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A NEW HISTOPATHOLOGICAL FEATURE IN THYROID PAPILLARY CARCINOMA: HYALINE BODIES

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SUMMARY: Thyroid papillary carcinomas differ from other thyroid carcinomas in behaviour and histopathologic features.
In our study, among 23 000 biopsies examined in the last 9 years in Dokuz Eylül Üniversity Medical Faculty, Deparment of Pathology, 9 thyroid papillary tumour cases (one thyroid papillary adenoma and eight thyroid papillary carcinomas) are presented. 7 of the cases are females and 2 are males. Their ages range between 18 and 78; the mean age is 41.
Histopathologic features including the characeristics like papillary structures, ground glass nuclei and psammoma bodies, are reviewed. The place and value of hyaline bodies, a new findings of ours in the histopathological diagnosis of thyroid papillary carcinoma is discussed.
Key Words: Thyroid papillary carcinoma, psammoma bodies, hyaline bodies.

INTRODUCTION

There are many etiological factors of thyroid carcinomas such as endemic goitre, adenomas, thyrotoxicosis, cases leading to long acting stimulation action of TSH, radiotherapy, and atom and hydrogen bombs (2,19).

In nonendemic regions, thyroid papillary carcinomas (TPC) are more common than the others (4). Especially in younger age groups radiotherapy applications to the head and neck regions, results in TPC later (8,10-12,19).

Some authors suggest that the development of TPC is due to long, standing TSH stimulation (8).

The most common type of thyroid carcinomas is TPC. In various laboratorios, 40-70 % of the cases are reported to be TPC (10,14).

Papillary carcinomas are not common than the other organ malignancies. However, in large number of autopies accult papillary carcinomas (OPC) smaller than 1 cm in diamater and clinically not diagnosed, are observed between 6-35,6 % cases. Because of this high percentage, OPC are normal signs in autospy series (8,11-17).

Thyroid OPC are seen puberty. In literature, there is one case at the age of 11 (8), but the papillary carcinomas are most common in middle age and in females (8,11,17).

Macroscopically, TPC are small in size, gray-white in colour and the borders are nondifferentiated. They are frequently nonencapsulated (8,10,14,18). Laskin defines them as partialy encapsulated (11). Sometimes, they can only be diagnosed microscopically. ın very large lesions, papillary structers are defined macroscopically (15). Therefore macroscopy is an important observation in definition of the tumour.

Microscopically, the tumour cells are arrenged in a row, their nuclei are pale and have the appearance of ground glass, and surround the papıllary structures of connective tissue. The cytoplasm of tumour cells in bright or oxyphilic (20). These cells are cubic, columnar or low columnar.

Psammom bodies are common TPC. These calcificated and spherical structures sug-

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gest that the tumours had appeared a long time ago (15). A possible explanation is that, psammom bodies develop from degenerated tumour cells in thyroid gland lymphatics (10).

On the other hand, structures which we call hyaline bodies are observed. Psammom bodies develop by precipitation of dystrophic calcium on these hyaline degeneration foci and areas on stromal connective tissue (6).

Microscopicall, under high power observation, nuclear cleaves and intracytoplasmic inclusion bodies appear in the tumour cells (20).

Especially in OPC, in some cases, tumour is composed of follicular stuructures. In these cases which have no in the presence of papillary structures or psammom bodies, the diagnosis can be made by ground glass nuclei (10). Ground glass nuclei are due to intranuclear inclusions (9,13). Capsular invasion ise observed in some cases (10).

In papillary carcinomas, there may be fibrosis despite lymphocytic infiltration, reflecting host reactions (10).

The lymph nodes are not palpable for a long period because they do not enlarge and change their constituents. Beside the lymph nodes, in rare cases hematogenous spread such as pulmonary and bone metastases are observed (11,17). Vessel invasion in primary tumour suggests the possibility of distant organ metastasis (9).

In additon, the distant metastasis of papillary carcinomas rarely lead to death (11, 13).

Our aim is to review the pathological specificities of TPC and reaxamine the histopathological features by using histochemical and immunperoxidase methods and to consider the hyaline bodies, a new histopathologic feature that we have determined in two cases.

MATERIAL AND METHOD

Starting with the foundation of Dokuz Eylül Üniversity Faculty of Medicine to date (5.11.1979-15.1.1989), 750 thyroid glands were studied in the Pathology Deparment and 15 of them were thyroid carcinomas. Of thes, 8 cases of TPC and one case of thyroid papillary adenoma studied by using light microscopy, histochemistry and immunperoxidase methods and the findings are discussed in the light of related literature (5). The morphological and histochemical characteristics of hyaline bodies are also studied together with the known histopathological properties of thyroid papillary carcinomas: the papillary structures, ground glass nuclei, vessel and capsula invasion and psammom bodies.

RESULTS

6 of our papillary carcinoma cases are women and 2 of them are men. The only case diagnosed as papillary adenoma is a 15 year old girl (Table 1). In our series of TPC, the youngest case was 18 years old and oldest was 78 years old, the mean age was 41.

Except of one case in our series clinical prediagnosis was nodular goitre.

Macroscopically; tumors were 5 mm and 3 cm in diameter. Their section sides were gray-white in colour, with an undetermined surrounding. Excluding the adenoma, they were unencapsulated.

Microscopically, the papillary structures were prominent in our, cases. The tumour cells with pale and ground glass nuclei lie in a row around the papillary structures of connetive tissue (Figure:1).

In the case of TPC which we have diagnosed by the metastatic foci of pulmonary tumour, vessel incasion was found in the primary tumour (Figure 2):

This was not observed in other cases in our series. Psammom bodies were observed in 2 cases of this series, hyaline bodies in 2, lymphocytic infiltration in 4, papillary structures and follicules in 5 and invasion to surrounding striated muscle fibres in 2 cases (Table 2) (Figure 3,4).

TABLE 1: Clinical features of 8 TPC cases in our series.

NUMBER		NAME	AGE/SEX	CLINICAL DX.	PATHOLOGICAL DX.
1.	103/81	HÖ	18/F	NG	TPC
2.	246/82	AM	78/F	Thyroid ca?	TPC
3.	1506/84	SK	15/F	NG	TPA
4.	1473/86	BG	30/M	NG	TPC
5.	1004/87	AM	48/M	NG	TPC
6.	1039/87	NP	31/F	NG	TPC
7.	2157/87	AB	32/F	NG	TPC
8.	4346/87	MG	34/F	NG	TPC
9.	4415/87	SE	62/F	Pulmonary tbc, tumor?	TPC
	4627/87	SE	62/F	TPC	TPC

TABLE 2: Histopathological features of 8 TPC and 1 TPA cases in our series.

NUMBER		CAPSULA	GROUND GLASS	PSAMMOM BODIES	HYALINE BODIES	LYMP. INF	FOLL. STR	VAS. INV.	PER INV.
1.	103/81	+	+	-	-	+	+	-	-
2.	246/82	-	+	-	-	+	-	-	-
3.	1506/84	+	+	-	-	-	+	-	-
4.	1473/86	-	+	-	-	+	-	-	-
5.	1004/87	-	+	-	+	+	-	+	+
6.	1039/87	-	-	+	-	-	+	-	-
7.	2159/87	-	+	-	-	-	+	-	-
8.	4346/87	+	+	-	-	-	-	+	+
9.	4415/87	-	-	+	+	-	-	-	-
	4627/87	-	+	-	-	-	+	+	-

TABLE 3: The histochemical properties of psammom and hyaline bodies.

	CONGO RED	PAS	VAN GIESON
PSAMMOM BODIES	Violet-blue	Purple-black	Purple-black
HYALINE BODIES	Pale orange	Violet	Purple-red

In additon, information about psammom and hyaline bodies were obtained by histochemical study with Congo-Red, PAS and Van Gieson stains (Tablo 3) (Figure: 5,6,7).

