Cystic thymomas and thymic cysts
A Review

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Six cases of large thymic cyst are described; five were cystic thymomas and one was non-neoplastic. Two of the thymomas were not only grossly degenerate but showed severe chronic inflammatory change, so that the diagnosis might be missed. The classification of cysts into congenital, inflammatory, and neoplastic groups is discussed. Cystic teratomata of the thymus, lymphatic cysts, and bronchogenic cysts are classed separately since thymic location does not affect their natural history. Cystic thymomas are still not well known clinically, and the literature on the subject is reviewed. It is probable that quite a few non-specific cysts of the anterior mediastinum are of thymic origin.

Tumours of the thymus are not as rare as was formerly supposed (Brit. med. J., 1963) although their relative incidence varies greatly in different series of primary mediastinal tumours and cysts and ranges from 7.5% to 43% (Le Roux, 1961). Thymic cysts, however, have received scant attention in the literature and most reports have failed to emphasize the different varieties of the lesion. In particular, the tendency to gross cyst formation in thymomas, which has long been recognized by pathologists, is often not appreciated by clinicians. When the cystic element predominates the thymic origin of the tumour may be missed (Davis, 1956). Although the clinical diagnosis of thymic cyst must ultimately await histological examination, it is hoped that a review of the subject will help the clinician in the differential diagnosis of mediastinal masses, especially as these cysts do not appear to be as rare as the literature suggests.

Material

The records of the Institute of Pathology and Department of Thoracic Surgery at the London Hospital were examined over the 16-year period from 1950 to 1965. Mediastinal tumours and cysts that were surgically treated during this period were reviewed. All cases of lymphoma and retrosternal goitre were excluded. The different lesions encountered are shown in Table I. The tumours classified as neurogenous included neurofibroma, ganglioneuroma, and neurilemmoma or their malignant counterparts.

Table I

<table>
<thead>
<tr>
<th>Type of Tumour</th>
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</tr>
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<td>Neurogenous</td>
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<td>Benign</td>
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<tr>
<td>Malignant</td>
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<tr>
<td>Thymoma</td>
<td>24</td>
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<td>2</td>
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<tr>
<td>Thymic cyst</td>
<td>1</td>
</tr>
<tr>
<td>Bronchogenic cyst</td>
<td>3</td>
</tr>
<tr>
<td>Pericardial cyst</td>
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</tr>
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<td>Haemangioma</td>
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</tr>
<tr>
<td>Gastro-enterogenous cyst</td>
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</tr>
<tr>
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</tr>
<tr>
<td>Fibroma</td>
<td>1</td>
</tr>
<tr>
<td>Hyperplastic mediastinal lymph nodes</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>93</td>
</tr>
</tbody>
</table>

Two cysts were classified as non-specific. The first was a thin-walled anterior mediastinal cyst which was incised as it could not be mobilized. No material was available for histology. The second was situated in the antero-superior mediastinum and consisted only of a thin fibrous wall lined by a single layer of flattened cells.

The benign teratomata comprised seven cysts and one solid lesion. Material for histological examination was not available in one, but the cyst contents were pathognomonic and the wall was described as being adherent to the thymus at operation. Five other cysts had normal thymic tissue present either in the cyst wall or immediately adjacent to it, whereas the remaining cyst had lymphoid tissue resembling...

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TUMOURS AND ITS MICROSCOPICAL CLASSIFICATION

malignant Lympho-epithelioma after matous picture Good, 1950). epithelial and tumour containing Solid with Solid (Table scopical descriptions thymic attached bronchi, that the indicated the period of the study and was found to be attached to thymus. However, careful histological examination indicated that the thymus was merely adherent to the cyst and did not form part of the wall.

Of the five bronchogenic cysts reviewed, none was related to the thymus. Three were attached to major bronchi, whereas the other two were related to oesophagus and situated in the posterior mediastinum.

The four pericardial cysts all lay in the right cardiophrenic angle, and microscopy revealed no attached thymic tissue, although one cyst had lymphoid foci in its wall.

