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Thyroid malignancy in multinodular goitre and solitary nodule

S. A. ABU-ESHY*†, A.-R. KHAN†, G. M. KHAN*, M. A. AL-HUMAIDI†, M. Y. AL-SHEHRI*†, AND T. S. MALATANI*†

Department of Surgery, Asir Central Hospital and †College of Medicine, King Saud University, Abha Branch, Abha, Saudi Arabia

This is a retrospective study of 361 thyroid specimens during a $6\frac{1}{2}$-year period with the objective of investigating the prevalence and pattern of thyroid malignancy associated with multinodular goitre (MNG) and solitary nodule (SN). Fourteen of 172 MNG (8%) and 16 of 105 SN (15.2%) were associated with malignancy, a statistically insignificant difference ($P = 0.06$). Unlike in males, malignancy was significantly commoner in females with SN than those with MNG ($P = 0.03$) and generally occurred at a significantly older age ($P < 0.05$). On analysing thyroid carcinoma and lymphoma separately, patients with SN had a higher incidence of carcinoma compared with those with MNG ($P = 0.01$). It is concluded that surgical intervention may be the appropriate method of treating male patients presenting with MNG. However, in females, conservative management of MNG should be adopted unless surgery is indicated depending on clinical judgement and, if feasible, the result of fine needle aspiration biopsy.

Keywords: malignancy, multinodular goitre, solitary nodules, thyroid.

The incidence of malignancy in multinodular goitre (MNG) varies from 4 to 17%[1] compared with 9 to 25% in solitary nodule (SN)[2]. The higher incidence of malignancy in SN when compared with MNG is debatable. Management of an SN has been refined by fine needle aspiration biopsy (FNAB), unlike MNG, in which a nodule of cancer can not be differentiated clinically or radiologically amidst other benign nodules[1]. Although many previous studies reported various incidences of malignancy associated with MNG and SN, none of these studies looked into sex differences. Therefore, we decided to perform this review to evaluate the prevalence of malignancy in MNG and SN in both sexes in order to make proposals for the management accordingly.

PATIENTS AND METHODS

Over a period of $6\frac{1}{2}$ years, from January 1987 to June 1993, the Pathology Department at Asir Central Hospital (ACH), Abha, Saudi Arabia, received 361 thyroid specimens. The incidence of malignancy was compared in clinically and/or histopathologically proven SN with that of MNG. Chi-square, Students' *t*-test and Fisher exact test were used for comparison at the 5% level of significance.

RESULTS

Among the 361 cases, there were 105 cases of SN and 172 cases of MNG. The results of the analysis of these cases are shown in Table 1. Of 105 patients with SN, 85 were female and 20 were male; the age ranged from 14 to 101 years (mean = 34.7 ± 14.2 years). Sixteen patients (15.2%) had thyroid malignancy. Among 172 patients with MNG, there were 23 males and 149 females; the age ranged from 7–120 years (mean = 37.7 ± 14.3 years). Fourteen patients (8%) had thyroid malignancy. The difference in the incidence of thyroid malignancy between patients with SN and those with MNG is not significant ($P = 0.06$). However, a significant difference was found between MNG and SN on analysing thyroid carcinoma and lymphoma separately ($P = 0.01$); carcinoma being higher in SN (13.6 vs. 4.2%). On analysing patients according to sex, we found that females had a significantly lower incidence of cancer in MNG (7.3%) compared with SN (16.5%) ($P = 0.03$). This difference was not noted in males. In this study, papillary carcinoma was encountered more frequently (8 of 11) in patients below 40 years of age with SN while all 9 cases of lymphoma were seen in patients above 40 years of age; seven of these patients presented with MNG. Two female patients with SN had follicular carcinoma and one had anaplastic carcinoma (Table 2). The incidence of thyroid malig-

Table 1 Malignancy in multinodular goitre (MNG) and solitary nodule (SN)

		Total	Cancer *n* (%)	Carcinoma	Lymphoma
MNG	Males	23	3 (13)	1	2
	Females	149	11 (7.3)	6	5
	Total	172	14 (8)	7 (50)	7 (50)
SN	Males	20	2 (10)	2	0
	Females	85	14 (16.5)	12	2
	Total	105	16 (15.2)	14 (87.5)	2 (12.5)

Correspondence to: Dr Saeed Ali Abu-Eshy, PO Box 54, Abha, Saudi Arabia.