Psammom bodies appear violet-blue with congo-red stain, but hyaline bodies appear pale orange with congo-red, violet with PAS and purple-red with van Gieson stain.

In the cases of this series, with immunoperoxidase method epidermal keratin was positive in all TPC and negative in TPA.

DISCUSSION

The specific properties of TPC are the spread to the cervicel lymph nodes by lymphatic vessels and their microcopically benign appearance. The metastases are especially found on the same side. Occult papillary carcinomas appear after cervical lymph node metastases (20) Cervical 1ymph node metastuses were wrongly named as "lateral aberrant thyroid" (1).

It is supposed that microcarcinomas smaller than 1 mm and limited are the initial

stage of thyroid papillary carcinomas (15). Occult papillary carcinomas develop after puberty and are on the same frequency in younger and older age groups. The dimensions of tumor also increase after the young adult stage. All of these confirm that TPC develop in young adults (8). In our series, the average age clinically was approximately 30 except for the case that was thought to have carcinoma.

The tumors show a follicular structure in the begining and are later surrounded by a connective tissue capsule and do not tend to spread (10). For the diagnosis of TPC, a detailed macroscopic examination is necessary. The actual frequency of these limited carcinomas is said to be higher than invasiye OPC (10). For this reason, some authors believe that these tumors are never invasive and never enlarge (10). In our series, authors follicular structures were seen beside the papillary structures.

It is claimed that limited OPC rarely develop to clinically invasive papillary carcinomas of unknown factors (10).

Occult papillary carcinomas are found between in 6-36 % of cases due to stimulation in may systemic autopsy studies. This ratio is 28 % in Japan, 15 % in USA; in Finlandia however, 52 OPC foci in 36 of 101 autopsies were reported by Harrach and Frassila. This observation is the highest percentage in the world (36. 6%). In this study, the diameters of OPC were smaller than 1 mm in 67 % of the cases. The frequency and dimensions of the tumour were not related to the patients age (10.16).

The specific finding in TPC is cervical 1ymph node metastasia observed in 20 % of the 518 cases studied by Sampson et al (16). The rate of extranodular metastases in papillary carcinoma is 4-8 % (11).

The most important microscopic finding in the differential diagnosis of borderline OPC that contains only follicular structures is the ground glass nuclei of tumour cells (8,15,17,20).

In the hot nodule appearance of the lesions in thyroid scannig, the finding of pale collodial vacuoles and no ground glass nuclei in microscopy are aids in the differential diagnosis of OPC and micropapillary structures in adenomatosis and diffuse hyperplastic goitre. The papillary structures seen in goitres are often restricted to the side facing the lumen of the cyst (15).

Immunohistochemistry is also used as a diagnostic feature. The papillary carcinoma cells stain positive with threoglobilin as do normal follicular cells. This feature helps to differentiate the neoplasms that originate from follicular cells of other neoplasms.

Positive staining with intermediate filament epidermal keratin is another speciality of papillary carcinoma cells while the normal follicular cells stain negative (8,11).

8 of TPC cases in our series stained positive with epidermal keratin in immunohistochemistry with the PAP technique.

The ratio of psammoma bodies is 61 % in large invasive papillary carcinomas (10), and 21 % in extratumoral tissues in papillary carcinomas. These structures are not seen in the normal thyroid. Only one case is reported of 2153 thyroids without cancer (15). In Patıroğlu's series, 40 (33,8 %) of 152 TPC contain psammom bodies (14).

The pathologist should consider TPC when psammom bodies are found in frozen sections, In our series, one of the cases 2 having psammom bodies was the pulmonary metastatic tumour.

In the microscopic study of the pulmonary tumour, the psammom bodies aid in the diagnosis together with the papillary structures and the ground glass nuclei (Figure: 8,10,11).

Frequently hyalin degenration is seen in stromal connective tissue of the tumour. This develops by a physical change in the stromal connective tissue collagen fibers. The collagen fibers make an nonnucleated homogenous structure by uniting together. At this time, the collagen fibers preserve their known staining properties (2). The changing in stromal connective tissue of papillary sturctures is observed as hyaline bodies. Hyaline bodies depend on the development of hyaline degeneration in stromal connective tissue of tumour papillary structures and are seen especially in the transverse sections of pa-

pillary structures.

Microscopically the hyaline bodies are elliptic or round and acellular, avascular, concentric, homogenous and hyalinised (Figure: 12). In 2 of the cases in our series, the hyaline bodies were prominent. One of these cases was in a pulmonary metastatic tumour, and was suspected as being a TPC in the thyroid gland; that was later confirmed investigations. The psammom boies develop precipitation of calcium on hyaline bodies were observed, there were also psammom bodies.

In fine needle aspiration biopsy, psammom bodies and vascular papillary sturctures sholud be considered in the diagnosis of TPC as well as intranucleer inclusions, papillary structures without vessels and metaplastic cytoplasm (13).

In a different series, the average age of TPC is between 37,5 and 49; in our series, it is 41.

The prognosis in papillary carcinoma is generally good. Ten years survival rate is reported in 80 % of the cases (12). Some authors suggest that the histological types of thyroid carcinomas are confusing (7). It is agreed that the primary tumor and its metastasis may be of different types and therefore the histopathological type of the primary tumor is not an important prognostic feature (7). According to, these the biological behavior of the thyroid carcinomas relate with the patients age and sex and histology (7). Prognosis is reported to be worse above 40 years in men than children, young adults and women (3). One case in our series was a 48 year old man and there was vascular and capsular invasion in histopathological study. Of interest was, one 62 year old case who presented with pulmonary metastasis.

According to Rosai, TPT is malignant in its biological behavior from the begining and question the existence of the benign TPA (15). It can also be suitable to think of TPT as a carcinoma because the real papillary adenomas are very rare.

In our series, there was only one case of TPA. This tumor was excised from a 15 year old girl, was macroscopically 1 cm, in diameter and well limited. Microscopically there was a capsul of manifest fibrous tissue.

It is reported that OPC must be more than 5 mm in diameter. In literature, there are tumors 6 mm in diameter and with metastasis. In thyroidectomy, there is no need for further invasive operation if there is no metastasis around the small OPC (10).

Occult papillary carcinoma should be kept in mind in cases where there is no thyroid pathology, clinically. Cases like these may appear with 1ymphogenous and hematogenous metastasis, althought both are rare features. Distant organ metastasis are very rare in OPC (8). For example Harach and Fransila report 8 metastatic cases in a wide search of 7 series (9). Of these only 2 cases were with pulmonary metastasis (9). In our 8 cases of the TPC series, one case was primarily diagnosed with pulmonary metastasis. In these cases,total embedding (paraffin) and many sections should be done, each 2-3 mm, to find the primary lesion in the thyroid (17).

In conclusion, the biological behavior of thyroid papillary carcinomas change according to the histopathological findings, and the patient's age and sex. A new finding, hyaline bodies, which we present in this article, should be considered in histopathological diagnosis together with the papillary structures of tumor epithelia, ground glass nuclei, capsula and vessel invasion and psammom bodies. The hyaline bodies are of value as a histopathological crietria supporting the other features either in the primary tumor or its metastasis.

FIGURES

1. *Ground glass apperance of tumour epithelial nuclei (HE, 2159/87, DEUMF Pathology Department).*
2. *Vascular invasion in thyroid papillary carcinoma (TPC) (HE, 4415/87, DEUMF Pathology Department).*

3.4. Tumour invasion to the capsular connective tissue (Masson, 1039/87, DEUMF Pathology Department).

5.6. The appearance of stromal hyaline degeneration areas in Congo Red stain. These areas had taken the appearance of hyaline body by hyalinisation and are concentric, nonvascular, noncellular and homogenious in same areas. Congo Red, 1004/87. DEUMF Pathology Department).

