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Tumours of the Thymus

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ABSTRACT

A series of 22 consecutive cases of thymic tumour was collected and the tumours were reclassified according to a modified classification scheme. Two-thirds of them were benign lympho-epitheliomas, though in one case pleural implants were noted. One-third of the tumours were clearly malignant (carcinomas, lymphomas and seminomas). In one of the seminomas and in a case of Hodgkin's disease of the thymus no signs of recurrence or metastases have been observed in 10 and 8 years respectively. The sex distribution was fairly equal except that all three seminomas were detected in young men. The malignant tumours usually gave rise to symptoms, while the benign ones did not. Four of the lympho-epitheliomas were associated with myasthenia gravis. No other associated syndrome was observed. The possibility that lympho-epitheliomas may be malignant is discussed.

INTRODUCTION

Considerable interest has been paid to tumours of the thymus in recent years. This is partly due to the increasing number of clinical syndromes observed in association with thymic tumours of different kinds, and partly to increased knowledge about the functions of the thymus. Consequently, in the last few decades reports on several series of thymic tumours have been published (among others 1, 4, 12, 13, 19, 24, 33, 36, 37). Nevertheless, there is still much confusion concerning the classification of these tumours, and further documentation would therefore seem justifiable.

MATERIAL AND METHODS

The 22 thymic tumours included in this study were diagnosed from 1961 to 1972 at the Department of Pathology, University of Uppsala (total number of specimens during this period 210, 720). All cases were diagnosed by biopsy. New thin sections were prepared from all paraffin blocks collected and these were stained according to van Gieson and with hematoxylin-eosin (H-E). These slides were re-examined and classified according to the histopathological scheme presented below.

HISTOPATHOLOGICAL CLASSIFICATION

There has been much confusion through the years concerning both the implication of the term 'thymoma' and the histopathological classification of thymic tumours. A number of classification schemes have been presented by different authors (for review see Galy & Renault (13)). In the present context 'thymoma' is used as a general description, meaning a tumour in the thymus or the thymic loge. The term says nothing about the possible malignancy of the tumour. This is best expressed by a name representing the histopathological diagnosis. The classification used in the present investigation corresponds in principal to those used by Seybold et al. (33), Galy & Renault (13), Shields (34) and Goldstein &B Mackay (14). It was found convenient on prognostic and histopathological grounds to subdivide thymic tumour into malignant tumours and usually benign tumours. A strictly histogenetic classification was found confusing and impractical. The classification scheme used is presented in Table I.

Lympho-epitheliomas are genuine thymic tumours. They contain two cell components, epithelial cells and lymphocytes, often in varying proportions in the same tumour. According to the main impression of the dominant cell type, the lympho-epithelioma is classified into epithelial cell, spindle cell, mixed, or lymphocytic type. Microscopically, no signs of malignancy are observed. Perivascular spaces, palisading of epithelial cells, rosette formation and cystic spaces are often seen (4, 5, 14, 29, 33, 36).

Table I. *Histopathological classification of thymic tumours*

I. *Usually benign tumours*
1. Lympho-epithelioma
Lymphocytic type
Mixed type
Epithelial type
Spindle cell type
2. Thymolipoma
3. Benign teratoma (dermoid)
II. *Malignant tumours*
1. Carcinoma
2. Malignant lymphoma
3. Malignant teratoma (seminoma)
4. Sarcoma

Table II. *Twenty-two cases of tumour of the thymus*

Abbreviations for tumour types: Sp=Spindle cell; M=Mixed; E=Epithelial; L=Lymphocytic; NS=Nodular sclerosis

Case no.	Age at operation	Sex	Symptoms/signs Myasthenia gr.	Duration	Treatment	Tumour appearance at operation	Histopathological diagnosis	Follow-up
1	68	♂	–	–	Surg. excision	Encapsulated, lobated, central calcification	Lympho-epithelioma (Sp)	Urinary bladder cancer after 11 years
2	45	♀	Palpable neck	1 year	Surg. excision	Encapsulated	Carcinoma	11 years
3	29	♂	Facial oedema, dysphagia	2 months	Surg. excision, radiother., cytostatics	Infiltrating surrounding tissues	Seminoma	10 years
4	11	♀	Cough	6 months	Surg. excision, radiother.,	Encapsulated	Lymphosarcoma	Died after 13 months
5	54	♀	Cough, mucus secretion	6 months	Surg. excision, radiother.,	Located in the right thymus lobe, engaging the superior vena cava	Hodgkin' disease (NS)	8 years
6	5	♂	–	–	Surg. excision	Connected with the right thymus lobe, well encapsulated	Dermoid	8 years
7	60	♀	–	–	Surg. excision	Encapsulated, lobulated	Lympho-epithelioma (M)	7 years
8	22	♂	Sternal tumour	6 months	Radiother., cytostatics	Invasion of sternum and mediastinum	Seminoma	Died after 3.5 years
9	55	♂	Cough	6 months	Surg. excision	Encapsulated	Lympho-epithelioma (E)	6 years
10	32	♀	Myasth. gravis	3 years	Surg. excision	Encapsulated. Connected with right thymus lobe	Lympho-epithelioma (M)	4 years
11	31	♂	–	–	Radiotherapy	Invasion of surrounding organs, metastasis in right lung	Seminoma	Died after 5 years
12	76	♀	Myasth. gravis	18 years	Surg. excision	Encapsulated, partly calcified	Lympho-epithelioma (E)	Died of myasth. gravis after 2 years
13	51	♂	–	–	Surg. excision	Encapsulated	Lympho-epithelioma (E)	3 years
14	33	♀	–	–	Surg. excision	Encapsulated	Lympho-epithelioma (L)	3 years
15	37	♂	Dyspnoea, oppression	3 months	Surg. excision, cytostatics	Widespread in the superior anterior mediastinum	Lymphosarcoma	Died after 2 months
16	64	♂	–	–	Surg. excision	Encapsulated	Lympho-epithelioma (M)	12 months
17	7	♀	Myasth. gravis	6 months	Surg. excision	Macroscopically normal thymus	Lympho-epithelioma (M)	18 months
18	65	♀	–	–	Surg. excision	Several tumours in the mediastinum, small implantations in the right pleura	Lympho-epithelioma (M)	12 months
19	50	♂	Myasth. gravis	6 months	Surg. excision	Encapsulated, partly cystic	Lympho-epithelioma (M)	12 months
20	42	♂	–	–	Surg. excision	Encapsulated	Lympho-epithelioma (M)	–
21	43	♀	–	–	Surg. excision	Encapsulated	Lympho-epithelioma (M)	–
22	62	♀	–	–	Surg. excision	Encapsulated	Lympho-epithelioma (M)	–

