Ultrasonographic features of papillary carcinoma: Five-year experience in thyroid refferal center

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UNDERUSE OF DIAGNOSTIC POSSIBILITIES IN PATIENTS WITH DIFFERENTIATED THYROID CARCINOMAS

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At an early stage thyroid carcinomas are often asymptomatic and are therefore mostly detected by a standardized diagnostic approach to thyroid nodules. The aim of this study was to examine which diagnostic tools were applied, finally leading to the diagnosis of thyroid cancer. We retrospectively screened the charts of 256 patients with a history of differentiated thyroid carcinoma at the Leipzig University Hospital. Missing data were retrieved from referring physicians and the patients were interviewed in a standardized manner. Preexisting thyroid diseases like goiter or thyroid nodules were present in 23% and 27%. Palpable nodules or nodule growth were noted by 37% and 15% of the patients. Nodules with diameter of more than 3 cm were noticed significantly more frequent than smaller ones. As a diagnostic procedure thyroid scintigraphy was performed most often in 78,5%. The scintigraphic appearance of carcinomas >10mm was isocaptant in 28%, warm in 2% and cold in 70%. Ultrasound results were available for 251 patients. No comment on the echogenicity was found in 54%, hypoechogenicity in 32% hyperechogenicity in 2%, echocomplexity in 8%, isodensity in 2% and cysts in 2%. Fine needle aspiration biopsy was performed for sonographically >10 mm nodules in 10%. It was non diagnostic in 26%, benign in 15% and malignant in 59%. Patients with a malignant FNAC underwent primary thyroidectomy significantly more often (65%) than patients without(50%). Only 16% of the patients were operated because of a preoperative suspicion of malignancy. Our data demonstrate that most patients later diagnosed with a thyroid carcinoma underwent primary thyroid surgery without a specific suspicion of malignancy. This could most likely mainly be due to the very infrequent use of preoperative FNAC, a high rate of non diagnostic FNACs and a lack of malignancy risk stratification by ultrasound criteria.

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MULTIFOCAL PAPILLARY THYROID CARCINIOMA ASSESSMENT IN PATIENTS WITH HASHIMOTO THYROIDITIS AFTER POSSIBLE RADIATION EXPOSURE

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Papillary thyroid carcinoma (PTC) sometimes develops within background of Hashimoto´s thyroiditis (HT). It is often difficult to differentiate between benign and malignant nodules due to vast variety of ultrasonographic HT representation. The aim of our work was to characterize the US and scintigraphic features of PTC in patients with HT and studied relatives of patients with HT and PTC. We prospectively studied 42 first-grade relatives (f30; m12; median age, 59 +/-14 yrs) of patiets with HT/ PTC. 38 of 42 studied patients (90%) were residents of North-eastern regions of Kazakhstan near from Nucleartestregion, prior to their repatriation to Germany. Initial investigation included clinical examination, sonography, ^{99m}Tc scan, thyroid hormone levels as well as anti-TPO and anti-Tg antibodies detection. Every case of PTC was confirmed by pathohistological examination. All pts had HT with high levels of thyroid Ab (TgAb, TPOAb). 17 of 33 autoantibody positive pts with suspicious multifocal non-uniform thyroid nodules (hypoechogeneic, with calcifications, presenting cold lesion in ^{99m}Tc scan and highly vascular) underwent thyreoidectomy. In 58%- 10/17 pts in this Group had multifocal PTC (up to pT3). US signs of calcifications in these pts have been revealed significantly frequently (P=0.05) than in Group without PTC, but al other features assumed as diagnostic parameters (size of nodules, shape, location in the gland,, tracer uptake) did not show any particular statistically difference between HT and PTC Groups.

A high prevalence (100%) of HT and multifocal PTC (25%) might be related to the fact, that a majority of pts were previously residents of Regions of Kazakhstan (probability of extensive radiation exposure). Indeed, a high incidence of HT/PTC, adjacent to the Semipalatinsk nuclear test site was reported. Our results justify a neccessity of screening for HT/PTC in this population group. Calcifications can be a useful indicator of enhanced PTC risk.

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POORLY DIFFERENTIATED FORMS OF THYROID CARCINOMA ARE OVER REPRESENTED IN CANCER DIAGNOSED AT AN ADVANCED STAGE. PRELIMINARY ANALYSIS OF A FRENCH PROSPECTIVE COHORT IN THE FRAME OF TUTHYREF NETWORK

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It is generally estimated that 5% of patients with thyroid cancer will develop distant metastases, and most of them had an advanced stage of the disease at presentation. Thirty per cent of them are resistant to radio iodine therapy and are called "refractory". Their long term survival is estimated to be less than 10%.

