

## The incidence of Thyroid Carcinoma in Multinodular Goiter: retrospective analysis

*Pier Paolo Gandolfi, Antonio Frisina, Maurizio Raffa\*, Flavia Renda\*\*, Orietta Rocchetti, Corrado Ruggeri\*\*, Alberto Tombolini*

Unit of Otolaryngology, Department of Surgery, Hospital of Sanremo, Sanremo (IM), Italy

\* Unit of Endocrinology, Department of Medicine, Hospital of Sanremo, Sanremo (IM), Italy

\*\* Department of Pathology, Hospital of Sanremo, Sanremo (IM), Italy

**Abstract.** Thyroid carcinoma (TC) is a relatively rare tumour, but it represents the most frequent form of cancer of the endocrine glands. Epidemiologically ascertained risk factors are ionising radiation, the presence of thyroid adenoma and multinodular goiter (MNG). Multinodularity of goiter should no longer be considered an indicator of probable benign disease. A retrospective analysis was performed on patients operated of MNG at the Unit of Otolaryngology, Sanremo Hospital (Italy) from January 1<sup>st</sup> 1995 to December 31<sup>st</sup> 2002, in order to establish the incidence of carcinoma. The results of this retrospective study, demonstrate that in 13.7% of the patients operated for goiter, the presence of a carcinoma was noticed in the definitive histopathologic examination. Such incidence percentage of MNG is in accordance with the data reported in published reports. Thus, the authors conclude that the risk of malignancy in MNG has not to be underestimated, and that a dominant nodule in MNG should be valued as if it were a solitary nodule in an otherwise normal gland.

**Key words:** Thyroid nodule, malignant nodule, thyroid carcinoma, multinodular goiter

### Introduction

Thyroid carcinoma (TC) is a relatively rare tumour, but it represents the most frequent form of cancer of the endocrine glands. It represents 1% of human neoplasias and its annual incidence is estimated worldwide from 0.5 to 10: 100.000 subjects in the world population (1). Such incidence is increased if cases of occult carcinoma are taken into consideration. This occult carcinoma is a non evident neoplasia, occurring with cervical nodal disease, or accidentally detected in a thyroid that has been removed for another pathology or during an autopsy (2). Epidemiologically ascertained risk factors are ionising radiation, the

presence of thyroid adenoma and multinodular goiter (MNG) (1). In published reports, the incidence of carcinoma in MNG is reported with a percentage that varies from 7% to 17% (3-8). Furthermore, it seems that there is no statistically significant difference between the incidence of TC in patients with a solitary nodule, as shown in the post-operation histopathologic exam, and those with MNG (6, 9). Thus, multinodularity does not seem to be a certain indicative factor of benign disease (5, 7, 8). The aim of the study is to carry out retrospective analysis of patients who have been operated for normal or hyperfunctioning MNG, in order to establish the incidence of the histopathologically documented carcinoma or of the

occult carcinoma found only after a complete histopathologic examination of the operated thyroid or whose clinical revealing occurred with the discovery of cervical node disease during the follow up.

**Materials and Methods**

A retrospective study on patients who have undergone a total thyroidectomy for normal or hyperfunctioning thyroid MNG, has been conducted at the Unit of Otolaryngology, Sanremo Hospital (Italy) from January 1<sup>st</sup> 1995 to December 31<sup>st</sup> 2002. During preoperative evaluation, all the patients underwent thyroid ultrasonography, and only in the cases with a suspect nodule during the ultrasound, a fine needle aspiration biopsy (FNAB) was conducted. Scintigraphy was never performed, since it has a low specificity and sensitivity in detecting thyroid cancer. In all the cases of multinodular nodules a total thyroidectomy was performed following the isolation and the preservation of the recurrent laryngeal nerves and of the parathyroid glands.

