Fine needle aspiration cytology and bethesda system: are they absolutely reliable in surgery?

İnce iğne aspirasyon sitolojisi ve bethesda sistemi: Cerrahide kesinlikle güvenilir mi?

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Özet

Giriş: Tiroid nodülü olan hastalar için ince iğne aspirasyonu (İİA) önemli bir tetkiktir. Bethesda sistemindeki 5 yıllık deneyimimizi retrospektif olarak analiz ettik.

Materyal ve Metod: Bu çalışmada, Ondokuz Mayıs Üniversitesi Tıp Fakültesi Genel Cerrahi Bölümü'nde, Ocak 2007 - Ekim 2012 tarihleri arasında uygulanmış olan 504 tiroid ince iğne aspirasyon sitoloji (İİAS) olgusu, tiroid sitopatolojisini değerlendirmede kullanılan Bethesda sistemiyle sınıflandırılmıştır.

Sonuçlar: İİAS sonuçlarında 117 (%23.21) tanesi Nondiagnostik veya yetersiz örnek ve 176 (%34.92) tanesi benign olarak bildirilmiştir. Önemi belirsiz atipi veya önemi belirsiz foliküler lezyon, foliküler neoplazm veya foliküler neoplazm şüphesi, malignite şüpheli ve malign sonuçlar ise sırasıyla 21 (%4.17), 23 (%4.56), 136 (%26.98) ve 31 (%6.15) olarak bulundu. Yanlış negatif ve yanlış pozitif sonuçlar sırasıyla %21.59 ve % 12.91 bulundu. Aynı zamanda İİAS sonucu malignite şüpheli olan vakalarda malignite oranı %36.76 bulundu.

Sonuç: İİAS ve tiroid sitopatoloji değerlendirmede kullanılan Bethesda sistemi, tiroid malignitelerinin ameliyat öncesi tanısında kullanışlı bir inceleme yöntemidir. Diğer taraftan, fizik muayene, ultrason bulguları ve İİAS sonuçları tiroid malignite tedavisinde beraber değerlendirilmelidir.

Anahtar Kelimeler: Tiroid, sitoloji, bethesda sistemi

Abstract

Background: Fine-needle aspiration cytology(FNAC) is an important test for evaluation of patients with thyroid nodules. We report a retrospective analysis of our 5 years' FNAC records based on Bethesda System.

Materials and methods: In this study, 504 cases of thyroid fine-needle aspiration cytology (FNAC), between the January 2007- October 2012 in Ondokuz Mayis University Medical Faculty Department of General Surgery, have been classified following the Bethesda System for reporting thyroid cytopathology .

Results: FNAC results have been reported nondiagnostic or unsatisfactory (ND/US) at 117 cases (23.21%) and benign at 176 cases (34.92%). Atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS), follicular neoplasm or suspicious for a follicular neoplas (FN/SFN), suspicious for malignancy (SM) and malignant were found at 21 (4.17%), 23 (4.56%), 136 (26.98%) and 31 (6.15%) cases respectively. False negative and false positive results were found as 21.59% and 12.91% respectively. Also, in the cases of suspicious for malignancy by FNAC, malignancy were found as 36.76%.

Conclusion: FNAC and The Bethesda System for Reporting Thyroid Cytopathology (BSRTC) is a helpfull investigative method in preoperative diagnosis of thyroid malignancies. On the other hand, evaluation with combination physical examination,ultrasound findings and FNAC results is the most proper treatment method of thyroid malignancies.

Key words: Thyroid, cytology, bethesda system

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Introduction

Fine-needle aspiration cytology (FNAC) has an essential role in the evaluation of patients with a thyroid nodule but only FNAC is not enough for diagnosis. Physical examination (lenfadenopaty, age, sex, a history of radiation therapy to the head or neck, hoarseness, etc.) ultrasound findings and FNAC results are used together for diagnosis of thyroid malignancy by physicians.

The Bethesda System for Reporting Thyroid Cytopathology (BSRTC) is commonly used for more than 4 years[1]. The biggest advantages of this system are preoperatively diagnosis and planning of surgical treatment of tyroid malignancies.

Cytopathological results of FNAC are commended in 6 groups as benign, nondiagnostic or unsatisfactory (ND/US), atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS), follicular neoplasm or suspicious for a follicular neoplasm (FN/SFN), suspicious for malignancy (SM) and malignant[1]. Results of false negative, false positive and lesions of undetermined significances are disadvantages of BSRTC.

