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Fine Needle Aspiration of the Thyroid: A Pathologist's Perspective

Oertel, Yolanda C

I have been aspirating palpable “lumps and bumps” for over 30 years and also interpreting aspirates performed by radiologists, endocrinologists, and other physicians; the last 9 years performing mostly thyroidal aspirates. What follows is based on my reflections and on the insight developed into the particular problem of thyroid nodules. We have to understand the limitations of fine needle aspiration (FNA) of thyroidal lesions. FNA is a diagnostic tool. Tools only work if they are handled properly. The five most important things I have learned in all these years are: (1) the role of the aspirator is crucial, (2) the technique is deceptively simple, (3) you have to have a team, (4) communication with the referring physician is essential, and (5) you have to persist.

THE ROLE OF THE ASPIRATOR IS CRUCIAL

I cannot overemphasize this premise. I believe that this still is overlooked in the literature. Frequently I read about how important it is to have an experienced cytopathologist interpreting the smears. The cytopathologist is only as good as the sample he obtains or receives. You can have the best cytopathologist in the world and he will not be able to diagnose your patient's nodule accurately if you only aspirated blood. Remember, that to acquire experience you must perform a sufficient number of aspirations. How many is enough? Only you will know. Also, you have to be self critical, and you must be a life-long learner. After 30 years I am still tinkering with my technique and getting better. In the last 9 years at the Washington Hospital Center I have aspirated over 10 000 patients (92% thyroids). There is a positive relation between “procedural experience” and outcomes. This is not restricted to FNA.

THE TECHNIQUE IS DECEPTIVELY SIMPLE

Again, I want to reiterate that not many “aspirators” realise that it is not only a matter of inserting a needle. The backbone of a cytological diagnosis is an adequate sample. What I see most frequently on submitted smears are haemodiluted samples. I believe that this is due to excessive suction. When dealing with thyroid lesions, you have to be an extremely gentle aspirator; even more gentle if the patient is hyperthyroid, or pregnant, or taking anticoagulants. I believe this technical problem can be overcome easily.

Remember that most patients are nervous, anxious and afraid (either of the procedure or about the results of the test), and their blood pressure will go up (“white coat syndrome”). This will contribute to easy bleeding. Hence, it is essential to learn how to get the patient to relax. Using an ice pack, performing the FNA with the patient sitting upright (rather than lying down), and applying pressure at the site of aspiration will prevent haematomas.

YOU HAVE TO HAVE A TEAM

You must realise that a team effort is required: the physicians involved in obtaining the samples, the technicians and technologists handling them (making the smears and staining them), and the

cytopathologists interpreting the aspirates must cooperate with each other, communicate, be willing to follow instructions, and pay attention to detail.

COMMUNICATE WITH REFERRING PHYSICIANS

It is essential that you communicate with the referring physician to achieve optimal management of the patient. The main means of communication for the pathologist is the cytopathology report. We are aware that there is dissatisfaction with our reports; that they are frequently “nebulous.” We should strive constantly to provide a clear and definite diagnosis, in a timely manner, and using standardized nomenclature.

You have to persist

In 1976, when I started performing FNAs at the George Washington University Medical Center, there was reluctance to accept this diagnostic tool. Now there is general agreement that it is the most valuable single test in assessing the nature of a mass in the thyroid gland. I want to share the following with you: Octavio Paz (Nobel laureate in literature) quotes the Spaniard B Pérez Galdós from *La Segunda Casaca*, 1883, “We see the instant triumph of the true idea over the false one, in the realm of thought, and we believe that just as quickly an idea can triumph over customs (or habits). Time has made customs so slowly and with so much patience, just as it made mountains; and only time, working every day (day in and day out) can destroy them. You cannot tear down a mountain with a bayonet.” So it will take us longer using a needle.

Who should aspirate?

Repeatedly, it has been reported that better results are obtained when the pathologist performs the FNAs. However, not many pathologists are willing to see patients and perform aspirations. Pathologists have been invisible and hence undervalued by patients. We are perceived as sedentary introverts, thought to be more controlling and less flexible than other physicians. Hence, whoever is willing to perform the procedure and to master it, should be the one to do it. Also, you have to consider the availability of “aspirators” in your geographical area. It is good to have “a mix of aspirators.”

What should the endocrinologist expect from the pathologist?