From a retrospective study of 45 patients with refractory thyroid cancer, we found that 90% of them were discovered at an advanced stage (pT3 > 2 cm, pT4 or M1). In collaboration with the Thyroid Cancer Registry of the Rhône-Alpes *region (TCRRA)* - a population-based collection of histologically proven incident cases - a prospective study was undertaken to identify the factors associated with poor outcome in a cohort of 400 patients with advanced thyroid cancer followed during 5 years. Anaplastic and medullary thyroid carcinomas were excluded. One hundred and sixty patients referred for iodine therapy after surgery, were prospectively included in 2010 and 2011. They corresponded to 12% of thyroid cancers annually diagnosed in the *TCRRA*. Preliminary analysis of the 119 first cases (female 67%, age 56; range 19–89 years) showed at diagnosis 104 pT3, 11 pT4 and 9 patients metastatic. As for histology, 88% were well differentiated thyroid carcinomas (papillary n= 95, follicular n= 9), and 12% (n=14) were poorly differentiated mainly from the insular subtype.

By comparison with the *TCRRA* population (n=5367 cases), there was a higher proportion of poorly differentiated thyroid cancer (3% vs 12%, $p<.001$) among patients with cancer diagnosed at an advanced stage.

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ULTRASONOGRAPHIC FEATURES OF PAPILLARY CARCINOMA: FIVE-YEAR EXPERIENCE IN THYROID REFFERAL CENTER

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Objective: To evaluate the ultrasonographic (US) features of thyroid nodules diagnosed by FNA (fine-needle aspiration) as papillary carcinoma (PC).

Methods: Thyroid US of patients (pts) with PC was retrospectively analysed from a 5-year period (2007–2012). Basic demographic data, thyroid mass, location and size of the nodules, US features: a) echogenicity (hypo-, iso-, hyper-, complex); b) vascularisation (yes/no); c) microcalcifications (yes/no) d) borders (regular/irregular) were evaluated. Neck US ability to detect lymph node metastasis in lateral neck compartments was also assessed.

Results: 122 PC nodules in 115 pts were detected. Mean age of pts was 48 years (range 13y to 80y), and the female/male ratio was 9:1. The PC nodules were located mostly in the lower third of right lobe of thyroid gland - 39 (29%), and the least common location was in the middle third of left lobe - 11 (8%). Nodules ranged in size from 5 mm to 29 mm, with mean 12.6 mm. Mean thyroid mass was 26 gr. 52% of nodules were hypoechogenic, 39% were isoechogenic, 2.5% were hyperechogenic and 6.5% were complex. Microcalcifications were present in 50% of the nodules, increased nodal vascularity was detected in 11.5% nodules and 20% of the nodules had irregular

borders. 31% of pts with PC had Hashimoto's thyroiditis as well. Ipsilateral lymph node metastases were detected in 5.2% pts.

Conclusions: The most common US features of PC nodules are hypoechogenicity and microcalcifications. Location of the nodule can be used to identify the pts with increased risk of PC. Irregular borders and increased nodal vascularity are present only in every fifth and ninth PC nodule, respectively. Our pts with nodules and Hashimoto's thyroiditis have increased risk of PC.

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FEASIBILITY OF REAL-TIME PCR TESTING FOR BRAF V600E MUTATIONS IN FINE-NEEDLE ASPIRATES OF THYROID TISSUE

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Objectives: BRAF mutations are common in papillary thyroid cancer (PTC). Those thyroid cancers with BRAF mutations are generally more aggressive that their counterparts without the mutation. Moreover BRAF mutation testing is helpful in the cytological preoperative diagnosis of suspicious/indeterminate thyroid nodules. Thyroid nodules are typically assessed with FNAs, which provide little DNA for molecular testing.

Methods: The performance of the **cobas**® 4800 BRAF V600 Mutation Test was assessed in FNA thyroid specimens. This test is a CE-marked, FDA-approved assay for detecting BRAF mutations in formalin-fixed paraffin-embedded tissue (FFPET) specimens of melanoma and thyroid. The assay can be performed in < 8 hours; analysis and result reporting is fully automated.