Atypia of undetermined significance or follicular lesion of undetermined significance (AUS /FLUS) is a new category in the Bethesda System for Reporting Thyroid Cytopathology for which repeat fine-needle aspiration cytology (FNAC) is recommended[1].

In this study, 504 cases of thyroid pathologies, FNAC had been applied by BSRTC are presented by comparing with histopathological results.

Material and methods

We retrospectively reviewed all reports on FNAC and thyroidectomy specimens submitted to the Pathology Department, Ondokuz Mayis University Medical Faculty from January 2007 to October 2012. All thyroid FNAC were categorized as previously described. FNAC have been performed via ultrasound-guided to all dominant thyroid nodules routinely by a radiologist.

Cytopathological results have been reported according to the BSRTC, compared with the histopathological results of thyroidectomy specimens. Specificity, sensitivity, positive predictive value (PV +) and negative predictive value (PV -) investigated by "NCSS 2004 And PASS 2005" program in computer.

Results

During the study period, 504 patient's FNAC and thyroidectomy specimens were submitted to the pathology laboratory. Of the 504 patients, 381 (75,59%) were women, and 123 (24,41%) were men. The mean age of patients was 49,3 (range 20–94) years.

FNAC results have been reported ND/US of 117 cases (23.21%) and benign of 176 cases (34.92%). AUS/FLUS, FN/SFN, SM and malignant were found of 21 (4.17%), 23 (4.56%), 136 (26.98%) and 31 (6.15%) cases respectively. Histopathological examination of thyroidectomy specimens were, diagnosed malignant of 145 (28.77%) patients in total.

False negative and false positive results were found as 21.59% and 12.91% respectively. Also, in the cases of suspicious for malignancy by FNAC, malignancy were found as 36.76% ***(Table 1)***.

Specificity, sensitivity, PV (+) and PV (-) summarized in ***(Table 2)***.

Discussion

Although FNAC and The Bethesda System for Reporting Thyroid Cytopathology (BSRTC) have been used worldwide commonly in recent years, they have not been standardised across institutions.

On the other hand, changing concepts especially in the treatment of well differentiated thyroid tumors, necessitate to evaluate of FNAC and reporting systems. In fact, changing from the bilateral lobectomy and radical neck dissection or prophylactic central lymph node dissection to simple observation, a lot of surgical/medical therapeutical methods have been reported for well differantiated thyroid carcinomas[2-4]. There are some studies found adequate only observation in papillary cancer without surgical intervention in last years. The rationale of these studies are acceptable 5 and 10 year overall survival for early-stage papillary cancers, 98% to 100%. İto et al, has reported 6.4% and 15.9% that growth of 3 mm or more in the 340 patients whom observation alone was done for papillary microcancer in 5 and 10 years. Lymph node involvement in these patients are 1.4% for 5 years and 3.4% for 10 years. Also, he has reported no recurrence in 109 patients who had delayed surgery[4].

Certainly, there are two important topics in survey and the treatment of thyroid malignancies; histopathological diagnosis and clinical staging (classification).

The main purpose of FNAC is to provide histopathological diagnosis preoperatively and to help the choice of surgical therapy. But the reliability of FNAC still remains controversial. Factors affecting the reliability of FNAC are the character of the lesion, the experiences of radiologist and pathologist who applies and evaluates biopsy. First of all, it is not possible to be sure that the samples have been taken from tumor. It is not possible to completely prevent false negative results although there are localized and more accurate ultrasound guided biopsies of the nodules and /or tumor samples. Especially in patients with microcancer, higher false negative results are inevitable.

Table 1: Comparison of the results of cytopathology and histopathology of the cases

İİAB	n	%	Benign n	Benign %	Malignant n	Malignant %
Nondiagnostic or insufficient	117	23.21	98	83.76	19	16.24
Benign	176	34.92	138	78.41	38	21.59
Atypia or follicular lesions of undetermined significance	21	4.17	17	80.95	4	19.05
Follicular neoplasm or suspicious for a follicular neoplasm	23	4.56	16	69.57	7	30.43
Suspicious for neoplasm	136	26.98	86	63.24	50	36.76
Malignant	31	6.15	4	12.91	27	87.09
Total	504	100	359	71.23	145	28.77

Pathologists contribute shaping of treatment by evaluating the several cells. The impact of these risk factors must be zero for an accurate diagnosis. However, it is not possible in reality.