**Results**

In this retrospective study of 81 operations performed for thyroid lesions in the period from 1995 to 2002 at the Unit of Otolaryngology Hospital of Sanremo (IM), the presence of MNG was found in 58 cases (71.6%) (Table 1). The total number of carcinoma cases was 25 (18 papillary cancer, 4 Hurtle carcinoma, 2 anaplastic cancer and 1 follicular cancer). In the 58 cases of MNG, 8 cases of carcinoma were found (13.7%) (Table 2). These 8 patients were

5 females and 3 males, all aged over 45 yrs. For all of these cases a thyroid ultrasonography was performed during the preoperative evaluation, in 5 cases a FNAB, while a scintigraphy was never performed. In the 5 cases where the FNAB was performed, no evidence of cellular atypia with benign colloid nodule was found in 2 cases (Figure 1), while in 3 cases a follicular tumour was reported. In all cases a total thyroidectomy was performed. At the definitive histopathological examination, 5 cases of papillary cancer (Figure 2), 2 Hurtle carcinoma and 1 follicular cancer were reported (Table 3). Hence, the incidence of occult carcinoma for the 58 cases of MNG was 8.6%. The 8 carcinomas were smaller than 2 cm in 7 cases, while in just one it was bigger than 2 cm. In this last

Table 2. Carcinoma in goiter

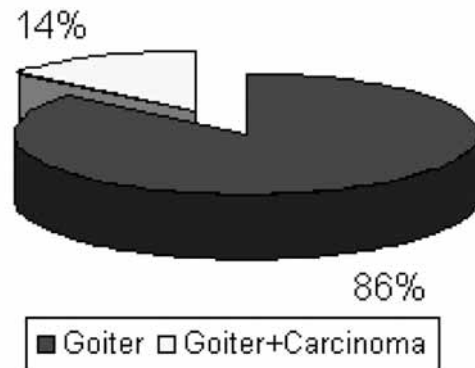


Table 1. 81 Cases with thyroid lesions

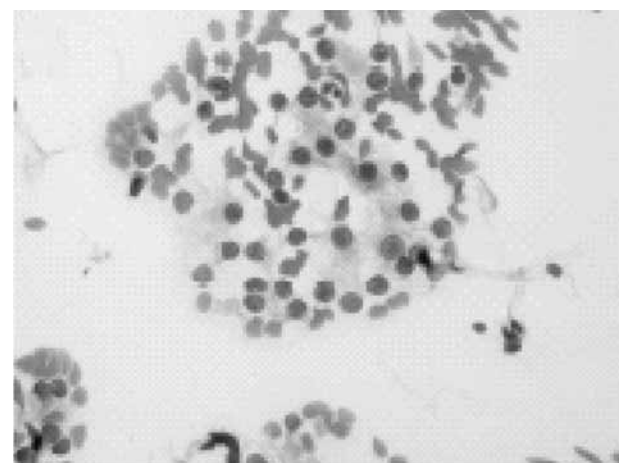
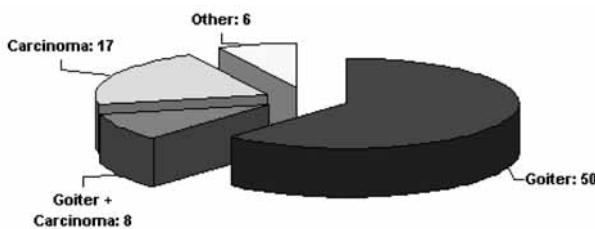


Figure 1. Cytology of the benign colloid noduel

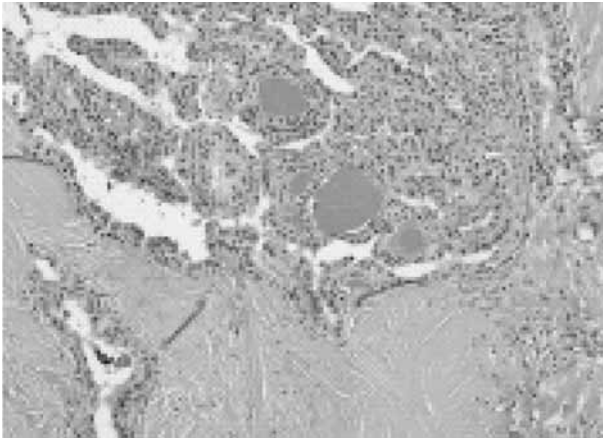
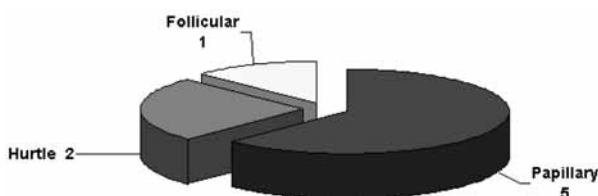


Figure 2. Histology of the papillary carcinoma

Table 3. Histological type of carcinoma



case post-operation radioiodine therapy has been carried out.