7. The violet-blue colour of psammoma body in Congo-Red stain and definite concentric lamellar sturcture (Congo Red, 4415/87, DEUMF Department Pathology).

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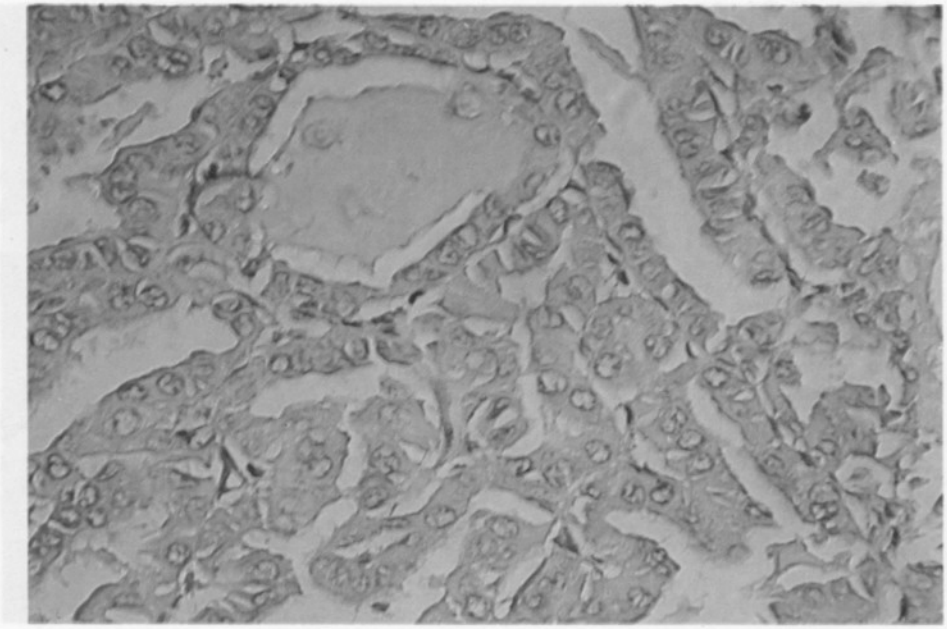

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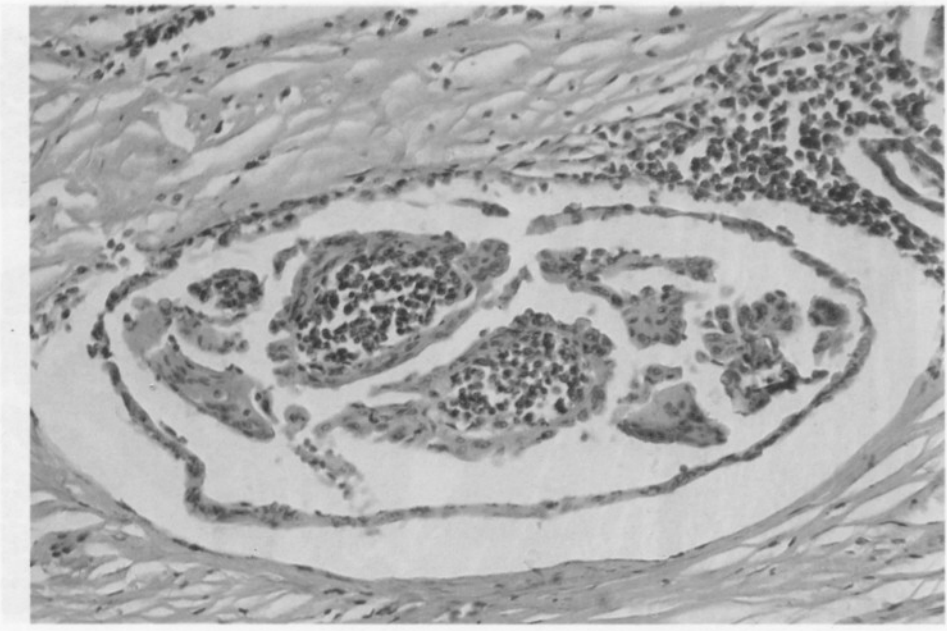

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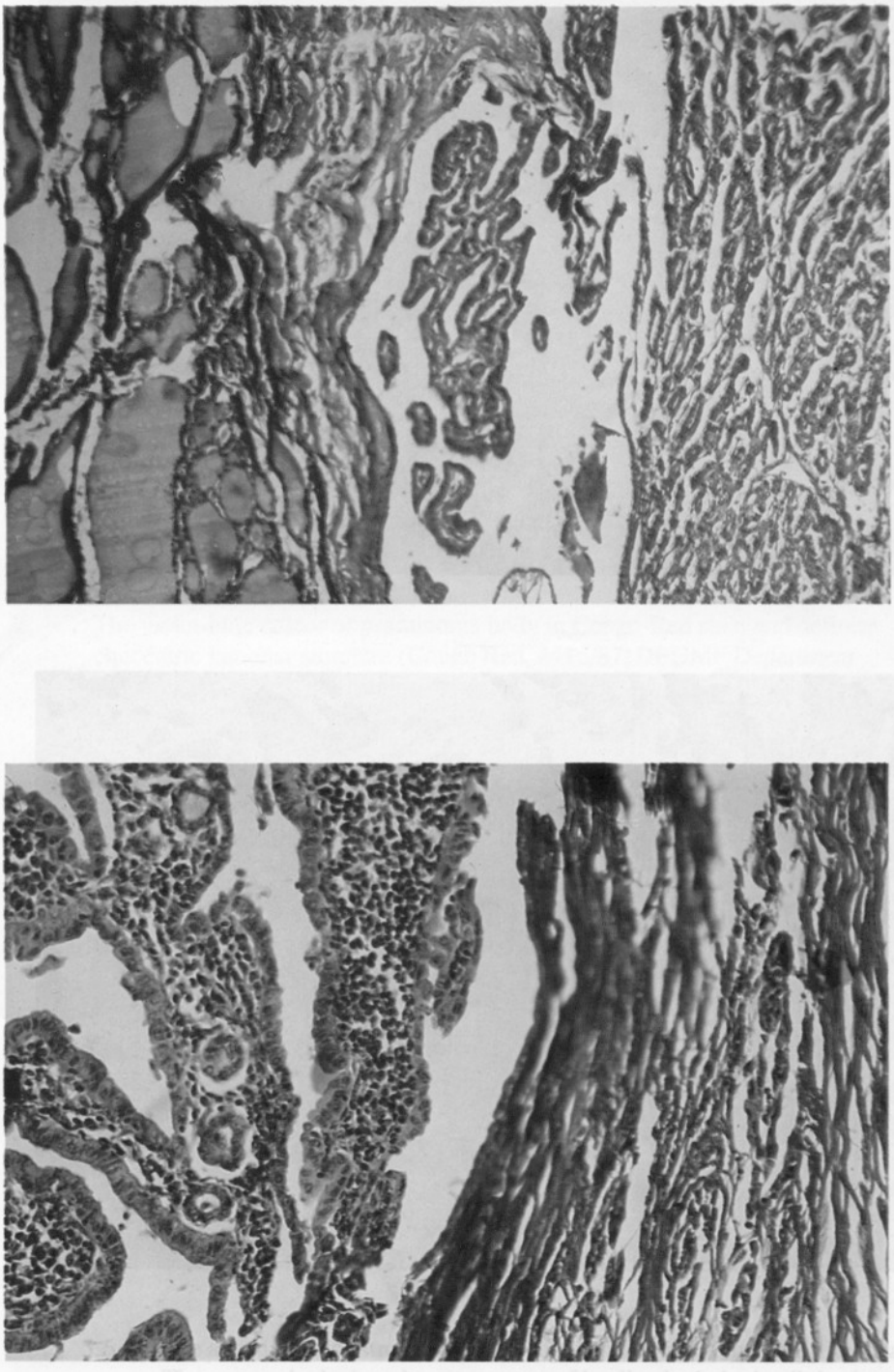

