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ARTICLE REVIEW

Histological findings in multinodular goiter

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لِّلَّهِ مَا فِي السَّمَاوَاتِ وَمَا فِي الْأَرْضِ ۗ وَإِن تُبْدُوا مَا فِي أَنفُسِكُمْ أَوْ تُخْفُوهُ يُحَاسِبْكُم بِهِ اللَّهُ ۖ فَيَغْفِرُ لِمَن يَشَاءُ وَيُعَذِّبُ مَن يَشَاءُ ۗ وَاللَّهُ عَلَىٰ كُلِّ شَيْءٍ قَدِيرٌ (284)

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DEDICATION

My family has showed me what the true meaning of life really is, what makes the journey worth it in the end. They showed me that no matter where the road leads, however many bumps, forks or traffic jams there are, the only thing that matters is that when you get where you set out to go, you are happy, and you know that the road keeps going on even after you pull over for a little while. They have showed me what it means to love, and to be loved, and how important both of those things are. They have helped make me who I am and continue to do so each and every day. My family is the constant in my life, the thing that is there when I close my eyes and is still there when I open them again. They say you can't choose family, and for that I am grateful, because if I could in fact choose my family, I would pick the one that I already have right beside me. I wouldn't trade my family for the world, and I feel like the luckiest girl in the world being able to call them mine.

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.....thank you for everything

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I would like to express my special thanks of gratitude to Dr. Thura Abbas as well as our university teaching doctors at diyala medical university who gave me the golden opportunity to do this wonderful project on the topic (Histological findings in multinodular goiter), which also helped me in doing a lot of Research and i came to know about so many new things I am really thankful to them.

Abstract

Introduction: A goiter simply means an enlarged thyroid. A goiter can either be a simple goiter where the whole thyroid is bigger than normal or a multinodular goiter where there are multiple nodules. Multinodular goiters can be either a toxic multinodular goiter (i.e. makes too much thyroid hormone and causes hyperthyroidism or non-toxic. (1) It is not known what causes multinodular goiters in most cases, but iodine deficiency (i.e. too little iodine in the diet) and certain genetic factors have been shown to lead to multinodular goiters. Multinodular goiter (MNG) is the most common of all thyroid gland disorders. MNG is the product of follicular cell genetic heterogeneity and the apparent acquisition of new cellular characteristics that become inheritable. The most common symptom of nodular goiter is a mass in the neck, but an enlarging gland may cause pressure symptoms. (3) Hyperthyroidism develops in a large proportion of MNGs after a few decades, frequently after iodine excess.

Review: the most common factors that may be involved in the evolution of multinodular goiter:

- **PRIMARY FACTORS:**
  - Functional heterogeneity of normal follicular cells, most probably due to genetic and acquisition of new inheritable qualities by (5) replicating epithelial cells. Gender (women) is an important factor.
  - Subsequent functional and structural abnormalities in growing goiters
- **SECONDARY FACTORS:**
  - Elevated TSH (induced by iodine deficiency,(6) natural goitrogens, inborn errors of thyroid hormone synthesis)
  - Smoking, stress, certain drugs
  - Other thyroid-stimulating factors (IGF-1 and others)
  - Endogenous factor (gender)

Aim: This narrative review summarizes the comprehensive information about histological findings in multinodular goiter. The aim of the current article review to focus on the importance of histopathological detection of different morphological type of multinodular goiter.

Conclusion: assessing patients with a multinodular goiter using histological examination with several other risk factors such as female gender, younger age, fewer overall nodules, and smaller nodule size should be considered in order to early detection of serious histopathological transformation which may end up with CA of the thyroid . Early histopathological diagnosis is essential in multinodular goiter as it will allow early treatment and good prognosis.

Introduction

A goiter is a swelling of the neck caused by a swollen thyroid gland. A goiter may be caused by a thyroid that isn't working properly. Iodine deficiency is the most common cause of goitre worldwide, particularly in countries where iodized salt is scarcely used. Selenium deficiency is also thought to be a cause. Hashimoto's thyroiditis is the most common cause of thyroiditis in countries that use iodized salt.