Thymic tumours were separated by their macroscopical descriptions into solid, cystic, and necrotic groups (Table II). No detailed histological classifica-

| TABLE II | MACROSCOPICAL APPEARANCES OF THE THYMIC TUMOURS |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| Appearance      | No.             | No.             | No.             | No.             |
| Solid           | 13              | 6               | 2               | 3               |
| Solid with multiple cysts | 2               | 3               | 1               | 1               |
| Up to 0-5 cm. diam. | 2               | 2               | 1               | 1               |
| Up to 1-5 cm. diam. | 3               | 3               | 2               | 1               |
| Including cysts >1-5 cm. diam. | 1               | 1               | 0               | 0               |
| Solid with areas of necrosis or haemorrhage | 3               | 3               | 2               | 2               |
| Minute           | 2               | 2               | 1               | 1               |
| Predominantly cystic | 4               | 4               | 4               | 4               |
| Total            | 26              | 26              | 20              | 20              |

tion was attempted, a thymoma being regarded as a tumour containing varying admixtures of lymphocytes and epithelial cells (Seybold, McDonald, Clagett, and Good, 1950). However, if spindle cells dominated the picture this was recorded (Table III). A 'granulomatous thymoma' was regarded as a lymphoma and excluded after review. Two undifferentiated malignant neoplasms from the thymic region are included; they had a microscopical appearance consistent with thymic carcinoma, but it is recognized that the presence of an undifferentiated tumour in the region of the thymus does not imply thymic origin.

Six 'thymic cysts' are reported in more detail. They include three large cystic thymomas and one simple cyst with normal thymic tissue in the wall. The remaining two cysts consisted of a calcified fibrous shell enclosing necrotic debris with a histological pattern believed to be due to massive degeneration in a thymoma. One of these was removed after 1965 and is not included in Tables I to III.

CASE REPORTS

CASE 1 A man aged 44 was referred to hospital after a shadow had been discovered on chest radiography at a routine medical examination. He was asymptomatic, and physical examination revealed no abnormal signs. Haemoglobin was 170 g./100 ml., but white cell and differential counts and E.S.R. were normal. An E.C.G. indicated slight left axis deviation. Chest radiography demonstrated an oval mass in the region of the right side of the heart (Fig. 1), which was shown to lie in close association with the heart shadow on tomography. Pulmonary function tests, which included measurements of ventilation and lung volumes, were normal.

Thoracotomy was performed on 19 August 1964. A lobulated cyst with a thin translucent wall was loosely attached to the pericardium but was not adherent to the lung or other mediastinal structures and was not obviously related to the thymus. It was excised and the patient made a complete recovery.

The cyst measured 10×9×7 cm. and was unicellular, containing opaque yellow fluid and refractile globules. On one area of the wall there was a raised polypoid mass, 4-5×3-5×1-5 cm., the cut surface of which revealed soft, friable, pink-grey tissue containing minute cysts (Fig. 2). The remainder of the wall was trabeculated and four small nodules up to 0-5 cm. diameter were also present. Microscopic examination of the polypoid tissue revealed a lymphoepithelioma of the thymus (Fig. 3) containing lakes of eosinophilic fluid. The rest of the wall was fibrous with areas of cholesterol clefts, foamy macrophages, and haemosiderin but contained no calcium.

Comment An asymptomatic cyst was situated in the antero-inferior mediastinum, and its nature was not certain until histological examination had been made.

CASE 2 A woman aged 21 developed myasthenic symptoms three months prior to admission and these gradually worsened in spite of neostigmine methylsulphate therapy. Examination showed ptosis and weakness of the face, palate, and limbs. There were no abnormal signs in the chest. Haemoglobin and white cell counts were normal. The chest radiograph showed an abnormal cardiac contour due to superimposition of a thymic tumour.

| TABLE III | MICROSCOPICAL CLASSIFICATION OF THE THYMIC TUMOURS AND ITS RELATIONSHIP TO CYST FORMATION OF ANY SIZE |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Lympno-epithelioma | 21              | 9               | 3               | 1               | 1               | 26              |
| Spindle cell     | 1               | 1               | 1               | 1               | 1               | 1               |
| Undifferentiated malignant | 2               | 2               | 2               | 2               | 2               | 2               |
| Total            | 26              | 10              | 8               | 8               | 8               | 8               |

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Case 1. Chest radiograph showing cyst at right cardio-phrenic angle.

Case 1. Cut surface of cyst showing thin translucent wall and single solid nodule.

Case 1. Lympho-epithelioma. H. and E. × 400.
A course of high-voltage radiotherapy was given and thymectomy was performed on 23 April 1955. The normal site of the thymus was occupied by a mass of fibrotic fat and the tumour was finally located far out in the left pleural cavity, where its extreme mobility made it difficult to palpate. It had drawn the entire thymus downwards and was situated in its lower pole. The gland remained attached to the superior mediastinum only by its vascular pedicle and two horns. Excision resulted in immediate improvement in the myasthenia.

The tumour was not invasive, measured 9·5 x 5·5 x 4·5 cm., and consisted of a capsule 0·5 cm. thick which enclosed a large cavity containing grey-white, pink, and amber material. At the lower pole there was a grey solid area 1·5 cm. in diameter containing small vesicles. Microscopy revealed a lympho-epithelioma in which epithelial cells predominated (Fig. 4), forming a lattice-work between cysts containing eosinophilic fluid and sometimes haemorrhagic material. A few flecks of calcium were present.

