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The Role of Fine-Needle Aspiration Biopsy in Diagnosing Pediatric Malignant Small Round Cell Tumors: Lessons from a Resource-Limited Setting

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ABSTRACT

Background: Malignant small round cell tumors (MSRCTs) in children are a heterogeneous group of neoplasms with overlapping cytomorphologic features, creating diagnostic challenges. Fine-needle aspiration biopsy (FNAB) is widely used in resource-limited settings as a minimally invasive diagnostic tool, but its accuracy in differentiating MSRCT subtypes remains debated. ***Method:*** This retrospective descriptive study reviewed pediatric MSRCT cases at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January 2020 to December 2024. Twenty-four patients aged 0–18 years with complete FNAB, histopathology, and immunohistochemistry data were included. Cytological features, background findings, and cytomorphologic patterns were compared with postoperative histopathology to assess diagnostic concordance. ***Result:*** Neurogenic tumors were the most frequent (41.7%), with Ewing's sarcoma as the predominant subtype (25%). The diffuse round cell pattern was the most common cytomorphologic finding (45.8%), followed by rosette formation (16.7%) and alveolar/pseudoalveolar patterns (8.3%). Distinctive features such as rosettes in neuroblastoma and retinoblastoma or alveolar arrangements in rhabdomyosarcoma enhanced diagnostic specificity, whereas diffuse patterns were less discriminative. FNAB showed good concordance with histopathology in nuclear morphology, cellularity, and growth patterns. Ewing's sarcoma consistently demonstrated small-to-medium nuclei with hypercellularity and diffuse arrangements, while osteosarcoma exhibited clustered patterns with hypocellularity. ***Discussion:*** FNAB provides valuable cytological insights into pediatric MSRCTs and demonstrates strong concordance with histopathology. However, nonspecific diffuse patterns limit its standalone diagnostic value. Integration with immunohistochemistry, particularly CD99 and FLI1 for Ewing's sarcoma, and molecular testing, where available, is essential to achieve diagnostic precision and guide timely therapeutic decisions.

Keywords: fine-needle aspiration biopsy; pediatric oncology; malignant small round cell tumor; cytomorphology; histopathology correlation.

INTRODUCTION

Malignant small round cell tumors (MSRCTs) in children represent a heterogeneous group of neoplasms characterized by small round cell morphology with a high nuclear-to-cytoplasmic ratio, fine chromatin, and scant cytoplasm [1]. This group encompasses various entities, including Ewing sarcoma/PNET, neuroblastoma, rhabdomyosarcoma, lymphoma, Wilms tumor, and desmoplastic small round cell tumor. Each entity carries distinct therapeutic implications and prognostic outcomes, making accurate diagnosis crucial [2].

However, the morphological similarities among these entities often pose significant diagnostic challenges. Therefore, a multimodal approach that integrates cytology, histopathology, immunohistochemistry, and, where available, molecular testing is essential to achieve diagnostic precision [3].

Globally, an estimated 300,000–400,000 new pediatric cancer cases are diagnosed annually, with approximately 30–40% comprising non-hematologic solid tumors, including MSRCTs [4]. In Asia, the burden is even greater, accounting for more than 50% of global cases, in line with the region's population proportion [5]. In Southeast Asia, including Indonesia, pediatric cancers are estimated to represent 3–5% of all new cancer cases, with 40–45% classified as solid tumors. These data highlight MSRCTs as a significant health problem in resource-limited settings [6].

In the diagnostic context, Fine Needle Aspiration Biopsy (FNAB) is a minimally invasive procedure widely utilized in developing countries due to its relative safety, rapidity, and cost-effectiveness [7].

In pediatric populations, FNAB plays a strategic role in establishing an initial diagnosis, guiding treatment planning, and reducing the need for more invasive surgical diagnostic procedures. Nevertheless, the accuracy of FNAB in differentiating among MSRCT entities remains a matter of debate, particularly in centers with limited access to immunohistochemistry or molecular facilities [8].

In Indonesia, data regarding the accuracy of FNAB in diagnosing pediatric MSRCTs remains scarce, despite the considerable case burden in tertiary referral hospitals. Accordingly, a systematic evaluation of the concordance between FNAB and postoperative histopathology is necessary to assess the reliability of this method in daily clinical practice [5]. The present study was designed to address this need by evaluating the concordance between FNAB and histopathological diagnoses in pediatric MSRCT cases at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, one of the leading tertiary care centers in Indonesia.

METHOD

Study Designs

This study employed a descriptive observational design with a retrospective approach. Secondary data were obtained from previously documented medical records of pediatric patients. The primary objective was to evaluate the concordance between FNAB findings and postoperative histopathological diagnoses in MSRCTs in children. The study was conducted at the Department of Anatomical Pathology, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, covering the period from January 2020 to December 2024.

