The Morphological Variants of Papillary Carcinoma of the Thyroid: A Clinico-Pathological Study - AFIP Experience

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Abstract

Many variants of papillary carcinoma of thyroid have been described. Identification of some of these may have prognostic hnpJications. Eighty-two cases of papillary carcinoma of the thyroid diagnosed at Armed Forces Institute of Pathology, Rawalpindi over a six year period were reviewed with the aim of identifying these variants. Fifty-eight (70.7%) were classical papillary carcinoma. Thirteen (15.9%) had fofficular variant, 6(7.3%) columnar cell variant and 3(3.7%) had tall cell variant. The mean age at diagnosis was 27 years for classical papillary carcinoma, 46 years for follicular variant, 61 years for columnar cell variant and 52 years for tall cell variant. The columnar cell variant had a more aggressive clinical presentation than others. Tall cell, columnar cell and diffuse scierosing variant have a poor prognosis. An effort should be made to identify them on histopathology so that specific therapy can be planned (JPMA 48:133,1998).

Introduction

Papillary carcinoma of the thyroid is the most common malignanc of thyroid comprising 80% of all cases of thyroid neoplasms[1]. These tumours have an excellent prognosis and cause little morbidity (more than 90% survival at 20 years)[1] with only <10% developing recurrence, distal metastasis (5-7%) or mortality[1-3]. However, mortality from thyroid malignancy exceeds mortality from cancers of all other endocrine organs, excluding the ovary[2].

Itis therefore, imperative tobe able to differentiate those cases which are at a risk of an aggressive clincal course from those that are likely to follow an indolent course. Risk factors that increase morbidity and mortality include olderpatient age (>50 years), male sex, growth characteristics of the tumour such as an increased size, multicentricity, lack of encapsulation, distant metastases, extrathyroidal extension of tumour and cell type or the histological varian[1-5].

The variants, which are said to be associated with a poor prognosis, include the tall cell[3], the columnar cell[6] and the diffuse scierosing variant[7-9]. Although most papillary cancers fit into the classical pattern, about 15-20% show certain morphological pattcrns which are said to have important prognostic implications[1,6,10].

Materials and Methods

Review of slides from eighty4wo cases of papillary carcinoma of the thyroid diagnosed at Armed Forces Institute of Pathology, Rawalpindi, from January, 1990 - June 1996, revealed more recently described variants.

Paraffin blocks alongwith Hernatoxylin and eosin stained sections were available for review in all cases. Criteria evaluated included size of tumour, multifocality, tumour encapsulation, soft tissue extension, nuclear features (ground glass change, grooving, pseudoinclusions and overlapping), psammornabodies, fibrosis, lymphocytic infiltrate along with more specific features such as clear cell

change, presence of tall or columnar cells etc.
The patient's age and gender were noted along with the mode of clinical presentation and the presence or absence of lymph node metastases. As efforts to obtain a follow-up after surgery to determine the duration of survival were not successful, this study therefore does not attempt to address the prognostic implications of various histological types.

Results

A retrospective analysis of 82 papillary thyroid carcinomas was made in order to subelassify them into their morphological variants. Of these, 58 were classical papillary carcinomas, while twenty-four were othervariants (Table I).

Table I. Papillary carcinoma and its variants.

Type of papillary carcinoma	No. of cases	%
Classical papillary carcinoma	58	70.7
Follicular variant	13	15.9
Columnar cell variant	6	7.3
Tall cell variant	3	3.7
Encapsulated	1	1.2
Occult	1	1.2
Total	82	

In the present study the mean age at diagnosis for classical papillary carcinoma was 27 years and the female to male ratio was 1:1(2:1 to 4:1 in other series)[1]. For follicular variant the meanage was 46 years, for columnar cell.variant61 years and for tall cell it was 52 years. The female to male ratio inthese was 1:2, 1:1 and 1:2 respectively.
The mode of clinical presentation varied. The patients with classical papillary carcinoma presented with multinodular goitre (28 cases), a solitary cold nodule (14 cases), cervical metastases (9 cases), symptoms of hyperthyroidism (2 cases), recurrent goitre (2 cases), hoarseness of voice (1 case), extrathyroid extension (1 case) and a mobile cystic swelling (1 case).
The follicular variant of papillary carcinoma also presented commonly as multinodular goitre or a solitary nodule (5 cases), recurrent laryngeal nerve paralysis (2 cases), hoarseness of voice and dysphagia (2 cases) - extrathyroid extension was seen in one case and lymph node metastases in 5 cases. Therefore, the incidence of nodal metastases was significantly higher in this group.
In columnar cell variant the clinical presentation was much morn aggressive. Three cases were of a

