

Multinodular goiter management in Western Saudi Arabia

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ABSTRACT

Objectives: The aim of this study was to provide epidemiological data and summarize the different modalities of management of multinodular goiters (MNG) in the Western Province of Saudi Arabia (KSA).

Methods: A total of 135 patients had MNG, which were diagnosed by ultrasonography at King Abdul-Aziz University Hospital in Jeddah, KSA between January 2003 and June 2004. The data collected includes the age, gender, physical examination of the thyroid gland (trifluorothymidine, free thyroxine, free triiodothyronine, thyroid stimulating hormone), ultrasonographic findings and Tc99 radioiodine nuclear scan of the thyroid gland, fine needle aspiration (FNA) of the gland and antithyroid antibodies. The study group was divided according to the thyroid status: nontoxic euthyroid MNG, hypothyroid MNG and toxic hyperthyroid MNG. The management of MNGs according to the patients' clinical presentations and thyroid status was reviewed.

Results: The mean age was 39 ± 12.66 years with a range of 10-79 years. Forty-two patients (31%), with no history of thyroid cancer, had ultrasound-guided FNA; 41 (97.6%) of the FNAs were benign. One FNA (2.3%) was positive for papillary carcinoma in a 56-year-old female patient. Thyroid antibodies (anti-microsomal antibodies and anti-thymoglobulin antibodies) were measured in 50 patients (37%). Thirty-one (62%) were

positive, 11 (35%) of which were positive in patients with documented hypothyroidism. All patients with hypothyroidism were treated with levothyroxine; however, only 25.6% with euthyroid MNG were treated with suppressive doses of levothyroxine. Twelve patients (44.4%) with toxic MNG were treated with antithyroid medications. Radioiodine therapy was not given to any patient with nontoxic MNG; however, 48% of those with hyperthyroid MNG received radioactive iodine treatment. Surgery was carried out in 25.6% of patients with euthyroid nontoxic MNG, and in 11 patients with toxic MNG. Nearly half of those with nontoxic MNG (46.5%) and 14.8% of those with a subclinical hyperthyroid MNG refrained from any therapy. They were followed-up by their clinician in the outpatient clinic.

Conclusion: Serum thyroid stimulating hormone levels, ultrasound and fine needle biopsy were the cornerstones of the diagnostic evaluation of patients with MNG. Review of the management of these patients was comparable to that found in the literature. The treatment strategy was similar to the recommendations by the American Thyroid Society; however, radioactive iodine treatment was not used as a treatment for patients with nontoxic goiters.

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The development a multinodular goiter (MNG) is a common clinical problem that poses important diagnostic and therapeutic issues for the surgeon, internist, radiologist and endocrinologist. It varies greatly in its manifestations. The goiter may be small and barely palpable, or it may clinically manifest as a single thyroid nodule detected by

physical examination.¹ On the other hand, the gland may be large enough to cause symptoms of obstruction. The patient may be euthyroid or thyrotoxic, and the thyroid gland may contain both hyperfunctioning and hypofunctioning (cold) nodules. It can also be the source of a thyroid carcinoma.² Multinodular goiters tend to be an

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especially important problem among geriatric patients, in whom it can cause substantial morbidity and mortality.³ Its diagnosis may be deceptively difficult, and its treatment is sometimes difficult but usually effective.

Few reports from the central area of the KSA described the epidemiology of MNG.^{4,5} The aim of this study is to provide epidemiological data of MNG in the Western Province of KSA. In this study, the diagnosis of MNG was made by ultrasonography. There were different modalities of treatment offered to those with as summarized in our study.

Methods. This cohort study consisted of all patients with MNG diagnosed by ultrasonography at King Abdul-Aziz University Hospital in Jeddah, KSA during a one and a half year period (from January 2003 to June 2004). The diagnosis of MNG based on ultrasound finding on the presence of different thyroid nodules: solid, cystic and mixed solid-cystic. Patients' notes were reviewed for age, gender, nationality and a detailed examination of the thyroid gland. All patients had a thyroid function test [free thyroxine (FT4), free triiodothyronine (FT3), thyroid stimulating hormone (TSH)], which was measured by radioimmunoassay using commercial kits. The clinic visits included a thyroid ultrasonography performed by a radiologist or Tm

99 radionuclear scan performed by a nuclear medicine physician. The radiological image findings revealed either a toxic MNG, nontoxic MNG or a cold nodule. Ultrasound guided fine needle aspirate (FNA) of all the nodules measuring at least 1 cm in maximum diameter (maximum of 4 nodules) and thyroid antibodies (anti-microsomal and anti-thyroglobulin antibodies) were reported.

