

## BENIGN AND MALIGNANT DOMINANT NODULE IN HASHIMOTO'S THYROIDITIS: A CLINICO-PATHOLOGIC STUDY ON A SERIES OF 342 PATIENTS

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**Background.** Hashimoto's thyroiditis (HT) is an autoimmune disorder which represents the most common inflammatory condition of the thyroid. HT occurs more frequently (up to 95% of cases) in women with age ranging from 30 to 50 years. It usually presents as a diffuse, firm, non-tender enlargement of the thyroid, due to the presence of micronodules imparting gland a resemblance to a hyperplastic lymph node. Some patients affected by HT may develop one or more nodules (> 1 cm), clinically evident or detected by ultrasonography, for which the term "dominant nodule" (DN) has been proposed. Due to the high rate of association between papillary thyroid carcinoma (PTC) and HT<sup>1</sup>, the detection of a DN larger than 1 cm is so alarming for clinicians that fine needle aspiration cytology (FNAC) is highly advised.

**Aim.** To investigate: i) the clinicopathologic features of DN in HT; ii) the association between HT, DN and PTC; iii) the predictive value of DN for a concurrent PTC elsewhere in the thyroid gland.

**Materials and Methods.** We selected a series of 342 patients with histologically proven HT (i.e. diffuse lymphocytic infiltration of the stroma with formation of lymphoid follicles and diffuse oxyphilic changes of the follicular epithelium). DN was defined as a nodule grossly or histologically detected, measuring  $\geq 1$  cm in its greatest diameter. The morphological features of "DN" were statistically correlated with clinical parameters. Benign or malignant tumors, especially PTC, were carefully searched on histological examination and correlated with clinical parameters, as well as with the occurrence of DN.

**Results.** We found that 48.5% of patients with HT had a "DN" ranging in size from 1 to 4.5 cm. In most cases (92.2%) DN was single, while in 7.8% at least two nodules were identified. Histologically most DN (78.3%) resulted to be benign, namely "hyperplastic follicular lesions (HFLs)". In contrast only 7.9% of DN resulted to be PTC (malignant DN). Surprisingly 65% of benign DN lacked inflammation and 55% were composed of non-Hurthle cells. Among the HFLs lacking inflammation, 55.6% were composed of Hurthle cells, while the 72.7% exhibited follicles lined by non-Hurthle cells. Notably, PTC was found in 25.7% (88 out of 342) of patients with HT. The majority of PTC (53.4%; 47 out of 88) were represented by microPTC (<1cm), as areas >1 cm (15.9%; 14 out of 88), or in the form of a DN (7.9%; 27 out of 342). In three patients with two DN, histological examination showed that both nodules were PTC, with a total of 30 PTC presenting as DN.

**Conclusions.** Our findings show that most DN (78.3%) in HT are histologically benign, namely HFLs, and not PTCs or follicular-derived neoplasms as commonly believed<sup>2</sup>. Unexpectedly a significant number of benign DN, despite their cellular composition (Hurthle or non-Hurthle cells), lacked any inflammatory component. Accordingly, pathologists should be aware of this possibility to avoid a misdiagnosis of follicular neoplasms in HT, either pre-operatively

(TIR3) or post-surgically. In addition our study first show that the detection of a benign DN is a protective factor for the occurrence of PTC.

### References

- Zhang Y, Dai J, Wu T, et al. The study of the coexistence of Hashimoto's thyroiditis with papillary thyroid carcinoma. *J Cancer Res Clin Oncol* 2014;140(6):1021-6.
- Mukasa K, Noh JY, Kunii Y, et al. Prevalence of malignant tumors and adenomatous lesions detected by ultrasonographic screening in patients with autoimmune thyroid diseases. *Thyroid* 2010.