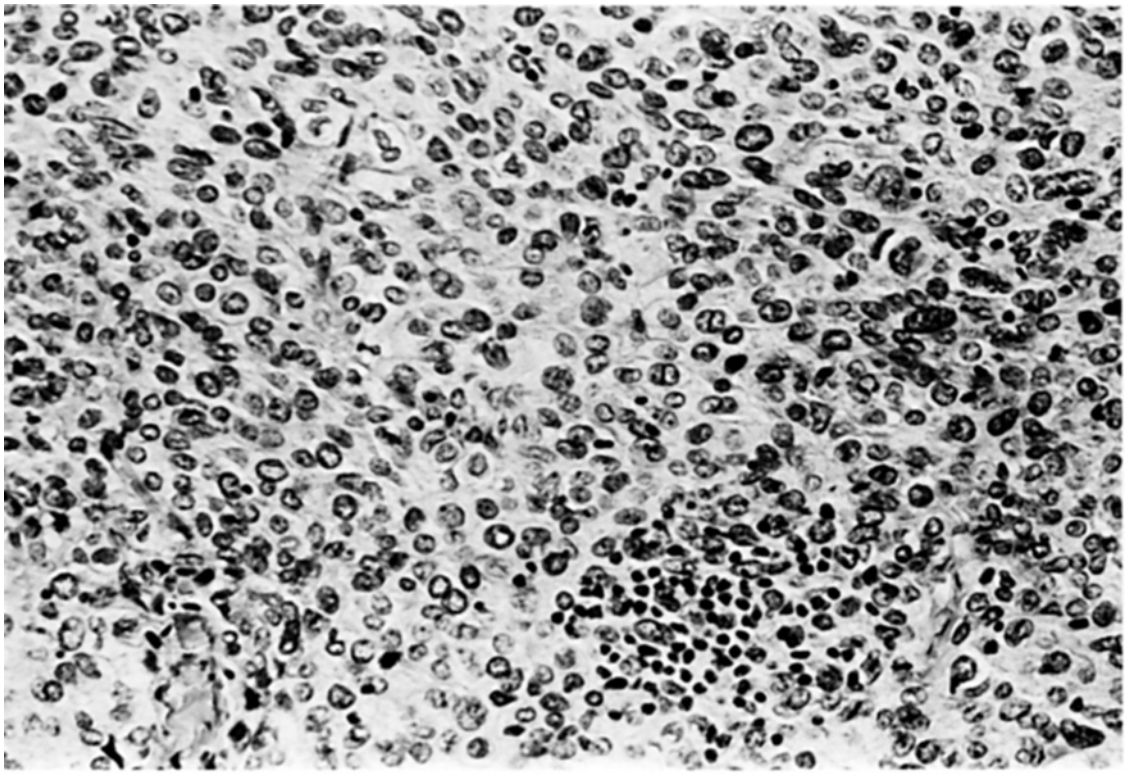


Fig. 1. Lympho-epithelioma, epithelial type (case 12). The epithelial cells are closely packed with somewhat varying nuclear shape but with no cytological signs of malignancy. No mitotic figures are observed. A small lymphocytic infiltrate is present (×460, H.-E.).

Thymolipomas contain abundant fat tissue derived from the normal fat tissue. In some thymolipomas hyperplasia of thymic tissue has been noted (5, 17).

Dermoids are unusual in the thymus. When present in this gland they show the same microscopic picture as elsewhere, though thymic tissue is seen in the immediate vicinity.

Carcinomas of the thymus are rare. Though the epithelial nature of these tumours often is obvious, the precise histogenetic origin is regularly obscure. A few squamous cell carcinomas have been described (5). Likewise, carcinoid resembling tumours in the thymus have been reported (22). Some thymic carcinomas seem impossible to classify in this respect, however, and are either designated as small cell carcinomas or large cell carcinomas.

Seminomas are relatively common among the malignant thymic tumours. Microscopically they resemble a seminoma of the testis or ovary, being composed of 'embryonal', dissociated large cells with abundant cytoplasm and polymorphous nuclei in a fibrous stroma (7, 11, 19, 26).

Malignant lymphomas often appear in the thymus,

Table III. *Age and sex distribution*

Age (years)	Total	Males	Females	Lympho-epi-theliomas	Malignant lymphomas	Malignant teratomas
0–10	2	1	1	1	–	–
11–20	1	–	1	–	1	–
21–30	2	2	–	–	–	2
31–40	4	2	2	2	1	1
41–50	4	2	2	3	–	–
51–60	4	2	2	3	1	–
61–70	4	2	2	4	–	–
71–	1	–	1	1	–	–
Total	22	11	11	14	3	3

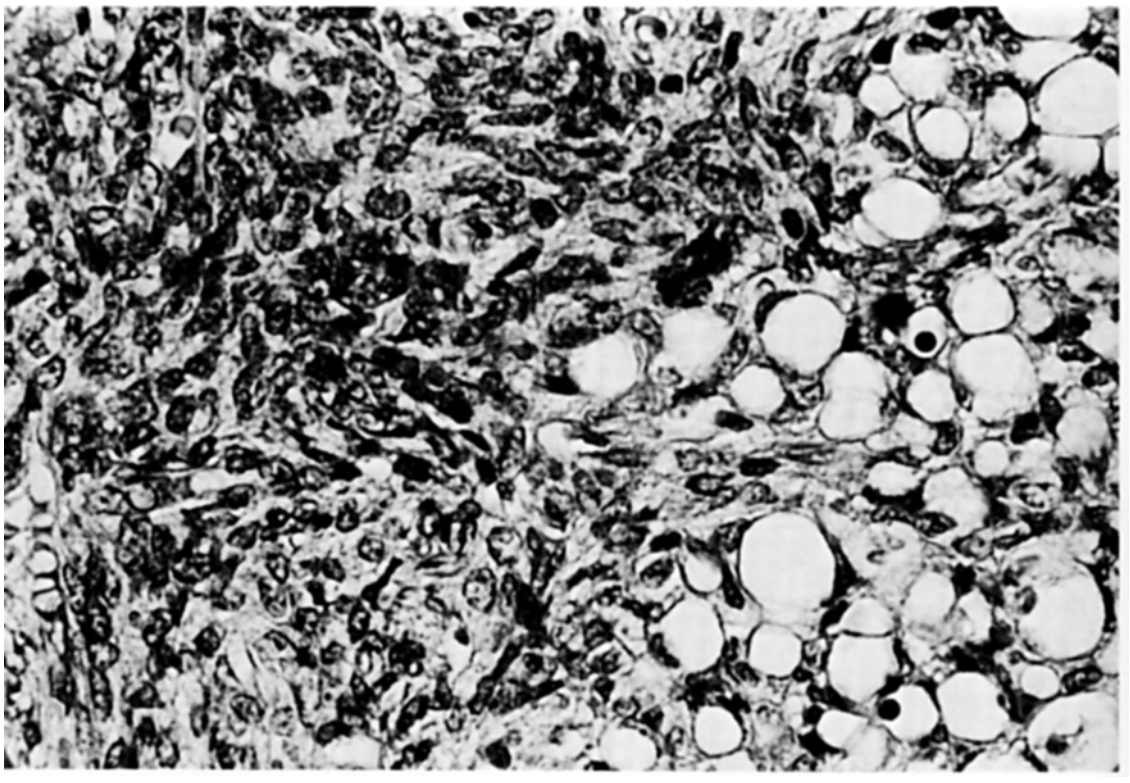


Fig. 2. Lympho-epithelioma, epithelial type (case 13). A cribriform arrangement is observed in parts of the tumour, with small clustered cystic spaces sometimes lined by a single layered endothelium (×460, H.-E.).

either primarily or secondary to a malignant lymphoma in other lymphoid tissues. All kinds of malignant lymphomas have been reported in the thymus (5).

