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Original research

The diagnostic accuracy of fine-needle cytology of Hurthle cell lesions; A comprehensive cytological, clinical and ultrasonographic experience

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ABSTRACT

Background: Fine-needle cytology (FNC) diagnosis and pre-operative classification of Hurthle cells (HC) lesions may be difficult. Rapid on-site evaluation (ROSE) enhances the efficiency of FNC, mainly when utilized in close combination to clinical and ultrasound (US) data.
Objective: to describe an experience on HC FNC with contextual clinical,US and ROSE evaluation and assess if this comprehensive approach improves the FNC accuracy of HC lesions.
Methods: FNC of 112 HC lesion were diagnosed and classified, according to the Bethesda system, by clinical, US and ROSE in one year. All the cases were controlled by follow-up and histology when performed.
Results: Eighty-five cases were diagnosed HC rich goiter or Hashimoto thyroiditis and were classified THY2; 5 cases were diagnosed hyperplastic nodular goiter and classified THY3A. Eight cases were diagnosed suspect neoplasia and classified THY3B. Two cases were diagnosed suspect HC papillary thyroid carcinoma (PTC) and classified THY4 and 2 cases were diagnosed HC-PTC and classified THY5. THY3B, THY4, THY5 and 1 THY3A were histologically controlled. FNC were confirmed in 14 out of the 17 THY3-THY5 cases.
Conclusions: A comprehensive diagnostic approach that include FNC, clinical data, US and ROSE improves the diagnosis and classification of HC lesions.

1. Introduction

Hurthle cells (HC) or oncocytic cells, are thyroid follicular cells with oncocytic appearance characterized by large hyperchromatic nuclei with prominent nucleoli and abundant granular eosinophilic cytoplasm [1–10]. HC are metaplastic follicular cells that are not specific for any corresponding pathological process. In fact, a variable amount of HC may be observed in all the thyroidal pathologies, starting from goiter up to all the possible thyroidal malignancies [1–12]. HC tumors, also called oncocytomas, can be benign (HC adenoma) or malignant (HC carcinoma) [12]. Both adenoma and carcinoma generally occur as a single, solid nodule, generally highly vascular and encapsulated in most of the cases. Microscopically neoplastic cells can grow in a follicular, solid-trabecular or papillary pattern. Solid and trabecular HC tumors, like the follicular counterparts, generally have a well-defined capsule and the differentiation between adenoma and carcinoma mainly depends on the presence or absence of capsule or vascular invasion [12]. Cytological atypia, anisonucleosis and mitoses may occur in any HC proliferation, including benign and malignant HC tumors. As a consequence, benign HC proliferations may show evident nuclear atypia and HC carcinoma can produce distant metastases to the lung, bone and less commonly in cervical lymph nodes with or without cytological atypia. HC unfavorable prognostic factors are: advanced age, tumor size, extra-thyroidal extension, vascular invasion and presence of metastases at diagnosis. Surgical excision of corresponding nodules or masses is the treatment of choice for both HC adenoma and carcinoma. Conversely goiter and thyroiditis with variable amount of HC do not require surgical treatment as first therapeutic choice at least, therefore the main task of preoperative diagnosis is the differentiation between non-tumoral HC lesions and HC tumors. Fine needle cytology (FNC) represents the main diagnostic procedure in the diagnosis of thyroidal nodule with generally highest levels of accuracy [1–10,13–22]. Cytological diagnoses are generally rendered according to the Bethesda classification [23–34] and, in our Institution, to the following recommendations by the Italian

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Society of Pathology and Cytopathology (SIAPEC). Bethesda classification include a six tiers categories, each of them corresponding to a cytological diagnosis of certainty with the exception of the category THY3 referring to follicular neoplasms that are not distinguishable on cytological sample. Since follicular proliferations include lesions with variable risk of malignancy, THY3 category was further divided into two subgroups:THY3A and THY3B according to the risk of malignancy with the purpose of reducing the percentage of nodules with indeterminate cytology to be submitted to surgery. Therefore, according to the Bethesda recommendations THY3A cases undergo to follow-up and or FNC repetition being THY3B deferred to surgical treatment. HC lesions are diagnosed in the same way of the follicular counterparts; nonetheless because of their peculiar cytological features, HC lesions offer additional difficulties to the FNC diagnosis [1–12,35–44]. FNC is utilized, more and more in close combination to clinical and ultrasound evaluation; moreover FNC efficacy is enhanced by rapid on-site evaluation (ROSE) of clinically or US suspected thyroidal nodules [45–49]. In the last years, a thyroid diagnostic unit has been set up in our Institution in which the contextual and synchronous clinical, US and cytological ROSE of the thyroid nodules is performed. The aim of this study is to present our experience on HC FNC and to assess if this approach improves the preoperative cytological diagnosis of HC lesions.

