

Citologia su agoaspirato nelle linfadenopatie superficiali in età pediatrica

Fine-needle aspiration cytology in children with superficial lymphadenopathy

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Abstract

Introduction: In pediatric population Fine-Needle Aspiration Cytology (FNAC) is slowly gaining acceptance in clinical management of Superficial Lymphadenopathy (SL). Our experience adds some data about the usefulness of this technique in diagnosing the cause of a SL and therefore guiding further treatment.

Patients and Methods: 238 FNAC were performed in 217 patients with SL, observed at our Institution from 2002 to 2006. The neck was the most frequent localization. The results were available within few hours. In cases of granulomatous findings, the samples were processed for microbiological and PCR test, in order to identify Mycobacteria.

Results: 174 were reactive lesions, 38 granulomatous lymphadenopathies, 24 malignant lesions, 2 specimens inadequate for diagnosis. Among the 174 reactive SL, 22 required an incisional biopsy after 1 month follow-up. Among the granulomatous lymphadenopathies, 13 children with Cat-Scratch Disease recovered, 25 with Mycobacteria infection underwent surgical excision. For 24 malignant lesions, the diagnosis was confirmed by further biopsy. Two false negative and no false positive were detected (sensitivity 92%, specificity 100%). No complications were encountered.

Conclusions: In our experience FNAC, performed by experienced cytopathologist, has revealed to be a fast, safe, non invasive and inexpensive method to achieve diagnosis in persistent SL. The

use of FNAC gave us the possibility to select patients for further investigation and/or surgical treatment. Incisional biopsy remains necessary to confirm the diagnosis in case of malignancy or doubtful lesions.

Riassunto

La Citologia su Ago-Aspirato (FNAC) sta lentamente ottenendo consensi nella gestione clinica delle linfadenopatie superficiali in età pediatrica. Nella nostra esperienza (238 procedure su 217 bambini in 4 anni) si è dimostrata essere un'importante strumento per discriminare lesioni neoplastiche da lesioni infettive, spesso anche consentendo la discriminazione tra linfadeniti acute e croniche da Micobatteri Atipici, consentendo quindi di programmare in maniera ottimale il successivo trattamento chirurgico.

Introduction

Swollen lymph nodes are quite a frequent event in pediatric age, and they often become the reason for a pediatric consultation. Causes may range from an infectious process, acute or chronic, to a malignant disease.

The first step is often represented by the pediatrician, and sometimes a detailed history and clinical examination are sufficient to give rise to a diagnostic suspicion. Anyway, in case of doubtful or persistent enlarged lymph nodes diagnosing represents a challenge for physicians. Other exams such as blood test (Lymphocytes Count, C-reactive protein (CRP), LAD dosage, immunologic assessments) and US scan can be useful. But in most cases, FNAC could play a major role as first line screening method^{1,2} as it allows us to obtain a cytological specimen directly from the swelling.

However, the use of FNAC in pediatric population has not yet been accepted worldwide for two reasons: the first because cytopathologists believed that cytomorphologic features are different in pediatric lesions as compared to those found in adults and secondly,

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because the interpretation of FNAC results could prove to be difficult and inconclusive.

In order to make a contribution to the literature on this subject, we have analyzed the results from a series of patients, observed in our Institution, who underwent FNAC for SL.

Patients and methods

We have evaluated the accuracy of this technique in a group of children with superficial lymphadenopathy who were observed at our Pediatric Surgery tertiary referral centre from July 2002 to May 2006. Patients were sent by the family physician or the family paediatrician, or by the paediatrician working at our emergency care unit sometimes consulted directly by parents facing a new-discovered neck swelling. The first clinical screening consisted in an accurate historical and clinical examination: sometimes patients underwent previous blood tests or US scans, so the decision to make a step over and go on with FNAC was easier to take.

The clinical suspicion was toward an acute infection in case of recent onset, with a firm, tender adenopathy, with or without warm and erythematous skin. In this case the search for a bacterial entry site was performed (upper respiratory airways in case of cervical adenopathy; extremities injuries in case of axillar or inguinal adenopathies). On the contrary, FNAC was considered useful in doubtful cases, especially if:

- Swelling was clinically persistent after more than 2 weeks of clinical observation or after more than 2 weeks from the onset of symptoms referred by patient or parents;
- Lymph-node dimensions, compared to the age of the patient, were: ≥ 2 cm if localized in the neck or axilla, ≥ 1 cm if supraclavicular, ≥ 2 cm if inguinal;
- Absence of local or systemic clinical signs of acute inflammation (fever, pain, skin hyperaemia).

US Scan and blood tests (lymphocytes count, CRP), Quantiferon plasmatic dosage of IgM and IgG for *Bartonella henselae*, Epstein-Barr Virus) were performed; however US Scan resulted to be much more significant to describe the physical findings of the lymphadenopathies.