Subject

The study population consisted of pediatric patients aged 0–18 years who underwent FNAB and surgical excision for malignant small round cell tumors during the study period. Of the 156 identified cases (97 males and 59 females), 24 patients had complete histopathological or immunohistochemical data available and were therefore included in the concordance analysis.

Eligible Criteria

The inclusion criteria comprised pediatric patients with complete medical documentation, including FNAB results, postoperative histopathology, and confirmed final diagnosis. Each case was required to have a valid medical record number along with corresponding identifiers. The exclusion criteria were cases referred to by other institutions for second opinion or review, as well as patients who had undergone FNAB procedures outside the hospital.

Data Collection

The data collection process was carried out in coordination with the Department of Anatomical Pathology, followed by the retrieval of medical record numbers and pathology examination identifiers (histopathology, immunohistochemistry, and FNAB) from the departmental archives. Subsequently, FNAB specimens were traced and retrieved, slides were re-examined, and the data were analyzed descriptively. The results of the analysis were then compiled into a structured report.

Diagnosis of Malignant Round Cell Tumors

The diagnosis of MRCTs was established through an integrated approach combining cytomorphology, histopathology, and immunohistochemistry (IHC). FNAB specimens were first evaluated for cytological features, including cellularity, nuclear morphology, nuclear-to-cytoplasmic ratio, chromatin pattern, and cytoplasmic characteristics. Particular attention was given to the presence of diagnostic features such as nuclear molding, rosette formation, or background neuropil. Postoperative histopathological examination of resected specimens, stained with hematoxylin and eosin, served as the reference standard for definitive diagnosis. Architectural patterns, mitotic activity, necrosis, and stromal characteristics were assessed to differentiate among entities within the MRCT spectrum.

Immunohistochemistry was applied in selected cases to resolve diagnostic ambiguity and to support lineage-specific classification. A panel of markers was employed according to the initial morphologic impression: CD99 and FLI-1 for Ewing sarcoma/PNET; Synaptophysin and Chromogranin for neuroblastoma; Desmin, Myogenin, and MyoD1 for rhabdomyosarcoma; LCA, CD20, CD3, and TdT for lymphomas; WT1 and cytokeratin for Wilms tumor and desmoplastic small round cell tumor; and additional markers as required. Cases were categorized as concordant when FNAB and histopathology yielded the same diagnosis, partially concordant when FNAB suggested the correct tumor category without specifying the exact entity, and discordant when the two modalities provided different diagnoses.

Data Analysis

Data collected from medical records, FNAB results, histopathology, and immunohistochemistry were analyzed descriptively. The evaluated variables included patient demographic characteristics (age and sex), tumor location, FNAB cytological findings, postoperative histopathological diagnoses, and immunohistochemical profiles in selected cases. Diagnostic concordance between FNAB and histopathology was determined by classifying each case into one of four categories: concordant (FNAB diagnosis consistent with histopathology), partially concordant (FNAB suggested the correct small round cell tumor category but did not specify the exact entity), discordant (FNAB and histopathology yielded different diagnoses), or inconclusive (incomplete data or non-diagnostic results). The findings were presented as frequency distributions, percentages, and summary tables to illustrate diagnostic concordance patterns between FNAB and histopathology in pediatric malignant round cell tumors.

Ethical Approval

This study received ethical approval from the Health Research Ethics Committee of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia (Approval No. 1874/LOE/301.4.2/I/2025). All research procedures were conducted in accordance with the principles outlined in the Declaration of Helsinki regarding medical research involving human subjects. Given the retrospective design of the study and the use of secondary data from medical records, the ethics committee waived the requirement for individual informed consent.

RESULT

Patient Demographics and Case Distribution

Between January 2020 and December 2024, a total of 24 pediatric malignant small round cell tumor (MSRCT) cases were identified at Dr. Soetomo General Hospital. The cohort consisted of 11 boys (45.8%) and 13 girls (54.2%), indicating a relatively balanced sex distribution with a slight female predominance. The annual trend demonstrated a gradual increase in case numbers, starting with 2 cases each in 2020 and 2021, rising to 3 cases in 2022, and peaking in 2023 with 12 cases (50% of the total) before declining to 5 cases in 2024 (Table 1). This temporal pattern highlights a notable clustering of cases in 2023, suggesting either improved case detection or a genuine rise in incidence during that period.