Beside malignant lymphomas, other *sarcomas* are extremely rare in the thymus. As far as is known only one case of myosarcoma has been described (12).

RESULTS

Age, sex

The ages of the patients at the time of the detection of the tumour ranged between 5 and 76 years of age (mean 43 years). The age distribution was fairly uniform, with a slightly increased frequency after the age of 31 years, and was the same for both sexes. For lympho-epitheliomas a slightly higher frequency was noted after the age of 41 years, while the few cases of malignant teratoma were seen in young men (range 22–31 years) (Tables II and III).

The sex distribution in the whole series was equal. Eleven of the patients were male, eleven female. The sex distribution among the different diagnoses was fairly uniform with the exception of the few malignant teratomas, which were found only in males (Tables II and IV).

Symptoms

Of the 15 patients with benign thymic tumours, only one (case 9) had symptoms (cough). The other 14 tumours were detected at a routine chest X-ray or during investigation of a diagnosed myastenia gravis.

All patients with malignant thymic tumours except one (case 11) had symptoms. The duration of symptoms/signs varied between two months (case 3) and one year (case 2). Three of the patients had cough or dyspnoea, two had a palpable tumour and one had facial oedema and dysphagia (Table II).

Associated syndromes

Except for myastenia gravis, no associated syndromes were recorded. Four of the 14 patients with a lympho-epithelioma had myastenia gravis (29% of lympho-epitheliomas, 18% of total material) of varying duration. Three of these patients were

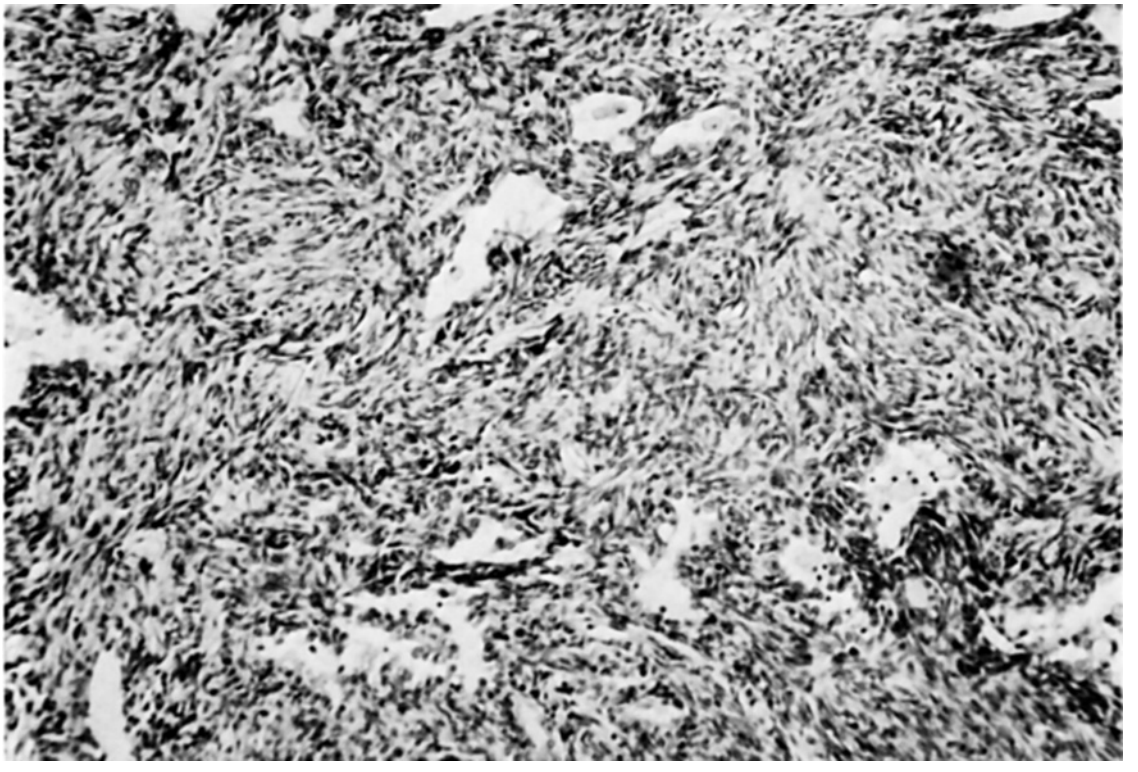


Fig. 3. Lympho-epithelioma, spindle cell type (case 1). The microscopic picture is dominated by spindle-shaped cells in strands. Several cystic spaces lined by single layered endothelium and containing a few lymphocytes are seen (×160, H.-E.).

female. The lympho-epitheliomas in these 4 cases were of the epithelial (case 12) or mixed (cases 10, 17 and 19) type.

Histopathology

The histopathological diagnoses in the 22 cases are summarized in Tables IV. Two-thirds of the tumours were lympho-epitheliomas, one was a benign teratoma and the remaining 7 were malignant.

Table IV. *Histopathological diagnosis in 22 tumours of the thymus*

Histopathological diagnosis	Number of cases		
	Males	Females	Total
Lympho-epithelioma	6	8	14
Epithelial	2	1	3
Spindle cell	1	–	1
Mixed	3	6	9
Lymphocytic	–	1	1
Benign teratoma (dermoid)	1	–	1
Carcinoma	–	1	1
Malignant lymphoma	1	2	3
Lymphosarcoma	1	1	2
Hodgkin's disease	–	1	1
Malignant teratoma	3	–	3
Total	11	11	22

The histopathological findings in the lympho-epitheliomas are summarized in Table V. No cytological signs of malignancy or mitotic figures were seen in any of these tumours. The microscopic characteristics of lympho-epitheliomas which have been reported by several authors were observed in varying frequencies. Fibrous trabeculae crossing the tumour were seen in all cases. Cystic spaces were observed in 50% of the tumours. Palisading of cells around blood vessels and rosettes of epithelial cells were seen in only 3 cases. In one case Hassall's corpuscles, and in another case lymphoid follicles, were seen in the tumour tissue. Normal thymus was identified outside the tumour in 5 cases, proving that at the time of operation the tumour had not involved the whole thymus. Capsular infiltration was noted in 50% of the lympho-epitheliomas. The significance of this finding is further discussed below.

In the malignant tumours cytological criteria of

malignancy were fulfilled, and in addition there were signs of infiltration of adjacent structures of the mediastinum and lack of encapsulation.

The carcinomatous tumour (case 2) was microscopically not encapsulated, and infiltrated surrounding fat tissue. Strands of fibrous tissue divided the tumour into alveolar structures, often with the tumour cells in solid strands. These cells were epithelial in appearance, with large nuclei, often with one or several small nucleoli. The cytoplasm was mostly abundant. Mitotic figures were frequently seen. In some places small cystic spaces were seen, some containing a hyaline substance.

The two lymphosarcomas (cases 4 and 15) were composed of lymphoid cells with sparse cytoplasm and dark nuclei with one or two small nucloli. Occasional epithelial cells, sometimes in isolated islets, were intermingled with the lymphocytes.

