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*Original Article*

# Clinical usefulness of fine needle aspiration cytology in patients less than 20 years old: a 10-year experience at a single institution

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**Abstract:** The purpose of this study was to identify the spectrum of cytological diagnoses and evaluate the diagnostic effectiveness of fine needle aspiration cytology (FNA) in patients less than 20 years old. The subjects were selected by retrospectively reviewing records from 1999 to 2009. Selected patients less than 20 years old underwent FNA. Cytological and histological slides of samples from the subjects were reviewed. Our study included a total of 909 subjects with a mean age of 14.6 years. The majority of the FNA samples were taken from lymph nodes (n = 448, 49.3%), with the remaining aspirates obtained from the thyroid gland (n = 247, 27.2%), soft tissues of head and neck masses (n = 106, 11.7%), salivary glands (n = 75, 8.3%), breasts (n = 18, 1.9%), skins (n = 9, 1.0%) and soft tissues of extremity (n = 6, 0.7%). The majority (87.6%, n = 796) of the FNA samples were categorized as 'benign', with the remaining designated as 'atypical lesion' (n = 18, 2.0%), 'malignant' (n = 24, 2.6%), or 'inadequate specimen' (n = 71, 7.8%). FNA accuracy was 92% for diagnosing cancer. Specificity and sensitivity were 99% and 63%, respectively. Our study first revealed that FNA has a high specificity for diagnosing cancer in various anatomical locations in young patients and can be confidently used as an effective tool for diagnosing malignancies in young individuals with a clinically suspicious lesion.

**Keywords:** Fine needle aspiration, cytology, children and adolescents, sensitivity, specificity

## Introduction

Fine needle aspiration cytology (FNA) has been widely used to as a primary diagnostic tool to examine lymphadenopathy, thyroid nodules, salivary masses, head and neck masses, breast masses, and other lesions in adults. Due to its minimally invasive nature, FNA possesses some advantages over biopsy [1-4]. A small number of studies have recently described the feasibility of using FNA as an excellent modality for diagnosing head and neck lesions in pediatric populations [1, 2].

However, this technique is still not widely accepted for use in pediatric patients due to the unknown sensitivity of this modality and lack of experienced cytopathologists who are familiar with pediatric cytology smears [1, 2]. We analyzed FNA results for lesions of patients less than 20 years old in our hospital. Using this technique, we determined that individuals in our study cohort had a wide spectrum of diseases and evaluated the usefulness of FNA as a primary diagnostic tool. To the best of our knowledge, this is the first study to evaluate the ability of FNA to diagnose lesions in various organs of young patients less than 20 years old in a single institution although studies have been performed examining a single organ series in a pediatric population or various organs in a general population.

## Materials and methods

Subjects for this investigation were identified by retrospectively reviewing data from the Pathology Department of Kyoungpook National University Hospital, Daegu, Korea collected between 1999 and 2009. Our university hospital is a tertiary care institution. We selected patients 20 years old or younger for FNA evalu-

**Table 1.** Categorical or regional distribution of cytological diagnoses according to patient age

| | Age (years) | | | | Total N (%) |
|---|---|---|---|---|---|
| | ≤ 5 (%) | ≤ 10 (%) | ≤ 15 (%) | ≤ 20 (%) | |
| Category | | | | | |
| Benign | 68 (87.2) | 92 (89.3) | 213 (90.3) | 424 (86.2) | 797 (87.7) |
| Atypical | 2 (2.6) | 0 (0.0) | 6 (2.8) | 9 (1.8) | 17 (1.9) |
| Malignant | 3 (3.8) | 3 (2.9) | 3 (1.3) | 15 (3.1) | 24 (2.6) |
| Inadequate | 5 (6.4) | 8 (7.8) | 14 (5.9) | 44 (8.9) | 71 (7.8) |
| Anatomical site | | | | | |
| Lymph node | 50 (64.1) | 60 (58.3) | 129 (54.7) | 209 (42.5) | 448 (49.3) |
| Thyroid gland | 1 (1.3) | 8 (7.8) | 56 (23.7) | 182 (37.0) | 247 (27.2) |
| ST of HN* | 14 (17.9) | 25 (24.3) | 24 (10.2) | 43 (8.7) | 106 (11.7) |
| Salivary gland | 7 (9.0) | 10 (9.7) | 20 (8.5) | 38 (7.7) | 75 (8.3) |
| Breast | 0 (0.0) | 0 (0.0) | 3 (1.3) | 15 (3.1) | 18 (2.0) |
| Skin | 3 (3.9) | 0 (0.0) | 3 (1.3) | 3 (0.6) | 9 (1.0) |
| ST of Ext† | 3 (3.9) | 0 (0.0) | 1 (0.4) | 2 (0.4) | 6 (0.7) |
| Total (N) | 78 | 103 | 236 | 492 | 909 |