2. Materials and methods

Over a 1-year period 1421 thyroidal FNC were performed at the Thyroid Diagnostic Unit of the Azienda Ospedaliera Universitaria of the University of Salerno. Cytological diagnoses were rendered according to the Bethesda classification as previously reported. FNC was performed under US guidance in all case and ROSE was performed in 411 cases on the basis of clinical or ultrasound criteria of suspect. Diff-Quik stained smears were immediately evaluated to assess the adequacy of the smear according to the current criteria applied for follicular lesions [15–17]. Namely adequate smear contained at least 6 groups of follicular cells with a minimum of 10 cells in each group. Inadequate cases were immediately repeated. At the time of the FNC and ROSE, clinical, serological and US data were obtained and discussed with the clinician. Therefore an accurate clinical, serological and US evaluation was immediately available and additional diagnostic material, hence additional FNCs, when needed, were obtained on the spot. HC reach proliferations were identified when more than 20% of all the follicular cells showed a clear oncocytic metaplasia [2,5]. Final cytological diagnosis was rendered according to the Bethesda classification and the HC component reported. HC lesions ranged from THY2 to THY5. According to the FNC diagnoses, cases classified as THY3A underwent to follow-up and repetition after six months, THY3B, THY4 and THY5 were requested for surgical treatment. Therefore cytological diagnoses, and namely HC rich lesions, were controlled by follow-up and by histological evaluation respectively. All the cases included in the present study were blindly by two of the authors (AC, PZ) with an highest level of concordance and classified according to the provided in the Bethesda System [23–27] guidelines.

3. Results

A significant high number of HC were detected in 112 cases. In all these cases the cells showed typical Hurthle cells features (well defined, abundant, finely granular cytoplasm, one or two enlarged, central or eccentrically located, round nuclei, evident or prominent nucleoli). In 85 cases of nodular goiter a variable amount of colloid, follicular cells and macrophages were present and were classified as HC rich THY2 (Fig. 1). In 10 cases, other than HC, a variable amount of lymphoid cells (mature small lymphocytes, follicular centre cells and plasma cells), and lymphoid “tangles” were present (Fig. 2). These cases were diagnosed as HC rich HT and classified THY2. The remaining 17 cases showed a remarkable high number of HC and were included in the present study. Regarding the clinic-pathologic characteristics of the cases, there were 15 females and 2 males. The age ranges between 17 and 82 years with an median of 49.5 years. The size of corresponding nodules ranged from 10 mm to 42 mm. As for the ultrasound pattern, 7 cases were isoechogenic, 7 cases were hypoecogenic and 3 cases were hyperperecogenic. In 2 cases (cases n. 14 and 16) microcalcifications were also present. As far as the FNC cytological features concerns, 5 cases showed a high cellularity and a percentage of HC higher than 20%, whereas a follicular cell component and scanty colloid in the background were still present (Fig. 3); these cases were classified THY3A. In 8 cases smears were monomorphous and represented almost exclusively by HC organized in small groups, rough follicular structures or isolated; colloid and follicular cells were absent (Fig. 4); these cases were classified THY3B. In 4 cases smears were monomorphous and represented almost exclusively by HC. These latter presented a papillary arrangement and in two of these case cytoplasmic nuclear inclusions were also detected (Fig. 5). These cases were classified THY4 and THY5 respectively. Four out of the 5 cases classified as THY3A underwent to clinical and US follow-up only that confirmed, up to now the FNC indication. Just one THY3A case (case n.4), because of the size and the US pattern was removed and the following histological examination revealed a HC adenoma. Eight cases classified as THY3B were treated surgically and the histological examination revealed five HC adenoma and three well-differentiated, capsule-invasive, HC carcinoma (Fig. 6). Two cases classified THY4, revealed to be HC adenomas and 2 THY5 were confirmed as papillary thyroid carcinoma, HC variant at the histological examination. Clinical, ultrasound cytological data, as well as follow-up and histological controls are summarized in Table 1.

4. Discussion

Hurthle cell (HC) may occur on FNC samples as component of different pathologies with different biologic significance and different therapeutic indications [1–22,31–44]. The main task of FNC, when dealing with HC lesions, is to distinguish HC rich, non-neoplastic lesions from HC neoplasm. At the same time, the identification and discrimination of HC neoplasms is important because of their high risk of malignancy that requires surgical treatment from those that can be followed over time because at very low risk. Therefore, the FNC report of HC lesions should be indicative of the specific pathological entities but also classify corresponding patients to a defined and identifiable diagnostic category. The classification

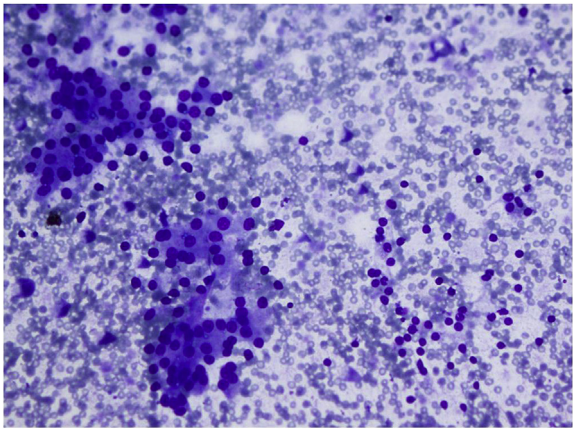

Fig. 1. FNC features of HC rich, nodular goiter. There are groups of HC and some follicular cells. This case was classified as THY2 (Diff Quik stain 270×).