

Thyroid neoplasms: A study of 1,039 cases at Chulalongkorn Hospital.

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Objective : *To determine the proportion of various tumors of thyroid gland and their relation to age groups and sexes of the patients.*

Methods : *The study was made by collecting data from official pathology reports of surgical specimens diagnosed as various thyroid tumors from the Department of Pathology, Chulalongkorn Hospital from January 1989 to December 1994.*

Results : *Of 2,057 specimens of thyroid glands, there were 1,039 (50.5 %) cases diagnosed as thyroid tumors. The 1,039 tumors were divided into two groups namely 1) Benign tumors 650 cases or 62.6 % and 2) Malignant tumors 389 cases or 37.4 %. The ratio of malignant to benign tumors was 38.9 : 650 or 1:1.7. Follicular adenoma comprises 99.4 % of benign neoplasms while papillary carcinoma is 73.8 % of malignant tumors. Female : male is 6.3 : 1 in all tumors. Follicular adenoma, carcinoma and papillary carcinoma are found most often in the third to fifth decades of*

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life. Anaplastic carcinoma has the mean age of 76 years old.

Conclusion : *There is a marked increase in the ratio of malignant to benign diseases from 1:7 in the study of Pongsabutra to 1: 1.7 in this study. The tumors are more common in female. There is a marked decline in the occurrence of anaplastic carcinoma. Follicular adenoma, carcinoma and papillary carcinoma are common in the third to fifth decades of life but anaplastic carcinoma is more common in the higher age group.*

Key word : *Thyroid neoplasms.*

สมบูรณ์ ศีลาวัฒน์, ชนพ ช่วงโชติ, พิไลวรรณ กลีบแก้ว, อัมพร แจ่มสุวรรณ. เนื้องอกของต่อมไทรอยด์:การศึกษาผู้ป่วย 1,039 ราย ในโรงพยาบาลจุฬาลงกรณ์. จุฬาลงกรณ์เวชสาร 2539 พฤษภาคม;40(5): 357-369

- วัตถุประสงค์** : เพื่อดูสัดส่วนของเนื้องอกของต่อมไทรอยด์ชนิดต่างๆ และความสัมพันธ์ต่อกลุ่มอายุ และเพศของคนไข้
- วิธีการ** : การศึกษาได้ทำโดยรวบรวมข้อมูลจากรายงานผลพยาธิอย่างเป็นการของชิ้นเนื้อทางศัลยกรรม ซึ่งวินิจฉัยว่าเป็นเนื้องอกของต่อมไทรอยด์ชนิดต่างๆ จากภาควิชาพยาธิวิทยา, ร.พ.จุฬาลงกรณ์ ตั้งแต่ มกราคม 2532 ถึงธันวาคม 2537
- ผลการศึกษา** : จากชิ้นเนื้อจำนวน 2,057 ราย มี 1,039 (50.5 %) รายที่วินิจฉัยว่าเป็นเนื้องอกของต่อมไทรอยด์ ซึ่งแบ่งเป็น 1) เนื้องอกชนิดธรรมดา 650 ราย หรือ 62.6 % และ 2) เนื้องอกชนิดร้ายแรง 389 ราย หรือ 37.4 % สัดส่วนของเนื้องอกชนิดร้ายแรงต่อเนื้องอกชนิดธรรมาคือ 389:650 หรือ 1:1.7 Follicular adenoma พบได้บ่อยถึงร้อยละ 99.4 ของเนื้องอกชนิดธรรมดา ส่วน Papillary carcinoma พบได้ 73.8 % ของเนื้องอกชนิดร้ายแรง สัดส่วนผู้หญิงต่อผู้ชายในเนื้องอกทุกชนิดเท่ากับ 6.3:1 Follicular adenoma, carcinoma และ papillary carcinoma พบมากที่สุดในช่วงทศวรรษที่ 3 ถึงทศวรรษที่ 5 ของชีวิต Anaplastic carcinoma พบในอายุเฉลี่ย 76 ปี
- สรุป** : สัดส่วนของเนื้องอกชนิดร้ายแรงต่อชนิดธรรมดาเพิ่มขึ้นจากการศึกษาที่ทำโดย น.พ.สุภรณ์ พงศบุตร จาก 1:7 มาเป็น 1:1.7 ในการศึกษาเนื้องอกโดยรวมจะพบในผู้หญิงมากกว่าในผู้ชาย Anaplastic carcinoma มีจำนวนลดลงมาก Follicular adenoma, carcinoma และ papillary carcinoma พบบ่อยในทศวรรษที่ 3 ถึงทศวรรษที่ 5 ของชีวิต แต่ anaplastic carcinoma พบมากในคนไข้ที่มีอายุสูงขึ้น