Distribution by Tumor Origin and Histological Subtypes

Analysis by tumor origin revealed that neurogenic tumors were the most common, comprising 10 cases (41.7%), with Ewing's sarcoma as the predominant subtype (6 cases, 25%; Figure 1), followed by neuroblastoma (3 cases, 12.5%; Figure 2) and retinoblastoma (1 case, 4.2%). Mesenchymal tumors accounted for 4 cases (16.7%), including rhabdomyosarcoma (2 cases), nephroblastoma (1 case), and osteosarcoma (1 case; Figure 3). Hematolymphoid tumors also represented 4 cases (16.7%), consisting of non-Hodgkin lymphoma (3 cases; Figure 4) and lymphoblastic lymphoma (1 case). The remaining 6 cases (25%) were classified as other entities, namely squamous cell carcinoma (3 cases), sialoblastoma (1 case), metastatic carcinoma, poorly differentiated (1 case), and germ cell tumor (1 case). These findings emphasize the predominance of neurogenic tumors, particularly Ewing's sarcoma, as the leading subtype in this pediatric cohort.

Cytomorphologic Patterns of FNAB

Analysis of cytomorphologic patterns in pediatric MSRCTs demonstrated that the diffuse round cell pattern was the most frequent, observed in 11 cases (45.8%), predominantly associated with Ewing's sarcoma, non-Hodgkin lymphoma, lymphoblastic lymphoma, nephroblastoma, and osteosarcoma. The round cell pattern with rosettes was identified in 4 cases (16.7%), typically in retinoblastoma and neuroblastoma, while the alveolar/pseudoalveolar pattern was noted in 2 cases (8.3%), corresponding to rhabdomyosarcoma. A single case (4.2%) exhibited a lobulated/segmented pattern, which may also occur in Ewing's sarcoma and rhabdomyosarcoma. Meanwhile, 6 cases (25.0%) were classified as undetermined patterns, encompassing germ cell tumor, squamous cell carcinoma, sialoblastoma, and metastatic carcinoma. These findings indicate that although the diffuse pattern predominates, distinctive morphologic features such as rosette formation and alveolar arrangements provide important diagnostic clues in narrowing the differential diagnosis of pediatric MSRCTs on FNAB (Table 2).

TABLE 1: Distribution of Pediatric Malignant Round Cell Tumors by Origin, Sex, And Year.

Tumor origin	Diagnosis	Boy	Girl	2020	2021	2022	2023	2024	Total
Neurogenic	Ewing's Sarcoma	0	6	0	1	1	3	1	6
	Neuroblastoma	2	1	1	0	0	1	1	3
	Retinoblastoma	0	1	0	0	0	0	1	1
Mesenchymal	Rhabdomyosarcoma	1	1	0	0	0	1	1	2
	Nephroblastoma	0	1	0	0	0	1	0	1
	Osteosarcoma	0	1	1	0	0	0	0	1
Hematolymphoid	Non-Hodgkin Lymphoma	3	0	0	0	0	2	1	3
	Lymphoblastic Lymphoma	1	0	0	1	0	0	0	1
Others	Squamous Cell Carcinoma	3	0	0	0	2	1	0	3
	Sialoblastoma	0	1	0	0	0	0	1	1
	Metastatic Carcinoma (Poorly Differentiated)	0	1	0	0	0	1	0	1
	Germ Cell Tumor	1	0	0	0	0	0	1	1
Total		11	13	2	2	3	12	5	24

TABLE 2: Distribution of Cytomorphologic Patterns in Pediatric Malignant Round Cell Tumors (2020–2024).

Cytomorphologic Pattern	Representative Diagnoses	n (%)
Diffuse round cell pattern	Ewing's sarcoma, non-Hodgkin lymphoma, lymphoblastic lymphoma, nephroblastoma, osteosarcoma	11 (45.8)
Segmented/lobulated pattern	Ewing's sarcoma, rhabdomyosarcoma	1 (4.2)
Alveolar/pseudoalveolar pattern	Rhabdomyosarcoma	2 (8.3)
Round cell pattern with rosettes	Retinoblastoma, neuroblastoma	4 (16.7)
Undetermined pattern	Germ cell tumor, squamous cell carcinoma, sialoblastoma, metastatic carcinoma	6 (25)

TABLE 3: Cytological Features and Background Findings of FNAB in Malignant Round Cell Tumors.