hard nodular gotire, in two of whom a clinical suspicion of carcinoma was raised. One patient had hard nodular goitre infiltrating into strap muscles while one presented with cervical lymph node metastases. In one case no history was available.

The tall cell variant on the other hand did not have any note- worthy mode of presentation. Of three cases, one presented as multinodular goitre and one as a solitary nodule of two years standing. The third case had extrathyroidal extension and was clinically suspected to have a thyroid malignancy.

On gross examination, no difference was found to exist between the different subtypes. All showed grey white well defined homogenous nodular masses with multifocality in 13 cases, a capsule was seen in 6 cases, while papillae were seen on gross examination inS cases. Other features were necrosis (14 cases), hemorrhage (11 cases) cystic degeneration (5 cases) and calcification (2 cases).

The microscopic features varied between different subtypes. In the classical variant the commonest histological finding was papillae with fibrovascular cores, lined by cuboidal to columnar cells having optically clear ground glass nuclei in44 cases. Focal ground glass change was seen in three cases while in ten cases no nuclear clearing was seen. Nuclear grooving was seen in 26 cases. In six cases it was unaccompanied by ground glass change. Prominent pseudo inclusions were seen in 4 cases. In one case it was particularly marked and associated with prominent nuclear grooves. We found overlapping of nuclei tobe a non- specific feature which invariably accompanied ground glass nuclei. Prominent nucleoli were seen in 6 cases. Only 20 cases showed psammoma bodies. Fibrosis and capsule formation was present in 14 cases with prominent lymphocytic infiltration in 3 cases. Other features included focal columnar cell, clear cell and Hurthie cell change (Figure 1).

