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Introduction
Metastases to the thyroid are rare (1.4–3% of malignant solid tumors). When present, metastatic cancers mimic the ultrasound image of the thyroid parenchyma, hindering diagnosis. Breast cancer rarely metastasizes to the thyroid.
Case
A 61-year-old woman was referred for goiterin the context of post-surgery evaluation for breast cancer. Thyrotropin (1.14 mIU/l), calcitonin (0.5 pg/ml) and parathyroidhormone (54 pg/ml) levels were normal. Thyroid ultrasound (US) showed a multinodular goiter with maximum nodule size of 4.2 cm at the left thyroid lobe (isoechoic with cystic degeneration areas, with few coarse calcifications and poor peripheral vascularization), scattered smaller hypoechoic nodules up to 4 mm in both lobes and few colloid cystsup to 7 mm, without abnormal lymph nodes. An US-guided FNA was performed at the largest left thyroid lobe nodule, showing benign nodular hyperplasia (Bethesda II). The patient was monitored by US and thyroid hormone testing. Elevated tumormarkers (Ca15–3) led to 18-FDG PET-CT scanning, following oncology consultation. Abnormal uptake (SUV max: 3.7) was noted in the area corresponding to the largest noduleat the left thyroid lobe. Total thyroidectomy was recommended (1.5 years after initial FNA). Histopathological examination revealed the presence of neoplastic infiltration in off-white areas of the right lower lobe of solid carcinoma with morphological and immunophenotypic characteristics compatible with breast tissue origin [CK8–18(+), CK19(+), GATA-3(+), ER(+ >80%), PGR(–), TTF-1(–), Thyroglobulin(–), p40(–), HBME-1(–), Galectin-3(–), S-100(–), Calcitonin(-), Ki67~30%].
Conclusion
In this patient, although FNA had been performed in the larger nodule that had the most suspicious featuresfor possible malignancy, it was considered that the increase in tumor markers and concomitant abnormal uptake in 18-FDG PET-CT increased the likelihood of cancer metastasis. However, histopathology after thyroidectomy revealed breast tissue metastasis in off-white areas at the right lower lobe where ultrasound had noted small hypoechoic nodules and colloid cysts. Although thyroid metastases are not very common, caution should be given especially when thyroid parenchyma lesions coexist with a recent history of malignancy.

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AEP878

Clinical case of autoimmune encephalopathy (Hashimoto) with a psycho-organic syndrome on the background of autoimmune thyroiditis

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Introduction
Hashimoto's Encephalopathy (HE) is an autoimmune inflammatory disease of the brain associated with the production of antithyroid antibodies.
Objective
A clinical case of treatment of severe autoimmune encephalopathy in combination with autoimmune thyroiditis and thyrotoxicosis is presented.
Results
A 59-year-old woman was transferred to the intensive care unit diagnosed with thyrotoxic crisis. Objectively: serious condition, inhibited, disoriented to personality, time and place, inadequate, productive contact is difficult, psychomotor agitation. Asymmetry of the nasolabial triangle. Swallowing is not impaired, movements in the limbs within normal. Normothermy. Heart rate 102 per minute, blood pressure 150/95 mmHg. From the anamnesis, about 5 years of thyrotoxicosis, takes thyreostatics, 3 years ago a similar episode of psycho-productive symptoms occurred, the patient was diagnosed with: 'Pseudodementia Syndrome'; mental status returned to normal without treatment. MRI of the brain: without pathology; in cerebrospinal fluid: protein 3.5 g/l, cytosis 2/3. In the blood and cerebrospinal fluid there is no DNA of herpes simplex virus, cytomegalovirus, Epstein-Barr virus. Procalcitonin and C-reactive protein are normal. Leukocytosis 10.7×10^9/l, urea 10.3 mmol/l, sodium 150 mmol/l, FT4 26.6, TSH 0.07, antibodies to TPO more than 1000. The conclusion of the council of doctors – autoimmune encephalopathy is possible, course of therapeutic plasmapheresis (No. 3) was prescribed in combination with pulse therapy with methylprednisolone (No. 5 of 1000 mg), followed by oral administration, a gradual dose reduction until complete cancellation. By the 7th day, the patient's state with pronounced positive dynamics, in consciousness, adequate, oriented to personality, time and place, some emotional lability and partial amnesia. By laboratory methods- transient hyperglycemia and protein-cell dissociation in cerebrospinal fluid. After 3 months, upon reaching the euthyroid state while taking thyreostatics, the patient underwent total thyroidectomy – without complications. Over the next 2 years, episodes of delirium and severe cognitive impairment were not observed.
Conclusion
It is necessary to consider each case of pronounced cognitive impairment with stroke-like symptoms in the prism of Hashimoto's encephalopathy, which requires timely and special treatment.