Thyroid gland is one of endocrine glands which has frequent pathological changes. Neoplasm comprises 52.5 % diseases which cause enlargement of thyroid glands.⁽¹⁾ Several risk factors related to thyroid cancers have been described by many authors such as diet,⁽²⁾ exposure to X-ray,⁽³⁾ reproductive and hormonal factors⁽⁴⁾ and goiter.⁽⁴⁾ The epidemiological studies of thyroid neoplasms have been conducted in several countries. As in most of the cancers at specific sites, the occurrence of thyroid cancer shows geographic and ethnic variations.⁽⁴⁾ The objective of this study is to find out if there are any changes in proportion of various thyroid neoplasms and their relation to the age groups and sexes of the patients from the study previously made in this hospital.⁽¹⁾

Materials and Methods

The study was made by collecting data from official pathology reports of surgical specimens diagnosed as various thyroid tumors (both benign and malignant) from the Department of Pathology, Chulalongkorn Hospital from January 1989 to December 1994. The total cases were 1,039. For the cases with unclear diagnoses, the slides were reviewed and the correct diagnoses were confirmed by senior staffs in the department. However, we did not review all of the slides. Regarding to ages of the patients, there were 73 patients whose ages were not recorded, therefore, only 966 cases were included for analysis.

The general materials used in this study were formalin-fixed paraffin embedded sections with routine hematoxylin and eosin stain Nec-

cessary special staining was provided in some cases.

Results

Of 2,057 specimens of thyroid glands, there were 1,039 (50.5 %) cases diagnosed as thyroid tumors. The 1,039 tumors were divided into two groups namely 1) Benign tumors 650 cases or 62.6 % and 2) Malignant tumors 389 cases or 37.4 %. The ratio of malignant to benign tumors was 389:650 1:1.7. (Table 1)

Of 650 cases of benign tumors, they consisted of 1) Follicular adenoma 646 cases or 99.4 % 2) Hurthle cell adenoma 3 cases or 0.5 % 3) Hemangioma 1 case or 0.2 % The 389 cases of malignant tumors consisted of 1) Papillary carcinoma 287 cases or 73.8 % 2) Mixed papillary and follicular carcinoma 6 cases or 1.5 % 3) Follicular carcinoma 81 cases or 20.8 % 4) Medullary carcinoma 1 cases or 0.3 % 5) Anaplastic carcinoma 5 cases or 1.3 % 6) Epidermoid carcinoma 4 cases or 1 % 7) Metastatic carcinoma 5 cases or 1.3 % which consisted of 2 cases of metastatic invasive ductal carcinoma from breast, 1 case of metastatic squamous cell carcinoma from larynx, 1 case of metastatic squamous cell carcinoma from esophagus and 1 case of metastatic adenocarcinoma from unknown primary site.

The ratio between female and male in all tumors was 897:142 or 6.3:1 and 570:76 or 7.5:1 for follicular adenoma, 238:49 or 5:1 for papillary carcinoma and 71:10 or 7:1 in follicular carcinoma.