Several studies have reported the prevalence of multinodular goiter in areas with adequate iodine intake (1-10). Tunbridge et al (1) discovered apparent goiters in 5.9 percent of 2,749 people in northern England in a detailed population survey with a female/male ratio of 13:1. Thyroid nodules were present in 0.8 percent of men and 5.3 percent of women, with a higher prevalence in women over 45 years old. The use of sensitive imaging methods and routine autopsy surveys results in a much higher incidence. Nodularity was observed in 30 to 50 percent of subjects in autopsy trials, and in 16 to 67 percent of subjects in prospective studies of randomly selected subjects on ultrasound (2). In Framingham, the prevalence of multinodular goiter was 1%, according to a population survey of 5234 people over the age of 60. (3). Singaporean data indicate a prevalence of 2.8 percent (4). In a study of 2,829 people between the ages of 31 and 38 in southwestern Utah and Nevada (USA), 23 percent had non-toxic goiter, which included 18 single nodules, 3 cysts, 38 colloid goiters, and 7 with no histological diagnosis. There was no mention of multinodular goiters, though some may have been present in the colloid and unidentified groups (5). In particular, the prevalence of multinodular goiter is less than 4% in iodine-sufficient countries (6). In countries where previous deficiency was fixed by universal salt iodination, elderly subjects can have a 10% incidence of nodular and multinodular goiter, which is due to a lack of dietary iodine in early adult life.

A goiter is classified as either nodular or diffuse. Nodular goitres which may consist of a single nodule (uninodular) or multiple nodules (multinodular).

- Uninodular goitre: one thyroid nodule; can be either inactive, or active (toxic) – autonomously producing thyroid hormone.
- Multinodular goitre: multiple nodules; can also be inactive (7) or toxic, the latter is called toxic multinodular goitre and associated with hyperthyroidism. These nodules grow up at varying rates and secrete thyroid

hormone autonomously, thereby suppressing TSH-dependent growth and function in the rest of gland. Inactive nodules in the same goitre can be malignant.Thyroid cancer is identified in 13.7% of the patients operated for multinodular goitre

- Diffuse goitre: the whole thyroid (8) appearing to be enlarged due to hyperplasia.

Non-toxic multinodular goiter

Iodine Deficiency: In the formation of a simple goiter, stimulation of new follicle generation appears to be needed. Many studies have found that iodine deficiency or failure of iodine metabolism by the thyroid gland, possibly due to congenital biochemical defects, may be a significant mechanism causing increases in TSH secretion(9).

On overage, the thyroidal iodine clearance of patients with nontoxic nodular goiter was found to be higher than that of normal people. This result was interpreted as a reflection of certain patients' suboptimal iodine intake(11-15).

Natural occurring goitrogens: Thyroid enlargement occurs in patients on occasion, either as a result of goitrogenic substances in their diet or as a result of medications prescribed for other conditions. Several natural occurring goitrogens are listed in Table (Modified and adapted from Medeiros-Neto & Knobel) (53)

Goitrogens	Agent	Action
Millet, soy beans	Flavonoids	Impairs thyroperoxidase
Cassava, sweet potato, sorghum	Cyanogenic glucosides metabolized to thiocyanates	Inhibits iodine thyroidal uptake
Babassu coconut	Flavoniods	Inhibits thyroperoxidase
Cruciferous vegetables: Cabbage, cauliflower, Broccoli, turnips	Glucosinolates	Impairs iodine thyroidal uptake
Seaweed (kelp)	Iodine excess	Inhibits release of thyroidal Hormones
Malnutrition, Iron deficiency	Vitamin A deficiency Iron deficiency	Increases TSH stimulation Reduces heme-dependent thyroperoxidase thyroidal activity
Selenium	Selenium deficiency	Accumulates peroxidase and cause deiodinase deficiency; impairs thyroid hormone synthesis

Inherited defects in thyroid hormone synthesis and resistance to thyroid hormone action: Stanbury (30-40) identified inherited goiter and congenital hypothyroidism as being associated with defective thyroperoxidase activity, resulting in impaired iodine organification in two goitrous siblings. Both of their siblings were mentally

disabled and had massive multinodular goiters. Over the next fifty years, a number of genetic defects in every stage of thyroid hormone synthesis were thoroughly identified.

It is possible that multinodular goiter is caused by a defect in either stage of thyroid hormone synthesis, as well as resistance to thyroid hormone action. Serum TSH would be elevated in both groups of thyroid hormone system defects, and goiter would be the logical result of a prolonged stimulation to development. When compared to other factors that can trigger multinodular goiters, a faulty thyroid hormone system and resistance to thyroid hormone action are relatively uncommon(25-29).