Histogenesis	Cytological Features	Background Findings
Ewing's Sarcoma	Presence of rosette formation, nuclear moulding, branching capillaries, scant eosinophilic matrix, and chromatin streaks	Erythrocytes; inflammatory cells
Neuroblastoma	Nuclear moulding, rosette formation, and chromatin streaks	Erythrocytes
Retinoblastoma	Nuclear moulding and chromatin streaks	Inflammatory cells; neutrophils
Rhabdomyosarcoma	Nuclear moulding, focal rosette formation, and chromatin streaks	Erythrocytes
Nephroblastoma	Nuclear moulding and chromatin streaks	Erythrocytes
Osteosarcoma	Pleomorphic cells with eccentrically placed nuclei and bluish cytoplasm	Eosinophilic matrix; erythrocytes
Non-Hodgkin Lymphoma	Presence of lymphogranular bodies and fine chromatin streaks	Relatively clean background
Lymphoblastic Lymphoma	Nuclear moulding, lymphogranular bodies, and chromatin streaks	Relatively clean background
Carcinoma (Poorly Differentiated), Sialoblastoma, Metastatic Carcinoma, Germ Cell Tumor	Pleomorphic cells with frequent mitoses, chromatin streaks, and eosinophilic matrix	Erythrocytes; inflammatory cells; necrotic debris

Cytological Features and Background Findings

FNAB of pediatric MSRCTs demonstrated characteristic cytological features according to tumor type. Ewing's sarcoma exhibited "rosette formation, nuclear moulding, branching capillaries, scant eosinophilic matrix, and chromatin streaks" with a background of "erythrocytes; inflammatory cells." Neuroblastoma and retinoblastoma showed "nuclear moulding and chromatin streaks," with additional "rosette formation" in neuroblastoma; their backgrounds consisted of "erythrocytes" or "inflammatory cells; neutrophils." Rhabdomyosarcoma and nephroblastoma demonstrated "nuclear moulding, chromatin streaks" with a background of "erythrocytes," whereas osteosarcoma was characterized by "pleomorphic cells with eccentrically placed nuclei and bluish cytoplasm" with "eosinophilic matrix; erythrocytes." Non-Hodgkin lymphoma and lymphoblastic lymphoma were defined by "lymphogranular bodies and chromatin streaks" with a "relatively clean background." Meanwhile, other entities such as poorly differentiated carcinoma, sialoblastoma, metastatic carcinoma, and germ cell tumor revealed "pleomorphic cells with frequent mitoses, chromatin streaks, and eosinophilic matrix" with a background of "erythrocytes; inflammatory cells; necrotic debris" (Table 3).

Correlation Between FNAB and Histopathological Findings

Correlation between FNAB and histopathological findings in pediatric MSRCTs demonstrated a generally good concordance in identifying key characteristics, including nuclear size, degree of cellularity, and cell arrangement patterns (diffuse versus clustered). Ewing's sarcoma consistently showed small-to-medium-sized nuclei with hypercellularity and predominantly diffuse patterns, with only a minority of cases presenting in clusters. Neuroblastoma and retinoblastoma were characterized by medium-sized nuclei with hypercellularity and diffuse arrangements, whereas rhabdomyosarcoma exhibited medium-to-large nuclei with diffuse hypercellularity. Nephroblastoma displayed medium-to-large nuclei with moderate

cellularity, while osteosarcoma differed by demonstrating clustered arrangements with hypocellularity. Non-Hodgkin lymphoma showed variable nuclear sizes (ranging from small-to-medium to large) but consistently exhibited diffuse hypercellular patterns, while lymphoblastic lymphoma demonstrated small-to-medium nuclei with diffuse arrangements and moderate cellularity. Other entities, including poorly differentiated carcinoma, sialoblastoma, metastatic carcinoma, and germ cell tumor, predominantly (80%) exhibited small-to-medium-sized nuclei with diffuse patterns, although some cases showed clustered arrangements; approximately 40% demonstrated hypercellularity. Overall, these findings confirm that FNAB reliably reflects the principal cytological features observed in histopathology, although variations in cellularity and cell arrangement remain important distinguishing factors (Table 4).

DISCUSSION

The findings of this study demonstrated that between 2020 and 2024, a total of 24 cases of MSRCTs in children were identified at the hospital, with a relatively balanced sex distribution and a slight female predominance. Interestingly, the sharp increase in cases in 2023, which accounted for 50% of the total, may reflect improved clinical awareness, better diagnostic access, or possible local epidemiological variation. This temporal trend is consistent with reports from other referral centers in Southeast Asia, where rising MSRCT case numbers have often been associated with advances in cytological and immunohistochemical diagnostic facilities [9].

Analysis by tumor origin revealed a predominance of neurogenic tumors, with Ewing's sarcoma as the most frequent subtype. This finding is consistent with international literature, which identifies Ewing's sarcoma as one of the most common MSRCTs in children and adolescents. Nevertheless, the presence of other entities such as rhabdomyosarcoma, lymphoma, and rarer tumors, including sialoblastoma and metastatic carcinoma, highlights the heterogeneity of the MSRCT spectrum in pediatric populations. Thus, this diversity underscores the importance of a multimodal diagnostic approach, as cytological morphology alone is often insufficient to distinguish between subtypes [10, 11].