I believe you and your patient deserve a prompt cytopathology report with a clearly stated diagnosis; an unambiguous report. A timely report is necessary but not sufficient. The report should be concise and “to the point” and should provide you with the information you need or will use for diagnostic and therapeutic decisions.

What do pathologists expect from endocrinologists?

We would like to receive an adequate sample that has been smeared properly. We need more than blood on the smears. Also, we need properly filled requisitions with legible demographics and relevant clinical information. It makes a difference whether the nodule was 1 cm or 5 cm in

diameter. We cannot (and should not) interpret smears in a vacuum. We want endocrinologists to understand that FNA has limitations and is no substitute for clinical judgment. Also, we need follow-up information to keep learning what we are doing right and to correct what we are doing wrong.

What should be aspirated? Why?

Any palpable lesion should be aspirated. This is because FNA will provide a diagnosis most rapidly, most accurately, and at the lowest cost to the patient (by eliminating the need for ordering additional unnecessary tests). Non-palpable lesions should be aspirated under sonographic guidance if the patient has a high-risk history or suspicious ultrasound findings.

Should a multinodular goiter be aspirated?

I believe it should. Concentrate on the firmer nodules (which are usually the smaller ones), but any discrete nodule can be aspirated. However, even if all aspirates are benign, this should not give us a false sense of security. Clinical judgment should dictate the course to follow. If there are symptoms of compression, if the lesion keeps growing, if cosmetically it is a problem, then one should consider surgical excision.

If the patient is going to have surgery, why subject her to an FNA?

The reason for aspirating is to avoid surprises. I have aspirated multinodular goiters and found unsuspected metastatic renal cell carcinoma and also medullary carcinoma; lesions that modified the surgical approach.

Would you aspirate a thyroid nodule incidentally found during CT scanning of the neck?

If I can palpate it, I would aspirate it. I believe that once one becomes aware of the presence of a thyroid nodule (even if it is asymptomatic and less than 1 cm), if it is palpable, it should be aspirated.

Do you recommend ultrasound-guided FNA of palpable lesions?

I do not think ultrasound is particularly helpful in palpable lesions. It has been reported that ultrasound-guided FNA may improve the yield. At those institutions where this happens, I believe it is because the ultrasonographer is more experienced and has a better technique. Hence the success rate depends on the operator rather than on the machine. I believe our insatiable embrace of the image knows no bounds and we use many more ultrasounds than needed. I agree with Shah that the value of ultrasound examination is quite limited.

What should be done when the aspirate is reported as unsatisfactory?

Repeat the FNA after a minimum lapse of 2 weeks; otherwise you will get another unsatisfactory specimen. Anytime you perform an aspiration you will cause some bleeding. If the lesion is small, and you repeat the aspiration after only a few days, you will be aspirating a haematoma

and that is what the pathologist will see on the slides (cholesterol crystals and haemosiderin-laden macrophages). However, if the lesion is large and there is no discoloration of the skin overlying it, a repeat FNA may be successful after only a few days. Usually it is best to wait one month.

If you know why you failed on the first aspirate, try to correct the problems. If the lesion bleeds easily or is difficult to aspirate, admit that you need help and refer the patient to an expert (when available).

What should be done when the aspirate is reported as suspicious or inconclusive?

In some of these cases, a repeat FNA after a suppressive trial of thyroid hormone for 6–8 months might be helpful. Also, if no other studies have been done prior to FNA, it would be helpful to perform a ^{131}I scan. An autonomous nodule with a “suspicious” cytology then may be spared from surgery.

What should be done when the aspirate is reported as benign?

The endocrinologist or clinician will determine whether suppressive therapy is necessary or not. From the pathologist’s point of view, we recommend a repeat FNA no sooner than a year. Why? If we missed a lesion, we will have a second chance to diagnose it. It has been an excellent educational experience to compare the consecutive aspirates.

What should be expected in a FNA report?

An FNA report should be concise and should highlight (emphasize) the important information that requires the referring physician’s attention. Also, it should allow for the collection of accurate and comprehensive data.

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Renal Cell Carcinoma

Ayala, Alberto G.; Ro, Jae Y.

