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"Second primary neoplasia": risk of thyroid and breast cancer. A preliminary study

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Background. Women with thyroid cancer are usually young and long-survivors, so they should have the same risk as general population to develop a breast cancer. Instead, some studies showed a frequency higher than expected of breast cancer in women operated for thyroid cancer. In our study we tried to confirm this finding and to analyse some possible risk factors.

Patients and methods. This retrospective preliminary study evaluated 95 women operated for thyroid cancer by total thyroidectomy from 1996 to 2009. A questionnaire was developed for this aim and validated with this first set of patients, who were interviewed by phone to investigate about their life style, previous therapies, other concomitant diseases and the presence of breast diseases. We excluded from our study patients dead by other causes than cancer (n=2), patients who could not be reached (n=22) and those refusing to answer to our questions (n=2), with a total drop out of 26/95 (27.3%). The mean follow up of the considered patients was 81. 0 months. Associations between development of a second cancer and covariates were evaluated with logistic models.

Results. We evaluated 69 questionnaires, from women with a mean age of 57.8±12.5 yrs. 38 women denied to have ever had any breast disease, 31 ones declared a breast disease. In particular, 6 of them suffered for breast cancer, while 25 were treated for benign breast diseases. When comparing the cancer group with the benign breast disease plus no disease group, a statistically significant association (at 95%) was found between the development of a second cancer and nulliparity, with a protective effect of at least one pregnancy (OR 0. 15; 95% CI 0. 03÷0.86). No significant associations were found with age, body mass index (BMI), smoke habits, physical exercise and concomitant metabolic diseases (from uni- and multi-variate models).

Conclusions. This preliminary study showed that the designed questionnaire is suitable for a larger survey (time of administration < 10'), with an acceptable rate of drop out. The sample was too little to drive conclusions but 6/69 cases of breast cancer in a rather limited period of observation seem to be a promising finding.

Hemangiosarcoma of thyroid: case report and literature review

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The hemangiosarcoma of thyroid is an uncommon malignant tumor (in literature incidence is about 2% of all thyroid neoplastic lesions espectially in Alpine regions) with poor prognosis (median survival 6 months), sometimes indistinguishable from anaplastic carcinoma. Therapy is difficult for local invasion and elevate rate of recurrence. We present a case of a patient, aged 75, with a pre-operative FNAC diagnosis of anaplastic carcinoma of the left lobe of thyroid gland. A total thyroidectomy with left latero-cervical lymphadenectomy was performed. The histologic examination showed an epithelioid hemangiosarcoma with negative lymph-nodes. After 20 day from surgery cervical and mediastinal recurrence appeared. The patient is still treated by radiation therapy. In conclusion, according to literature, we can affirm that hemangiosarcoma, has to be inclu-

ded in differential diagnosis of thyroid tumors. The distinction between hemangiosarcoma and other epithelial neoplastic lesions of thyroid (e. g. positivity for CD31, CD34, Vimentin, Galectine 3 and negativity for cytokeratine 19, cytokeratine 5.2, pancytokeratine) can be difficult. For its aggressive behavior, therapy is based on radical surgery when possible and, in case of recurrence, on conservative treatments such as radiotherapy.

Poorly differentiated non insular thyroid cancer: case report

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Due to the high morbidity's and mortality's rate poorly differentiated thyroid cancer (PDTC) is still now an important oncological and surgical challenge. PDTC accounts for about 5-10% of all thyroid cancers and therefore the sclerosing, solid and columnar cells are the most aggressive variants. PTC is further subdivided in insular, hystologically recognized with positive hymmunoreaction for Tg, TTF1 and P53 (0-38%), and *non insular cells.* Even with similar clinical and prognostic characteristics the second variant is more associated with other thyroid cancers and with recurrent disease. A man 74 years underwent to total thyroidectomy and left central lymphoadenectomy for PDTC non insular. Three months later the follow up revealed a recurrence of the tumor with lateral node (patient in iodine-131 treatment) for which is now in external beam radiation therapy. Intersting in this case was the lymph node involvment higher in lateral lymph nodes than in central one. Surgery remains the first choice of therapy. The responsiveness of PDTC to radiation is uncertain and randomized studies are still necessary for the cancer's uptake.