## Conclusions

Traditionally patients with MNG have been considered less at risk of malignancy than those with single nodule. However, published reports show that the incidence of malignant tumours in patients with single nodule does not differ from those with MNG (6, 9). MNG is a risk factor for epidemiologically ascertained TC (1). In fact, the induction of TC following a diet lacking in iodine, was demonstrated in mice and a confirmation is given by the reduction of the mortality rate for TC registered in Switzerland following the supplement of iodine in table salt (10). Epidemiological studies have demonstrated how the incidence of carcinoma in patients with MNG is higher than the incidence of the general population (11, 12). In our re-

trospective study, for 13.7% of the patients operated for MNG, during the definitive histopathological examination, a pattern of MNG associated to carcinoma was evidenced. In accordance with published works, the histopathological type of carcinoma more frequently associated to MNG was shown to be the papillary (62.5%) (12). Among the instrumental exams to diagnose the malignancy of a thyroid nodule, ultrasound and scintigraphy help in raising a suspect, however, the most efficient method is the FNAB. Nevertheless, even if the pre-operation FNAB is negative, it does not exclude with certainty the possibility of a carcinoma, especially in MNG where the error in sampling the right area is greater. In fact, an incidence of 8.6% of occult carcinoma was evidenced in cases operated for MNG. Such evaluation error may lead to the performance of a non radical operation, and thus, to the need of a second operation or radiotherapy. In all cases of treated goiter, a total thyroidectomy was performed. Such radical treatment in case of carcinoma guarantees an oncological radicality, and allows to evidence eventual local or distant metastases. The post-operation radioiodine therapy has been carried out in just one case inasmuch the carcinoma was bigger than 2 cm. In conclusion, the risk of malignancy in MNG has not to be underestimated, and a dominant nodule in MNG should be valued as if it were a single nodule in an otherwise normal gland.

## References

1. Franceschi S. Epidemiologia del carcinoma della tiroide. In: Miani P eds. Il carcinoma della tiroide. Pisa: Pacini Editore, 1992; 13-29.
2. Miani P, Piemonte M, Bacchi G, Miani C. Fattori prognostici e risultati terapeutici nel carcinoma della tiroide. In: Miani P eds. Il carcinoma della tiroide. Pisa: Pacini Editore, 1992; 167-97.
3. Cole WH. Incidence of carcinoma of the thyroid in nodular goiter. *Semin Surg Oncol* 1991; 7 (2): 61-3.
4. Koh KB, Chang KW. Carcinoma in multinodular goitre. *Br J Surg* 1992; 79 (3): 266-7.
5. Mathai V, Idikula J, Fenn S, Nair A. Do long-standing nodular goitres result in malignancies? *Aust N Z J Surg* 1994; 64: 180-2.
6. McCall A, Jarosz H, Lawrence AM, Paloyan E. The incidence of thyroid carcinoma in solitary cold nodules and in multinodular goiters. *Surgery* 1986; 100 (6): 1128-32.

7. Pelizzo MR, Toniato A, Piotto A, Bernante P. Cancer in multinodular goiter. *Ann Ital Chir* 1996; 67 (3): 351-6.
8. Sachmechi I, Miller E, Varatharajah R, et al. Thyroid carcinoma in single cold nodules and in cold nodules of multinodular goiters. *Endocr Pract* 2000; 6 (1): 110-2.
9. Hossein G. Changing concepts in the diagnosis and management of the thyroid nodules. *Endocrinology and Metabolism Clinics of North America* 1997; 26 (4): 777-800.
10. Franceschi S, Talamini R, Frassina A, Bidoli E. Diet and epithelial cancer of the thyroid gland. *Tumori* 1990; 76: 331-8.
11. Francis SG. The problem of nodular goitre. *Med Clin N Am* 1991; 75: 195-209.
12. Clark OH, Quan-Yang D. Thyroid cancer. *Med Clin N Am* 1991; 75: 211-34.

---

Received: 12 January 2004

Accepted: 10 June 2004

Correspondence: Alberto Tombolini, MD

Unit of Otolaryngology

Department of Surgery

Hospital of Sanremo

Via Giovanni Borea, 56

18038 Sanremo (IM), Italy

Tel: +39 0184/536374

Cell: 335/5414308

Fax: +39 0184/536371

E-mail: albertotombolini@yahoo.it