The majorities of renal cell carcinomas (RCCs), represented by conventional clear cell, papillary and chromophobe RCC, and collecting duct carcinoma, are not difficult to diagnose with conventional histology. However, there is a 5% to 10% selective group of RCC that present different morphologic features as well as different clinical behavior. Because of the rarity of these special types of RCC, diagnosis is often difficult. In this issue, we explore in depth the clinicopathologic features of these neoplasms including the XP11 translocation RCC, tubulocystic carcinoma, end stage renal disease associated RCC with oxalate deposition, and the mucinous tubular spindle cell carcinoma. In addition, complementary articles included in this issue review immunohistochemistry in all renal neoplasms and the utilization of virtual

karyotyping of single nucleotide polymorphism (SNP) arrays in the diagnosis of granular/oncocytic renal cell neoplasms.

The RCC displaying Xp11 translocation is a rare pediatric neoplasm that is often difficult to diagnose as it has a varied morphology including features that closely resemble those of conventional clear cell RCC. Because RCCs with clear cell morphology in adults are seldom investigated for the Xp11 translocation, the possibility exists that this lesion may be found more often in adult patients. The translocations involve a breakpoint at Xp11.2 that results in gene fusions involving the TFE3 transcription factor gene which maps to this locus.

Mucinous tubular spindle cell carcinoma is a rare form of RCC that presents an indolent behavior although metastatic disease has been well documented in a few reports. As the name implies, it has a characteristic growth pattern consisting of tubules, mucinous stroma and spindle cells that have bland nuclear features, different from atypical spindle cells in sarcomatoid RCCs. Rare cases may develop a dedifferentiated component. Some immunohistochemical similarities to papillary RCC have been described; however, cytogenetic abnormalities are reported to be different.

Tubulocystic carcinoma is a rare renal tumor histologically characterized by closely packed tubules and cysts lined by a single layer of cuboidal cells with eosinophilic cytoplasm, prominent nucleoli, and not uncommonly a hobnail appearance. This tumor has a bland cytologic and histologic appearance and may be misinterpreted as a benign neoplasm; hence the importance of its recognition. This tumor was considered by some authors as a low grade collecting duct carcinoma. However, the clinicopathologic presentation including morphologic features, immunohistochemical and molecular profile, does not support its origin from the collecting ducts of Bellini. This distinct renal epithelial neoplasm has a possible relationship to papillary RCC.

Renal neoplasms frequently develop in the cystic kidneys of end stage renal disease patients treated by long-term dialysis. Although a wide variety of renal neoplasms may be seen in these patients, there is only one tumor characterized by deposition of calcium oxalate crystals in the tumor cells. This type of RCC has distinctive clinicopathologic features and appears to be seen only in kidneys with acquired cystic kidney disease on long-term dialysis. It has a varied growth pattern and characteristically displays abundant extracellular calcium oxalate crystals.

As time goes on, oncologists are rapidly beginning to use targeted therapies directed to specific cell types of renal neoplasms; thus, proper classification of renal cell neoplasms is a must. There is no question that new methodology is being currently used, but such technology is not yet fully available for utilization in current surgical pathology practice. Yet, in the very near future we will have methodology available for the common practice of surgical pathology. We are witnessing the increasing utilization of FISH and CISH analysis as important tools in the final diagnosis of numerous sarcomas. Molecular analysis with SNP microarrays (virtual karyotyping) is now a rapidly developing technique that provides important karyotyping information which is a key for a definitive diagnosis, supplementing the classic morphology of the renal tumors. In this issue, the utilization of this analysis applied to the challenging diagnosis of oncocytic tumors is addressed.

Considering that new markers are being developed often and that it is difficult to keep up with such a vast amount of new knowledge, an overall review of the immunoprofile of renal cell neoplasms is included in this issue. Furthermore, common daily diagnostic problems such as oncocytoma versus chromophobe RCC, papillary RCC versus metanephric adenoma,

conventional RCC versus Xp11 translocation RCC, and others are addressed. This discussion also reviews the immune profile of tumors suspected of being metastatic RCC.

In summary, within the category of RCCs, the recent literature has drawn attention to the presence of new rare entities causing potential confusion with known RCC categories. The histopathology of recently described unusual kidney tumors is herein presented, emphasizing new or unusual aspects. Although awareness of these entities will lead into a reasonable diagnostic interpretation, immunohistochemistry and SNP karyotyping will provide the key for the characterization of these rare entities.