The three seminomas (cases 3, 8 and 11) were all partly encapsulated, with tumour tissue penetrating the capsule. A fibrous stroma was present. The tumour cells appeared mostly epithelial, but cellular polymorphism was prominent. The cytoplasm was mostly abundant. The nuclei were hyperchromatic and pleomorphic, with one large nucleous or one to several small nucleoli. A few cells with two nuclei were seen. Nuclear membranes were often distinct. Mitotic figures and some necrotic areas were seen. Small lymphocytic infiltrates were present, mainly in or near the fibrous trabeculae.

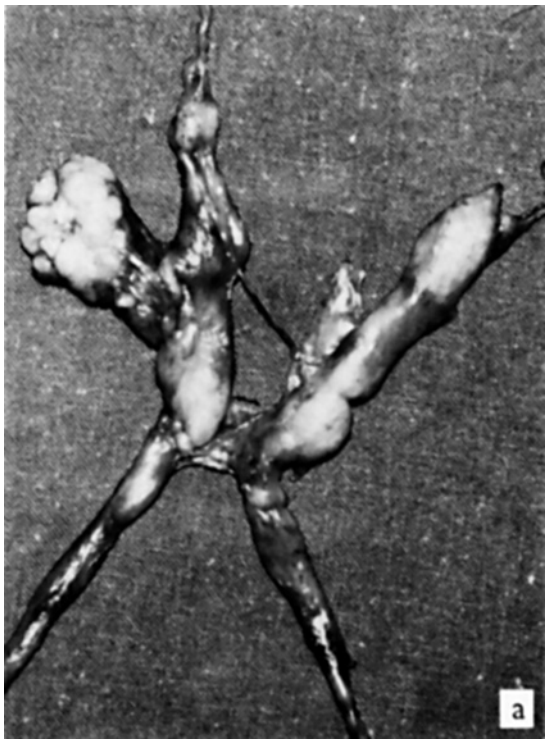
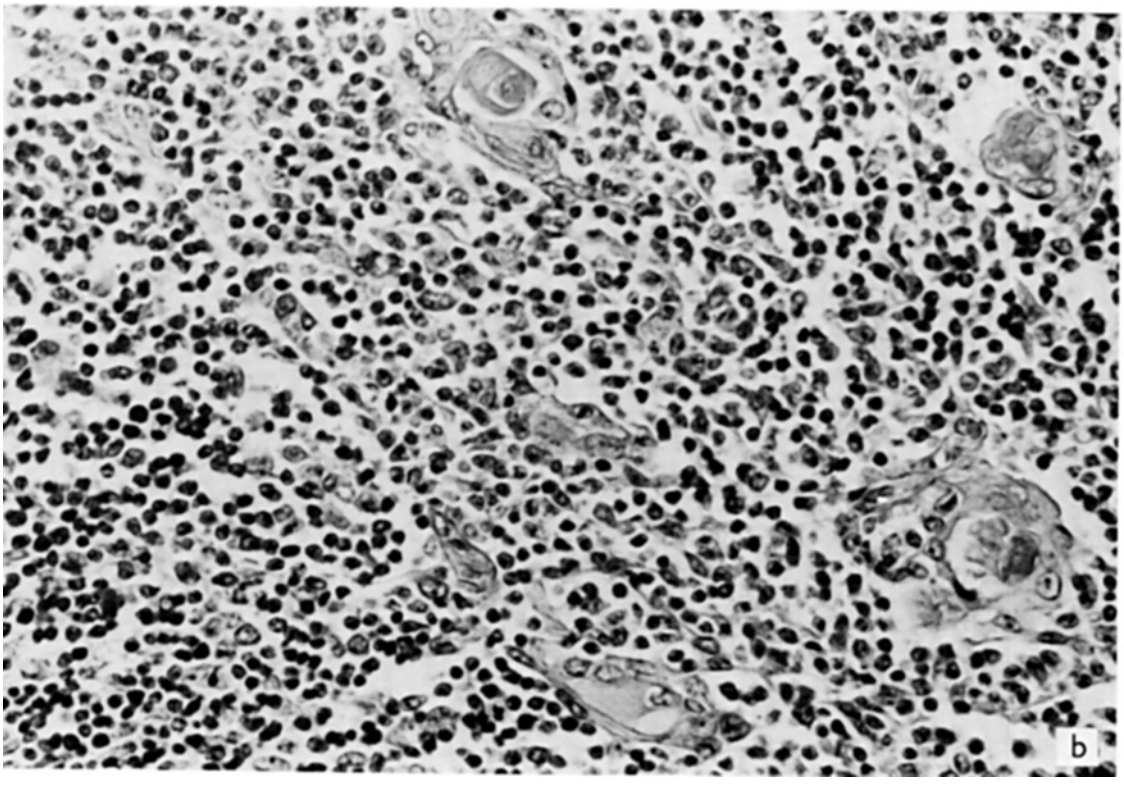


Fig. 4. Lympho-epithelioma, mixed type (case 10). (*a*) Gross appearance of the resected thymus with a walnut-sized tumour in the right thymic lobe. (*b*) Microscopic picture showing a mixture of lymphocytes and polyhedral epithelial cells. Aggregates of epithelial cells are seen in a Hassall's corpuscle-like arrangement (×460, H.-E.).

Table V. *Histopathological findings in 14 lympho-epitheliomas*

Abbreviations: E=Epithelial, Sp=Spindle cell, L=Lymphocytic, M=Mixed

Case no.	Normal thymus outside tumour	Hassall's corpuscles within tumour	Lymphoid follicles inside tumour	Cystic spaces	Palisading of cells, rosettes	Fibrous trabeculation	Capsular infiltration (L, E)	Cytological signs of malignancy	Mitotic figures
1	–	–	–	+	+	+	+(E)	–	–
7	–	–	–	–	–	+	–	–	–
9	–	–	–	+	–	+	–	–	–
10	+	–	–	+	–	+	+(L)	–	–
12	–	–	–	–	–	+	–	–	–
13	+	–	–	+	+	+	+(L, E)	–	–
14	–	–	–	–	–	+	+(L)	–	–
16	–	–	–	–	–	+	+(L, E)	–	–
17	+	+	–	–	–	+	–	–	–
18	–	–	–	+	–	+	+(L, E)	–	–
19	+	–	+	+	–	+	–	–	–
20	–	–	–	–	+	+	–	–	–
21	+	–	–	+	–	+	+(L)	–	–
22	–	–	–	–	–	+	–	–	–



Follow-up

Of the 14 patients with a lympho-epithelioma, 2 have died, one of cancer in the urinary bladder, one of myastenia gravis. In three of these 14 patients (cases 20–22) the observation period has been too short for follow-up (less than one year). No signs of recurrency have been observed in the other patients, though in one of them (case 18) pleural implants were observed at operation.

It is of interest that the one patient with carcinoma (case 2) is still alive after 11 years of observation, though all cytological criteria of malignancy were fulfilled at the time of diagnosis.

Of the patients with a malignant lymphoma in the thymus, the two with lymphosarcoma have both died within 13 and 2 months of diagnosis. The patient with Hodgkin's disease of the thymus is still alive after 8 years of observation (case 5).

Two of the patients with malignant teratoma (cases 8 and 11) died of the tumour 3½ and 5 years following diagnosis. It is interesting that one patient (case 3) is still alive after 10 years without any signs of recurrence.