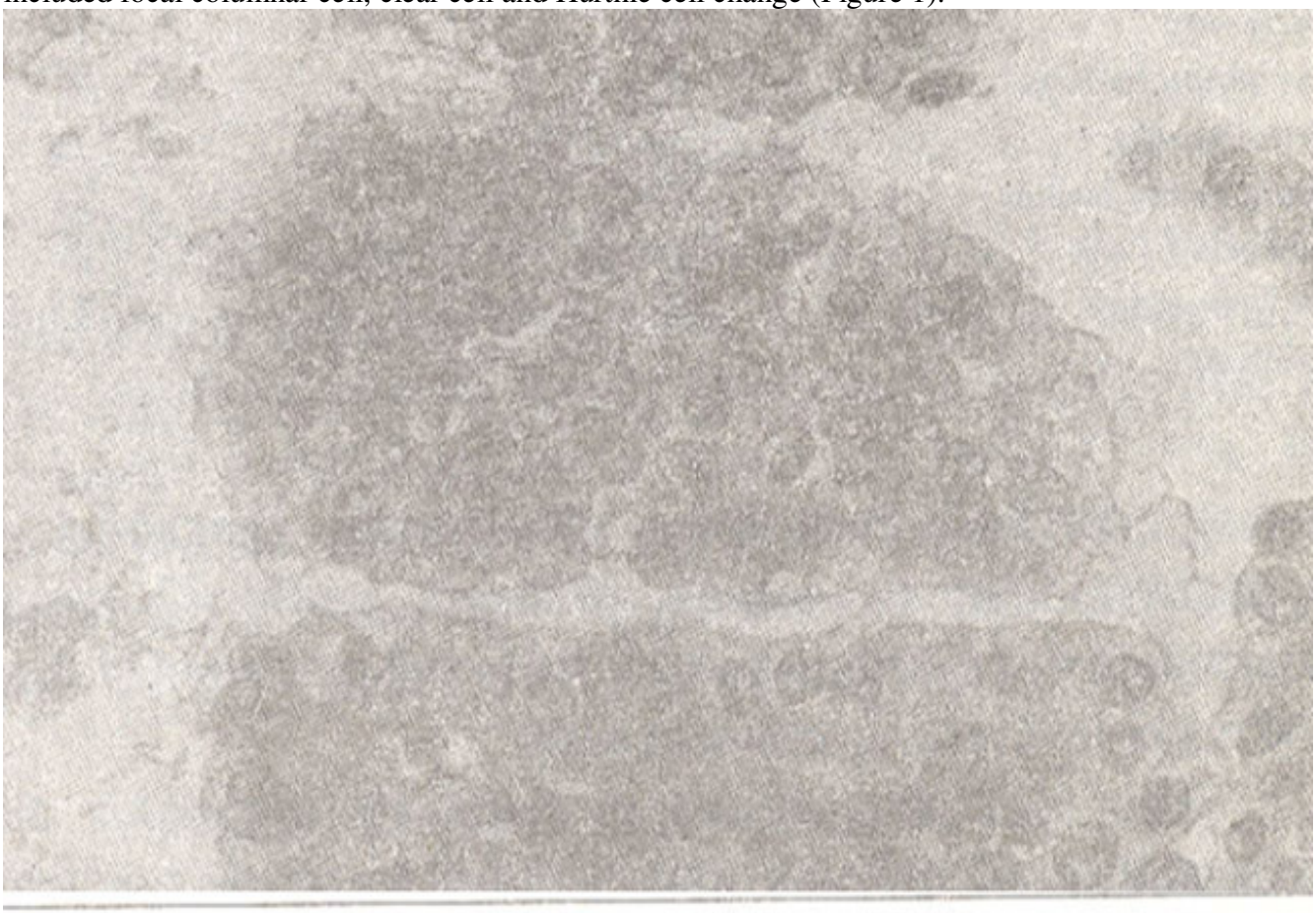

Figure 1. Hurthle cell change in papillary carcinoma. (Hematoxylin & eosin, x 400)

In the follicular variant of papillary carcinoma 9 cases (70%) showed ground glass nuclei and 10 (77%) cases had overlapping nuclei with peripheral scalloping of colloid (Figure 2).