Venerdì, 19 ottobre 2018

Sala Cassiopea – 9:00 - 12:30

## PATOLOGIA FETOPLACENTARE

### SHOULD THE PATHOLOGIST TALK TO THE PATIENT? FETAL POST AUTOPSY INTERVIEW: TOOL OF THERAPEUTIC MANAGEMENT, GRIEVING PROCESS AND RISK CONTROL

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**Background.** Clinical-pathological autopsies are decreasing all over the world, with the exception of fetal post mortem examinations which, according to Italian law, are mandatory from the twelfth week of pregnancy.

**Objectives.** We analyzed the experience of parents in relation to abortion providing, through post mortem examination and following interview, clinical and emotional care and offering critical information for the consideration and planning of a subsequent pregnancy.

**Materials and Methods.** All fetal post autopsy interviews carried out at Ospedale Policlinico San Martino in the period January 1, 2013 – July 1, 2018 have been included in the retrospective study. Bereaved parents, sometimes advised by clinicians, asked to meet the gynecopathologist, specialized in fetal, placental and perinatal field, who performed post mortem examinations. All autopsies have been reported with a standardized check-list based protocol including macro and microscopic analyses, together with placental examination. A standardized check-list based record followed every pathologist-parent meeting.

**Results.** Among the 214 post mortem fetal examinations (gestational age 12 – 42 weeks), 74 pathologist-parent interviews have been requested (34.6%), following both miscarriages (62.2%) and induced abortions (37.8%). Mothers, usually pregnant for the first time (mean age 34 years old), often brought along a family member, being the partner most of the time (56.8%). Although the mean mother age is nearly the same and the pathologist approach doesn't differ in both the miscarriage and abortion courts, women who experienced a miscarriage late in pregnancy asked for a post autopsy interview to obtain information to face with

the mourning and for medicolegal issue. Miscarriage etiology is more frequently placental, while abortions are often induced due to fetal pathologies.

**Conclusions.** Fetal autopsy and placenta examinations are critical in miscarriage and abortion investigation, providing information for an effective prevention. Gynecologist and genetist have a crucial role in the planning of a subsequent pregnancy especially in miscarriages and abortions, respectively. The management of polymalformative genetic syndromes emphasizes the importance to work in a multidisciplinary team, collaborating with gynecologist, radiologist and genetist. The pathologist, meeting the parents, offers a clear explanation about fetal post mortem examination and may help them in coping with bereavement and post mortem decision-making, preventing potential unfounded medicolegal issues. It is imperative that the pathologist remains impartial throughout the meeting with the patient, but, at the same time, is able to offer the sympathy that may be called for in grieving process. Overall, in our experience, pathologist-parent interaction has been positively perceived, with sporadic difficulty due to sociodemographic barriers and previous psychiatric disorders.

## GINECOLOGIA

### ATYPICAL ENDOMETRIAL HYPERPLASIA AND EARLY ENDOMETRIAL CANCER: A NOVEL FERTILITY-SPARING TECHNIQUE AND THE ROLE OF PATHOLOGY