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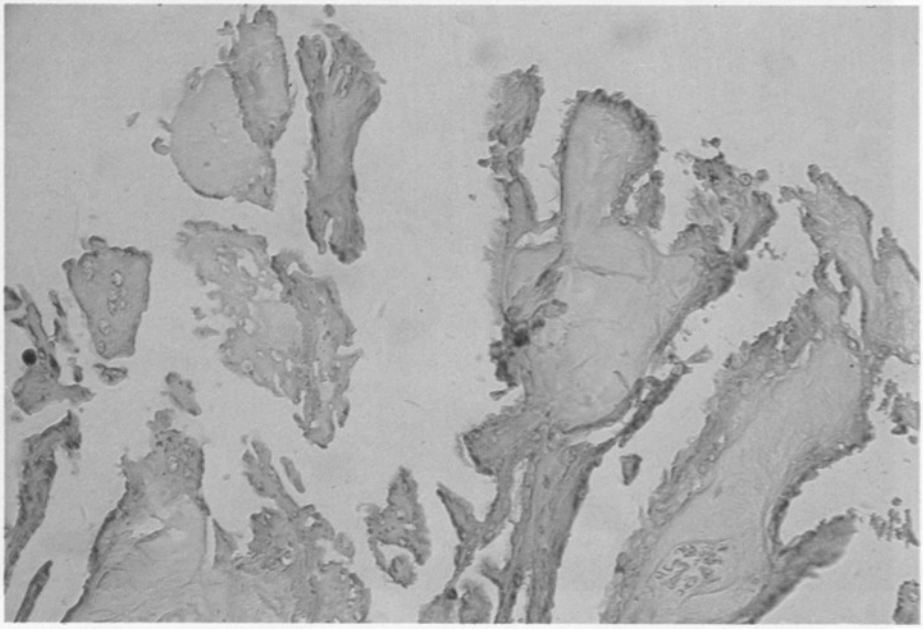

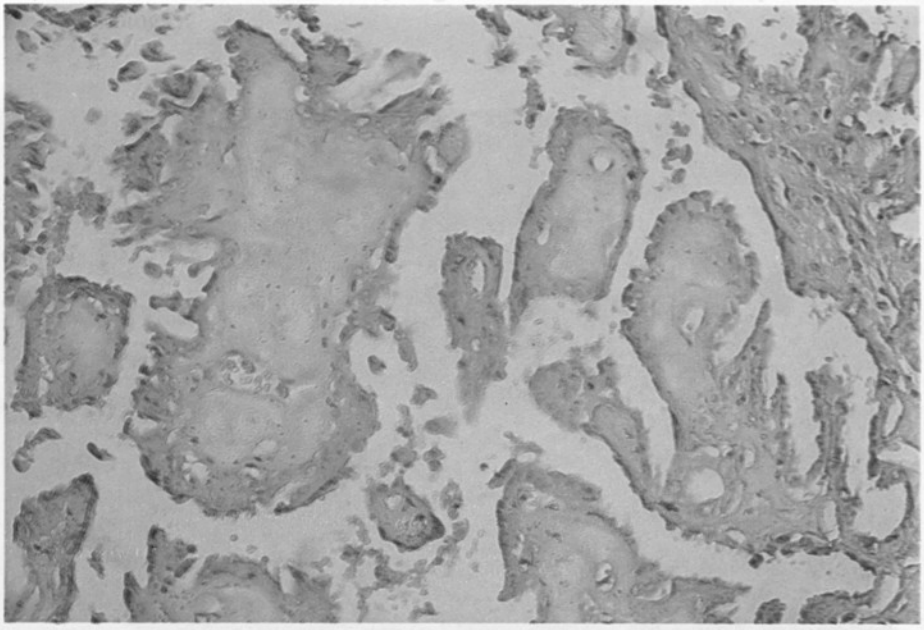

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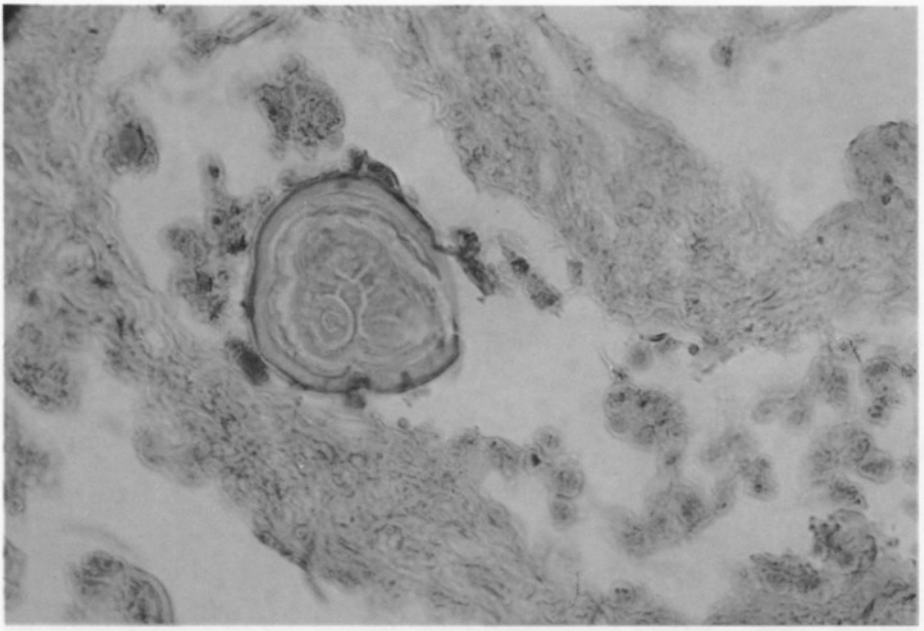

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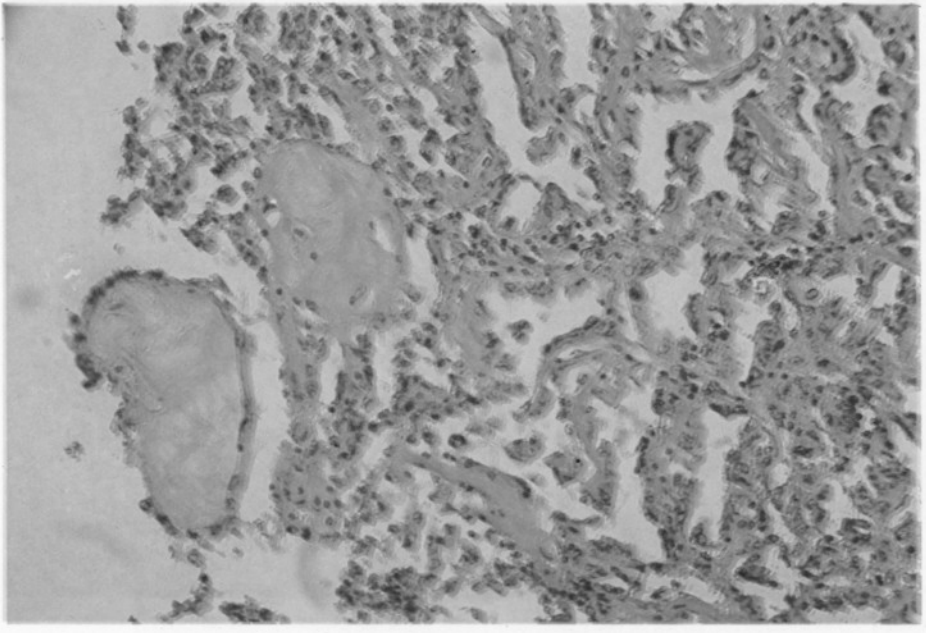