*Soft tissue of the head and neck, †Soft tissue of an extremity.

ation to diagnose their clinically palpable masses.

For FNA, the palpable mass was stabilized with digital palpation and the overlying skin was cleaned with an alcohol swab. We usually did not induce general or local anesthesia. Experienced cytopathologists performed the aspiration using a 23 G needle attached to a 10 mL syringe. The aspirates were expelled onto glass slides and smeared. The smear was air-dried and stained with Diff-Quik (or Giemsa) to assess the adequacy of the specimens. Four to five smears were immediately fixed in 95% ethanol and stained using the Papanicolaou method for final diagnostic evaluation. The needle and syringe were then rinsed in formalin for cell block preparation. When necessary for diagnosis, special or immunohistochemical staining was performed on the cell blocks. The smears were diagnosed by cytopathologists who obtained the aspirates.

We reviewed the FNA cytology smears and subsequent histology sections recovered from the subjects. The samples were categorized according to the final cytological diagnosis as 'inadequate specimen', 'benign', 'atypical lesion', or 'malignancy'. Sensitivity, specificity, negative and positive predictive values, and accuracy of the FNA were calculated based on the histopathological diagnoses.

## Results

Nine hundred and nine patients with a mean age of 14.6 years (8 months to 20 years) were included in this study, and included 504 females and 405 males. The subjects were divided according to age at 5-year intervals. Ulti-mately, the current study included 78 patients 0 to 5 years old, 103 patients 6 to 10 years old, 236 patients from 11 to 15 years old, and 492 patients 16 to 20 years old. The majority (87.6%) of FNA samples were categorized as 'benign' with the remaining classified as 'atypical lesion' (2.0%), 'malignant' (2.6%), or 'inadequate specimen' (7.8%). The majority of the FNA samples were taken from lymph nodes (n = 448, 49.3%) while the remaining aspirates were obtained from the thyroid (n = 247, 27.2%), soft tissues of head and neck masses (n = 106, 11.7%), salivary glands (n = 75, 8.3%), breast (n = 18, 1.9%), skin (n = 9, 1.0%) and soft tissues of extremities (n = 6, 0.7%). **Table 1** presents the categorical or regional distribution of cytological diagnoses according to age.

The most common diagnoses based on the FNA samples obtained from the lymph node was benign reactive lymphoid hyperplasia (n = 281, 62.7%) followed by necrotizing lymphadenitis (n = 62, 13.8%), and chronic granulomatous inflammation (n = 39, 8.7%). One hundred and eighty (72.9%) aspirates from the thyroid glands were diagnosed as nodular hyperplasia with the remaining identified as follicular tumors (n = 26, 10.5%), papillary carcinoma (n = 14, 5.7%), atypical lesion (n = 6, 2.4%), Hashimoto's thyroiditis (n = 5, 2.0%), and medullary carcinoma (n = 1, 0.4%). Aspirates of soft tissues in head and neck lesions were most commonly diagnosed as benign cystic lesions (n = 52, 49.1%); the second most common diagnosis was acute inflammation (n = 16, 15.1%). In salivary gland, pleomorphic adenoma (n = 24, 32%) was the most common disorder followed by benign lesions (n = 18, 24%)