Ages of the patients ranged from 6 years old to 84 years old with the mean age of 37.8

years old. Most tumors were found often in the third to fifth decades of life but anaplastic, epidermoid and metastatic carcinoma were found

in the higher age groups with the mean ages of 76, 62.3 and 58.2 years old, respectively. (Table 2-5)

Table 1. The total number of cases in each and all thyroid neoplasms. In 1,039 cases, 73 cases have no record in ages.

	Number of cases			Ranges of ages					
	Female	Male	All	Female		Male		All	
				minimum of age	maximum of ages	minimum of ages	maximum of ages	minimum of ages	maximum of ages
1) Follicular adenoma	570	76	646	6	82	9	75	6	82
2) Hemangioma+Hurthle cell adenoma	4	-	4	24	74	-	-	24	74
3) Papillary carcinoma	238	49	287	12	81	16	84	12	84
4) Mixed papillary and follicular carcinoma	4	2	6	22	35	29	58	22	58
5) Follicular carcinoma	71	10	81	19	63	20	83	19	83
6) Medullary carcinoma	1	-	1	43	43	-	-	43	43
7) Anaplastic carcinoma	4	1	5	64	84	82	82	64	84
8) Epidermoid carcinoma	3	1	4	48	73	56	56	48	73
9) Metastatic carcinoma to thyroid gland	2	3	5	48	63	56	67	48	67
Total	897	142	1,039	-	-	-	-	-	-



Figure 1. Demonstrates follicular adenoma with fibrous capsule surrounding the tumor. There is no evidence of capsular invasion seen.

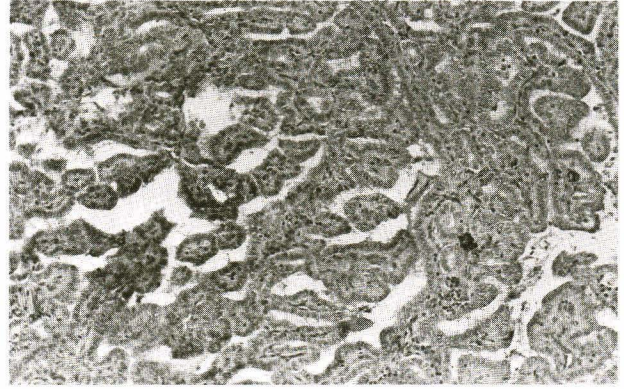


Figure 2. Demonstrates papillary carcinoma showing formation of true papillae and the characteristic ground glass nuclei.

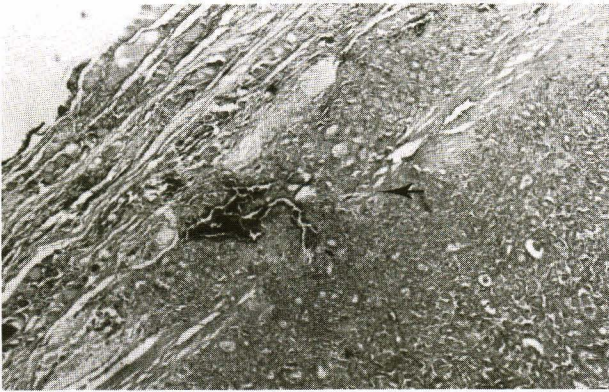


Figure 3. Demonstrates follicular carcinoma showing tumor invasion through the fibrous capsule. (Arrow)



Figure 4. High power feild of follicular carcinoma showing capsular invasion. (Arrow)

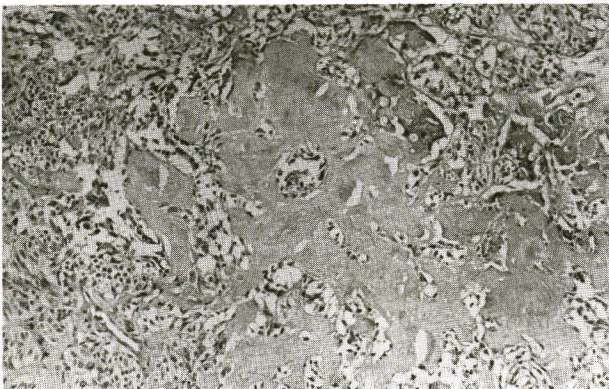


Figure 5. Demonstrates medullary thyroid carcinoma. Broad bands of amyloid are present at the center. The tumor cells are arranged in organoid nests separated by a scant fibrovascular stroma.