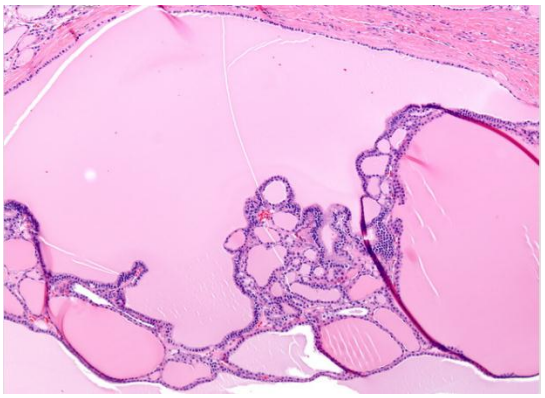
Toxic multinodular goiter

It is a common cause of hyperthyroidism in which there is excess production of thyroid hormones from functionally autonomous thyroid nodules, which do not require stimulation from thyroid stimulating hormone (TSH)(5)

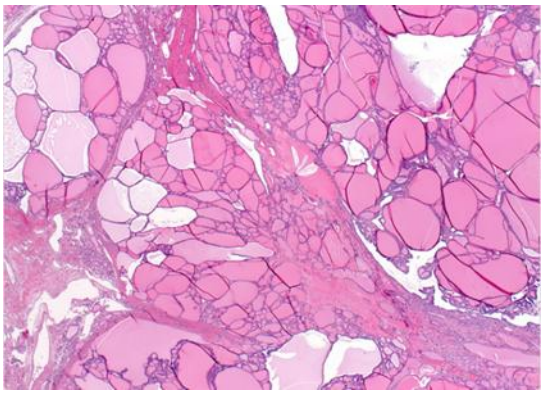
- Iodine deficiency leading to decreased T4 production.
- Induction of thyroid cell hyperplasia due to low levels of T4. This accounts for the multinodular goitre appearance.
- Increased replication predisposes to a risk of mutation in the TSH receptor.
- If the mutated TSH receptor is constitutively active, it would then become 'toxic' and produces excess T3/T4 leading to hyperthyroidism.

Microscopic findings in multinodular goiter

Microscopic analysis of multinodular goiters reveals a wide range of appearances

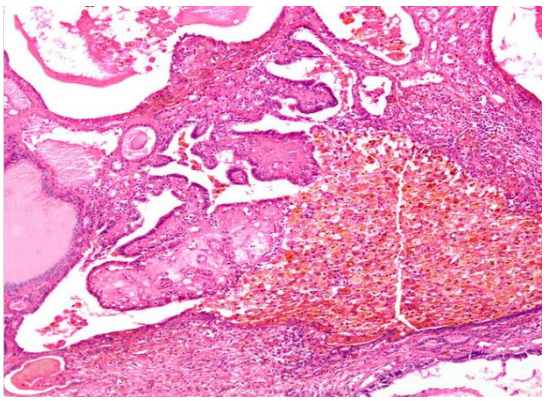


Follicular hyperplastic changes: Thyroid hyperplasia is a physiologic reaction of the follicular epithelium to hormonal changes that cause disruptions in the thyrotropin-releasing hormone and thyroid-stimulating hormone feedback mechanisms. The most common form of this phase is intermittent goiter (diffuse or nodular hyperplasia), a disorder that can be triggered by a number of factors. The photomicrograph (1) shown has variably-sized follicles. In addition, in a multinodular goiter, some of the large dilated follicles may have a cluster of small active follicles at one pole. Sanderson polsters are what they're called. Some multinodular goiters can have a dominant nodule that is difficult to differentiate from a follicular adenoma. (30-40)



Sanderson polsters

Metastatic changes: Thyroid nodules are normal, found by palpation in at least 4% of the population in iodine-sufficient areas and by ultrasonography in more than half of patients with the remainder asymptomatic. They may be linked to local compressive symptoms, resulting in dysphagia and a disruption in thyroid hormone development, as well as thyroid cancer. Ultrasound results are gradually being used to help differentiate malignancy in MNG patients. Microcalcifications, hypoechoic appearance, irregular boundaries, and increased vascularity have all been linked to an increased risk of cancer. Some clinicians use radioactive iodine scanning to help classify "cold" nodules in order