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AEP879

Influence of Sodium Iodide symporter expression level on recurrence rate in differentiated thyroid cancer

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The ability of thyroid cell to accumulate iodine is due to presence of sodium iodide symporter (NIS). Differentiated thyroid cancer (DTC) maintain ability to express NIS and thus it makes possible to perform RAI treatment. In case of DTC cells loss the ability of NIS protein production and cell membrane embedding that leads to RAI treatment fail.
The aim of our study was to find a relationship between the level of preoperatively defined NIS and recurrences-free survival after RAI in DTC patients.
Materials and methods
Our study included 205 patients with highly differentiated thyroid cancer. In all patients the level of NIS expression was detected by flow fluorocytometry method in a fine-needle biopsy material. The criteria for inclusion in the study were RAI therapy in the postoperative period, the ability to follow up the patient in the postoperative period up to 60 months. All patients were operated.
Results
RAI therapy was performed in 130 patientsin the postoperative period. Recurrence was detected in 50 patientsin the follow-up period of 60 months. Total thyroidectomy (TT) with central lymph node dissection (CLD) was performed in 72.5% (58/80) of cases in the group without recurrence, compared with the group of patients with detected recurrence, where this operation was performed only in 24% (12/50) of cases. Lateral neck compartment cervical lymph node dissection was performed in 40% of patients in the group with developed recurrence of the disease and in 17.5% of patients without recurrence of the disease. The liner discriminant analysis (LDA) revealed the level of NIS expression less than 1% significantly correlate with the risk of recurrence ($P=0.000037$). In the group of patients with recurrence, the level of NIS expression less than 1% was detected in 31 patients (62%), while in the group without recurrence only in 17 (21.2%).Thus, the recurrence-free survival after RAI is significantly lower in patients with NIS expression less than 1% in primary tumor compared to patients with NIS expression level more than 1%. TT with CLD was performed in all patients with low NIS expression in the group without disease recurrence and decrease in the number of recurrences is possibly associated with the volume of surgical treatment.
Conclusions
The level of NIS expression can be used as a prognostic marker of disease recurrence, particular after RAI. The level of NIS expression less than 1% in the primary tumor is suspicious of RAI-refractory DTC.

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AEP880

Clinical practice survey on BRAF V600E role in the therapeutic decision in indeterminate thyroid cytology

Giulia Brigante[1,2], Andrea Craparo[1,2], Elisa Pignatti[3], Marco Marino[3], Livio Casarini[1], Samantha Sperduti[1], Gisella Boselli[1,2], Gianluca Margiotta[1,2], Vincenzo Rochira[1,2] & Manuela Simoni[1,2]
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Introduction
The use of multigene panels in thyroid nodule diagnosis is still limited, due to high costs and need for *ad hoc* sampling. Since *BRAF-V600E* is the commonest genetic alteration in differentiated thyroid cancer, this is the mostly tested genetic parameter in clinical practice.
Aim
To evaluate the use of *BRAF* mutation analysis in wash-out liquid from fine needle aspiration (FNA) in clinical practice, characterizing the cases in which it is requested, and the consequences of genetic test result on therapeutic decisions.
Methods
We considered all the subjects tested for *BRAF-V600E* among those attending the Endocrinology Unit of Modena for FNA between January 2014 and November 2018. After written informed consent, washing fluid was collected together with cytological sample and stored at –20°C. If the clinician deemed it necessary, the sample was thawed, DNA was extracted and genetic test was performed by the high-resolution melting protocol previously described[1]. We collected cytology of nodules according to the 2010 *SIAPEC-IAP* Italian Consensus, and when surgical treatment was performed, histology.
Results
Out of a total of 7112 subjects submitted to FNA, *BRAF* analysis was requested for 681 (9.6%), for a total of 898 nodules: 97% of nodules were indeterminate at cytology, mainly TIR3A (low risk); 2% suspicious or diagnostic for cancer, and genetic test was requested to estimate prognosis; 1% were suspect nodules at ultrasonography with unsuspicious cytology. Only 22 nodules were mutant (*BRAF*+).Most of them were already high risk or suspicious lesions at cytology (64%). One third were TIR3A. Considering the prevalence of *BRAF* mutation among cytological classes of the whole group, only 1% of TIR3A were *BRAF*+. Twenty *BRAF*+ patients were addressed to surgery (one lost at follow-up, one refused): 5% underwent hemithyroidectomy, 25% total thyroidectomy and 70% total thyroidectomy plus central lymph nodes dissection. They all had papillary thyroid cancer. Since 64% of *BRAF*+ were TIR3B-4-5 at cytology, they had surgical indication even before the genetic test. Among the 14 subjects treated with central neck dissection, only 2 had suspect metastasis before surgery; among those who would have had no indication, one third had metastases (only 1 among TIR3A and 2 among TIR3B).
Conclusions
Despite the development of panels, single gene tests are still requested, mainly for nodules with indeterminate low risk cytology. *BRAF* mutation in TIR3A is rare and leads clinicians to more invasive surgery, with questionable clinical utility.
Reference
1. Marino *et al. Eur Thyroid J* 2015 **4**(2) 73–81.
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AEP881