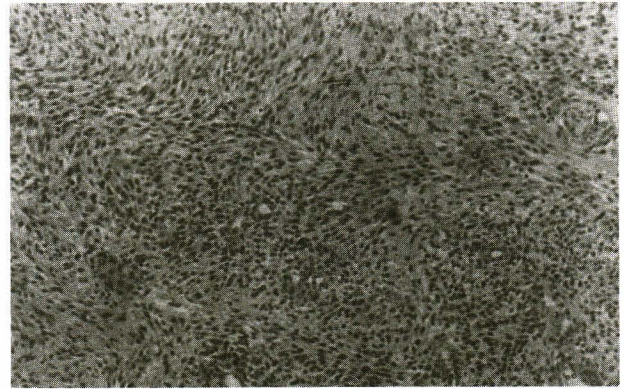


Figure 6. Demonstrates anaplastic carcinoma with spindle shaped cell patterns

Table 2. Demonstrates the number of cases, the ranges of ages, the mean age and the standard deviation in each tumor. Only 966 cases were included for analysis because there were 73 cases whose ages were not recorded.

Thyroid tumor	Female		Male		All		SD		
	Number of cases	Mean age	Number of cases	Mean age	Number of cases	Mean age	F	M	All
1) Follicular adenoma	524	35.3	74	38.4	598	35.7	13.53	15.77	13.85
2) Hurthle cell adenoma	2	49	-	-	2	49	35.36	-	35.36
3) Papillary carcinoma	222	39.4	47	44.6	269	40.3	14.47	18.08	15.25
4) Mixed papillary and follicular carcinoma	4	27.5	2	43.5	6	32.8	6.14	20.51	13.23
5) Follicular carcinoma	66	38.3	10	47.8	76	39.5	12.76	21.32	14.36
6) Medullary carcinoma	1	43	-	-	1	43	-	-	-
7) Anaplastic carcinoma	4	74.5	1	82	5	76	9.54	-	8.92
8) Epidermoid carcinoma	3	65.5	1	56	4	62.3	12.58	-	10.00
9) Metastatic carcinoma to thyroid gland	2	53.7	3	62.7	5	58.2	9.19	5.86	7.05
Total	828	37	138	42.2	966	37.8		14.89	

F
SD = 14.17

M
SD = 17.61

Table 3. Number of cases in each age group of follicular adenoma. Forty-six cases were excluded from the analysis because of the lack of the data about ages of the patients.

Ages	Number of cases
0-10	5
11-20	70
21-30	178
31-40	148
41-50	98
51-60	59
61-70	28
71-80	11
81-90	1
Total	598

Table 4. Number of cases in each age group of papillary carcinoma five cases were excluded from the analysis because of the lack of the data about ages of the patients.

Ages	Number of cases
0-10	0
11-20	17
21-30	71
31-40	67
41-50	51
51-60	32
61-70	23
71-80	6
81-90	2
Total	269

Table 5. Number of cases in each age group of follicular carcinoma five cases were excluded from the analysis because of the lack of the data about ages of the patients.

Ages	Number of cases
0-10	0
11-20	4
21-30	24
31-40	19
41-50	14
51-60	9
61-70	5
71-80	0
81-90	1
Total	76