BSRTC has began to be used increasingly common since 2009. Accordingly, the results of FNAC meets in six basic groups.

Seninger et al. reported that there were nondiagnostic 180 (9.3%), negative for malignancy 512 (26.3%), atypical 27 (1.4%), suspicious of malignant 729 (37.5%), and malignant 497(25.6%) cases in series of FNAC with 1945 cases[5]. Also Bongiovanni et al. and meta-analysis of 8 studies including 25,445 cases reported the rate of FN/SFN was 10.10% in[6]. The groups' rates in Seningers' study were found respectively 12.86, 59.36, 06.09, 2.67 and 5.42% in his study[5].

Comparing with FNAC results inaccording to BSRTC and histopathological diagnosis of operative specimens, the risk of malignancy have been found 0-11.76, 1-13.9, 5-17.09, 29.5-75, 81-99% in the groups of benign, ND/US, AUS/FLUS, SM and malignant respectively[1,5,7].

In Davoudi's study, FNAC comparing with the frozen-section results, the indeterminant, benign, and malignant rates were found 7%, 96%, and 64% respectively[8].

It was reported that the rate of incidental thyroid cancer was 8.9% in patients whose FNAC was defined as bening in study of Negro [9].

These results showed that 51.9-77% of cases detected in the exact result, but in the rest ones the results are inadequate to determine. In these cases, FNAC should be repeat or washing should be done to ensure that result. The discussion about the time of repeat FNAC is still present. Some authors have suggested early repetition, while others believe that 3 months time should be given

Table 2: Statistical analysis of benign, suspicious for neoplasm and malignant acording to Bethesda System

	Spesifity	Sensitivity	PV (+)	PV (-)
Malignant-Benign	% 81.657	% 43.548	% 46.552	% 79.769
Benign- Suspicious for neoplasm	% 50.923	% 56.790	% 25.698	% 79.769
Benign-"Suspicious for neoplasm+Malignant"	% 45.695	% 67.593	% 30.802	% 79.769

for pathological changes associated with the procedure to return to normal.

Nagarkatti et al. found that the malignancy rate was 13.64% in repeat FNAC series with 51 cases, where the first FNAC result had been AUS/FLUS[10]. Similarly, Chen et al. reported that in 26 cases showed a AUS/FLUS series, repeat FNAC results were the same at diagnosis in 6 (23.08%), and 2 were (7.69%) Follicular/Hurthle cell neoplasm, 4 were (15.38%) malignancy suspected[11].

In fact, the results of FNAC are not exact still[10]. Washing is in the research phase and aims to investigate thyroglobulin in lymhp node involvement in the washer fluid[12].

Another important problem of FNAC beside inadequacy is false negative and false positive results. False negative results, delays the treatment, while pushing the patient and the surgeon to the comfort, false positive results can cause with unnecessary surgery.

In literature, authors have reported 0.9-11.6% false negative and 1-19% false positives in FNAC studies[1,5,7-9,13,14]. In the cases of thyroid nodules with macrocalcification, Lee et al, has detected the false positive value and false negative value were 9.09 and 1.49%, respectively[15]. In our series, false negativity rate of 21.59% which is higher than the literature, but the false positivity rate of 12.91% is compatible with it.

In Bongiovanni meta-analysis of the sensitivity, specifity and diagnostic accuracy were found 97, 50.7 and 68.8%, respectively[6]. In the study of Seningen et al, in groups of thresholds of atypical, suspicious, and positive cytologic sensitivity of FNAC were found as 94.5, 94.1 and 65% respectively[5]. Gharib et al. reported the specifity 65-98% and sensitivity 72-100% according to the groups[13]. Also, PV (+) and PV (-) values were 55.9-97.7% and 92-96.3% in this study. In our series specifity,sensitivity and PV (+) values were lower than the literature.

Conclusion

BSRTC is a useful evaluation method for cytologic analysis. As a result, FNAC is a helpfull investigative method in preoperative diagnosis of thyroid malignancies. This is useful for management the treatment in experienced hands. However, the false negative and false positive results should keep in mind as the risks of the method.

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