TABLE 4: Cytological characteristics of FNAB compared with histopathological findings in malignant round cell tumors.

Histogenesis	Cytological Findings
Ewing's Sarcoma	All cases (100%) demonstrated small-to-medium-sized nuclei. The majority (83.3%) exhibited hypercellularity with predominantly diffuse patterns, while a minority (1/6 cases) presented in clusters.
Neuroblastoma	Two-thirds of cases (66.7%) showed medium-sized nuclei with hypercellularity; most (2/3) demonstrated a diffuse arrangement.
Retinoblastoma	Characterized by medium-sized nuclei arranged diffusely with marked hypercellularity.
Rhabdomyosarcoma	All cases exhibited medium-to-large nuclei arranged diffusely with hypercellularity.
Nephroblastoma	Displayed medium-to-large nuclei arranged diffusely with moderate cellularity.
Osteosarcoma	Demonstrated medium-to-large nuclei predominantly arranged in clusters with hypocellularity.
Non-Hodgkin Lymphoma	Exhibited variable nuclear sizes (one small-to-medium, one medium-to-large, and one large); all cases showed diffuse arrangements with hypercellularity.
Lymphoblastic Lymphoma	Demonstrated small-to-medium-sized nuclei arranged diffusely with moderate cellularity.
Carcinoma (Poorly Differentiated), Sialoblastoma, Metastatic Carcinoma, Germ Cell Tumor	Most cases (80%) exhibited small-to-medium-sized nuclei, predominantly diffuse in pattern (4/5 cases), with one case showing a clustered arrangement; 40% demonstrated hypercellularity.

Cytomorphologic analysis of FNAB revealed that the diffuse pattern was the most common finding (45.8%), followed by rosette formation (16.7%) and alveolar/pseudoalveolar patterns (8.3%). The predominance of the diffuse pattern in Ewing's sarcoma, lymphoma, and nephroblastoma underscores its limited specificity, necessitating correlation with additional cytological features. In contrast, distinctive patterns such as rosettes in neuroblastoma and retinoblastoma, or alveolar arrangements in rhabdomyosarcoma, provided greater diagnostic value. Therefore, cytomorphologic patterns may serve as an initial clue, but confirmation requires integration with immunohistochemistry and histopathology [12, 13].

The cytological features observed in FNAB were consistent with classical descriptions. For example, nuclear moulding and chromatin streaks in neuroblastoma and retinoblastoma, or lymphogranular bodies in lymphoma, remain well-recognized hallmarks. Moreover, background elements also played an important role: the presence of erythrocytes and eosinophilic matrix in osteosarcoma, or necrotic debris in metastatic carcinoma, aided in differentiating entities with otherwise overlapping nuclear morphology. This emphasizes that FNAB evaluation should not only focus on tumor cells but also consider the cytological background [13, 14].

Correlation between FNAB and histopathology in this study demonstrated good concordance, particularly in nuclear size, cellularity, and cell arrangement. For instance, Ewing's sarcoma consistently showed small-to-medium nuclei with hypercellularity and diffuse patterns, in line with histopathological findings. Conversely, osteosarcoma exhibited a distinct clustered arrangement with hypocellularity, highlighting that variations in cellularity can serve as an important discriminator. Overall, FNAB proved reliable in reflecting the principal histopathological features, although it cannot replace examination of intact tissue [15, 16].

These findings carry important clinical implications, particularly in referral centers with limited resources. FNAB, with its high sensitivity in detecting nuclear patterns and cellularity, can serve as an effective initial screening tool. However, given the morphological overlap among entities, FNAB interpretation must always be correlated with immunohistochemical studies, such as CD99 and FLI1 expression in Ewing's sarcoma, or other more specific markers. Through such an integrative approach, diagnostic accuracy can be enhanced and therapeutic decisions expedited [16, 17].

Despite the consistency observed between FNAB and histopathology, several limitations should be acknowledged. The relatively small number of cases and the single-center design limit the generalizability of these findings. In addition, not all cases were supported by a complete immunohistochemical panel, which may reduce the strength of diagnostic confirmation. Future studies should therefore involve larger, multicenter cohorts and incorporate molecular techniques such as FISH or RT-PCR to detect specific translocations (e.g., EWSR1-FLI1 in Ewing's sarcoma). In this way, the validity of the findings will be strengthened and contribute more broadly to the global literature on pediatric MSRCTs.