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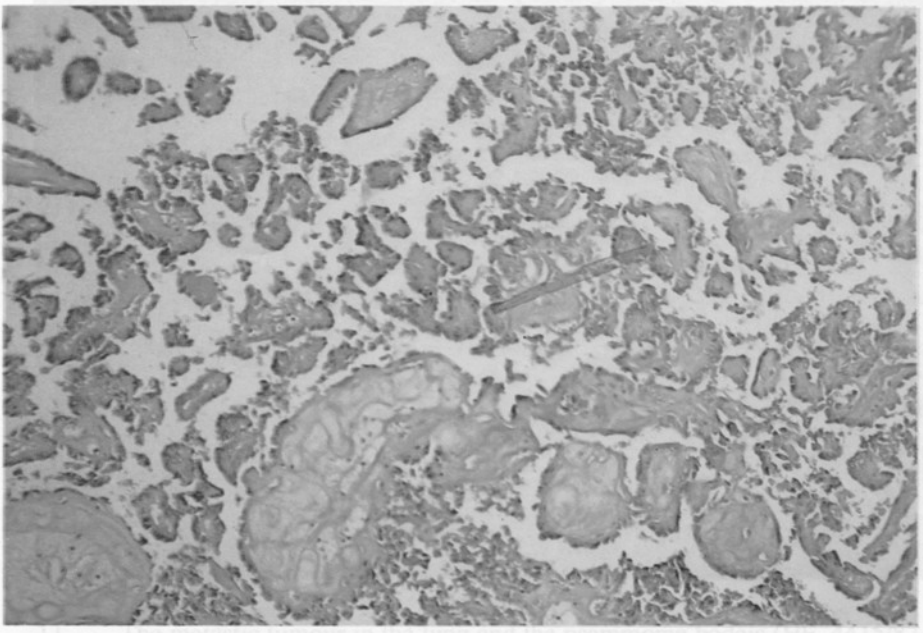

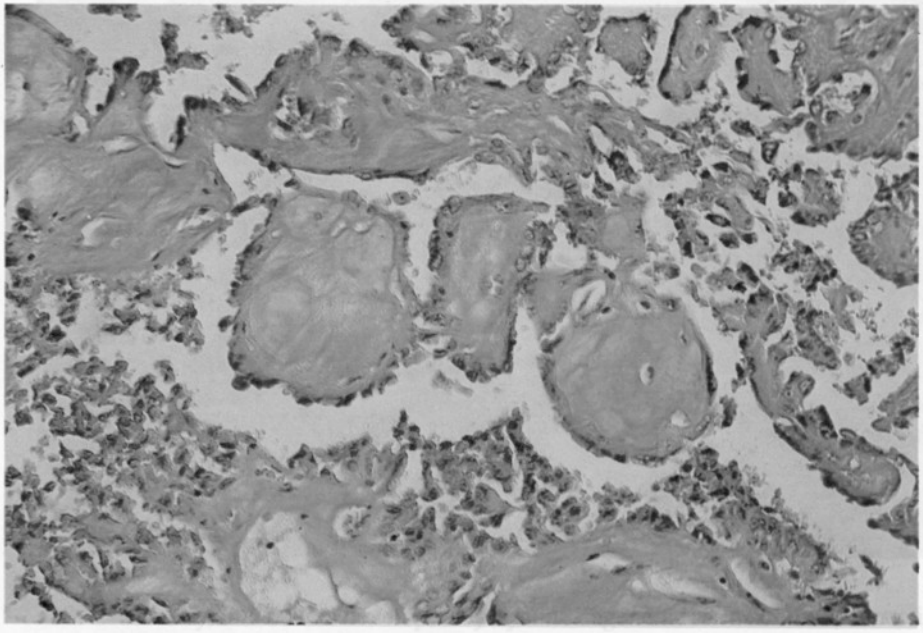

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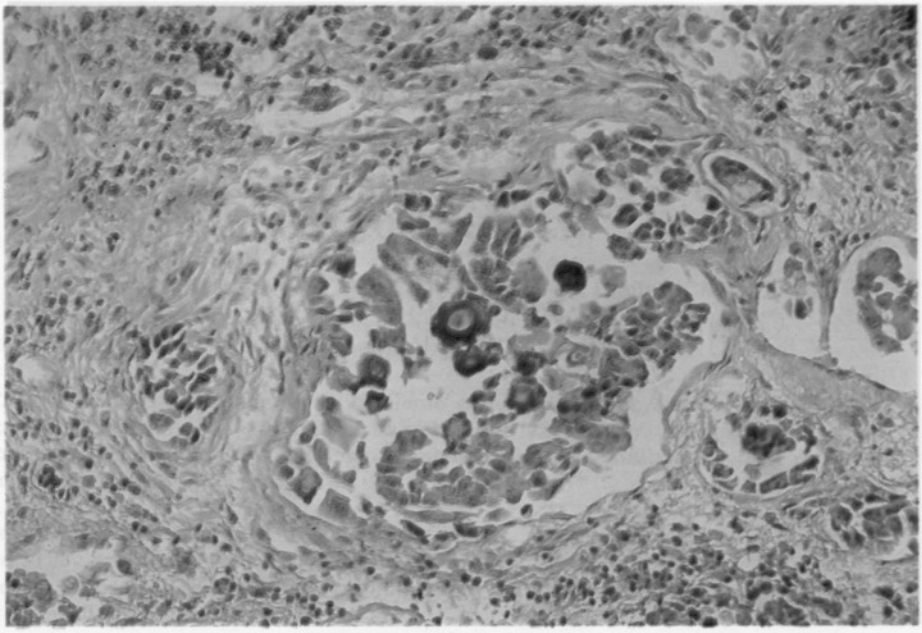

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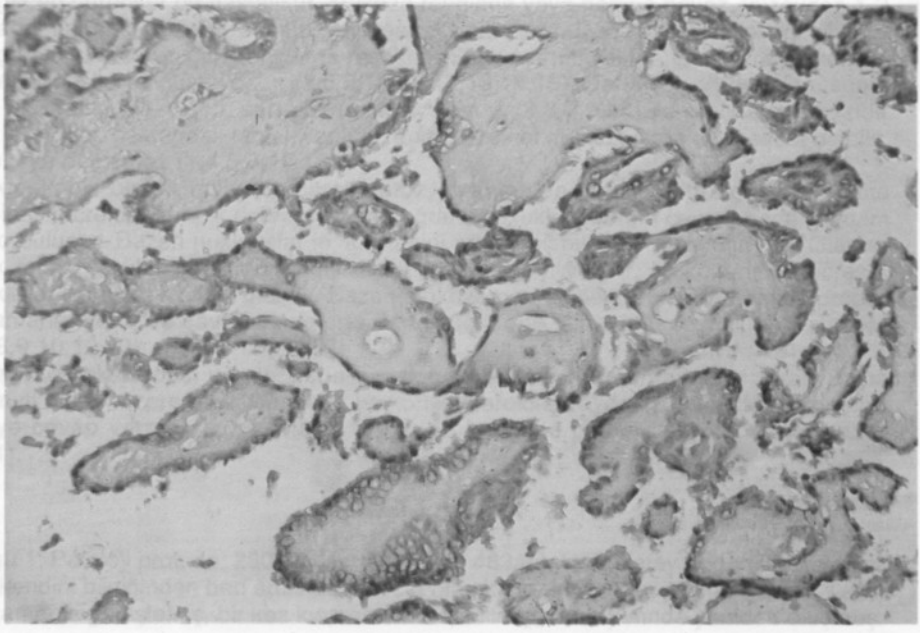