Cellular composition

E	Sp	L	Type of lympho-epithe-lioma
+	+++	+	Sp
++	+	++	M
+++	+	+	E
++	−	++	M
+++	−	+	E
++	+	+	E
+	−	+++	L
++	+	++	M
++	−	++	M
++	−	++	M
++	−	++	M
+	++	++	M
++	−	++	M
++	−	++	M

DISCUSSION

Frequency of thymic tumours

Comparison between materials of thymic tumours published by different authors is somewhat difficult. This is due to the fact that different classification schemes have been used and that some authors

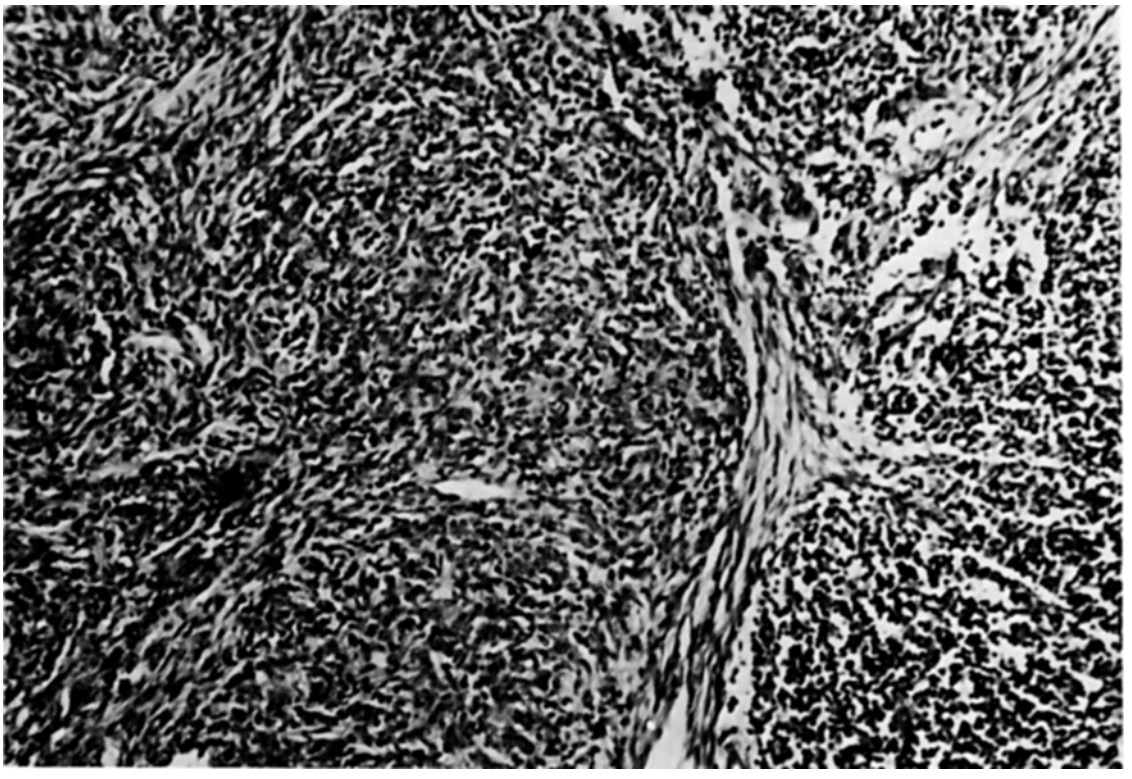


Fig. 5. Lympho-epithelioma, mixed type (case 16). A mixture of epithelial cells and lymphocytes is seen in varying proportions. Strands of spindle cells are seen (×160, H.-E.).

exclude certain thymic tumours from their materials. Some authors do not even state what definition of 'thymoma' or 'thymic tumour' they use or do not seem to be aware of the occurrence of different types of thymic tumours. In the present small series all thymic tumours and tumours of the thymic loge encountered during a period of 12 years have been collected.

It was found that two-thirds of these tumours were lympho-epitheliomas, i.e. usually benign thymic tumours. The remaining one-third were clearly malignant. Of the 14 lympho-epitheliomas, when classified according to the dominant cell type, one was lymphocytic, nine were mixed, three were epithelial and one was of the spindle cell type.

Bernatz et al. (4) reported a series of 138 thymic tumours, excluding all other tumours but lympho-epitheliomas. They found that 30% of these lympho-epitheliomas were lymphocytic, 30% were of mixed type, 16% of epithelial type and 24% of

Table VI. *The relation of different malignancy criteria to different thymic tumours*

	Partial or total lack of encapsulation	Infiltration of capsule if encapsulated	Local initial recurrence, implants	Initial invasion of adjacent structures	Distant metastases	Stromal invasion or lack of tumour stroma	Cytological signs of malignancy
Lympho-epitheliomas	Rarely	50% (present investigation)	2% (8)	10–20% (4, 24, 29, 33)	Exceptional cases (16)	–	–
Thymic carcinomas, lymphomas, seminomas	+	+		+	+	+	+

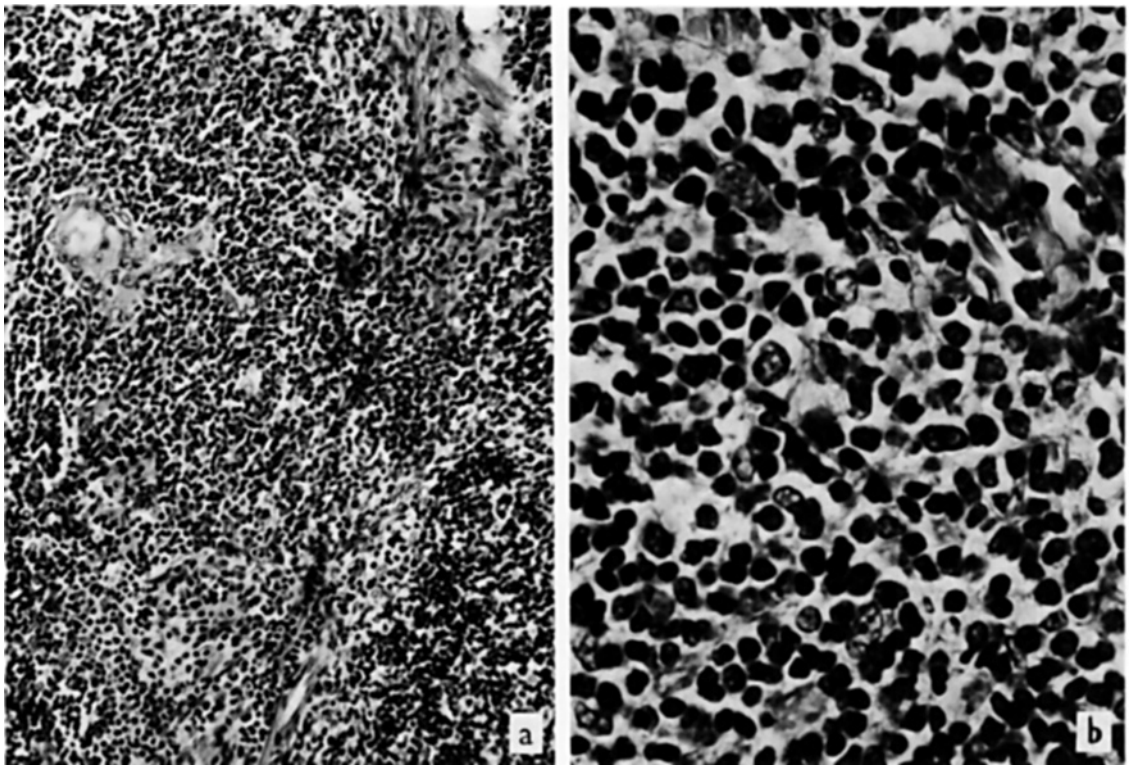


Fig. 6. Lympho-epithelioma, lymphocytic type (case 21). The dual composition of lympho-epitheliomas is still obvious. There is a predominance of small well differentiated lymphocytes in an epithelial reticle. No cytological signs of malignancy or invasion of the capsule are seen. Aggregates of epithelial cells are observed in some places. (*a*) ×160, (*b*) ×640, H.-E.