The diagnostic value of basal and calcium-stimulated procalcitonin for the diagnosis of medullary thyroid cancer: Preliminary results from a multicentric experience

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Background
Calcitonin (CT) is the most sensitive marker for MTC diagnosis. By the way, many pre-analytical, analytical and post-analytical pitfalls worsen its accuracy. Procalcitonin (proCT), a CT precursor, has been suggested as a valuable complementary test in MTC diagnosis, given its stability and the reproducibility between different assay kits.
Material and methods
basal CT (bCT) and proCT (bproCT) and stimulated CT (bCT) and proCT (sproCT) (2–5–10 and 20 minutes)were measured in 37 patients (14M, 23F; median age: 55 years, range: 5–77 years) that underwent surgical excision. At the histological report, 22 were MTC, while the others were C-cell hyperplasias (HCCs) or non-C-cell lesions. 17/37 (45.9%) were carriers of a *RET* mutation. Calcium gluconate at the dose of 25 mg/Kg based on adjusted body weight was administered. bproCT was considered positive when ≥0.04 mg/l, while CT when ≥10 ng/l.
Results
there was a correlation between bCT and bproCT ($P<0.0001$, $r=0.75$). A significant correlation was found between MTC tumor size and bproCT ($P=0.0062$, $r=0.58$), as well as with bCT ($P=0.01$, $r=0.54$).Positive bproCT showed higher specificity than positive bCT in the diagnosis of MTC with respect to non MTC lesions (CCHs or other lesions) (53% vs 40%), with higher positive predictive value (PPV) (70% vs 66.6%). The combination of elevated bCT and bproCT increased the specificity of bCT value from 40% to 67% and its PPV from 67% to 75%. bCT and bproCT showed the same accuracy in *RET*-wild-type (*RET*wt) and *RET*-mutated patients. Applying ROC curve, we could identify a cut-off of 0.07 mg/l for bproCT, able to identify a MTC (sensitivity=68%, specificity=87%, AUC=0.764, $P=0.0009$), regardless of the gender. There was a correlation between sCT and sproCT ($P<0.0001$, $r=0.64$). A positive correlation existed between MTC tumor size and sproCT ($P=0.0018$, $r=0.64$) and with sCT ($P=0.0001$, $r=0.75$). Higher values of median proCT increase were found in MTC versus non-MTC (median increase of 0.22 mg/l in MTC versus 0.02 mg/l in non-MTC, $P=0.0003$). Applying the ROC curve, a sproCT value>0.19 was able to identify an MTC (sensitivity=72%, specificity=93%, AUC: 0.806, $P<0.001$), regardless of the gender. Combining bproCT and sproCT specificity for MTC increased up to 93% (94% VPP).
Conclusions
proCT calcium-stimulated levels are significantly higher in MTC than in non-MTC and are correlate with tumour size. Basal and stimulated proCT can be used in combination with bCT and sCT to increase its specificity in biochemical diagnosis of MTC.
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AEP882

***In vitro* modeling of thyroid cancer cells and fibroblasts interplay**

Elisa Stellaria Grassi[1], Viola Ghiandai[2], Gabriele Pogliaghi[3], Laura Fugazzola[3,4,5] & Luca Persani[1,3,5]
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Thyroid cancer (TC) is the most common endocrine tumor and its incidence has increased faster than in any other malignancy. Although TCs are usually well differentiated, disease recurrence or persistence is high, because of local and distant metastasis and therapeutic resistance. Among the different genetic alterations, BRAFV600E is the most frequent one. Several studies tried to establish a correlation between BRAFV600E and patients outcome, with controversial results. Nevertheless, the activation of different BRAF downstream pathways influences immune response, matrix remodeling and intra- and extra-cellular pH. All these alterations substantially modify tumor microenvironment and may enhance the survival of cancer-initiating cells and promote therapy resistance. The aim of the study is to investigate the role of BRAF in cancer-associated fibroblast matrix deposition and remodeling in *in vitro* 2D and 3D systems obtained from immortalized and patients-derived cells. In particular, the use of conditioned media and co-cultures of TC cells with different genetic background and fibroblasts is used to generate different extracellular matrices (ECM). The ECM themselves and their effects on cell growth and survival is then analyzed by different techniques, such as western blot, immunofluorescence, real-time PCR, colony assay, sphere formation assays and proliferation assays. Our results show that TC cells with BRAFV600E mutation can significantly increase the proliferation and activation of fibroblasts in respect with BRAF WT TC cells and normal thyrocytes; fibroblasts that have been conditioned with BRAFV600E TC cells can produce an ECM that is thicker and has a different fiber pattern than the one produced from fibroblasts conditioned with BRAF WT TC cells and normal thyrocytes. Moreover, the different matrices differentially influence the survival of BRAF mutated and WT TC cells. As second step, we are currently evaluating the effects of different drugs that acts against BRAF downstream effectors involved in matrix remodeling and metabolism alterations. In conclusion, our *in vitro* model can partially recapitulate the complex environment of human tumors and can be a useful tool for the screening of different anticancer drugs.
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