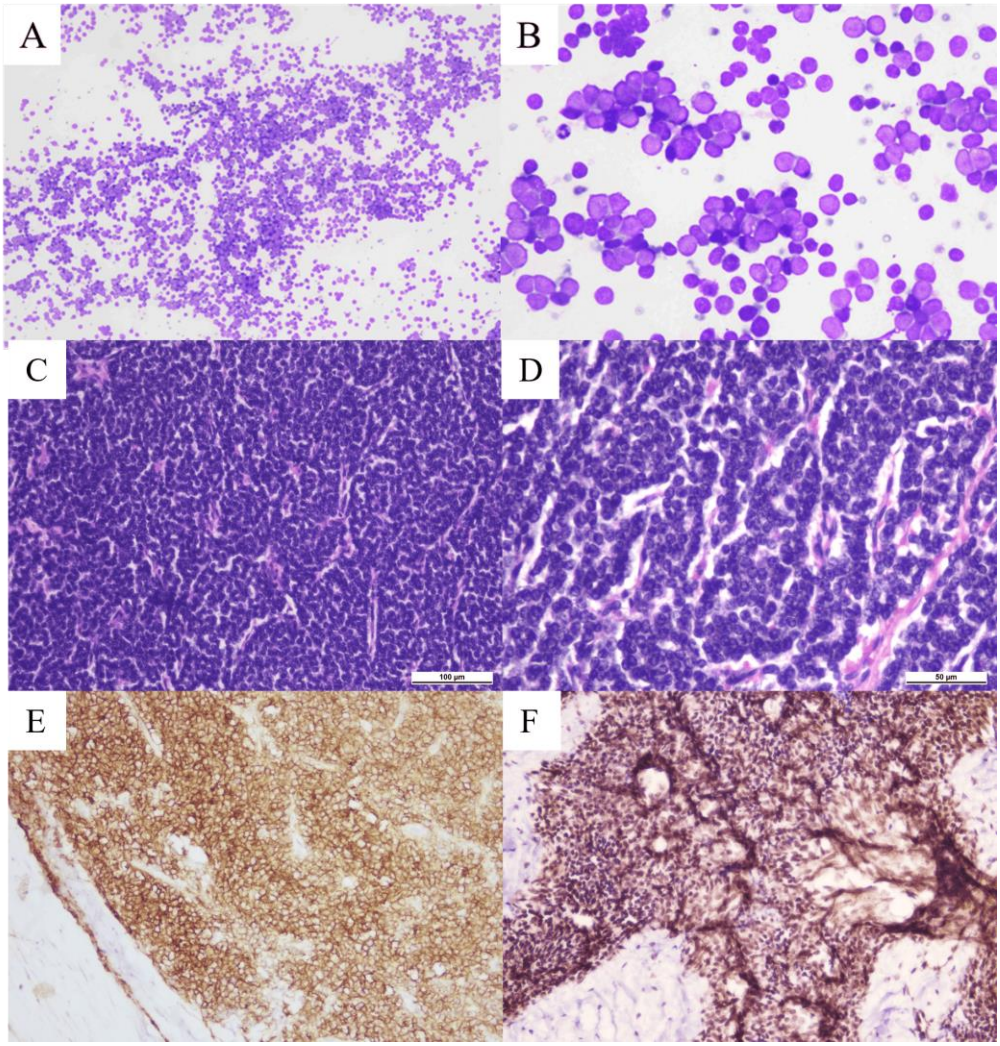

FIGURE 1: Microscopic features of Ewing sarcoma. (A) Magnification 100×; (B) Magnification 400×; (c) Histopathological features of Ewing sarcoma; (E) Immunohistochemistry positive for CD99; (F) Immunohistochemistry positive for FLI-1. Samples are taken from a 7-year-old female patient.