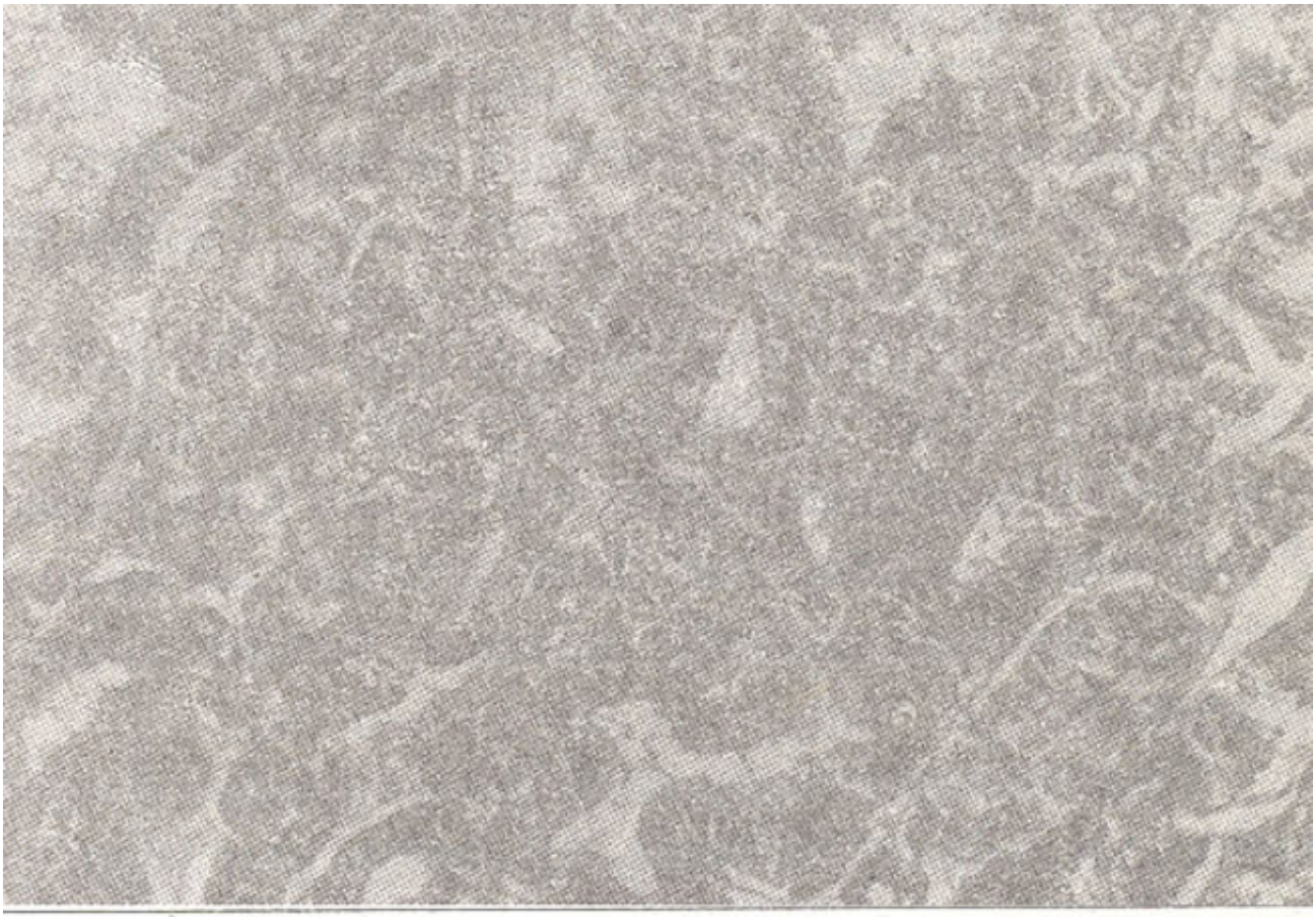

Figure 2. Follicular variant of papillary carcinoma showing peripheral scalloping of colloid (H&Ex100).

Grooving was seen in one case only. Thick nuclear membranes with prominent nucleoli were seen in 2 cases. In4 cases no optically clear nuclei were found and the diagnosis was based on the occasional presence of micropapillae. Another consistent finding was the presence of fibrosis with broad fibrous septa traversing the tumor. Micropapillae were seen in 7 cases and psammoma bodies in 2 cases only (Table II).

Table II. Clinical, gross and microscopic features of papillary carcinoma and its variants.

	Classical papillary carcinoma	Follicular variant	Columnar cell variant	Tall cell variant
Age (mean)	27 years	46 years	61 years	52 years.
Sex (F/M)	2:1	1:2	1:1	1:2
Tumour size (range of diameter)	- 0.7 - 4 cm - Multifocal (10 - Gross papillae (5) Necrosis and haemorrhage (11) - Cystic (4)	4 cm	4.5 cm	5.5 cm
Clinical presentation	- Multinodular goitre (28) -Solitary nodules (14) -hyperthyroidism (2) -Cervical lymph node Metastases (4)	- Multinodular goitre (3) -Cold nodule (2) -Hoarseness of voice metastases (1) & Dysphagia (2) -Lymph node mets (5)	Hard nodular goitre (3) -Strap muscle (1) infiltration -Lymph node	- Multinodular goitre (1) - Solitary cold nodule (1)
Metastases	4	5	1	0
Microscopic appearance		Micropapillae (7)		
Ground glass nuclei	44	9	2	2
Grooving	26	1	1	0
Pseudoinclusions	4	0	1	0
Overlapping	54	10	0	0
Psammoma bodies	20	2	1	0
Fibrosis	14	8	0	0
Lymphocytic infiltrate.	3	2	0	0

All the 6 cases of columnar cell variant showed pseudostratification of nuclei with basal vacuolation. Four cases showed pale cytoplasm while 2 cases had eosinophilic cells. Acinus formation and tubule formation was seen in 2 cases. Focal clear cell change was seen in one case while one case showed Hurthle cell change with prominent psammoma bodies.