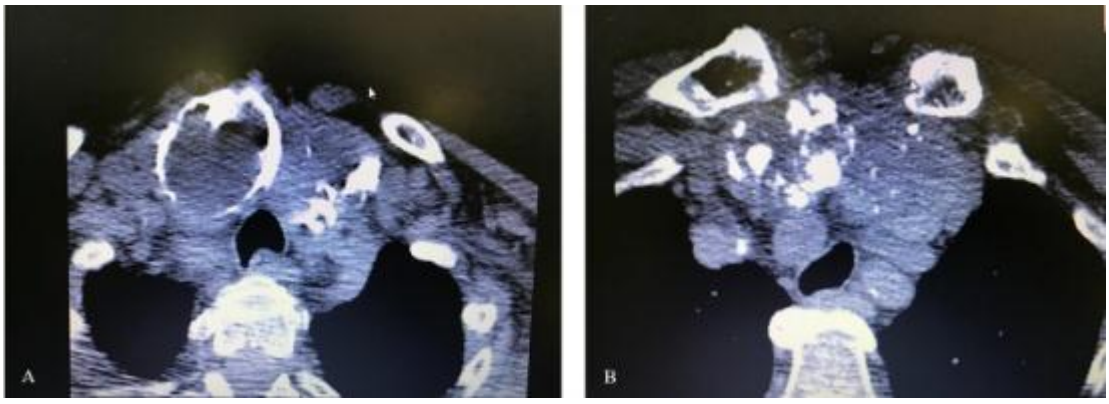


to better determine which nodules should be biopsied. Several studies have shown that preoperative ultrasonography and FNA have an 84 per cent to 88 per cent9 negative predictive value for excluding thyroid cancer in patients who undergo thyroidectomy for MNG. (42)However, a more recent study reported that FNA was able to detect only 46 per cent of the total thyroid cancers discovered at pathological evaluation of the surgical specimen, even though nearly half of the cancers missed by FNA were more than 1 cm in size.(45-50)

Mixed pattern of calcifications (both micro- and macrocalcifications)

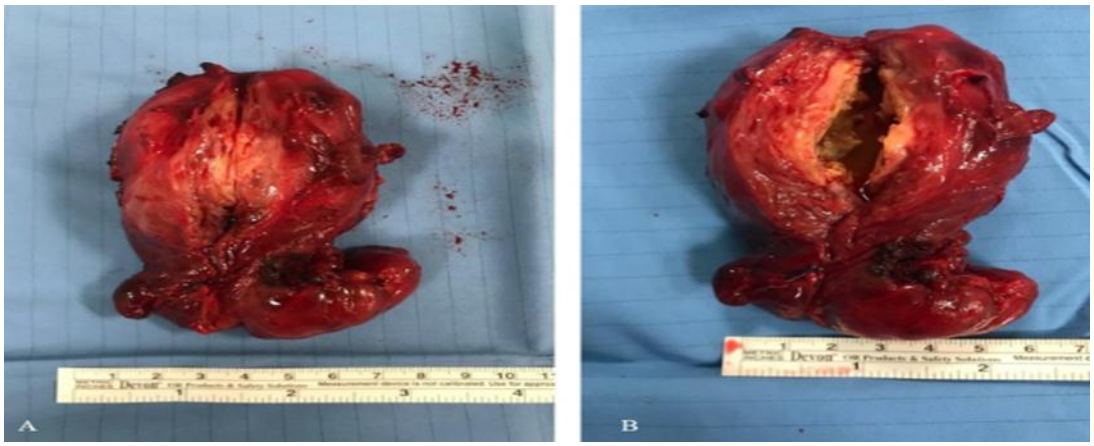
Calcifications are a typical ultrasonographic finding in thyroid nodules, and calcification patterns may help distinguish between benign and malignant nodules. However, Due to a relatively high rate of false negatives and nondiagnostic radiologists,(43) the role of fine-needle aspiration (FNA) is the gold standard method .Thyroid calcifications are classified into two types based on their diameter and echogenic characteristics: microcalcifications (less than 2 mm in diameter) and macrocalcifications (greater than 2 mm in diameter with a posterior acoustic shadow). Microcalcification has been found to be closely linked to papillary thyroid carcinoma, occurring in up to 40% of cases.On the other hand, such macrocalcification patterns, such as annular or "egg-shell" calcification, are less specifically associated with cancer. (44)

The CT scan showed the posterior dislocation of the epiaortic vessels and lateral dislocation and compression of the pharynx.