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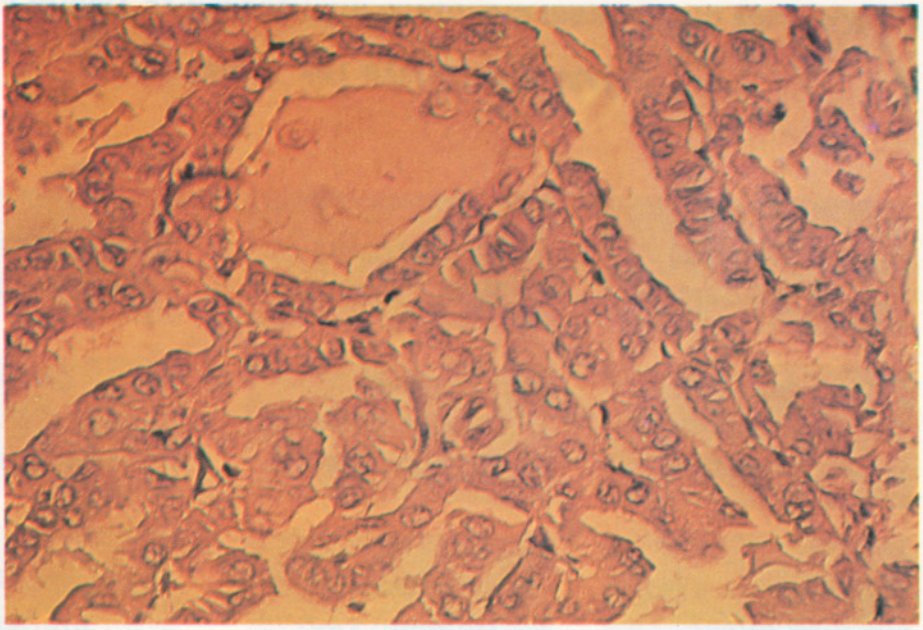

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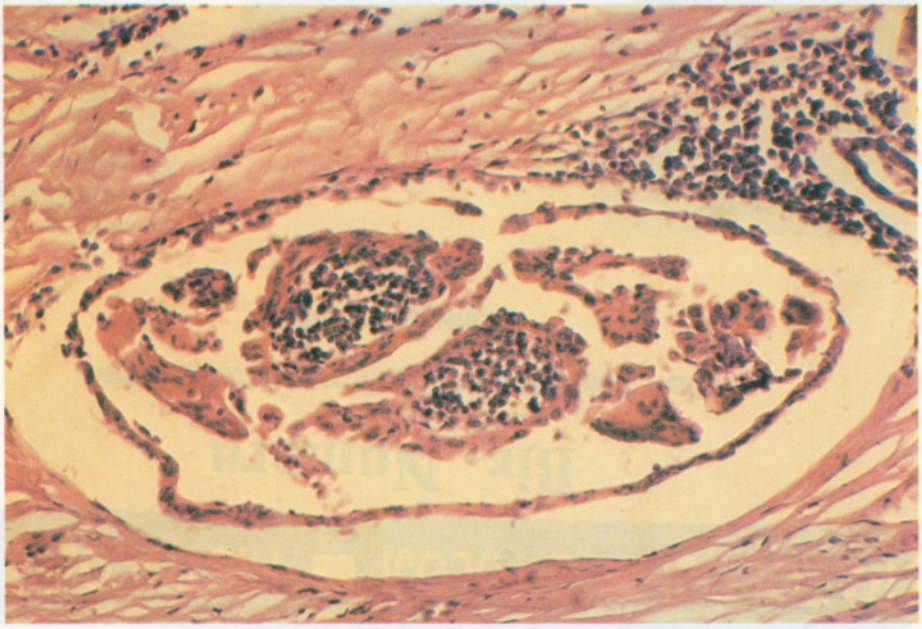

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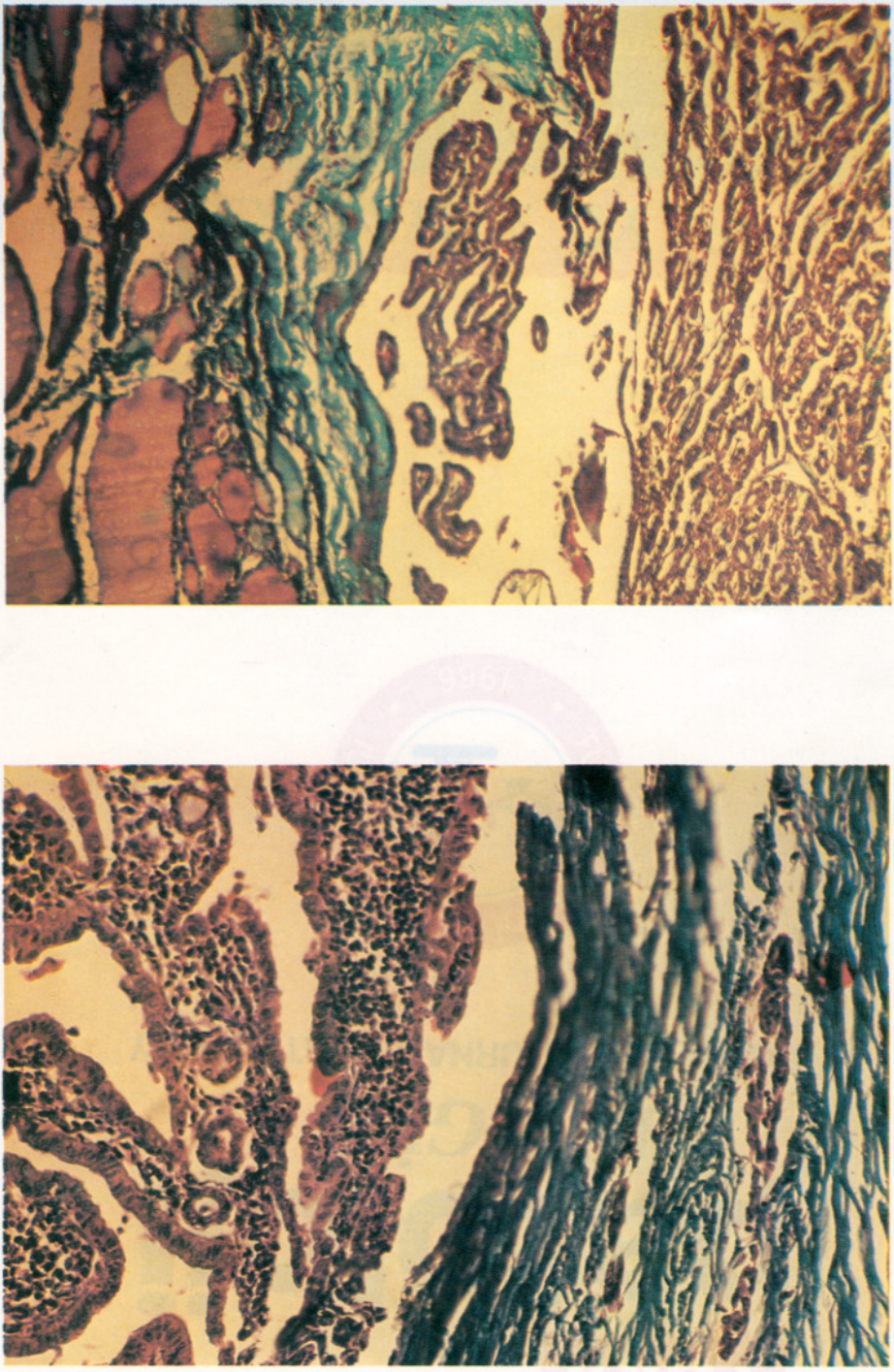