spindle cell type. These figures are quite different from our own, where the frequency of the mixed type, in particular, is considerably higher. Watanabe (36) published a seris of 70 thymomas, i.e. lympho-epitheliomas, and found 24% of lymphocytic, 36% of mixed, 21% of epithelial and 19% of spindle cell type. These frequencies conform better with ours, though the comparison is uncertain due to the small number of tumours in our series. Variations in the relative frequency of different types of lympho-epitheliomas also probably in part reflect different standards in evaluating the lymphocyte and spindle cell components used by different authors.

Comparison between relative frequencies of other tumours of the thymus is still more difficult. Among 106 thymic tumours, Lattes (24) found 14 (13%) tumours that were not classified as lympho-epitheliomas. Of these 14, three were classified as atypical epithelial thymomas with granulomatous focuses, seven as granulomatous thymomas, and four as seminoma-like tumours. (O'Gara (29) found that among 51 tumours from the anterior mediastinum, in addition to 16 lymphoepitheliomas, there were three cases of thymic carcinoma, 10 malignant lymphomas, 10 teratomas (five benign cystic, five malignant), and eight unclassified tumours. Both these authors have noted the occurrence of malignant teratomas in the thymus and in the anterior mediastinum. The frequency of malignant lymphomas in the thymus is difficult to estimate in both series. In Lattes' material no malignant lymphomas are noted, with the possible exception of Hodgkin's disease. In O'Gara's series the 10 malignant lymphomas may include tumours in mediastinal lymph nodes. In our own material three cases (14% of the total material) of seminoma were observed. In comparison with the figures just cited, this seems to be a very high frequency. Further comparison of the total occurrence and relative frequency of malignant thymic tumours is impossible and must await further investigations.

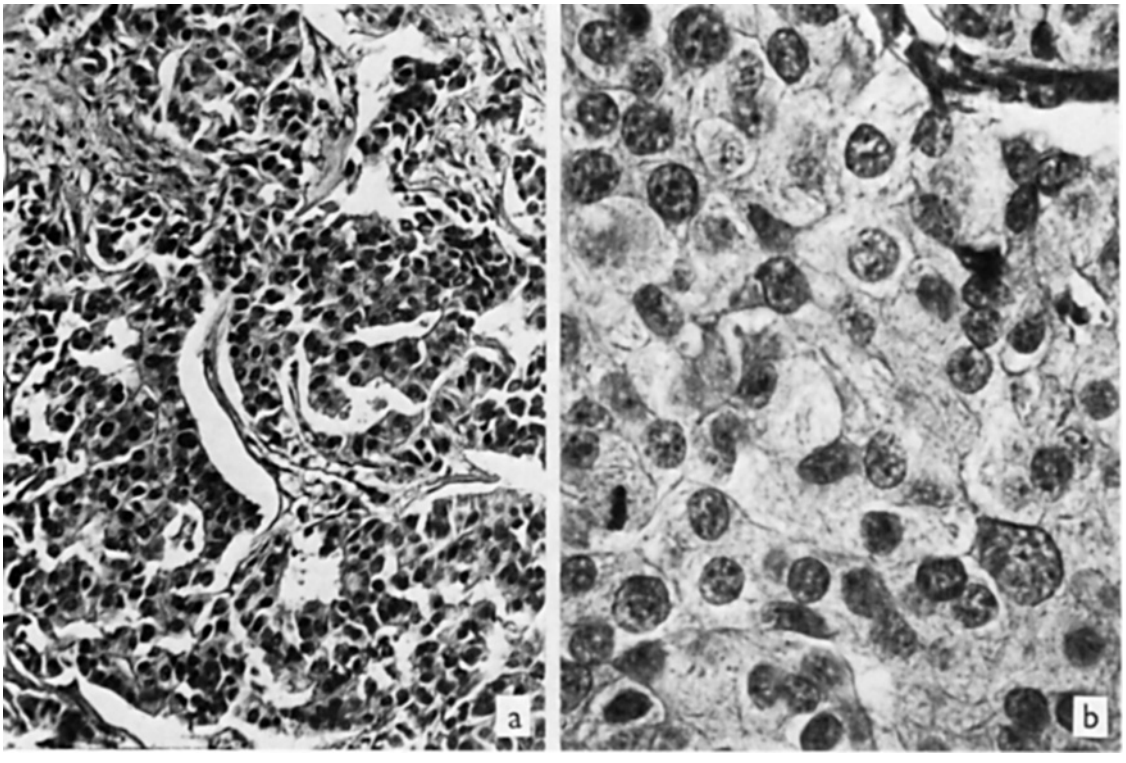


Fig. 7. Thymic carcinoma (case 2). The tumour is composed of atypical epithelial cells in sheets and cords separated by a relatively rich stroma. The tumour cells have rounded, sometimes irregular nuclei with or without a few small nucleoli. Bizarre nuclei are sometimes seen. Cytoplasm is abundant. Mitotic figures are relatively frequent. (*a*) ×160, (*b*) ×640, H.-E.

Malignancy of thymic tumours

The malignancy of thymic tumours, especially lympho-epitheliomas, has been repeatedly discussed in the literature. Castleman (5) stated that since the thymoma did not metastasize it was not a malignant tumour, even if local invasion and pleural implants occurred. There seem to be no histological signs which can distinguish these invasive tumours from the non-invading ones (33). One author concluded that predicting the prognosis in cases of typical thymomas on purely histopathological grounds was "useless guess-work" (24).

Lympho-epitheliomas have been found to recur after excision even in the absence of local invasion at operation. This recurrence may be manifested either as mediastinal masses or as pleural/pericardial implants. This tendency to recurrence has been estimated to be less than 2% (8).

Several reports on thymomas with distant metastases have been made. It can seriously be questioned if several of these tumours really can be classified as lympho-epitheliomas, i.e. thymic tumours without any histopathological signs of malignancy (15, 27, 28). Guillan et al. (16) have reported one case of thymoma, however, evidently a lympho-epithelioma, with distant metastases to the abdomen, and this case seems to be one of the first well documented cases in this respect. The authors have listed 11 further cases from the literature, described in less detail, without having carefully questiond each histopathological diagnosis. The case described by Rachmaninoff & Fentress (31) is doubtful but may represent a lympho-epithelioma with distant metastases.