Laparoscopic approach to adrenal tumors associated with other abdominal endocrine tumors

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Introduction. Laparoscopic resection is nowadays the gold standard surgical approach for all kinds of adrenal tumors, even larger or malignant in selected cases. Laparoscopic adrenalectomy can be performed through different approaches: lateral or anterior transabdominal approaches, lateral or posterior extraperitoneal (retroperitoneoscopic) approaches. Lateral transabdominal approach remains the most used laparoscopic approach worldwide, due to its easy feasibility and reproducibility, but in case of contemporary presence of other abdominal tumors or extra-adrenal involvement, anterior approach becomes preferable.

Patients and results. The Authors report their experience in diagnosis and surgical approach to adrenal tumors associated with other abdominal tumors of endocrine origin (arising from pancreas, small and large bowel, urinary bladder or paraganglia), focusing on the importance of correct preoperative diagnosis and localization, in order to correctly program the laparoscopic surgical approach.

Conclusions. Co-incidence of different tumors of endocrine, even if actually not included in MENs classification, may represent the effect of a genetic mutation/polymorphism. For this reason these patients should be adequately investigated, in order to identify any possible gene mutation and tha possible presence of further tumors, as in the case of neurofibromatosis, VHL disease. Once a correct and precise diagnosis is established, synchronous laparoscopic resection, when feasible, represent the gold standard surgical approach.

Syndromic adrenal and extra-adrenal pheochromocytomas

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Introduction. About 24 per cent of phaeochromocytomas and sympathetic paragangliomas appear in familial cancer syndromes, including multiple endocrine neoplasia type 2, von Hippel-Lindau disease, neurofibromatosis type 1 and PCC-paraganglioma syndrome (PGL). Identification of these syndromes is of primary importance for patients and their relatives. Surgical resection is the treatment of choice for both PCC and PGL, but controversy exists about the management of patients with bilateral or multiple tumours.

Patients and results. 24 patients affected by hereditary pheochromocytoma or paragangliomas were surgically treated in our Institution. The following variables were studied: (1) clinical and diagnostic data: age, mutation, clinical features, levels of catecholamines and catabolites in a 24-h urine sample, computerized tomography (CT) scan and iodine-131 meta-iodobenzylguanidine (MIBG) scintigraphy results, and genetic screening; (2) surgical treatment; and (3) follow-up and recurrence.

Conclusions. Genetic testing for syndromic or familial pheochromocytomas and paragangliomas should become routine clinical practice. Patients and family members with proven mutations should be entered into a standardized screening protocol. The preferred treatment of pheochromocytomas and paragangliomas is laparoscopic surgical resection; to avoid the lifelong consequences of bilateral adrenalectomy, cortex-sparing adrenalectomy should become the treatment of choice in the next future.

Intraoperative recurrent laryngeal nerve monitoring in thyroid surgery

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The injury of recurrent laryngeal nerve is the most terrible complication in the thyroid surgery. Several factors can influence the possibility of damaging the nerve, including the thyroid pathology and the surgeon's experience. The intraoperative recurrent laryngeal nerve monitoring (NIM) is considered a safe procedure, even if it is not yet largely used by the surgeons. The use of NIM gives several advantages: the capability to evidence straight away any possible damage caused to the nerve and the possibility to distinguish the nerve (after its direct simulation) from the vascUlar and fibrous structures. Important limits of this procedure are the cost and the false negatives.

From February 2009 to November 2009 we observed 188 patients (167 total thyroidectomies and 21 total thyroidectomies with lymphectomy). All patients underwent pre-operative indirect laryngoscopic examination to evaluate vocal cords mobility. Seven cases of unilateral postoperative recurrent laryngeal nerve injuries were observed. In our experience, NIM is very useful in recurrent goiter, where identification of recurrent laryngeal nerve can be very difficult due to scar tissue. Greater experience is necessary to establish real advantages of NIM.