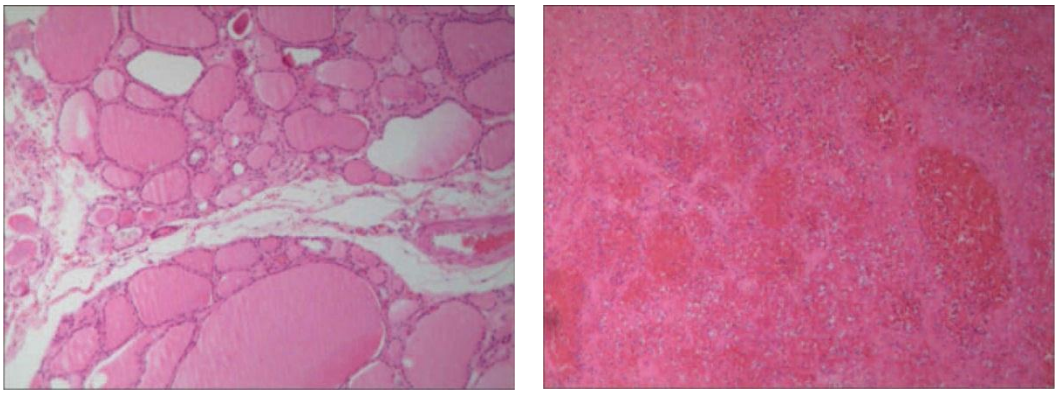
A. Calcified nodule with "egg-shell" pattern. B. Microcalcification spots in the same nodule.

Macroscopically, the presented photo showed a nodule with a weight of 130 g that was partially cavitated and extremely hard when cut.



A. Macroscopically complete calcified nodule. B. Calcified rim when cut.

. **Multinodular Goiter Spontaneous Hemorrhage:** However, the cause of spontaneous thyroid hemorrhage is unknown. Venous bleeding is the most likely cause of goiter hemorrhage. According to the literature, the Valsalva maneuver can cause thyroid hemorrhage by increasing venous pressure. As a result, a related external occurrence, such as apparently insignificant straining at defecation, is often seen in spontaneous hemorrhage cases. (Wen-Hui Lei, 2015)



Pathological outcomes showed sludged blood and infiltration of inflammatory cells (EvG stain, original magnification ×100) (Lei, 2016)

Fibrosis changes in patient with multinodular goiter

Histolopathological finding in patient with fibrosis changes is that the nodule was surrounded by a fibrous capsule (fig. (fig.4).4). The histopathological diagnosis was RT associated with FA. The patient was started on thyroid hormone (thyroxine) replacement therapy after the surgery. A CT scan of abdomen and

thorax, in addition to blood analysis, was also performed to evaluate RT associated with other fibrosis. These revealed no systemic evidence of fibrosis. Neck USG was performed after 6 months postoperatively showed no progression in fibrosis. Masson's trichrome histochemical staining revealed the fibrous nature of the RT-associated connective tissue. Atrophic residual follicular epithelium was discovered (fig. (fig.1,1,2,2,3,3).3). There was nodular hyperplasia with lymphocytic infiltration in the left lobe. FA was diagnosed in one of the nodules protruding from the gland. (J., 2012)