**Table 2.** Cytological diagnoses for various anatomic locations

| Cytological diagnosis | Number (N) | % |
|---|---|---|
| Lymph node | 448 | |
| Benign reactive lymphoid hyperplasia | 281 | 62.7 |
| Necrotizing lymphadenitis | 62 | 13.8 |
| Chronic granulomatous inflammation | 39 | 8.7 |
| Benign, non-specific | 15 | 3.4 |
| Acute inflammation | 11 | 2.5 |
| Atypical lesion | 9 | 2 |
| Malignant lymphoma | 6 | 1.3 |
| Hemangioma | 1 | 0.2 |
| Malignant lesion | 1 | 0.2 |
| Papillary carcinoma, metastatic | 1 | 0.2 |
| Inadequate specimen | 22 | 4.9 |
| Thyroid gland | 248 | |
| Nodular hyperplasia | 180 | 72.9 |
| Follicular tumor | 26 | 10.5 |
| Papillary carcinoma | 14 | 5.7 |
| Atypical lesion | 6 | 2.4 |
| Hashimoto's thyroiditis | 5 | 2.0 |
| Medullary carcinoma | 1 | 0.4 |
| Inadequate specimen | 15 | 6.1 |
| Soft tissue of the head and neck | 106 | |
| Benign cyst | 52 | 49.1 |
| Acute inflammation | 16 | 15.1 |
| Hemangioma | 5 | 4.7 |
| Pilomatricoma | 4 | 3.8 |
| Mucocele | 2 | 1.9 |
| Chronic inflammation | 2 | 1.9 |
| Adenoid cystic carcinoma | 1 | 0.9 |
| Atypical lesion | 1 | 0.9 |
| Calcifying epithelioma | 1 | 0.9 |
| Inadequate specimen | 22 | 20.8 |
| Salivary gland | 75 | |
| Pleomorphic adenoma | 24 | 32.0 |
| Benign | 18 | 24.0 |
| Chronic inflammation | 16 | 21.3 |
| Acute inflammation | 4 | 5.3 |
| Benign lymphoid hyperplasia | 2 | 2.7 |
| Hemangioma | 2 | 2.7 |
| Mucocele | 2 | 2.7 |
| Pilomatricoma | 1 | 1.3 |
| Warthin's tumor | 1 | 1.3 |
| Neurilemmoma | 1 | 1.3 |
| Inadequate specimen | 4 | 5.3 |

including epidermal cysts, brachial cleft cysts, and non-diagnostic benign lesions. The cytological diagnoses obtained for our FNA samples are summarized in **Table 2**. Overall, the most common diagnosis was benign reactive lymphoid hyperplasia of the lymph node followed by nodular hyperplasia of the thyroid gland. Papillary carcinoma of the thyroid gland was the most common malignancy while the next most common disorder was malignant lymphoma.

Excision biopsy after FNA was performed for 182 cases (20%). Out of these, 75.3% and 24.7% of the specimens were histopathologically confirmed as benign or malignant lesions, respectively. The atypical category included 10 cases involving the lymph nodes, six cases involving the thyroid, one case involving soft tissues of the head and neck, and one case involving soft tissues of an extremity. Out of 28 cases, 11 requiring surgical follow-up consisted of six cases involving the lymph nodes, four cases involving the thyroid, and one case involving the soft tissue of an extremity. These were histopathologically diagnosed as benign (n = 4, 36%) or malignant (n = 7, 64%) lesions.

Excluding the 24 cases of atypical lesions, ones for which inadequate specimens were recovered, and indeterminate cases, the accuracy of FNA was 92% for determining a cytological diagnosis of cancer based on the histopathological diagnosis. Sensitivity and specificity were 63% and 99%, respectively. Positive and negative predictive values were 95% and 91%, respectively. Results of the overall and organ-specific statistic analyses are summarized in **Table 3**.

## Discussion

FNA in the current study was more frequently performed in older children. Our study revealed that the most common diagnostic category, based on FNA findings, was 'benign' (n = 796, 87.6%) for all age groups. The majority of cases of FNA were obtained from lymph nodes followed by thyroid gland, head and neck masses, salivary gland and soft tissue. The most common cytological diagnosis was benign reactive lymphoid hyperplasia followed by nodular

**Table 3.** Diagnostic effectiveness of FNA for various anatomical locations

| | Accuracy (%) | Specificity (%) | Sensitivity (%) | PPV[‡] (%) | NPV[§] (%) |
|---|---|---|---|---|---|
| Lymph node | 86 | 97 | 38 | 75 | 87 |
| Thyroid gland | 90 | 100 | 76 | 100 | 86 |
| ST of HN[*] | 100 | 100 | 100 | 100 | 100 |
| Salivary gland | 93 | 93 | 0 | Not available | 93 |
| Breast, ST of ext[†], Skin | 100 | 100 | Not available | Not available | 100 |

[*]Soft tissue of the head and neck, [†]soft tissue of an extremity, [‡]positive predictive value, [§]negative predictive value.