Discussion

Thyroid neoplasms comprise 50.5 % of all thyroid specimens obtained in the Department of Pathology in Chulalongkorn Hospital. This percentage is similar to the study made by Pongsabutra⁽¹⁾ during 1965-1975. There was a marked change in ratio of malignant and benign tumors. The ratio of malignant and benign tumors in this study is 1:1.7 while the ratio in Pongsabutra's work was 1:7⁽¹⁾. The reasons behind a marked increase in the proportion of thyroid cancer should be further investigated. Many authors have been trying to study to find risk factors of thyroid cancers. They include ionizing radiation,⁽⁵⁾ radiotherapy to the head and neck,⁽⁶⁾ goiter and reproductive and hormonal factors (the number of pregnancies and exogenous estrogen).^(7,4,5) Moreover, there are evidences that

a diet rich in starchy foods and fats is associated with elevated risk, while vegetables and fruits may be protective.⁽²⁾ Akslen et al⁽⁷⁾ found that women in some occupations such as fishing, ships and crew were at increased risk of thyroid cancer. Kolonel et al⁽⁸⁾ has indicated high consumption of seafood (especially shellfish) may be a risk factor. For us, the increase in the incidence of thyroid cancers in this study may be due to the combination of these factors such as the high consumption of food rich in starch and fat or the intake of exogenous estrogen etc. However, we do not know the exact causes of this change but further study may help us to find the answers.

In benign tumors, follicular adenoma comprises 99.4 % while in Pongsabutra's⁽¹⁾ study, it was 98.3 % the remainders of benign tumors

are hurthle cell adenoma (0.5 %) and heman-gioma (0.2 %) which were not found in Pongsa-butra's series.⁽¹⁾

For malignant tumors, the largest group is papillary carcinoma which comprises 73.8 % of malignant neoplasms. Follicular carcinoma is the second one comprising 20.8 %. The remainders are medullary carcinoma (0.3 %), anaplastic carcinoma (1.3 %), epidermoid (1 %), metastatic carcinoma (1.3 %) and mixed papillary and follicular carcinoma (1.5 %). In the previous study,⁽¹⁾ the pure papillary carcinoma was 52.7 %, pure follicular carcinoma was only 6.9 %, mixed papillary and follicular carcinoma was 27.9 % and anaplastic carcinoma was 10.07 %. These findings show a little increase in incidence of follicular carcinoma and a marked decrease in anaplastic carcinoma. In most series, papillary carcinoma accounts for 40-70 %, follicular carcinoma about 10-28 % and anaplastic carcinoma 10-20 %, while medullary thyroid carcinoma accounts for less than 5 %. Tumors with a combination of papillary and follicular structures have the biologic behavior of papillary carcinoma and should therefore be classified as such instead of as mixed carcinoma.⁽⁶⁾ In the series of Demeter et al,⁽⁹⁾ anaplastic thyroid carcinoma represents 5 % of all cases of thyroid carcinoma and 76 % of the patients had a previous benign or malignant disorder of the thyroid gland before the diagnosis of anaplastic carcinoma. This finding has given rise to the hypothesis that many anaplastic carcinoma arise from dedifferentiation of well-differentiated carcinoma.⁽⁹⁾ In addition, the occurrence of anaplastic thyroid carcinoma in previously benign

goiters in the same series also supports the hypothesis that anaplastic tumors can arise from any abnormal thyroid tissue that has degenerated into a more primitive, undifferentiated, and aggressive cell line. If this is true, identification and resection of this abnormal tissue before it dedifferentiates could prevent the development of this tumor.⁽⁹⁾ In the series of Pettersson et al,⁽¹⁰⁾ the incidence of anaplastic carcinoma had a steady decline during 1958-1981. This may be related both to improved diagnostic accuracy and to a decline in the occurrence of goiter.

As in other series, this study also shows striking female predominance with the sex ratio of 7.5:1 for follicular adenoma and 5:1 for all malignant tumors. Hormonal or other factors related to reproduction may, in part, explain this sex difference.⁽⁷⁾

Follicular adenoma is found mostly in the third to fourth decades of life which is 54.5 %. The mean age is 35.7 years old. It is rare in the age below 10 years old which were found only 5 cases and in the age of 81-90 years old which was found only 1 case. Papillary carcinoma may occur at any age but are found most often in the third to fifth decades.⁽¹¹⁾ In our series, the ages of the patients range from 12 to 84 years old with the mean age of 40.3 years old. 70 % of the patients are in the third to fifth decades of life. Follicular carcinoma have a peak incidence in the fifth and sixth decades of life in general.⁽¹¹⁾ but in our series, the incidence is highest in the third and fourth decades with the mean age of 39.5 years old. Anaplastic carcinoma is more common in older patients⁽⁹⁾ and the mean age in this study is 76 years old.

