69:1067–1073.
11. Layfield L, Glasgow B, Ostrzega N, Reynolds C. Fine needle aspiration cytology and the diagnosis of neoplasms in the pediatric age group. Diagn Cytopathol 1991;7:451–461.
12. Silverman J, Gurley M, Holbrook T, Joshi V. pediatric fine-needle biopsy. Am J Clin Pathol 1991;95:653–659.
13. Liu E, Bernstein J, Sculerati N, Wu H. Fine needle aspiration biopsy of pediatric head and neck masses. Int J Pediatr Otorhinolaryngol 2001;60:135–140.
14. Howell L. Changing role of fine-needle aspiration in the evaluation of pediatric masses. Diagn Cytopathol 2001;24:65–70.
15. Cohen MB, Bottles K, Ablin AR, Miller TR. The use of fine-needle aspiration biopsy in children. West Med J 1989;150:665–667.
16. Kardos T, Maygarden S, Blumberg A, Wakely P, Frable W. Fine needle aspiration biopsy in the management of children and young adults with peripheral lymphadenopathy. Cancer 1989;63:703–707.
17. Wakely PE, Kardos TF, Frable WJ. Application of fine needle aspiration biopsy to pediatrics. Hum Pathol 1988;19:1383–1386.
18. Chirdan L, Bode-Thomas F, Chirdan O. Childhood cancers: Challenges and strategies for management in developing countries. Afr J Pediatr Surg 2009;6:126–130.
19. Davidson A, Hendricks M. Priorities in childhood cancer. S Afr J Child Health 2007;1:96–97.
20. Chhieng D, Cohen J-M, Cangiarella J. Cytology and immunophenotyping of low- and intermediate-grade B-cell non-Hodgkin's lymphomas with a small-cell component: A study of 56 cases. Diagn Cytopathol 2001;24:90–97.
21. Jaffe E, Harris N, Stein H, Isaacson P. Classification of lymphoid neoplasms: The microscope as a tool for disease discovery. Blood 2008;112:4384–4399.
22. Dong H, Harris N, Preffer F, Pitman M. Fine needle aspiration biopsy in the diagnosis and classification of primary and recurrent lymphoma: A retrospective analysis of the utility of cytomorphology and flow cytometry. Mod Pathol 2001;14:472–481.
23. Mayall F, Darlington A, Harrison B. Fine needle aspiration cytology in the diagnosis of uncommon types of lymphoma. J Clin Pathol 2003;56:821–825.
24. Mourad W, Tulbah A, Shoukri M, et al. Primary diagnosis and REAL/WHO classification of Non-Hodgkin's lymphoma by fine-needle aspiration: Cytomorphological and immunophenotypic approach. Diagn Pathol 2003;28:191–195.
25. Zeppa P, Marino G, Troncone G, et al. Fine-needle cytology and flow cytometry immunophenotyping and subclassification of non-Hodgkin lymphoma: A critical review of 307 cases with technical suggestions. Cancer Cytopathol 2003;102:55–65.
26. Dey P, Amir T, Al Jassar A, et al. Combined applications of fine needle aspiration cytology and flow cytometric immunophenotyping for diagnosis and classification of non Hodgkin lymphoma. CytoJournal 2006;3:24.
27. Pohar-Marinsek Z. Difficulties in diagnosing small round cell tumors of childhood from fine needle aspiration cytology samples. Cytopathology 2008;19:67–79.
28. Barroca H. Fine needle biopsy and genetics, two allied weapons diagnosis, prognosis and target therapeutics of solid pediatric tumors. Diagn Cytopathol 2008;36:678–684.