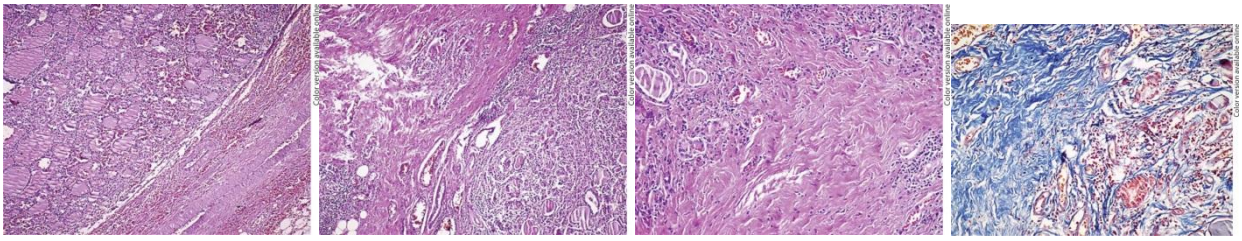


Figure 1 figure 2 figure 3 figure 4

Cystic changes with multinodular goiter

Multinodular goiter (MNG) is the most common thyroid problem, responsible for 80% to 85% of thyroid pathology, and is encountered in up to 5% of the general population [13]. Goiters are three times more common in females and peak during the fifth and sixth decades. Initial pathologic change is always diffuse cellular hyperplasia of the thyroid acini that eventually becomes clinically apparent as a diffuse goiter. As this process continues into adulthood, the clusters of thyroid follicles, surrounded by eosinophilic infiltrate, accumulate colloid material and form micro-nodules that further progress to macro-nodules (MNG). In a longstanding process ,these macro-nodules undergo colliquative necrosis because follicular hyper-plasia causes compression of the supplying blood vessels [14]. This leads to cavitation with accumulation of serous fluid, colloid substance, or oldblood, because hemorrhage into these cysts is common. Coarse (‘‘egg shell’’) calcifications often develop in the areas of degeneration, and sometimes can compromise sonographic assessment of a nodular goiter. Terms such a scystic, colloid cystic and hemorrhagic thyroid hyperplasia or goiters are in common use. Cystic hyperplasia or goiter is the only cystic disease of the thyroid. These are false cysts that do not have epithelial lining; true thyroid cysts are exceedingly uncommon. US allows for differentiation between cystic and solid nodules. True thyroid cysts are exceedingly rare. Most cystic nodules are hyperplastic lesions or adenomas that have undergone degeneration and hemorrhage.

Review

1) Hyperplastic changes

In 2008, **Maria Delia** had Studied 300 consecutive cases of hyperplasia of the thyroid to evaluate morphologic features that could potentially be mistaken for neoplastic conditions. Florid papillary hyperplasia of follicular epithelium was observed in 13% of cases, in several instances closely resembling the papillary structures of papillary thyroid carcinoma. Foci displaying nuclear clearing closely resembling "Orphan-Annie" nuclei were present in 15% of cases. Nuclear grooves and pseudonuclear inclusions were also identified focally in 8% of cases. Cytologic atypia was observed in 7% of cases, including nuclear enlargement, multinucleation, and nuclear pleomorphism with prominent nucleoli. Mitoses were observed in 6% of cases and averaged 1 to 2 per 20 high-power fields. This finding was usually seen in the more cellular areas in cases characterized by a solid, microfollicular pattern of growth. Psammoma bodies were observed focally in 4 cases (1.3%). Infiltration of adjacent skeletal muscle by benign hyperplastic follicles was seen in 3 cases (1%). Another unexpected finding in 2 cases was the identification of small clusters of normal thyroid follicles within the sinuses of lymph nodes located adjacent to the gland (>1%). The presented study confirms that thyroid hyperplasia can sometimes display features that may be confused for a malignant neoplastic process. Awareness of such features and their recognition are of importance to avoid a misdiagnosis of malignancy.

Dige-Petersen and **Hummer** evaluated basal and TRH-stimulated serum TSH levels in 15 patients with diffuse goiter and 47 patients with nodular goiter (11). They found impairment of TRH-induced TSH release in 27% of the patients with nodular goiter, suggesting thyroid autonomy, but in only 1 of the 15 with diffuse goiter. They concluded that by the time the goiter is well developed, serum TSH levels and TSH production rates are usually normal or even suppressed.

2) Malignancy changes in patients with multinodular goiter (MNG)

J Surg Res, 1791 patients were involved in the study; they underwent thyroid surgery between May 1994 and December 2009. Of those patients, a total of 838 patients underwent surgery for a multinodular goiter during the study period. A final pathologic diagnosis of malignancy post-surgery was found in 31% (n=260) of MNG patients (Table 1). The cancer was in the largest nodule in only 37% (n=95) of cases. Of the 260 patients with malignancy, 113 (44%) had a foci of cancer <1 cm.