Follicular adenomas are usually solitary.⁽⁶⁾ They are characteristically surrounded by a capsule that is grossly and microscopically complete.⁽⁶⁾ Microscopically, the architectural and cytologic features are different from those of surrounding gland⁽⁶⁾ but are more or less uniform throughout the lesion. Adenomas may exhibit a variety of patterns : normofollicular (simple), macrofollicular (colloid), microfollicular (fetal) and trabecular or solid (embryonal).⁽⁶⁾ These various patterns have no clinical differences.⁽⁶⁾

Papillary carcinoma is rarely encapsulated but instead infiltrates surrounding thyroid parenchyma.⁽¹¹⁾ Grossly, most cases are solid, whitish, firm and clearly invasive; less than 10 % are surrounded by a complete capsule.⁽⁶⁾ Microscopically, This tumor usually forms true papillae and has characteristic nuclear changes.⁽⁶⁾ The nuclear features of papillary carcinoma, which are as important diagnostically as the presence of papillae, consist of :

- 1) Ground glass nuclei. This change is present in sections obtained from paraffin-embedded material regardless of the fixative used but is less apparent or absent altogether in frozen sections or cytology material.⁽⁶⁾

- 2) Nuclear pseudoinclusions. These represent invaginations of the cytoplasm and appear as sharply outlined acidophilic formations.⁽⁶⁾ This feature is readily apparent in specimens from frozen sections and aspiration.⁽⁶⁾

- 3) Nuclear grooves.⁽¹¹⁾

Mitoses are nil or absent.⁽⁶⁾ Mostly, they show extensive fibrosis, usually in the form of bands traversing the tumor.⁽⁶⁾

Psammoma bodies are seen in approximately half of the cases.⁽⁶⁾ These structures are almost never found in follicular and medullary carcinomas, and so, when present, are diagnostic of papillary carcinoma.⁽¹¹⁾ These laminated basophilic structures arise from necrosis of individual tumor cells.⁽⁶⁾ Immunohistochemically, the tumors are reactive for low and high molecular weight keratin.⁽⁶⁾ Reactivity for thyroglobulin is the rule.⁽⁶⁾ There is also positivity for EMA, CEA (occasionally), vimentin and ceruloplasmin.⁽⁶⁾ Laminin and other basement membrane components are also identifiable.⁽⁶⁾ Ultrastructurally, the most distinctive feature of the cells of papillary carcinoma is the highly indented nuclear membrane, with formation of pseudoinclusions and multilobation.

Follicular carcinoma. These neoplasms are typically encapsulated that are sometimes difficult to differentiate from follicular adenoma.⁽¹¹⁾ Grossly, they are grey to tan to pink on transection.⁽¹¹⁾ On occasion, they are translucent when large colloid-filled follicles are present.⁽¹¹⁾ Central fibrosis and foci of calcification are often found.⁽¹¹⁾ Microscopically, follicular carcinomas have variable pattern in their architecture.⁽¹¹⁾ Whatever the pattern, the nuclei lack the features typical of papillary carcinoma and psammoma bodies are not present.⁽¹¹⁾ The diagnosis of follicular carcinoma depends largely on the identification of capsular and /or blood vessel invasion.⁽⁶⁾ Immunohistochemically, follicular carcinomas are reactive for thyroglobulin, low molecular weight keratin, EMA, S-100 protein, and basement membrane components such as laminin and type IV collagen.⁽⁶⁾ Ultrastructural

appearance of lectin-binding pattern are not significantly different from those of adenoma.⁽⁶⁾