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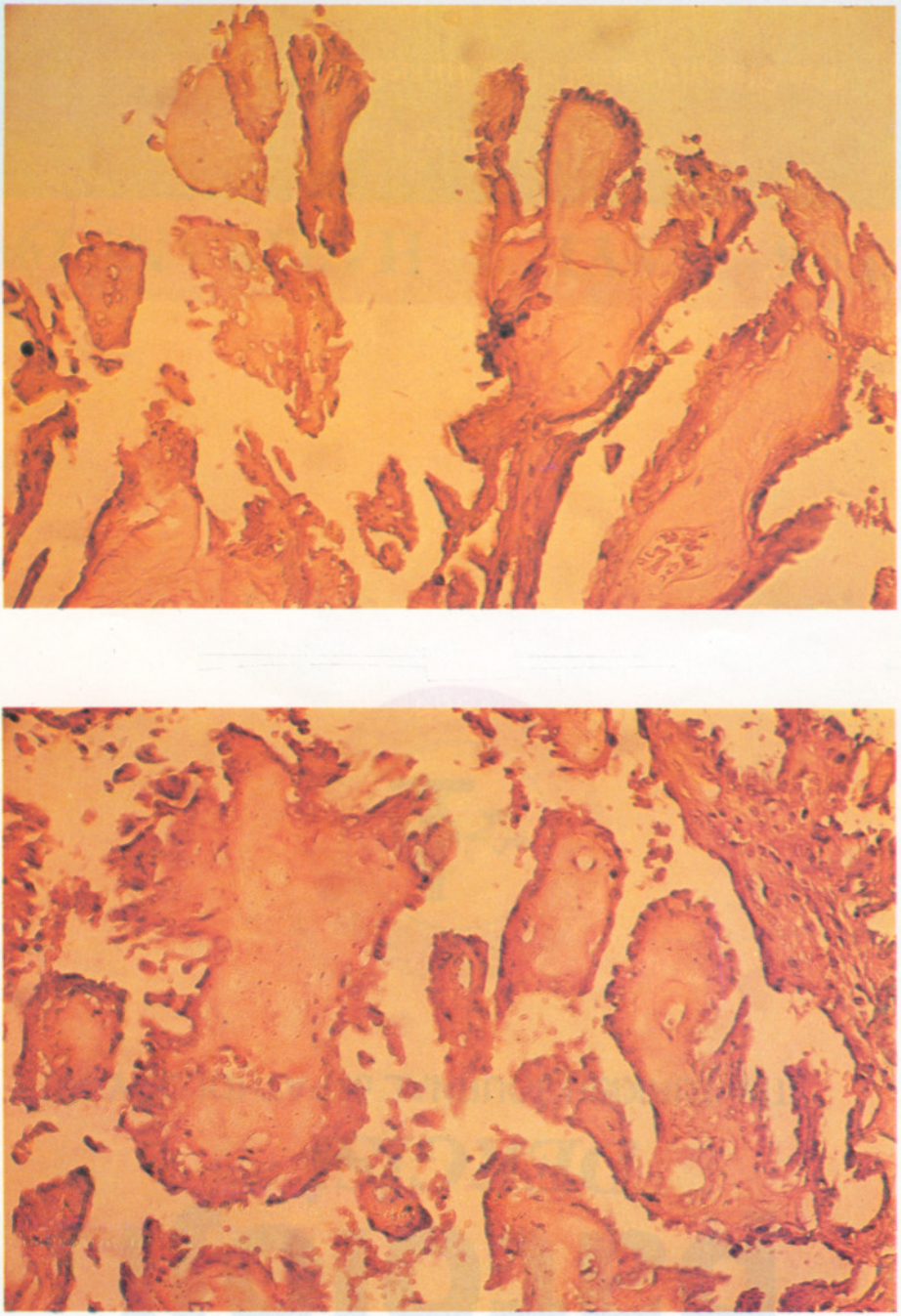

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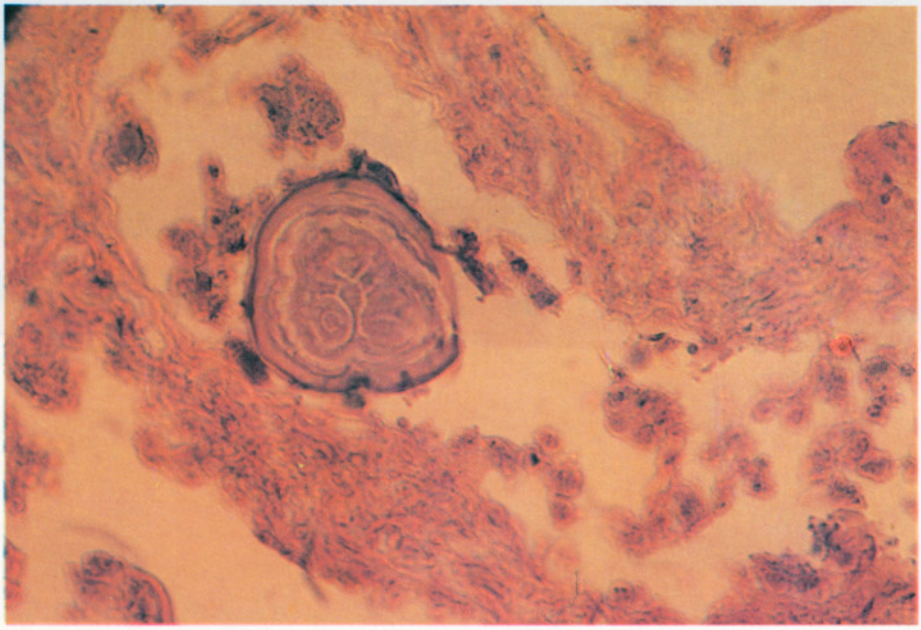