Table 2 Distribution of thyroid carcinoma

	Multinodular goitre			Solitary nodule		
	Males	Females	Total	Males	Females	Total
Papillary	0	6	6	2	9	11
Follicular	0	0	0	0	2	2
Medullary	1	0	1	0	0	0
Anaplastic	0	0	0	0	1	1
Total	1	6	7	2	12	14

nancy was found to be significantly higher ($P < 0.01$) in patients above 40 years of age in both sexes (Table 3).

DISCUSSION

A long-standing and hitherto unresolved issue is whether MNG is significantly associated with carcinoma[3]. The diagnosis of malignancy in SN is easily made by different methods such as surgical excision of the palpable nodule or aspiration biopsy. However, the incidence of malignancy in MNG is reported to range from 4–17%[1]. This variation is due to several factors, which include, but are not limited to, the following.

(1) Method of diagnosis, whether surgical excision or aspiration biopsy.

(2) Expertise in interpretation of the aspiration biopsy.

(3) Care in microscopic sectioning. In some centres, pathologists submit a few representative sections, whereas in others, the entire specimen is sectioned.

(4) The ambiguity in the pathogenesis of MNG. Mild dietary deficiency of iodine, slight impairment of hormone synthesis, increased iodide clearance from the kidneys and presence of thyroid-stimulating immunoglobulins had been suggested as various causes. Therefore, geographical and racial factors play an important role in the pathogenesis of MNG and thus associated cancer. It is not surprising, therefore, to see such heterogenous data from different populations.

A nodule harbouring malignancy in MNG cannot be distinguished clinically or radiologically in order to obtain a FNAB from it. This makes the early detection of cancer in MNG a very difficult task. In a study reported from Malaysia[1], 7.5% of patients with MNG had foci of malignancy. In another study from the USA, the incidence of carcinoma in MNG was 13% and was not significantly different from SN in which malignancy was seen in 17%[2]. However, the incidence of malignancy in solitary cold nodule is generally considered to be higher than that of MNG[4].

Table 3 Mean age for malignant and benign goitres

	Mean age in years	
Histopathology	Multinodular goitre	Solitary nodule
Benign	36.4	32.7
Malignant	52.2	46.1

In our study, we found the incidence of malignancy to be 8% with MNG and 15.2% with SN. The difference is not statistically significant. This finding is in agreement with that of McCall et al.[2], the reported studies from Riyadh, Saudi Arabia[5,6], and that by Belfiore et al.[7]. When we separated the sexes in our study, we found that females, unlike males, had significantly lower incidence of malignancy in MNG (7.3%) compared to SN (16.5%). Furthermore, exclusion of thyroid lymphoma resulted in a significant difference in the incidence of thyroid carcinoma between MNG and SN; being higher in the later. The results of our study also showed that the incidence of malignancy in males with SN was 10% and in females 16.5%; the difference is not statistically significant. MNG in males contained foci of malignancy in 13% and in females 7.3%, a statistically insignificant difference.

Although the malignancies associated with MNG are usually follicular or papillary carcinomas[8–11], our study showed a higher frequency of thyroid lymphoma. This could well be a translation of the high lymphoma rate in our area, which ranks as the third most common among other malignancies[12].

In conclusion, our study, supported by other reports in the surveyed literature, revealed insignificant difference in the incidence of thyroid malignancy between MNG and SN. Therefore, we think that surgical intervention may be the appropriate modality of treating MNG in males. However, since a large proportion of MNG are benign in females, conservative approach should be undertaken and the decision to perform surgery should be based on the clinical judgement and, if feasible, the result of FNAB.

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