Medullary thyroid carcinomas are neuroendocrine neoplasms of parafollicular (C) cell origin.⁽¹¹⁾ Grossly, two patterns can be discerned. 1) discrete tumors in one lobe or 2) numerous nodules that usually involve both lobes.⁽¹¹⁾ The sporadic neoplasms tend to originate in one lobe.⁽¹¹⁾ The familial type are usually bilateral and multicentric early in their course.⁽¹¹⁾ The tumor tissue is commonly firm, pale, gray to tan, and infiltrative.⁽¹¹⁾ Histologically, the tumor cells are usually polygonal or spindled and disposed in organoid nests separated by a scant to abundant fibrovascular stroma.⁽¹¹⁾ In some tumors, the neoplastic cells are disposed in trabecular or ribbon patterns⁽¹¹⁾, and in others, the growth pattern may be carcinoid-like nests, glandular (tubular-and follicular), or pseudopapillary.⁽⁶⁾ In somewhat fewer than half of the cases, the stroma contains broad bands of amyloid.⁽¹¹⁾ Ultrastructurally, membrane bound secretory granules that represent sites of storage of calcitonin and other elaborated products are invariably presents.^(6,11) Immunohistochemically, the tumor cells are reactive for keratin, NSE, chromogranin A,B, and C, synaptophysin and opioid peptides and for calcitonin.⁽⁶⁾ They are also consistently positive for CEA and degenerally negative for thyroglobulin.⁽⁶⁾

Anaplastic carcinomas basically have three histologic patterns 1) spindle cell carcinomas, 2) giant cell lesions and 3) small cell carcinoma.⁽¹¹⁾ Infrequently, admixtures of papillary and follicular carcinoma are found in this tumors suggesting transformation of a better dif-

ferentiated carcinoma into an anaplastic one.⁽¹¹⁾ Immunohistochemically, the most useful marker is keratin.⁽⁶⁾ Vimentin is consistently present in spindle cell component.⁽⁶⁾

Epidermoid carcinoma mostly merges with undifferentiated areas, so that the tendency has been to place the tumor into the anaplastic category.⁽¹²⁾ A residual component of papillary carcinoma is sometimes found in these neoplasms.⁽¹²⁾ In the presence of obvious epidermoid carcinoma involving the thyroid, the possibility should be considered of secondary direct involvement from a tumor of larynx or trachea or a metastasis from lung or other sites.⁽⁶⁾

Hurthle cell tumors. Tumors included in this category are those in which more than half of the cell population is made up of hurthle cells.⁽⁶⁾ Grossly, the tumors are characteristically solid, tan, and well-vascularized.⁽⁶⁾ Microscopically, the pattern of growth may be follicular, trabecular/ solid, or papillary.⁽⁶⁾ The nuclei may show pleomorphism and prominent nucleoli.⁽⁶⁾ The cytoplasm has a distinct granular acidophilic quality.⁽⁶⁾ Ultrastructurally, the cells are packed with mitochondria showing abnormalities in size, shape, and content.⁽⁶⁾ Immunohistochemically there is reactivity for thyroglobulin, CEA.⁽⁶⁾ Hurthle cell tumors with follicular or solid/trabecular patterns should be diagnosed using analogous criteria to those employed for follicular neoplasms of non-hurthle cell types, i.e., the presence of capsular and/or vascular invasion should be used as the criterion for malignancy.⁽⁶⁾

Summary

Thyroid neoplasms comprise 50.5 % of

2,057 thyroid specimens obtained in the Department of Pathology in Chulalongkorn Hospital during January 1989 to December 1994. There is a marked increase in the ratio of malignant to benign diseases from 1:7⁽¹⁾ to 1:1.7. Among the malignant tumors, anaplastic carcinoma has a marked decline in its occurrence. The sex difference of the tumors in overall shows female preponderance with the ratio 6.3:1. Follicular adenoma, papillary carcinoma and follicular carcinoma are found most often in the third to fifth decades of life but anaplastic carcinoma is more common in the higher age group.

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