In one case marked edema of the stroma of the papillae was seen, strongly reminiscent of chononic villi. Focal tall cell change was seen in one case.

The tall cell variant histologically exhibited a trabecular patternofgrowthcomposedofcords andtrabeculae (Figure 3)

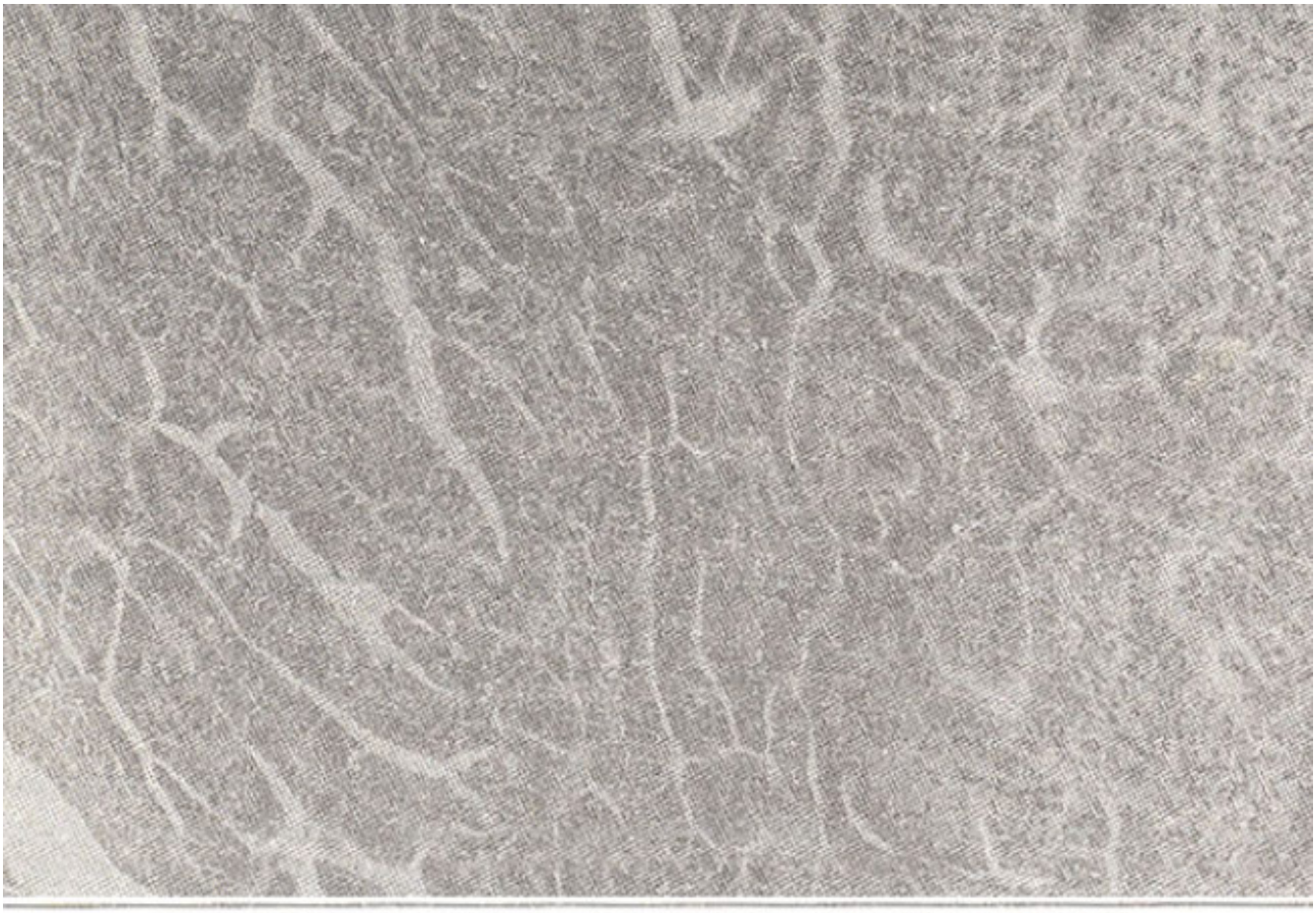

Figure 3. Tall cell variant showing trabeculae and papillae (H&E x100).

lined by tall cells fulfiling the described criteria of a cellular height width ratio of >2:1 with basal nuclei and eosinophilic cytoplasm[1-3]. Papillae were found in abundance in 2 cases. The surrounding thyroid showed a ground glass change in 30-40% nuclei (Figure 4).