Ectopic parathyroid gland misunderstood with preoperative scintigraphy Tc-99 MIBI: a case report

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Recurrent hyperparathyroidism is an uncommon complication after parathyroidectomy with an incidence of 1-10%. The current management is strictly connected to the Surgeon's experience. For consequent metabolic and symptomatologyc advantages surgery remains in 90% of the cases the first choice of therapy with accetable rates of morbidity.

A man 79 years old operated of left inferior parathyroidectomy for prymary hyperparathyroidism, for the persistence of higher intraoperative and post operative value of PTH underwent to scintigraphyc exam with Tc-99 MIBI that showed an ectopic mediastinal parathyroid gland preoperatively misunderstood. The negative results of the scintigraphyc examen was probably due to the great radiopharmaceutical interaction with the adenom. The precence of the ectopic gland was also confirmed by RMN. In consideration of age, comorbidity and negative evidence of gastroenteric and renal implications the patient is medically treated before of an eventual new surgical approach.

Recurrent hyperparathyroidism should be carefully evaluated. Surgical approach indicated in 95% of patients has to be compared with age, comorbidity, renal function. Pre-operative evaluation has a key-role for the exclusion of an adenoma in the ectopic gland.

Management of suspicious cervical lymph nodes in patient being considered for total thyroidectomy

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Background. In the surgical thyroid diseases, it is common occurrence to find pre-operative enlarged cervical lymph nodes (LN) in patients treating for a benign disease, with a definitive diagnosis of differentiated thyroid cancer.

Patients and methods. In our study a pre-operative

thyroid ecocolor-Doppler was executed in 46 patients involved in total thyroidectomy, performing FNAB with US guidance for 55 suspicious cervical LN: an aspirate aliquot was smeared for cytological examination and another was frozen for subsequent PCR analysis to detect the mRNA of Tg and the TSH-receptor, while Tg was measured in the needle washout only in 42 LN.

Results. A 100% correspondence between genetic and histopathological diagnosis was observed in the 49/55 nodes (89%). The genetic analysis resulted more sensitive (100%) and accurate (100%) than both the cytological analysis (24% inadequate samples, 17% false negative diagnoses) and the Tg measurement in the aspirates (39% false negative).

Conclusion. Our experience demonstrates that after a total thyroidectomy, if histopathological diagnosis is malignant, it is required a loco-regional lymphectomy. This could be avoided by identifying pre-operative metastatic lymph node. Objective of our work is to assess the true cost-benefit of this protocol and its applicability in terms of morbidity.

Medullary thyroid cancer: a case report

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Medullary thyroid cancer (MTC) accounts for about 3-10% of all thyroid cancers with a mortality rate of 13,4%. MTC is further subdivided in the sporadic, familiar, MEN associated variants. Age, stage of disease, lymphnodal metastasis and surgery are prognostic factors for survival.

A woman 54 years, operated 10 years before of total thyroidectomy in another hospital, according to imaging evidence and higher values of calcitonin, underwent to lateral cervical limphoadenectomy. Hystology was positive for metastatic involvment of medullary thyroid cancer. One year later the follow-up revealed a recurrence of the tumor in superior mediastinal left lymph nodes surgically treated. Since the patient has been without signs of tumor recurrence or metastases.

Surgical treatment represents the gold standard for MTC also in locoregional recurrence of tumor. Calcitonin values, even after long time from first surgical approach, are predictable of lymph nodal recurrent involvement. Radiotherapy is until now useful just in selected cases and many investigations of new chemotherapeutic agents are still performed.

The role of sentinel node approach in the treatment of breast cancer

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Introduction. Factors influencing the choice of treatment of breast cancer are the TNM, histological type, grading, age of patient, presence of lymphatic or vascular invasion, degree of tumor growth, the presence of RE and RP, presence oncogene HER. In the past axillary dissection was the diagnostic method to highlight the lymph node invasion. Today the technique of sentinel lymph node, the first lymph node draining the tumor, can to screening patients with lymph node metastasis.