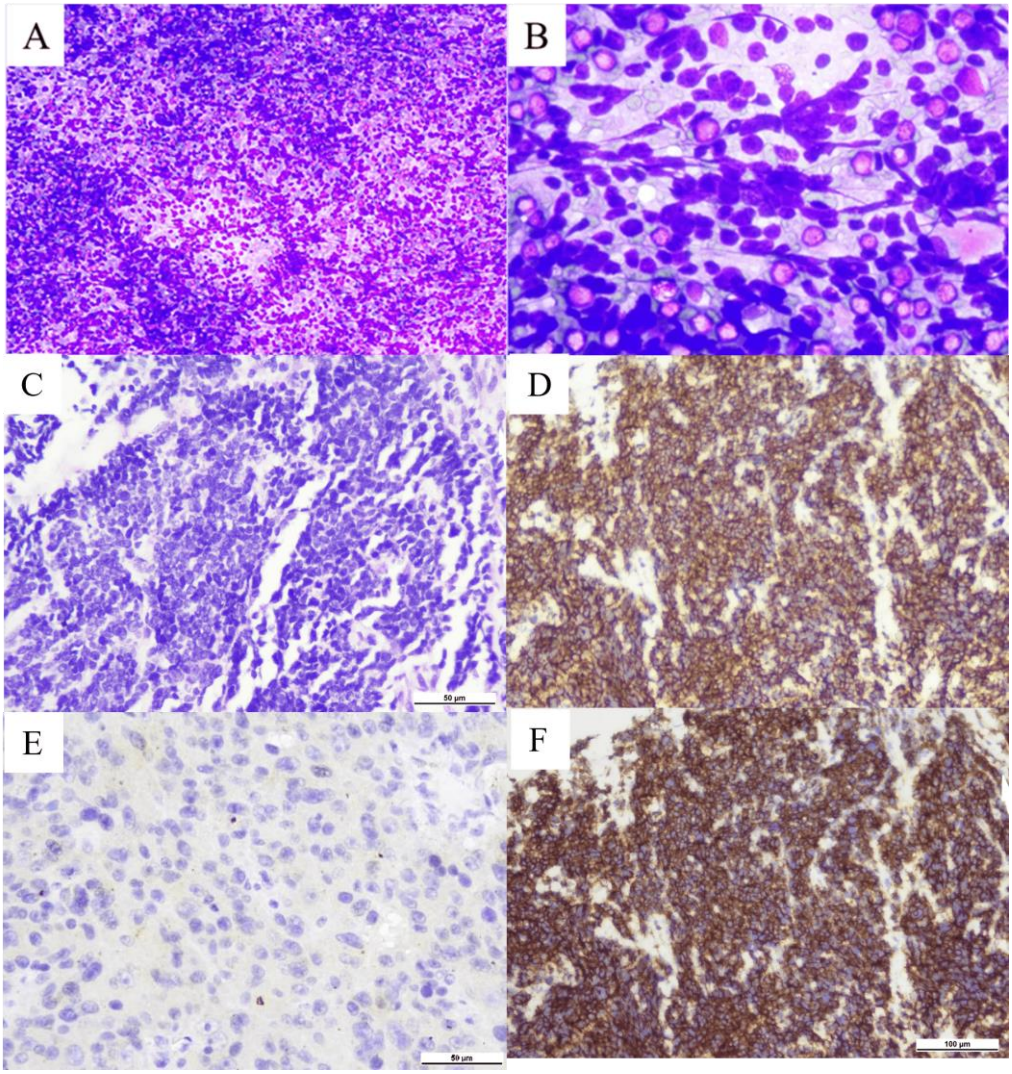

FIGURE 2: Microscopic features of neuroblastoma. (A) Magnification 100×; (B) Magnification 400×; (C) Histopathological features of neuroblastoma; (D) Immunohistochemistry positive for Synaptophysin; (E) Immunohistochemistry negative for CK; (F) Immunohistochemistry positive for Chromogranin. Samples are taken from a 2-year-old male patient.