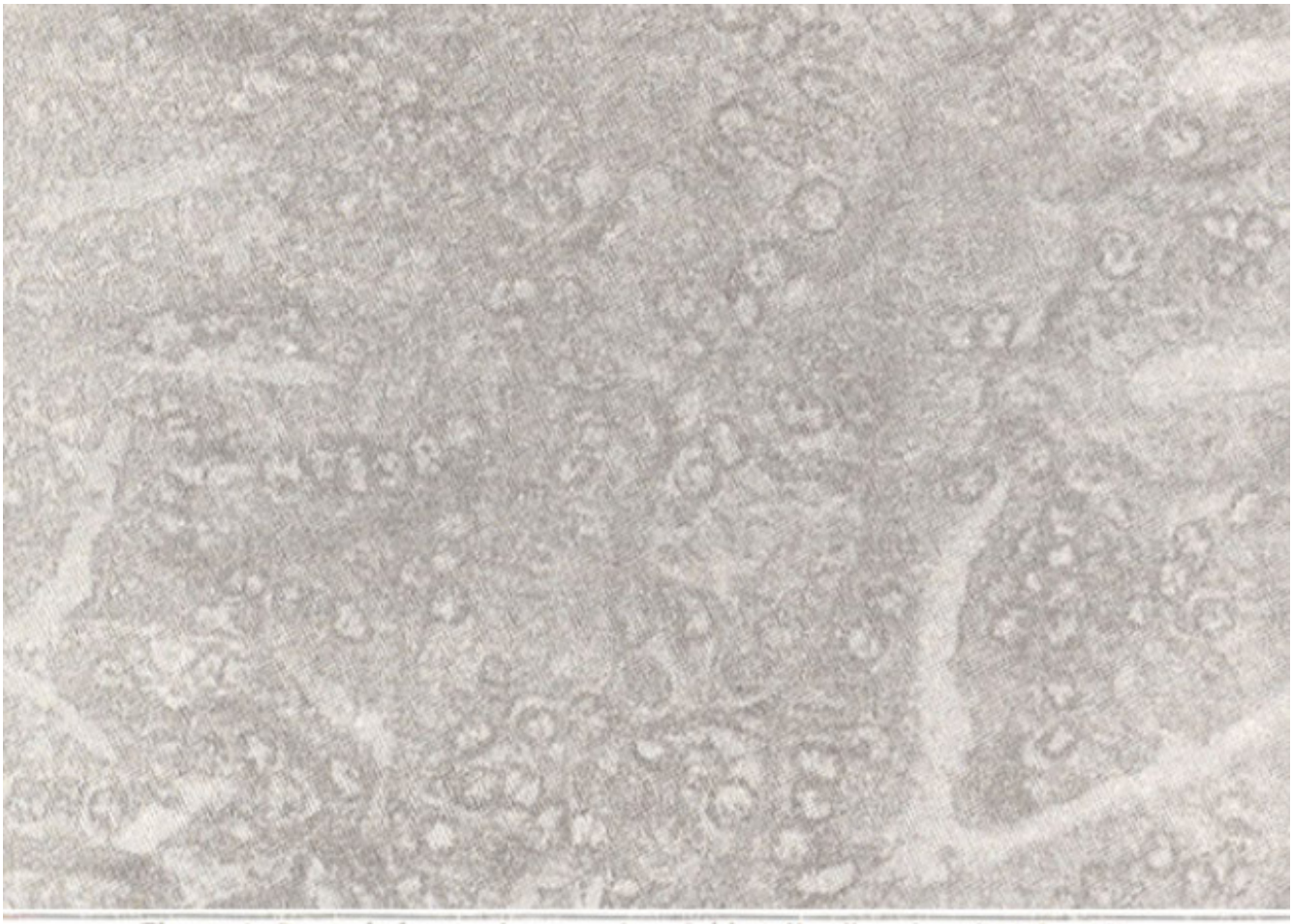

Figure 4. Ground glass and grooved nuclei in tall cell variant (H&Ex400)