Patients and methods. 341 patients, 339 female and 2 males, aged between 27 and 83 years, 284 with breast cancer T (clinical) 1, 57 with T2, all with clinically negative lymph node status. 339 undergo quadrantectomy and 2 mastectomy in male patients. All patients were informed of the aims of the procedure and signed informed consent. The diagnosis of breast cancer was previously determined by fine needle biopsy or core needle biopsy. For the identification of sentinel lymph node the vital staining and radioactive tracing methods were applied.

All blue-enhancing lymph nodes were removed. All lymph nodes removed were examined histologically: if they were metastatic, complete axillary lymph node dissection was made.

Results. Rate of identification of sentinel lymph nodes of 97% (331/341 cases), the most frequent histological type was ductal carcinoma (260 cases), lymphvascular invasion was found in 128 patients, the neural invasion in 61 patients, ER positivity was 288/332 of histological samples and the PR positivity was 283/332. Over-expression of HER2/neu was: 180 patients were negative, 30 patients had a positive +1, 23 patients had a positive +2, 35 patients were positive +3. The sentinel node was positive for metastasis in 31.7% (108/341 cases), micrometastases were found in 22 patients and isolated tumoral cells in 1 case. The average number of sentinel nodes removed was 1.8, the sentinel node was the only positive lymph node in 57 of 108 patients (52,8%).

Discussion. From the literature review, including 2.753 patients, the detection rate of sentinel node was about 93.5% (range 83-100%) with negative predictive value equal to 97, 2% (range 93-100%), an accuracy of 97.5% (range 93-100%) and false-negative rate of 4.6% (range 0-15%). Positive node in 52.8% of cases (57/108).

As can be seen from our study and the literature review, histological negativity of the sentinel node has a negative predictive value of almost 100%. This means that not highlight tumor foci in the sentinel node is strongly indicative of histological negativity for all other nodes, so you can avoid complete axillary dissection, with the inevitable early and late complications associated with this procedure: lymphedema, injury of thoracic anterior medial and lateral thoraco-dorsal nerve, long thoracic nerve, the nerve intercostobrachial, subacromial bursitis, retractile scars, biomechanical and postural results, thoraco-epigastric superficial thrombophlebitis (Mondor's disease).

Conclusions. The diagnostic accuracy in this experiment is high. We conclude that complete axillary lymph node dissection is not necessary when the sentinel node is negative, i. e. in 50-60% of cases; that results in decreased morbidity.

Harmonic Focus™ in thyroid surgery: our experience

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Introduction. Total thyroidectomy has a complication rate of less than 2%. The goal of thyroid surgery is to preserve recurrent nerve and parathyroid glands. An accurate haemostasis is mandatory: a bleeding can obstruct an appropriate view of recurrent nerve or parathyroid glands and can lead to accidental injury of them. Today various technologies for haemostasis and dissection are available to the surgeon. Harmonic Focus™ is an ultrasonic scissor which can be used for safe dissection, coagulation and cut.

Patients and methods. Our study is a retrospective analysis of two groups of patients who have undergone total thyroidectomy: the first one (n=300) has undergone total thyroidectomy from November 2007 to June 2008 with traditional coagulation devices; the second group has undergone total thyroidectomy from June 2008 and July 2009 with Harmonic Focus™.

Results. We have compared operative time, post-operative stay, drainage blood loss, incidence of hypoparathyroidism, haematomas and recurrent nerve injury among the two groups. Operative time was significantly reduced in Harmonic Focus™ group (with a mean decrease of operative time of 15%).

Analysis of calcemia showed a decreased incidence of permanent hypoparathyroidism in Harmonic Focus™ group (2% *vs* 5,7% of the other group).

Conclusions. Post-operative stay was lower in Harmonic Focus™ group (82% of patients were discharged in second post-operative day in Harmonic Focus™ group *vs* 73% of the other group). We found no significant differences of recurrent nerve injury (1% in both groups) and haematomas (0,5% in both groups).