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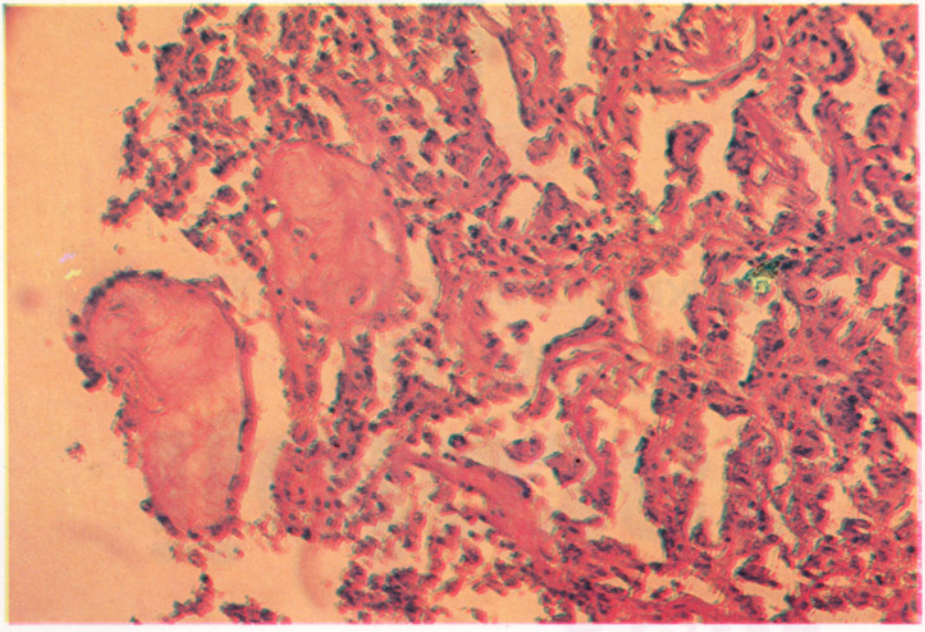
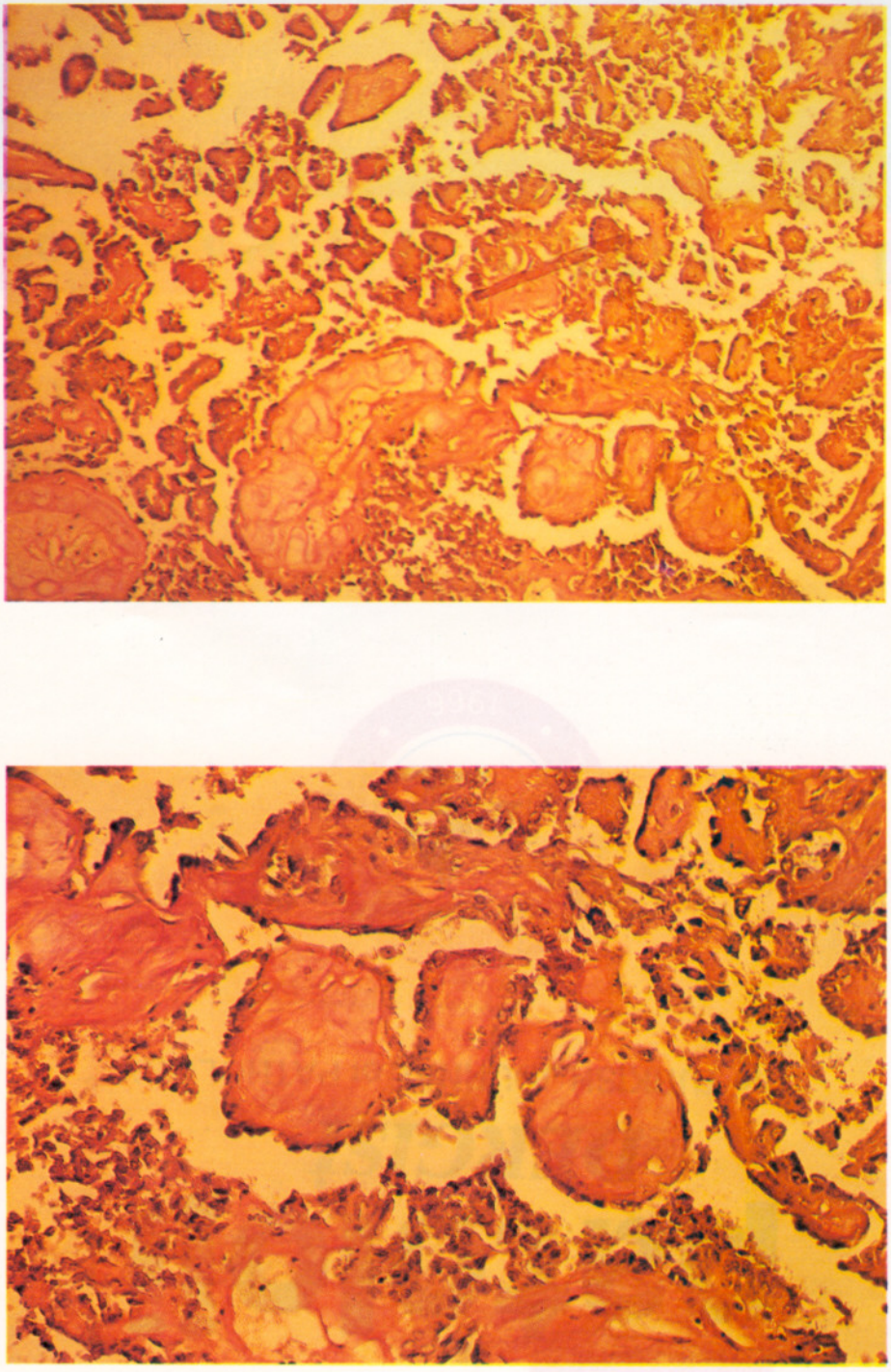
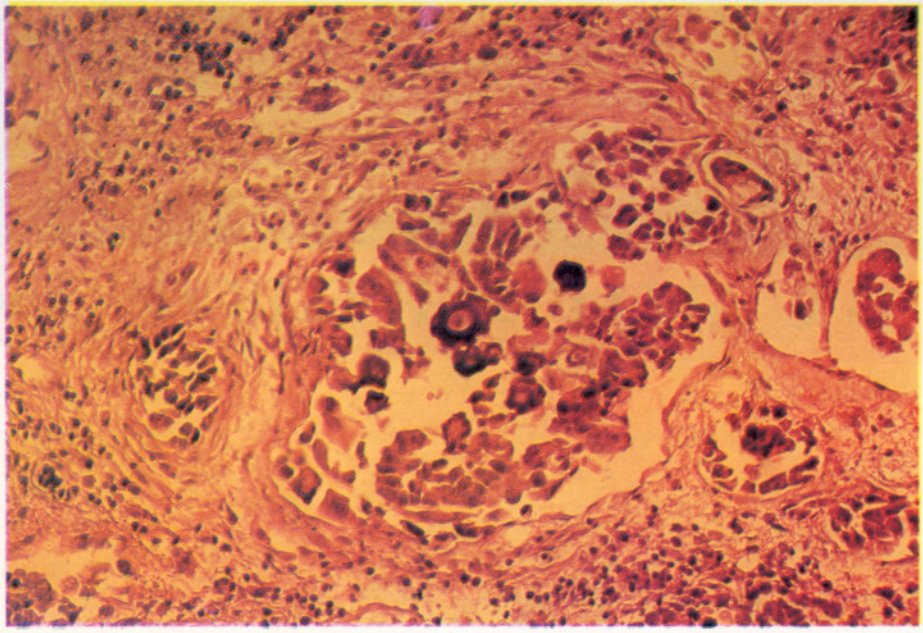


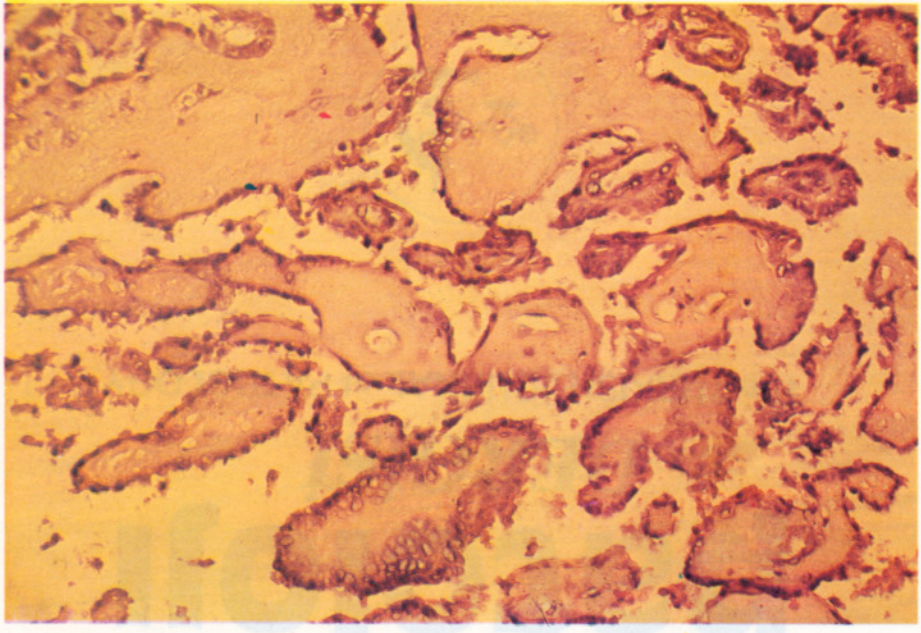
8. Hyaline bodies'appearance with van Gieson stain in the case of TPC having pulmonary metastasis (van Gieson, 4415/87 DEUMF Department of Pathology).



9.10. The other areas and the hyaline bodies with van Gieson stain in the same case.



11. The metastic tumour in the lung and the psammoma bodeis (HE, 4415/87 DEUMF Pathology Deparment).



12. The hyaline bodies developed by hyaline degeneration in stromal connective tissue in the transverse section of papillary structures surrounded by tumour epithelium (HE, 1004/87, DEUMF Pathology Department).