**Table 4.** Comparison of the findings from our study and previous investigations evaluating FNA as a diagnostic tool

| Reports | Specificity | Sensitivity | Accuracy |
|---|---|---|---|
| General population | | | |
| Flynn et al. | 99 | 82 | 91.4 |
| Fiere et al. | 91.6 | 70 | 85.3 |
| Young et al. | 97.1 | 91.5 | 94.5 |
| Platt et al. | - | - | 91 |
| Franco et al. | 100 | 86.4 | 93.6 |
| Pediatric population | | | |
| Chang et al. | 63 | 100 | 81 |
| Byun et al. | 96 | 86 | - |
| Mobley et al. | 97.1 | 94.4 | - |
| Our study | 99 | 63 | 92 |

hyperplasia of the thyroid gland, necrotizing lymphadenitis, and chronic granulomatous inflammation. In the current study, FNA produced one false positive and 12 false negative results and FNA was found to have a diagnostic accuracy of 92%, 63% sensitivity, and 99% specificity.

The distribution of cytological diagnoses in our study was very similar to those of previous reports [1, 5], except that chronic granulomatous inflammation in lymphadenopathy was identified in up to 8.7% of cases. The most common cause of lymphadenopathy in pediatric populations is benign reactive lymphoid proliferation due to a self-limiting viral infection or inflammatory reaction and chronic granulomatous inflammation is usually rare [5, 6]. The high rate of chronic granulomatous inflammation identified in current study may be due to the fact that tuberculosis is endemic in South Korea. In contrast to adult lesions [6, 7] which have a high malignancy rate (13% to 48%) with metastatic carcinoma as the most common malignant lesion, our study revealed that the malignancy rate of young patients less than 20 years old was relatively low (2.6%) while both thyroid papillary carcinoma and malignant lymphoma were the most typical malignant lesions. Inadequate specimens were collected for 7.8% of all cases (see **Table 1**), similar to the proportion reported in previous studies (3% to 7%) [1, 3, 5].

FNA has been widely accepted as a useful, convenient, and cost-effective diagnostic tool for adult patients with some advantages over open biopsy [1, 4, 8]. A small number of studies have described the usefulness of FNA for diagnosing head and neck lesions in children and adolescents [1, 2]. However, FNA has still not been broadly accepted for use in pediatric populations due to the unknown sensitivity of this technique along with lack of familiarity with pediatric cytology smears and difficulties with obtaining sufficient aspirates associated with inadequate patient control [1, 2, 4, 9]. According our analysis which performed to evaluate the diagnostic usefulness of FNA in patients less than 20 years old, the FNA accuracy and specificity observed in the current study were very similar to the rates reported in some studies which described the diagnostic effectiveness of FNA in pediatric patients [3, 5, 10-18] or in general patient populations [19]. However, the sensitivity we observed was slightly lower than that found in previous studies. **Table 4** details the comparison of our study results with those of other reports.

In the current investigation, most false negative findings were obtained from the lymph node and thyroid gland. When analyzing the 12 false negative cases (five involving the lymph node, five involving the thyroid glands, and two involving the salivary gland), four were cytologically diagnosed as thyroid adenomatous hyperplasia (three) and lymphoid reactive hyperplasia (one). Surgical follow-up identified follicular carcinoma (three) and metastatic thyroidal papillary