In an attempt to analyse criteria of value in predicting the benign or malignant behaviour of thymic tumours, Jain & Frable (20) reviewed a series of 32 tumours of this gland. They found that benign thymomas, i.e. lympho-epitheliomas, were grossly well encapsulated and nodular in appearance. Malignant thymomas (classification not specified) showed capsular and local infiltration and satisfied criteria of malignancy. Unfortunately, the intriguing

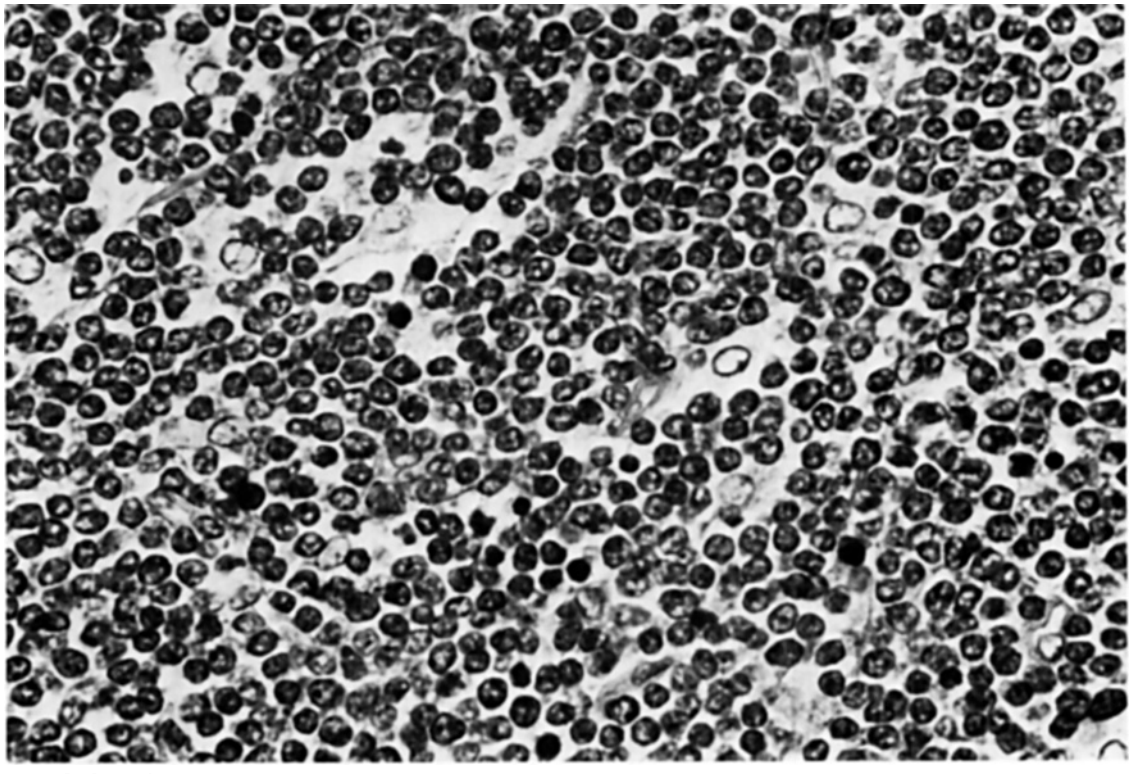


Fig. 8. Thymic lymphosarcoma (case 15). A predominance of moderately well differentiated lymphocytes is seen. The lymphocytes have somewhat irregular nuclei, sometimes with one or two small nucleoli. A discrete network of epithelial cells is present (×460, H.-E.).

problem of invasion and local recurrence of lympho-epitheliomas has been neglected in their investigation.

The relations of different malignancy criteria to different types of thymic tumour are summarized in Table IV. To conclude, (i) lympho-epitheliomas are evidently thymic tumours without cytological signs of malignancy (cellular pleomorphism, frequent mitotic figures etc.) and with benign clinical course. (ii) Occasionally there is partial lack of encapsulation, with infiltration of adjacent mediastinal structures. (iii) In spite of initial non-invasiveness, local recurrence can occur after total surgical excision. (iv) Rarely, distant metastases can be seen. Histopathological differentiation between these groups of lympho-epitheliomas is impossible.

The significance of capsular infiltration in lympho-epitheliomas is difficult to evaluate. In our series, small capsular infiltrates were noted in 50% of the tumours. In case 18, pleural implants were observed at operation and capsular infiltration of both lymphocytes and epithelial cells was seen at microscopic examination. Whether this capsular infiltration has any bearing upon the pleural implantation in this case cannot be determined. The possible role of capsular infiltration in lympho-epitheliomas must await further evaluation of the possible role of lymphocytes and of epithelial cells in these tumours.

Malignant thymic tumours can be differentiated fairly easily from lympho-epitheliomas on histopathological grounds. The importance of a correct diagnosis in cases of malignant thymic tumours must be stressed, however. Concerning thymic seminomas, it has been concluded that these tumours are primary in the mediastinum (9) and possibly thymic in origin (11, 24, 32). Several reports have stressed the relatively good prognosis in these cases following surgical excision and postoperative radiotherapy. El-Domeiri et al. (7) reported that pure seminomas were less aggressive than other germ cell tumours in the mediastinum. They reported a survival of 10 years or more in 4 out of 9 patients with seminomas of the anterior