In one case focal clearing of the cytoplasm (Figure 5)

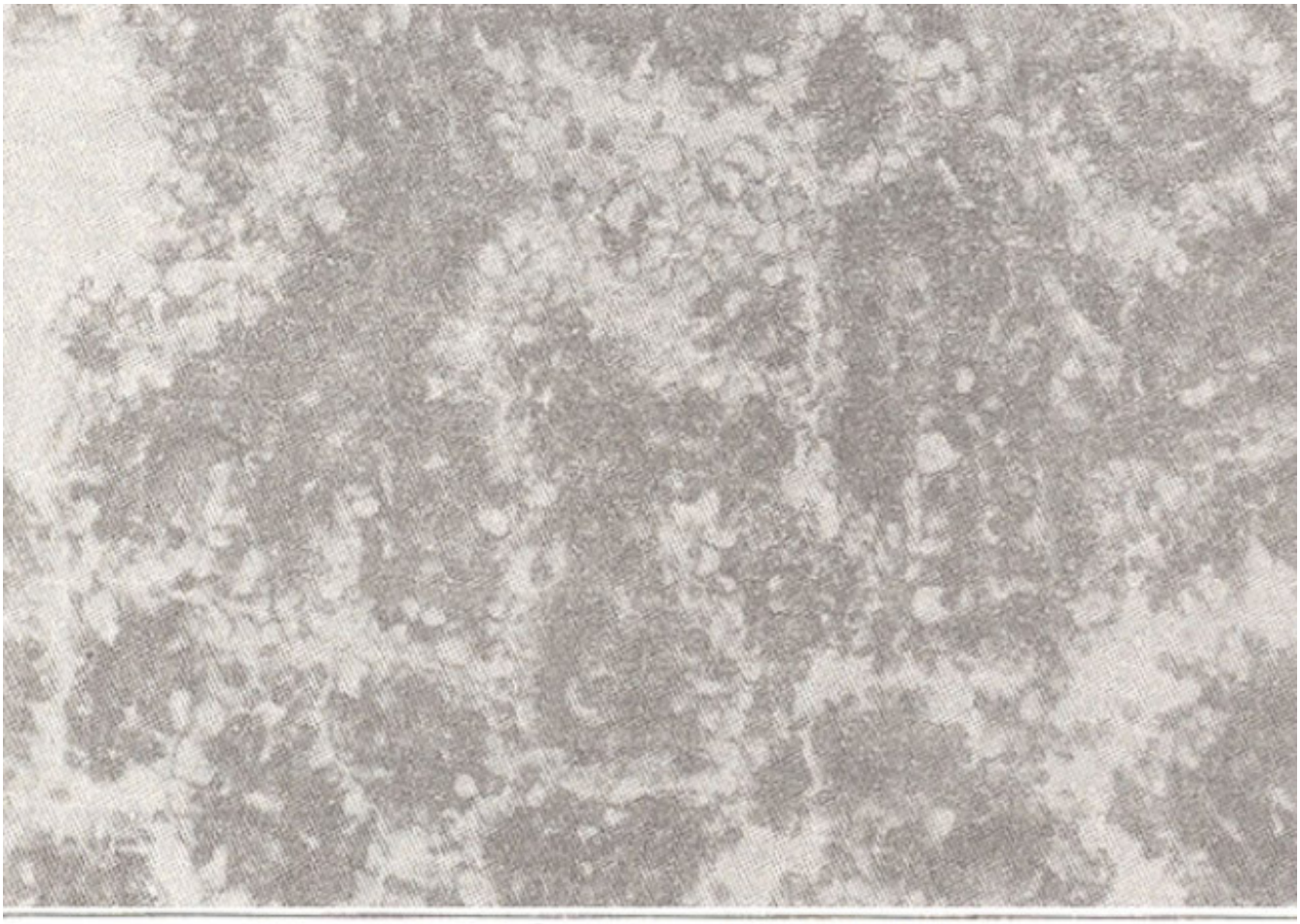

Figure 5. Focal clear cell change in TCV (H&Ex100).

was present while in another small pools of mucin were seen.