Results: 31 thyroid FNAs were tested with the cobas BRAF test, including 27 specimens of PTC, 1 case of nodular hyperplasia, and 3 cervical lymph node metastases of PTC. In 30 cases (97%), DNA was isolated from stained smears. All FNAs used in the study were fixed in 96º ethanol and stained with Papanicolau. DNA was isolated in duplicate using the cobas DNA isolation kit and Nucleospin DNA extraction kit. Although < 5 ng/ul of DNA was isolated in 11/31 samples using the cobas kit, and in 16/31 using the Nucleospin kit, valid test results were achieved for all 31 specimens using cobas DNA isolation kit and in 29 using the Nucleospin kit. V600E mutations were detected in 22/31 (71%) specimens. Sanger sequencing was performed on 16/31 specimens and yielded concordant results with the cobas test in all cases.

Conclusions: Despite the low DNA yields, it is feasible to use the **cobas** test to detect BRAF mutations in FNAs of thyroid nodules. Although the cobas reagents are designed to work with FFPET, DNA yields from cytological stained smears using the cobas DNA isolation kit were adequate for mutation testing.

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FIRST UK THYROID CANCER AWARENESS CAMPAIGN

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Introduction: Thyroid cancer is potentially curable, yet late presentations still occur. Current guidelines recommend that newly discovered palpable thyroid nodules should be investigated.

Objectives: To promote public awareness of thyroid lumps and thyroid cancer.

Methods: Butterfly Thyroid Cancer Trust in partnership with the Newcastle Thyroid Cancer clinical team hosted an awareness event. A professionally produced video was shown via the Butterfly website, YouTube and on local TV. A dedicated website to promote the event was launched (www.neckcheck2011.org.uk). The event took place in a busy shopping mall on a Saturday morning in September 2011. Several volunteers including twelve thyroid experts took part. A seating area for fifty was provided in front of a screen, which projected educational material on thyroid cancer. Members of the public who thought they had thyroid lumps had the opportunity to be examined by a member the medical team.

Results: Members of the public began arriving at 8.30am. By 10am the queue was three hundred deep. Admission to the event had to close at 5 pm. The medical team examined one thousand necks. Average waiting time was ninety minutes. Forty people were identified as requiring further investigation. A fast track clinic was arranged in advance in anticipation of this. Pathology has confirmed two new thyroid cancers. Feedback from the public was positive and many asked for this event to be repeated annually.

Conclusion: There is a great demand by the public to learn about thyroid lumps and thyroid cancer. Wide advertising, appropriate choice of venue and joint hosting by a patient led organisation and thyroid experts appear to be important factors in making the event attractive. The yield of thyroid cancer among people who think they may have thyroid lumps or thyroid cancer is very low. This experience will be valuable in planning further awareness events.

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RATE, TIME AND RISK FACTORS FOR RECURRENCE IN PATIENTS AFFECTED WITH DIFFERENTIATED THYROID CANCER (DTC): A 10 YEAR PROSPECTIVE STUDY

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Background: It is known that 10–15% of DTC will recur during the 30–40 years after their clinical remission but it is still not well defined which are the prognostic factors of recurrences. Aim of this study was to evaluate the recurrence rate, the time of recurrence and the prognostic factors in a series of DTC patients who were declared free-of-disease between 1999 and 2001 and then prospectively followed up for more than 10 years.

Methods: We analyzed 138 DTC patients: 126(91.3%) with a papillary histotype(PTC) and 12(8%) with a follicular histotype(FTC). Patients were followed with annual clinical and biochemical controls. The evidence of detectable levels of serum thyroglobulin(Tg) or the identification of lymph-node at neck ultrasound suggested the recurrence. Clinical and pathological features were reported in a database.

Results: During a follow-up of 10 years, we observed 11/138(7.97%) recurrences, 6 of whom (6/11, 54.5%) happened within the first five years from the clinical remission. Among the several possible prognostic factors that we analyzed only an advanced stage at diagnosis ($p< 0.02$), a more aggressive variant ($p< 0.01$) and an older age at diagnosis ($p< 0.04$) were significantly correlated with the recurrence rate. Conversely, sex, intra or extrathyroidal extension, presence of lymph-node or distant metastases *per se* and the ATA risk level did not correlate with the recurrence rate.

Conclusions: About 8% of recurrences were observed in a series of DTC, who were defined in clinical remission according with the most recently defined criteria, and prospectively followed-up for at least 10 years after the definition of their cure. More than 50% of recurrences were found within the first five years from the remission. Among several, the significant poor prognostic factors for the recurrence were the most aggressive histological variant, the advanced stage and an older age at diagnosis.

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FREQUENT INCIDENCE OF *BRAF* MUTATION IN POST-CHORNOBYL PAPILLARY THYROID CARCINOMA

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Papillary thyroid carcinoma (PTC) is a most common endocrine malignancy. PTCs commonly demonstrate a *BRAF* mutation resulting in thymine-