FNAC was performed by a skilled cytopathologist using two techniques: Fine Needle Aspiration (FNA) and Fine Needle Sampling (FNS). The procedures were performed without any sedation and the preparation of each patient was the identical. In most cases a local anaesthetic cream (mixed lidocaine 2.5% and prilocaine 2.5%) was applied between 60 and 90 minutes before the procedure. When required, the sampling was guided by an ultrasound scan. In both techniques the lymph node was immobilized by one hand and the skin disinfected.

The FNA technique involved aspiration of the cell samples through a needle introduced into the lymph-node by applying negative pressure created by a syringe. The calibre of the needle varied between 23 and 27 gauge. The aspirated tissue was dropped onto a glass slide, spread, air dried and stained with May-Grunwald-Giemsa stain. The

aspiration was usually repeated, if a microbiological examination was called for or if the first sampling seemed inadequate.

The FNS technique, with a thinner needle (27 gauges), was mainly employed when the structure of the lymph node was solid. To obtain adequate cellular sample, the needle was moved back and forth very slightly whilst angled in different directions and depths within the lymph-node before being withdrawn.

The sample obtained was detached by the cutting edge of the needle and conducted into the lumen by capillary force. The needle was removed and connected to a syringe filled with air. The material was expelled onto a glass slide and prepared using the same technique described above.

The Pathologist decided the number of samples to be taken during the procedure. Median number of punctures was 2 per patient: if the aspirated material was sufficient for both cytological examination and microbiological researches one was considered to be enough, otherwise the exam was repeated two or three times.

Verbal preliminary results were available within few hours after the biopsy. Definitive written results were ready within 24-48 hours, especially if a neoplastic lesion was present. In the granulomatous lymphadenitis the results needed a microbiological confirmation.

Results

238 FNAC aspirates were performed in 217 patients; 126 males and 91 females, aged between 3 months and 17 years (median age of 7.5 years).

The neck was the most involved site (94%) the others were axillar (4%) and inguinal localizations (2%).

Various ancillary studies were carried out using the same sample to yield a highly specific diagnosis. These include culture methods, acid-fast bacteria staining, immunocytochemistry, cytogenetics, flowcytometry, electron microscopy and Polymerase Chain Reaction (PCR) for *Mycobacteria*.

An acute reactive lymphadenitis was detected in 174 cases (73%), a chronic granulomatous lymphadenitis in 38 cases (16%), a malignant lesion in 24 cases (10%). In 2 cases (1%) the specimens were inadequate.

The 174 lesions diagnosed as reactive lymphadenitis were followed up as outpatients to control their development. Figure 1 resumes the results.

Of these, 152 cases (87%) healed spontaneously, whilst 22 (13%) required further investigation as they did not show any signs of spontaneous resolution at one month follow up or if they had demonstrated some clinical alteration such as increased volume or consistency. An incisional biopsy was performed in all 22 cases. In 20 of 22 cases a sub-chronic reactive lymphadenitis was diagnosed, whilst in 2 cases a lymphoma (1 Hodgkin Disease and 1 Anaplastic Large T-Cells Lymphoma) was found.

The 38 granulomatous lymphadenopathies were further investigated using microbiological tests. Atypical *Mycobacteria* was found in 25 cases (66%), while the remaining 13 (34%) were Cat-Scratch

Disease that healed spontaneously without any further medical or surgical therapy. Atypical Mycobacteria were treated with a planned complete excision of the involved lymph nodes.

Malignancy was diagnosed in 24 patients by FNAC. These data were confirmed by a surgical biopsy in 13 of the 24 cases or by a bone marrow biopsy in the remaining 11 cases where a haematological malignancy was suspected.

The 2 cases with inadequate specimen underwent a surgical biopsy and an acute reactive lymphadenitis was detected.

No complications followed the FNAC aspirates.

Discussion

Palpable lymph nodes are a very frequent occurrence in the pediatric population even in absence of systemic illness or infection (about 55%).⁴ Blood tests and imaging evaluations may be helpful but rarely do they complete the diagnosis especially when the enlarged nodes are not clearly inflammatory. In some cases an antibiotic therapy is given, but if the lesion persists, a histological evaluation is mandatory.⁵ Since the first report in literature in 1961,⁶ clinicians have progressively increased their confidence in this rapid and minimally invasive diagnostic technique. The utility of FNAC in diagnosing superficial lesions is now assessed through important clinical studies and reviews, especially for thyroid nodules,⁷ breast cancer and other neoplastic lymphadenopathies. In paediatric patients, there has been some resistance to the spread of this technique, particularly due to the characteristics of paediatric lesions. But over the years, many experiences have been reported in literature^{8,9,10} leading to the technique becoming widely used in the evaluation of peripheral lymphadenopathies.