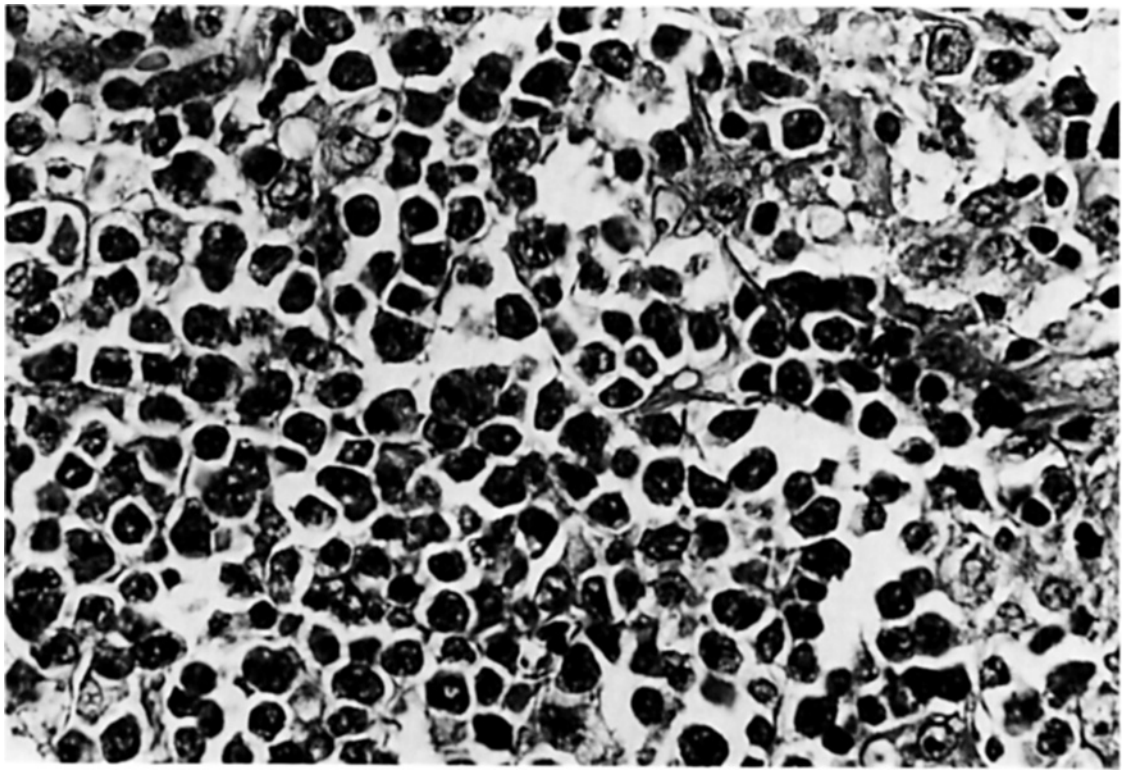


Fig. 9. Thymic lymphosarcoma (case 4). In this case the picture is dominated by undifferentiated lymphoblasts with relatively large irregular nuclei and sparse cytoplasm. The nuclei often contain small nucleoli. A few epithelial cells are still discernible (×460, H.-E.).

mediastinum. Bagshaw et al. (2) reported 13 mediastinal seminomas treated by irradiation only, and the five-year survival was 50%. In our own series three cases of seminoma were included. One patient died after 3½ years, and one after 5 years, and the third patient is still alive without signs of recurrence 10 years after operation. These findings are in full accord with earlier reports. The prognosis in lymphosarcoma involving the thymus is less favourable. The two patients included in our series died within 2 and 13 months, respectively. We have found no earlier report dealing solely with lymphosarcomas of the thymus. Benjamin et al. (3), however, have reported a series of mediastinal malignant lymphomas. Their four patients with lymphosarcoma all died within 28 months. These data also correspond with our results.

Myasthenia gravis and thymic tumours

The association between certain thymic tumours and other diseases is well established. Most important of these associations is the simultaneous occurrence of lympho-epithelioma and myasthenia gravis (6, 14). Hematopoietic depression (18), immunopathy (21), Cushing's disease (10) and various collagenoses (23, 30, 35) are other diseases known to occur concomitantly with different thymic tumours.

In the present study four cases of lympho-epithelioma combined with myasthenia gravis wre observed. As noted above, these four lympho-epitheliomas comprised 29% of all the lympho-epitheliomas in the series and 18% of the total material. This high incidence of myasthenia gravis among patients with thymic tumours has been noted by several investigators and the association is now considered highly significant (4, 10, 19). In earlier reports the occurrence of myasthenia gravis was noted only in cases of lympho-epithelioma of the epithelial type (5). This view has now been revised. Nowadays, myasthenia gravis is seen in association with all types of lympho-epithelioma, except the spindle cell type (24). In our 4 patients with

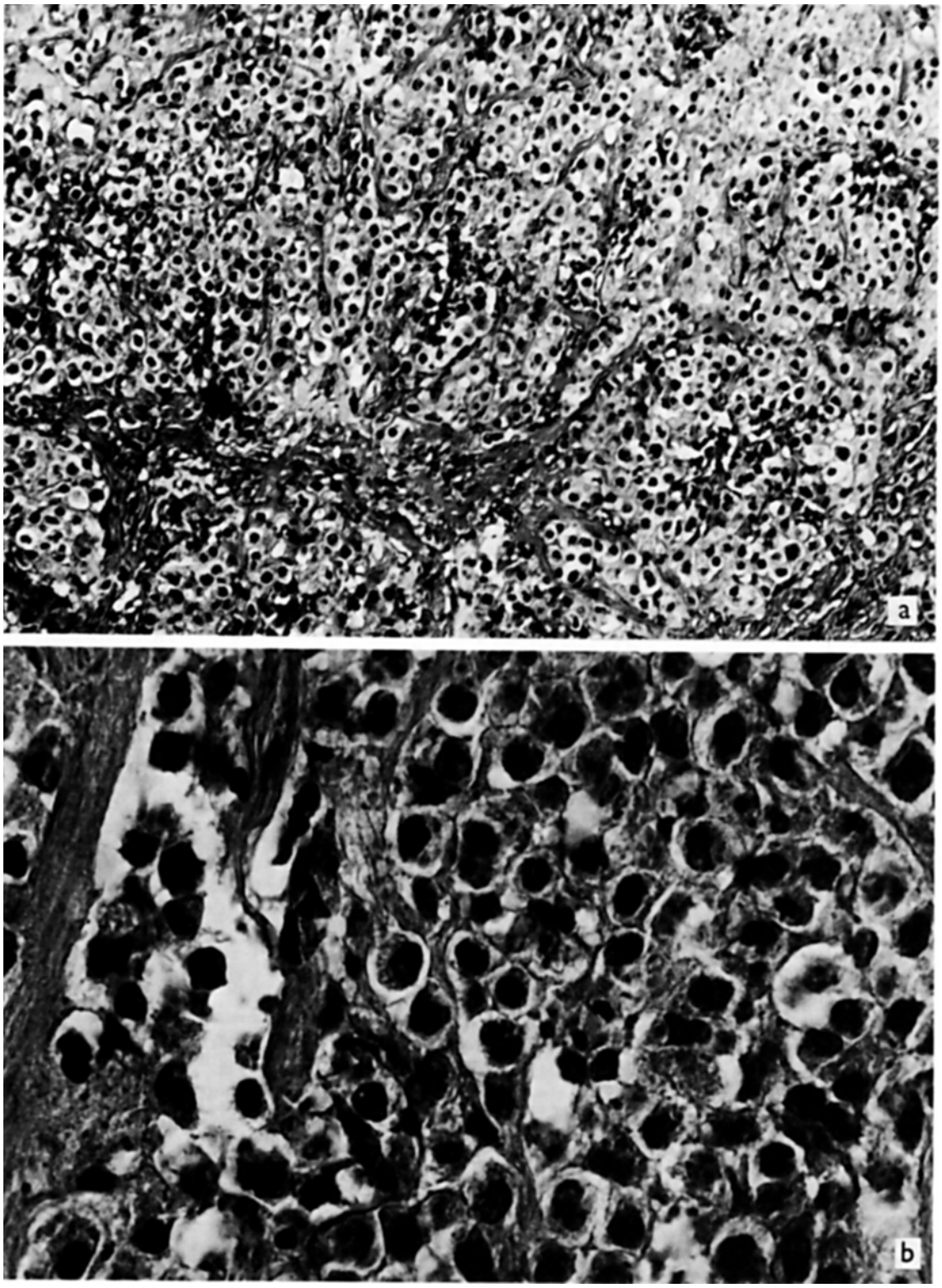


Fig. 10. Thymic seminoma (case 3). In a relatively rich stroma, often highly atypical dissociated cells with rich cytoplasm and hyperchromatic nuclei are seen. Bizarre nuclei and binucleated forms are observed, as well as mitotic figures. (*a*) ×150, (*b*) ×640, H.-E.

myasthenia gravis the lympho-epitheliomas were of the mixed (3 cases) or epithelial type (1 case), thus confirming this latter view.

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