The mode of therapy, which was elected according to the different clinical presentations of MNG (follow up of patients without treatment, medical therapy, thyroidectomy or radioactive iodine treatment) was noted. The clinical presentations of MNG were divided into 3 groups according to their thyroid status: euthyroid, hyperthyroid or hypothyroid. The results were expressed as mean \pm SD or median (range).

Results. A total of 135 patients (120 females and 15 males); with a female to male ratio of 8:1 were evaluated at the radiology department by ultrasonography for MNG. Forty-eight patients (35.6%) were Saudis and 87 (64.4 %) were non-Saudis; the non-Saudi and Saudi ratio was 1.8:1. The mean age was 39 ± 12.66 years with a range of 10-79 years.

Sonographic and Tm 99 radioiodine nuclear scan findings. Ultrasonography revealed MNG in all patients, 12 patients (9%) had a solitary cold

Table 1 - Mode of therapy according to the thyroid status of multinodular goiter.

Trifluorothyrimidine	Nontoxic MNG (Euthyroid)		Toxic MNG (Hyperthyroid)		MNG (Hypothyroid)	
	n	(%)	n	(%)	n	(%)
<i>N patients</i>	86	(63.7)	27	(20)	22	(16.3)
<i>Mode of therapy</i>						
FT4 (12 - 22 pmol/L)	13 \pm 0.92		37.75 \pm 26.22		10.39 \pm 3.22	
FT3 (2.8 - 7 nmol/L)	3.02 \pm 2.32		13.92 \pm 7.9		4.11 \pm 1.19	
TSH (0.27-4.2 IU)	1.66 \pm 3.2		0.01 \pm 0.32		23.7 \pm 23.13	
<i>Mode of treatment</i>						
Follow up without treatment	40	(46.5)	4	(14.8)		
Levothyroxine	22	(25.6)	0		22	(100)
Antithyroid medication	0		12	(44.4)		
Thyroidectomy	22	(25.6)	3	(11)		
Radioactive iodine	0		13	(48)		
MNG - multinodular goiter, FT3 - free triiodothyronine, FT4 - free thyroxine, TSH - thyroid stimulating hormone.						

nodule. T99 radioiodine nuclear scans carried out in 70 patients (52%) revealed toxic MNG in 23 patients (33%), 42 patients (60%) had nontoxic MNG and only 5 patients (7%) had a solitary cold nodule.

Cytological findings after fine-needle aspiration. Forty-two patients (31%) with no history of thyroid cancer had ultrasonography-guided FNA, 41 of them (97.2%) were benign including undetermined and inadequate cases. One FNA (2.3%) was positive for papillary carcinoma in a 56 years old female patient.

Thyroid antibodies. Thyroid antibodies (anti-microsomal antibodies and anti-thyroglobulin antibodies) were measured in 50 patients (37%). Thirty-one (62%) were positive. Eleven of them (35%) were positive in hypothyroid patients, 15 (30%) in euthyroid patients and 5 (10%) in patients with a toxic MNG.

Modalities of treatment according to thyroid status in patients with a multinodular goiter. All patients with hypothyroidism were treated with levothyroxine (L-thyroxine); however, only 25.6% with euthyroid MNG were treated with a suppressive dose of L-thyroxin (mean dose was 81 ± 32 mg daily) to suppress the serum TSH to a level between 0.1 and 3I U. These patients used L-thyroxin therapy continuously for several years. Twelve (44.4%) of those with a toxic MNG were treated with antithyroid medications (11 cases with neomercazole and one patient with propylthiouracil during her pregnancy). Radioiodine therapy was not given to anyone with nontoxic MNG. However, 48% of those with hyperthyroid MNG were treated with radioactive iodine with a mean dose of 18.6 ± 5.7 Mci. Three of those patients were treated initially with antithyroid medications for one year. Surgery was carried out in 25.6% of patients with euthyroid nontoxic MNG and in 11 patients with toxic MNG; one in whom surgery was carried out after failure of medical treatment. A near total thyroidectomy was the preferred surgery. Nearly half of those with nontoxic MNG (46.5%) and 14.8% with a subclinical hyperthyroid MNG refrained from any therapy. They were followed up by their clinician in their own clinic. (Table 1)