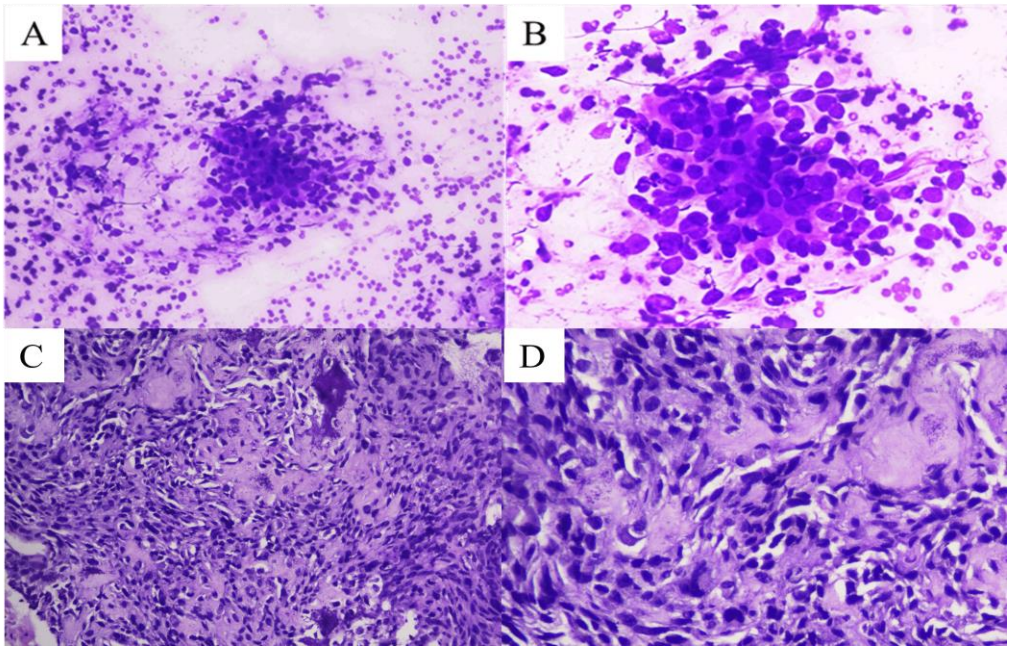

FIGURE 3: Microscopic features of osteosarcoma osteoblastic type from an 8-year-old male patient. (A) Magnification 200×; (B) Magnification 400×; (C,D) Histopathological features showed a tissue section with tumor growth consisting of proliferating anaplastic osteoblasts with round-oval nuclei, some eccentrically positioned, pleomorphic, hyperchromatic, moderately narrow cytoplasm, >20/10 HPF mitoses, embedded in a faint eosinophilic matrix that forms a lace-like pattern.

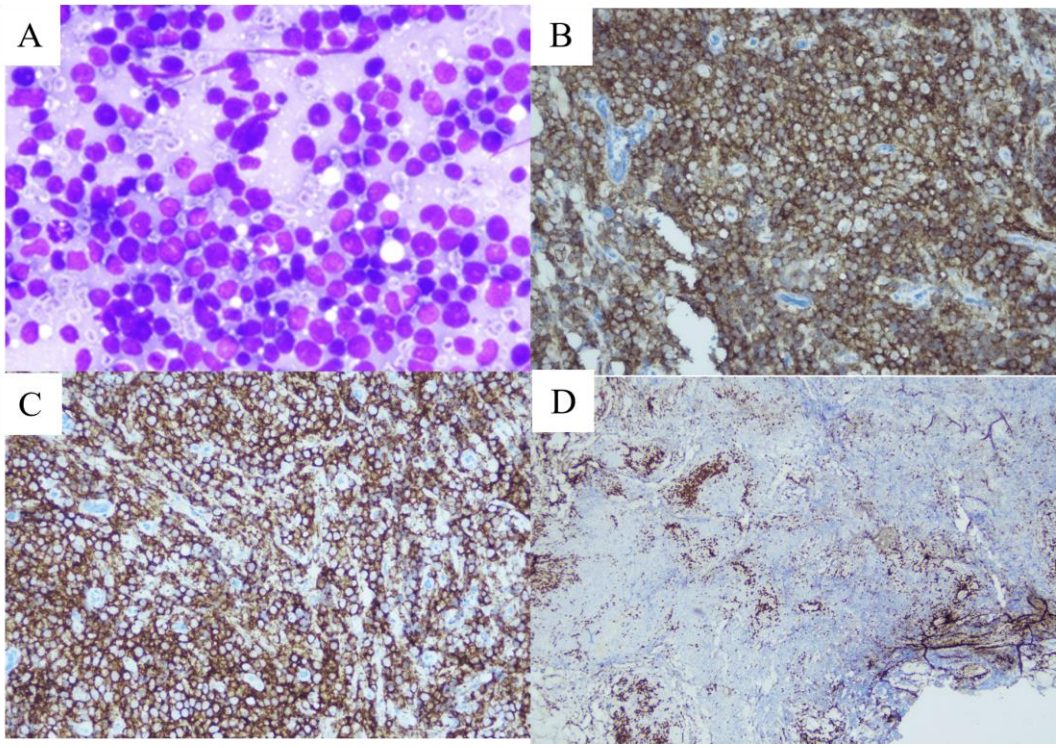

FIGURE 4: Microscopic features of Non-Hodgkin lymphoma (B-cell type). (A) The cytology section shows small-to-medium nuclei arranged diffusely with moderate cellularity. Magnification 400×; (B) Immunohistochemistry shows diffuse positivity for CD45; (C) Immunohistochemistry negative for CD20; (D) Immunohistochemistry negative for CD3, confirming B-cell lineage. Samples are taken from a 17-year-old male patient.

CONCLUSION

This study demonstrates that FNAB provides valuable cytological insights into pediatric MSRCTs, showing strong concordance with histopathological findings in terms of nuclear morphology, cellularity, and growth patterns. Neurogenic tumors, particularly Ewing's sarcoma, emerged as the most frequent subtype, while distinctive features such as rosette formation in neuroblastoma and retinoblastoma or alveolar arrangements in rhabdomyosarcoma enhanced diagnostic specificity. Nevertheless, the predominance of nonspecific diffuse patterns underscores the limitations of FNAB when used in isolation. Accordingly, integration with immunohistochemistry, especially CD99 and FLI1 for Ewing's sarcoma and, where available, molecular techniques, is essential to achieve diagnostic precision, optimize therapeutic decision making, and strengthen the evidence base for pediatric MSRCTs in both resource-limited and advanced clinical settings.

Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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