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Synchronous Tumours of the Female Genital Tract

Naveena Singh

About 1–2% of women with gynaecological cancers are found to have two or more simultaneous independent primary malignancies. Low stage multiple primaries must be distinguished from metastasis from one to other site for correct management. Synchronous tumours in the ovary and endometrium are the commonest combination. Most of these can be accurately categorised by standard histological criteria. Molecular testing has been advocated for valuable adjunctive information in ambiguous cases but must be interpreted with clinicopathological correlation: loss of heterozygosity, pTEN or beta-catenin gene mutational analysis, microsatellite instability and most recently gene expression profiling have all been used. The pattern of beta-catenin immunohistochemical expression has been reported to be of value. A very low percentage of women with synchronous primaries in the uterus and ovary are HNPCC patients and testing for mismatch repair gene mutations is unnecessary in all cases, even if young; the diagnosis of HNPCC should be based on standard criteria. Women with endometrial cancer under 50 are more likely than older patients to have a synchronous ovarian cancer. Rarer combinations of synchronous tumours are less well studied but may also represent a mixture of unusual patterns of metastasis and multifocal origin; these are discussed briefly.

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Indications for Routine Pathologic Examination of Specimens Removed During Trauma Operations

Gertz R, Salim A, Teixeira P, Ley EJ, Inaba K, Chandrasoma P et al.

BACKGROUND: Surgical specimens removed during trauma operations are routinely submitted for examination by pathology. This practice has not been systematically evaluated and the incidence of abnormal results from these examinations remains unknown. The objective of this

study was to identify the incidence and management implications of abnormal findings at pathology review of trauma specimens.

METHODS: This is a retrospective chart and pathology review of all surgical specimens obtained during laparotomy or thoracotomy for trauma between January 1, 1993 and December 31, 2005. Reports were assessed for significant abnormal findings, including malignancy, infectious processes, and chronic inflammation. Additional clinical and demographic data were obtained. The main outcome measure was any change in management due to the pathology result.

RESULTS: A total of 1686 specimens were obtained from 1307 trauma patients. Ten patients (0.8%) were identified as having clinically significant abnormal findings on pathology. Six findings (0.5%) were evidence of malignancy. The pathology reports did not alter care in any patients. In all instances malignancy was known or highly suspected prior to specimen examination based on other diagnostic modalities or gross examination during surgery. Patients with an abnormal finding were significantly older than the patients with normal pathology reports (70.5 vs. 30.4, $P < 0.0001$).

CONCLUSIONS: The routine pathology review of specimens obtained during trauma operations did not alter patient care and should not continue. In all instances of abnormal pathology, preoperative imaging or gross intraoperative findings led to increased suspicion of occult disease. The suggestion of abnormalities on imaging or intraoperatively warrants pathologic examination, especially in older patients.

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Pathologic Evaluation of Sentinel Lymph Nodes in Oral Squamous Cell Carcinoma

Trivedi NP, Ravindran HK, Sundram S, Iyer S, Kekatpure V et al

BACKGROUND: The objective of this study was to determine the relative efficacy of different methods of pathologic evaluation of sentinel lymph nodes.

METHODS: In this prospective study, sentinel nodes were evaluated for occult metastasis using frozen section, imprint-cytology, hematoxylin-eosin staining, serial step sectioning (SSS) with hematoxylin-eosin, and immunohistochemistry (IHC). Metastases were classified into macro metastasis (>2.0 mm), micro metastasis (0.2 mm-2.0 mm), isolated tumor cells (<0.2 mm).

RESULTS: Occult metastasis was detected in 20 of 80 patients. Frozen section and imprint cytology identified metastasis in 10 of 20 patients, hematoxylin-eosin stain in 13 patients; SSS upstaged the disease in a further 7 patients (9%). Frozen section detected macro metastasis in 7 of 8 cases but failed to detect smaller metastases (missed micrometastasis in 4 of 7 and isolated

tumor cells in 5 of 5). SSS upstaged the disease by 10%, and sensitivity and negative predictive value of SSS with hematoxylin-eosin stain were 90% and 97%, respectively.

CONCLUSION: Frozen section and imprint cytology are not effective in identifying occult metastasis. IHC and SSS are required to identify micro metastasis and isolated tumor cells.

Head Neck. 2010 Feb 9. [Epub ahead of print]