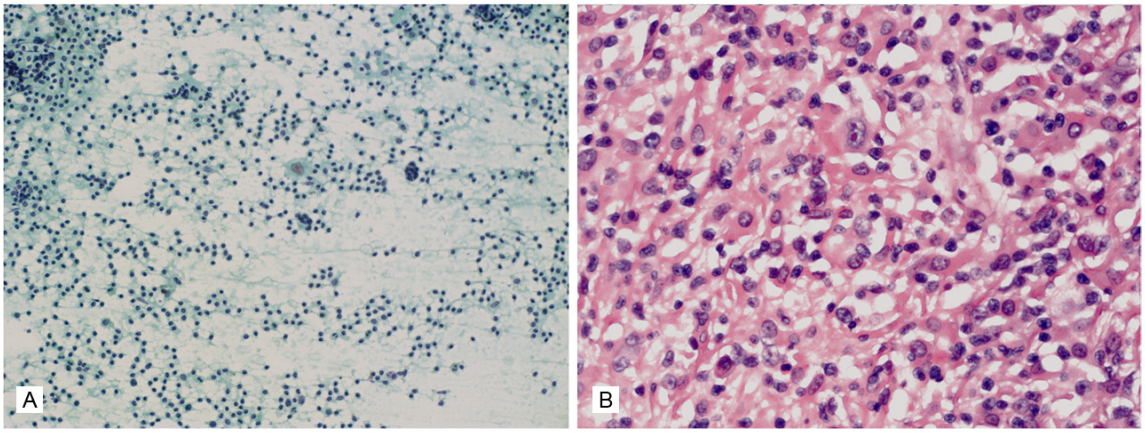


**Figure 1.** Cytological and histological findings from a 5-year-old girl with cervical lymphadenopathy. A: Smear showing various reactive inflammatory cells and a large mononuclear cell that seems to be a Hodgkin cell (Papanicolaou stain, 200x magnification). The patient was misdiagnosed as having reactive lymphoid hyperplasia because diagnostic Reed-Sternberg (R-S) cells were not identified in the smear and scattered large mononuclear cells with acidophilic nucleolus were scanty. B: Histological section showing mononuclear R-S cell variants (Hodgkin cells) and diagnostic R-S cells with two large nuclei along with a large amount of eosinophilic cytoplasm. R-S and Hodgkin cells are mixed with lymphocytes, neutrophils, eosinophils, and histiocytes (hematoxylin and eosin stain, 400x magnification).

carcinoma (one), respectively. When reviewing the smears, all four cases had cytological findings insufficient for typical histological diagnosis. When these four cases were excluded, FNA sensitivity increased up to 71%.

When closely examining lymph node FNA results with low sensitivity in the current study, the four cases which were cytologically misdiagnosed as benign reactive lymphoid hyperplasia were histologically identified as unspecified peripheral T cell lymphoma (one case) and Hodgkin's lymphoma (three cases). Although the smears were retrospectively reviewed after histological evaluation, it was difficult to diagnose these cases as malignant lymphoma because all smears were composed of mixed inflammatory cells with minimal or absent nuclear atypia and scanty large atypical cells. Generally, lymph nodes are notorious as one of the most difficult organs to evaluate with cytopathology. Some types of lymphomas are so rare that they may be not encountered during a general pathologist's career and cytological sampling can be inadequate for diagnosing partial lymph node involvement or fibrosis [20, 21]. Identifying T cell or small cell lymphomas is usually more difficult than B cell or large cell lymphomas; thus, diagnostic sensitivity of cytological-based methods is very dependent on the relative cellular composition of lymphoma lesions. In addition, the difficulty of diagnosis is increased for lower grade lymphoma with a minimal degree of cytologic atypia or Hodgkin's lymphoma with scanty Reed-Sternburg cells, similar to cases in our study that were misdiagnosed based on cytological evidence (see **Figure 1**). To overcome these difficulties and improve diagnostic sensitivity, the use of ancillary tools (molecular techniques, flow cytometry, fluorescence *in situ* hybridization, and immunohistochemistry) is important when dealing with lymph nodes. It may also be very helpful to contact a lymph node specialist.

Statistical findings from the current and previous studies [3, 5, 11, 19] demonstrated that FNA has high specificity and can be confidently used as a tool for diagnosing malignancies in young patients with a clinically suspicious lesion, thereby avoiding unnecessary invasive surgical procedures. Although this is first study to reveal that FNA has a high specificity and accuracy for diagnosing cancer in various anatomical locations in young patients, considering the low sensitivity observed in our study, both cytopathologists and clinicians should be aware that a relatively large number of false negative diagnoses can be obtained by FNA. Frequent communication between the pathologists and attending physicians is essential to obtain a correct diagnosis using FNA. In addition, cytopathologists should be familiar with

pediatric smears, and make accurate diagnoses through the additional use of ancillary tools and adequate consultation with specialists.

## Disclosure of conflict of interest

None.

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