	Database (n=1791)	MNG (n=838)
% Malignancy	30% (n = 537)	31% (n = 260)
% Cancer < 1 cm	30% (n = 162)	44% (n = 113)

Malignancy was identified pre-operatively in 47% (123) patients. Of the 137 cancers not recognized pre-operatively, 61 (45%) were >1 cm in size. Pre-operative FNA was performed on 204 patients with malignancy on final pathology, and malignancy was suspected or confirmed by FNA evaluation in only 60% (n=123). Of the 81 cancers that FNA evaluation missed, 44% (61) were greater than 1 cm in size. Excluding patients with malignancy that was known pre-operatively, unexpected malignancy was found in 16% of the overall MNG population.

Demographically, the majority of patients in both the malignant and non-malignant groups were female, however the percentage of males was higher in the malignant group than in the non-malignant group (28% vs. 17%, P<0.001).The mean age of patients in the malignant group was younger than those in the non-malignant group (47±0.9 vs. 53±0.6, P<0.001).

	No Malignancy (n=578)	Malignancy (n=260)	P-value
% Female	83%	72%	<0.001
Mean Age (years)	53±1	47 ±1	<0.001
Pre-op TSH	1.65	2.22	0.30

	No Malignancy (n=578)	Malignancy (n=260)	P-value
Pre-op T4	1.17	1.23	0.39
% 5+ nodules	43%	21%	<0.001
Mean gland weight (gm)	50 ±2.8	31±2.5	<0.001
Largest Nodule Size (cm)	3.1±0.1	2.2±1	<0.001

(Table 2) shows the risk factors for malignancy found in the study, which include younger age and female gender. Patients with malignant nodules had smaller nodules, smaller thyroids, and fewer nodules on pathology than patients with benign findings.

The presence of malignant thyroid nodules was negatively correlated with the thyroid gland weight. The mean thyroid gland weight was lower in the malignant group compared to the non-malignant group (31±2.5 gm vs. 50±2.8 gm, P<0.001). There were also fewer nodules in the malignant group. The percentage of patients having 5 or more nodules was much less in the malignant group than that in non-malignant group (20.9% vs. 42.6%, P<0.001). In addition, the largest nodule size was smaller in malignant group (2.32±0.09 cm vs. 3.05±0.09cm, P<0.001). Pre-operative TSH and free T4 levels did not differ significantly between the two groups.

The results indicate that a smaller tumor size is associated with a higher risk of malignancy as demonstrated in final pathology.

The results above was confirmed by **Erbil et al**, which discovered a link between a smaller thyroid volume and a higher detection rate of suspected malignant thyroid nodules in patients with MNG. The study showed that thyroid gland volumes smaller than 38 ml had a 48-fold increase in the rate of detecting suspected thyroid cancer. The reasons for the negative correlation between tumor size and malignancy rate are not clear, but it is likely do to a selection bias as all of the patients underwent thyroid surgery and in the absence of suspected malignancy, patients with smaller nodules do not routinely undergo surgical intervention. The reason that the presence of more nodules is associated with a lower risk of malignancy may be that growth stimulating factors that lead to large goiters do not necessarily stimulate the formation of malignancy.

3. Calcifications incidence in patients with multinodular goiter

The study was done by **S K Kakkos** which involved 188 patients with thyroid disease, including 37 with thyroid cancer, were included in the study. Each patient underwent preoperative, high-resolution sonography to evaluate the thyroid gland for the presence of calcifications.

The highest incidence of calcification was found in thyroid cancer patients (54%), followed by multinodular goiter (40%), solitary nodular goiter (14%), and follicular adenomas (12%). The incidence of cancer was significantly higher in calcified nodules (29%) than in noncalcified nodules in the entire group (14%) ($p = 0.019$), with a relative risk of 2.5. In the group of solitary thyroid nodules, the incidence of cancer in the calcified nodules (55%) was higher than in the nodules without calcification (23%) ($p = 0.016$). Multiple noncalcified thyroid nodules harbored cancer in only 5% of cases. Compared with multiple noncalcified thyroid nodules, the solitary calcified nodules demonstrated a relative risk of 22.8%. In both the solitary and multiple nodules, the relative risk in the presence of calcification was about the same, around 4%. Patients younger than 40 years with calcified nodules constituted a high-risk group, with a relative risk of 3.8% versus 2.5% in patients older than 40 years with calcified nodules.