Lateral spread of energy in the use of innovative hemostatic devices in thyroid surgery: experimental study in the pigs

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Introduction. To value the existence of lateral spread of energy using electrothermal radiofrequency and ultrasonic hemostatic devices and the possible effects on recurrent nerve through an experimental study in the pigs.

Materials and methods. We used 10 pigs. The tissues near the recurrent nerve were treated with each of the two devices at the distance of 1, 2, 3, 4 and 5 mm. During the application we measured the temperature range on the exposed nerve. The side of nerve exposed to the action of devices was dissected, fixed and examined with electron microscope and at the same time were dissected also 2 cm of the nerve above the site of application of device that we used like control sample.

Results. Range temperature average was 5,8°C using the electrothermal radiofrequency device while the median value was 5,5°C; using ultrasonic device range temperature average was 5,3°C while the median value was 4,5°C. In everyone of the treated nerve's piece, with both devices, we found perineural edema, but it was found also in the pieces that we use as control samples.

Conclusions. The use of these technologies in thyroid surgery causes a slight temperature increase in adja-

cent tissues inversely proportional to distance between the nerve and the site of application of device and directly proportional to the amount of treated tissue, but there aren't differences between the treated nerve and the control samples at the osservation with electron microscope.

Video-assisted thoracoscopic removal of mediastinal parathyroid adenomas: two cases successfully treated (film)

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Introduction. In 1% to 2% of cases of primary hyperparathyroidism the disease is sustained by an adenoma deep located into the mediastinum, being inaccessible through the neck. In these patients a trans-sternal approach is traditionally required, but video-assisted thoracoscopic surgery (VATS) represents an effective alternative option.

Patients and methods. We report the cases of two female patients, with mediastinal parathyroid adenomas pointed out by MIBI scintigraphy and confirmed by CT scan. In the first one a cervical exploration had already been carried out, because a previous scintigraphy did not show any anomalous mediastinal uptake. In both cases the adenoma was located in the anterior mediastinum, respectively before the ascending aorta and in the paraaortic right region. VATS was performed through three thoracoports placed in the right axillary region. In one case the excision of a clearly evident lesion was very easy; in the other one the adenoma was not visible, and the adipose tissue of precaval triangle including right residual thymic tissue was completely excised. Patients were discharged without complications and normocalcemia was achieved in both.

Conclusions. Our experience confirms that VATS is an effective, minimally invasive and safe procedure for the treatment of ectopic parathyroid adenomas deep located into the mediastinum. Where the lesion cannot be recognized, a wide excision of adipose tissue in the area where the adenoma is located including residual thymic tissue is required. Otherwise, intraoperative ultrasound (that we have not used) can assist and allow a less extensive resection.

Forgotten goiter. Our experience

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Forgotten goiter is a very uncommon clinical event. It refers to masses "origined" from thyroid gland after total thyroidectomy. The difference between *forgotten* goiter and *recurrent* goiter is determined by the lack of a continuity between cervical and residual mediastinal mass.

Our experience refers to the period from September 2002 to December 2009. We observed 4 patients with forgotten goiter after *total* thyroidectomy performed for cervicomediastinal goiter. All patients were female (median age 60 yrs). A range of 2 months - 25 years elapsed from first thyroidectomy and the new surgical intervention. In three cases the resection of "residual" thyroid required partial sternotomy

No malignant thyroid neoplasm was found. In one case we registred a transient paralysis (< 6 months) of the recurrent laryngeal nerve. No postoperative hypoparathyroidism or bleeding were observed. Mean postoperative hospitalization were one day longer than patients undergoing total thyroidectomy (3 vs 2 days).

Forgotten goiter exposes patients to diagnostical and therapeutical problems. Differential diagnosis is not difficult. Currect diagnosis needs TC and MR. The forgotten goiter is often due to an incomplete resection of a cervicomediastinal goiter. Also an experienced Surgeon can run into difficulties in some eveniences, like a *bunch* multinodular goiter, *forgetting* a part of the goiter in the mediastinum. Surgical treatment needs a sternal split, rarely a thoracotomy; hardly ever a cervicotomy as way of access.