Discussion. Patients with MNG are a relatively common clinical problem especially in areas of frank or borderline iodine deficiency. Although most goiters are benign and asymptomatic, there are several factors to be considered. The goiter may give rise to local discomfort and may, in cases of large goiters, cause mechanical obstruction of the upper airway, like one patient in this study who presented with a huge goiter and airway obstruction. Goiters have an annual growth potential of up to 20%, which can complicate treatment.⁶ That is, if treatment is

delayed, surgery may ultimately be required.⁷ Progressive autonomous function of thyroid nodules can cause overt thyrotoxicosis in 5–10% of patients with MNG within a 5-year period. Even more frequently, patients develop subclinical thyrotoxicosis with its potential for atrial fibrillation. Three of our patients presented initially with atrial fibrillation.³ Finally, thyroid cancer presents in approximately 5% of patients with MNG. However, only one patient (0.7%) in our series was detected to have papillary carcinoma.⁸ This could be explained that (97.2 %) FNA were benign including undetermined and inadequate.

King Abdul-Aziz University Hospital (KAUH), Jeddah is a referral center in the Western area of KSA with no specific limitations in accepting patients whether Saudis or non-Saudi residents. This explained why 64.4% of our patients were non-Saudi residents. The diagnosis of MNG was based mainly on ultrasound records rather than a clinical setting like endocrine or thyroid clinic. However, a policy of KAUH that all goiter patients undergo ultrasound examination, which may create biased on the results. There are several international surveys in the management of goiter amongst North American as well European clinicians have been reported, which show disagreement in the treatment recommendation.^{9,10} The evaluation of patients with multinodular goiters includes determination of thyroid function, estimation of goiter size, and exclusion of malignancy and assessment of local symptoms. The evaluation should begin with determination of the serum TSH level. If the TSH level is suppressed, serum levels of the other thyroid hormones (FT4 and FT3) should be determined followed by a radioactive iodine uptake test.¹¹ A toxic MNG is treated with radioactive iodine or surgery.¹² Subclinical hyperthyroidism may be observed for a transient period of time and then resolved. Our management of toxic MNG corresponds to that reported in the literature.¹³ A normal serum concentration of TSH suggests the presence of nontoxic MNG. Cytological evaluation by FNA helps the management strategy.¹⁴ That is, in a patient with benign goiter, periodic evaluation (including thyroid palpation, determination of serum levels of TSH and imaging studies) is helpful in the management. Cytologically suspicious or malignant MNG should be treated surgically.¹⁵ Surgical excision is preferred in patients with nontoxic MNGs who have local compression symptoms or for cosmetic concerns. In recent years, radioiodine therapy has been advocated for patients with large nontoxic MNG.¹⁶ In several studies, Huysman et al¹⁷⁻¹⁹ reported results of successful treatment with radioiodine in nontoxic MNG: symptomatic improvement in 71% of patients, a decrease in tracheal deviation in 20% and an increase in tracheal lumen in 36%. None of the patients with a

nontoxic MNG in our study were treated with radioactive iodine therapy. This could be due to the fact that most patients suffering from MNGs were managed by internists, primary care physicians or surgeons, who were not members of any thyroid association and consequently not updated in the management of thyroid disorders.²⁰

Multinodular goiter rarely presents with an increased TSH level; however, 16.3% of our patients were hypothyroid and had a high TSH level. Those cases most probably had Hashimoto's thyroiditis, irrespective of the ultrasonographic diagnosis of nontoxic MNG, as 62% had a high titer of positive thyroid antibodies.

This is the first study from Jeddah showing the epidemiology of MNGs in the Western Province of KSA. Serum TSH, ultrasound and fine needle biopsy are the cornerstones of the diagnostic evaluation of patients with MNG. Review of the management of our patients was comparable to that found in the literature. The treatment strategy was similar to recommendations made by the American Thyroid Society. However, radioiodine treatment was not used for treatment of nontoxic goiters in our region.

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