The main reason for performing a FNAC in a persistent lymphadenopathy is to exclude a malignant disease. The incidence of a malignant cervico-facial lesion in children is much lower than in adults (4-5%),¹¹ but this possibility has to be excluded. It is not uncommon for children to present for evaluation of a mass, especially in the head and neck region. The majority of these lesions are inflammatory in nature, but malignant neoplastic lesions are included in the possible aetiologies, even if rare. Primary head and neck lesions account for 5% of these cancers, while 70% of head and neck malignancies are represented by lymphoreticular malignancies (Lymphomas) and Soft Tissue Sarcomas (Rhabdomyosarcoma is the most common in children).¹² Neuroblastoma is the most common solid malignant tumour in infants less than a year old.

A lesion may not necessarily be homogeneous, and with FNAC only a small portion of any mass is sampled. Consequently any needle biopsy may miss the true lesion in a bloody, necrotic, or fibrotic mass.¹³ FNAC also is unable to give a specific diagnosis if the histological architecture has to be defined.

Moreover, FNAC requires not only a very experienced cytopathologist, but also a close relationship with the clinician in order to obtain the detailed history, and to assist the cytopathology in palpating the lesion or helping during an US guided FNAC. A skilled

cytopathologist should be able to make an immediate evaluation of the quality of the direct sample and also to give a preliminary diagnosis.³ In our experience the adoption of FNAC as first diagnostic tool for patients with SL that have lasted more than two weeks without infectious signs, has been shown to be worthwhile. FNAC showed a sensitivity of 92% with only 2 false negatives and a specificity of 100% with any false positives. A surgical biopsy was found to be necessary in concluding the diagnosis in only 10% of patients: 24 cases of 238 performed FNAC (22 persistent reactive lymphadenopathies and 2 inadequate samples).

Reported complications are ecchymosis, hematoma, a draining sinus tract, tumor tracking. However we did not encounter any important adverse effects, as reported by Ramadan and Buchino.^{11,14}

We believe that FNAC should be the first step in the diagnostic process of a persistent SL, due to its inherent safety, simplicity, rapidity and high cost-effectiveness.

References

- Rapkiewicz A, Thuy Le B, Simsir A, et al. Spectrum of head and neck lesions diagnosed by fine-needle aspiration cytology in the pediatric population *Cancer* 2007;111(4):242-51.
- Koo V, Lioe TF, Spence RA. Fine needle aspiration cytology (FNAC) in the diagnosis of granulomatous lymphadenitis *Ulster Med J*. 2006;75:59-64.
- Liu ES, Bernstein JM, Sculerati N, et al. Fine needle aspiration biopsy of pediatric head end neck masses *Int J Pediatr Otorhinolaryngol*. 2001;60:135-40.
- Park YW. Evaluation of neck masses in children *Am Fam Physician* 1995;51:1904-12.
- Knight PJ, Muline AF, Vassy LE. When is lymph node biopsy indicated in children with enlarged peripheral nodes? *Pediatrics* 1982;69(4):391-6.
- Cavaroc M, Terrasse J. Pathological cytology and puncture biopsy with the fine needle *Sem Hosp*. 1961;37:1469-71.
- Lundgren CI, Zedenius J, Skoog L. Fine-needle aspiration biopsy of benign thyroid nodules: an evidence-based review *World J Surg*. 2008;32:1247-52.
- Layfield LJ, Reichman A. Fine needle aspiration cytology: utilization in pediatric pathology *Dis Markers* 1990;8:301-15.
- Gamba PG, Messineo A, Antonello LM, et al. A simple exam to screen superficial masses: fine-needle aspiration cytology *Med Pediatr Oncol*. 1995;24:97-9.
- Ponder TB, Smith D, Ramzy I. Lymphadenopathy in children and adolescents: role of fine-needle aspiration in management *Cancer Detect Prev*. 2000;24:228-33.
- Buchino JJ, Jones VF. Fine needle aspiration in the evaluation of children with lymphadenopathy *Arch Pediatr Adolesc Med*. 1994;148:1327-1330.
- Anderson GJ, Tom LW, Womer RB, et al. Rhabdomyosarcoma of the head and neck in children *Arch Otolaryngol Head Neck Surg*. 1990;116:428-31.
- Wakely PE Jr. Merits of fine-needle aspiration biopsy in children: head and neck *Diagn Cytopathol*. 1992;8:299-301.
- Ramadan HH, Wax MK, Boyd CB. Fine-needle aspiration of head and neck masses in children *Am J Otolaryngol*. 1997;18:400-4.