Discussion

Recent studies have brought to light the importance of subtyping of papillary carcinoma of the thyroid, since many histological variants have been associated with an aggressive biological behaviour and a grave prognosis[1-3]. As the immuno-histological profile and flow cytometry findings of the aggressive and non- aggressive variants are similar, morphology[3-4] is the only way of identifying these variants, so far[2].

Papillary carcinoma has high incidence in countries having iodine - sufficient or iodine - excessive diets, comprising about 80% of all the thyroid cancers[1]. Ground glass nuclei were the most consistent finding found in 76% of our cases (97-100% in other series)[1,5]. Similarly psammoma bodies were found to occur in 34% cases (40% in other series)1,11,12. Cervical lymph node metastases were present in 15.5% of our cases (50% in other series)[1,12,13]. Prominent nucleoli, an uncommon finding[11-13] were seen in 6 cases, in association with well formed papillae.

In the present study we had two cases that showed prominent Hurthle cell change in some areas. In both these cases an unusually large number of psammoma bodies were found. To our knowledge no such association with hurthie cell change has been reported so far. Reports on Oxyphilic or Hurthie cell papillary thyroid carcinoma are coming up[10] but a psammomatous variant has not been mentioned.

The follicular variant of papillary thyroid carcinoma (FVPTC) was the commonest variant diagnosed in

our study. Thirteen (16%) of the 82 cases FVPTC represented a figure similar to the 13% found in a study carried out by Tielens et al[14]. FVPTC tends to be smaller than classical papillary carcinoma and is more likely to be encapsulated[15]. In this study the size ranged between 1-4 cm. Multicentricity was found only in three cases. Psammomabodies weit uncommon (3/13 cases) micropapillae were seen in 6 cases while the most consistent finding seen in eight of 13 cases was complete or partial encapsulation with intratunioral fibrosis. Another study by Isarangkul[15] has also analyzed the association between dense and frequently hyalinized fibrosis and papillary careinoma, to assess the possibility of using this finding as another diagnostic criterion for this type of thyroid caicinoma. This may specially be helpful when other classic criteria are absent or inconspicuous as in frozen section. The presence of ground glass nuclei alone cannot be taken as evidence of FVPTC and a conglomerate of features must be taken in consideration when making this diagnosis. We found the same criteria useful for the diagnosis of FVPTC that have been followed by Tielens et al[15] in their study i.e., a follicular architecture occupying at least 80% of the neoplasm and atleast two nuclear features typical of papillary carcinoma. Although FVPTC is considered to be simply a diagnostic curiosity, with no serious prognostic implications, in this study four of the thirteen cases presented with recunent laryngeal nerve paralysis and hoarseness of voice with extrathyroidal extension in one case.

The frequency of columnar cell variant[6,16], another ominous subtype of papillary carcinoma in the present study was 7%, the meanagebeing 6l years. The clinical presentation of these was clearly an indicator of their aggressive clinical behaviour. In our cases focal tall cell change, focal clear cell change and focal Hurthie cell change was seen in some of these tumours. Therefore, although morphologic heterogeneity is found commonly in papillary carcinomas, we found it to be more prevalent in the columnar cell variant.

The tall cell variant (TCV) of papillary carcinoma, had a much lower incidence (4%) in our study compared to the 10-12% reported by otheis[1,17] and more in accordance with Johnson's study (4%)[18]. The reasons for these differences could be racial orgeographical. The average age of the patients was 52 years comparable to the 57 years reported by others[3].

In one case mucin-like pools of colloid were seen. TCV has been described in association with other types of thyroid cancers such as mucin-producing careinoma, anaplastic, squamous cell, columnar cell[19] and clear cell carcinoma[17]. Therefore, a careful search for these should be made where indicated. In view of the prognostic implications of the variants of papillary carcinoma, it is important for pathologists to specify the variant of papillary carcinoma in their diagnosis. An awareness of the more aggressive variants among surgeons and pathologists calls for a more careful search for specific gross, microscopic and clinical features in these cases. This may be important in planning therapy.

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