Sonography may detect thyroid calcifications, which is particularly useful in cases involving a single nodule or a young person. In these circumstances, the existence of calcifications should increase the possibility of malignancy. Because of the low cancer incidence in patients with multiple noncalcified thyroid nodules, a more conservative approach might be acceptable in such situations.

Another study which was carried out by **Fabrizio Consorti** to confirm the predictive value of calcifications in thyroid nodules as a risk factor for malignancy and to detect aspects specific for tumors. In a set of 196 patients (33 differentiated thyroid carcinoma, 9 follicular adenomas and 154 multinodular goiters with dominant nodule) calcifications were detected by post-operative sampling. Calcifications were significantly more frequent in differentiated thyroid carcinoma (DTC) than in benign diseases (DTC 39.4%, adenoma 11.1%, goiter 20.1%) but their considered characteristics (size, number, position, location in the gland, sonographic features of the nodule) did not show any particular difference between DTC and benign diseases. The frequency of calcifications in the series was higher in older patients (mean age 59.4 +/- 13.7 vs. 52.1 +/- 13.1 in patients without calcifications, $p < 0.001$) and this could imply that their onset is time-dependent. Calcifications can be a useful indicator of enhanced risk, to be considered in the overall diagnostic process.

4. Multinodular Goiter Spontaneous Hemorrhage

Wen-Hui Lei,,A 63-year-old woman with ESRD who had been on hemodialysis for 6 years presented to a nephrologist in April 2015 with a 1-day history of large neck swelling, hoarseness, and progressive dysphagia. A review of the records showed a 1-year history of grape-sized nodular goiter on either lobe with no hyperthyroid or hypothyroid symptoms. When admitted to the hospital, the patient had difficulty swallowing and healthy vital signs. A significant nodular goiter was found on physical examination, but there were no cervical or axillary lymphadenopathies; respiratory sounds were natural on chest auscultation. The platelet and coagulation functions in the blood were regular. Despite the operational risks to the patient with end-stage renal disease, an immediate partial thyroidectomy was successfully performed. Postoperative histopathology indicated spontaneous hemorrhage in a multinodular goiter.

5. Fibrosis changes in patient with multinodular goiter

Eur Thyroid J. 2012, Due to a multinodular goiter and thyroiditis, a 42-year-old woman was referred to the outpatient clinic. The patient was euthyroid, and thyroid function tests came out normal. Thyroid antibodies (thyroid peroxidase antibody and thyroglobulin antibody) were present in high concentrations.. According to the Bethesda method, fine-needle aspiration cytology was conducted, and the results were consistent with ‘suspicious for a follicular neoplasm.' The patient underwent a complete thyroidectomy as a result of the clinical findings, which included weight loss and sweating, as well as the cytological results, which indicated a follicular neoplasm. RT with FA was the histopathological diagnosis. Following surgery, the patient was started on thyroid hormone (thyroxine) replacement therapy and was treated for further fibrosis caused by RT. According to the Bethesda system, FNAC was compatible with ‘suspicious for a follicular neoplasm' [10]. The patient underwent a complete thyroidectomy as a result of the clinical results and the suspicious cytological result. Dissection of the thyroid gland proved difficult during surgery due to fibrotic extensions to the perithyroidal soft tissues.

The thyroid gland was damaged and extensively replaced by dense fibrous tissue with lymphocytic infiltration, according to histopathological review. There were a lot of lymphocytes, plasma cells, and eosinophils, but no neutrophils, granulomatous tissue, or malignancy, supporting the RT diagnosis. The surgical material was examined under the microscope and found to be free of Hurthle cells.

Conclusion

1) The most common benign finding in multinodular goiter was hyperplasia of the follicular cells due to the disruptions in the thyrotropin-releasing hormone and thyroid-stimulating hormone feedback mechanisms.
2) The most common malignant finding in multinodular goiter was papillary carcinoma which it is the main histopathologic subtype in the patients with CA.
3) There is correlation between the age of the patients, gender, weight of the tumor and malignant changes. The results indicate that a smaller tumor size is associated with a higher risk of malignancy as demonstrated in final pathology. (Res, 2009) ,also many report showed that females are more likely to have multinodular goiter than males (Qureshi IA, 2015)
4) The histopathological examination is important in all thyroid specimens to detect unexpected Pathology which may end up with malignant transformation.

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