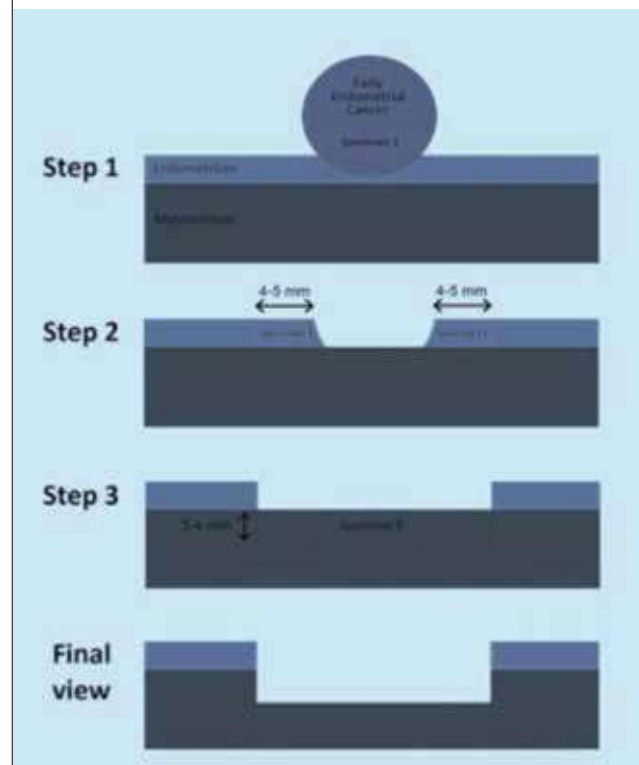
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**Aim.** Atypical endometrial hyperplasia (AEH) is a preneoplastic diseases characterized by an irregular proliferations of crowded endometrial glands with evident cytologic atypia. AEH is the precursor of endometrioid-type endometrial cancer EEC<sup>1</sup>. The treatment of choice for AEH and early EEC should be total hysterectomy<sup>2,3</sup>. However, these lesions are often diagnosed in young women with desire of pregnancy, and a fertility-sparing approach is required. To date, progestins are widely used as a conservative treatment for AEH and well-differentiated EEC at stage FIGO IA without invasion of the myometrium<sup>3</sup>. Among the several different fertility-sparing treatments, the levonorgestrel-releasing intrauterine system (LNG-IUS) is considered the most effective one<sup>2,4</sup>. Our aim was to evaluate safety and effectiveness of the combination of hysteroscopic endometrial focal resection with LNG-IUS for AEH and EEC in young women to preserve their fertility, highlighting the importance of pathological diagnosis.

**Materials and Methods.** Our study was designed as a retrospective case series (Canadian Task Force Level II-3). The medical records of 69 consecutive patients from 2007 to 2017 with diagnosis of AEH (n=55) or EEC (n=14) meeting inclusion criteria were reviewed. All patients were treated at the Obstetrics and Gynecology Unit, University Federico II, Naples, Italy. On patients with AEH, hysteroscopic resection preserving the basal layer of the endometrium was performed. On patients with EEC, hysteroscopic resection in three steps according to Mazzon's technique<sup>5</sup> was performed as follows: 1) removal

**Figure 1.** Schematic representation Mazzon's technique: (1) removal of the exophytic tumor (specimen 1); (2) removal of 4-5 mm of adjacent endometrium (specimen 2); (3) removal of 3-4 mm of underlying myometrium (specimen 3).



of the exophytic tumor (specimen 1); 2) removal of 4-5 mm of adjacent endometrium (specimen 2); 3) removal of 3-4 mm of underlying myometrium (specimen 3) (Fig. 1). The histologic examination of the specimens was performed at the Anatomic Pathology Unit, University Federico II, Naples, Italy. In order to include women in the fertility-sparing treatment, specimen 1 should be diagnosed as endometrioid type, well differentiated endometrial cancer without lymphovascular space invasion; specimen 2 should be cancer-free, indicating that the lesion was focal; specimen 3 should be cancer-free as well, demonstrating that the myometrium was not infiltrated. Subsequently, LNG-IUS was inserted and maintained for at least 12 months. Patients were followed for a total of 24 months with serial hysteroscopic biopsies. **Results.** Rates of response, live birth and recurrence were assessed. Out of 55 patients with AEH, 51 (92.7%) achieved a complete response, 2 of whom (3.9%) had subsequent relapse, 3 (5.5%) showed partial response, while only 1 (1.8%) was non-responder with stable disease. Out of 14 patients with EEC, 11 (78.6%) achieved a complete response, 2 of whom (18.2%) had subsequent relapse, 1 (7.1%) showed partial response, while 2 (14.3%) were non-responders (1 stable disease and 1 progression). Among 25 patients who had removed LNG-IUS, 10 (40%) gave birth after natural conception in the last twelve months of follow-up.

**Conclusions.** The combination of hysteroscopic resection with LNG-IUS as fertility-sparing treatment of AEH and EEC showed similar response and live birth rates compared to those reported in literature for progestins alone, but a considerably lower relapse rate<sup>6</sup>. We advocate the use of this combined approach as an alternative fertility-sparing option for AEH and ECC, highlighting the importance of pathological diagnosis to avoid both under- and over-treatment.