Comment The presence of myasthenia led to the detection of a paracardiac shadow that was not immediately obvious. The unusual position of the tumour made it difficult to locate at operation. Its cystic nature was not appreciated until it was sectioned and may have been the result of radiotherapy.

CASE 3 A woman aged 48 presented with myasthenia gravis of three months' duration comprising diplopia, ptosis, intermittent dysphagia, dysarthria, and weakness of the jaw muscles, face, and limbs. The physical signs were complicated by hysterical overlay. A skull radiograph, haemoglobin, E.S.R., and W.R. were normal. The white cell count was 3,200 per c.mm. with a normal differential count. An E.C.G. showed ventricular ectopic beats. An E.M.G. indicated myasthenic myopathy. A chest radiograph showed a round opacity at the right hilum and tomography confirmed that it lay in the anterior mediastinum (Fig. 5).

Thoracotomy was performed on 3 August 1960 and a spherical tumour was found in the right lobe of the thymus. It was encapsulated and not invasive. Thymectomy was performed. Post-operative recovery was satisfactory and the myasthenia has improved gradually but still requires drug therapy.

The thymus weighed 54 g. The left lobe was fatty and the right lobe was expanded inferiorly by a fibrous-walled cyst, 3·4 x 3·4 x 3 cm., the wall of which was 0·2 cm. thick. It contained numerous cholesterol crystals in red-brown fluid, many thin grey or yellow septa, and one soft white nodule, 1 cm. in diameter. Microscopical examination showed extensive cystic degeneration in a lympho-epithelioma (Fig. 6). The cyst contents showed necrotic debris, cholesterol clefts, foam cells, and eosinophilic fluid. The thin wall was composed of hyalinized collagen containing foci of lymphocytes and flecks of calcium. Some small cysts were partially lined by compressed epithelial cells vaguely resembling endothelium.

Fig. 4. Case 2. Lympho-epithelioma. H. and E. x 125 (above); x 400 (below).
Comment The occurrence of myasthenia gravis led to a search for a thymoma, which was cystic due to necrosis.

CASE 4 A man aged 34, whose chest radiograph was normal in 1948, underwent mass miniature radiography in 1965 and a shadow was discovered. Chest radiography and tomography indicated that there was a calcified cyst in the right anterior mediastinum (Fig. 7). He was asymptomatic apart from a smoker’s cough, and there were no abnormal physical signs.

The cyst was excised on 9 March 1966 and measured $7 \times 5 \times 4$ cm. The cut surface showed a thin rim of calcification enclosing brown, pulvaceous, semi-solid, and crystalline material which was more fluid in the centre. Histologically, the wall was composed of hyaline fibrous tissue with areas of calcification and contained cholesterol clefts, foam cells, foreign body giant cells, haemosiderin, granulation tissue, and eosinophilic debris (Fig. 8). Vestiges of lymphoid tissue were present in the wall and a small area resembling a lympho-epithelioma remained. No normal thymic tissue was present outside the wall.

FIG. 8. Case 4. Cyst wall showing (left) foam cells and cholesterol clefts; (right) lymphoid tissue. H. and E. ×125.


Comment An asymptomatic calcified cyst was discovered on radiography. The histological pattern was mainly due to inflammation, but a suggestion of thymomatous origin was present. Final proof would rest on evidence of intrathymic origin, but no normal thymic tissue was found.

CASE 5 A woman aged 53 had become gradually more breathless for five years. Two months before admission she developed pneumonia which was followed by transient pain in the right chest and back, so that chest radiography was performed and revealed a lobular opacity in the anterior mediastinum (Fig. 9). Physical examination was normal. Haemoglobin, white cell and differential count, sputum culture, and bronchoscopy were normal.

Thoracotomy on 14 May 1957 demonstrated an oval cyst arising from the lower right pole of the thymus adherent to the upper lobe of the right lung, pericardium, and phrenic nerve. The cyst was not invasive, thymectomy was performed, and she has been in good health ever since.

The cyst measured $8 \times 7 \times 5$ cm.; its wall was red-brown flecked with orange and was 0.2 cm. thick. There was one major loculus filled with brown fluid. After fixation, the inner surface was found to be partly covered by inspissated grey material with a subsidiary cyst ($3 \times 1$ cm.) on one side, part of which contained blood clot. Histological examination revealed severe chronic inflammation with granulation tissue, plasma cells, foamy macrophages, haemosiderin, cholesterol clefts, foreign body giant cells, and necrotic debris (Fig. 10). The wall was composed of hyaline fibrous tissue containing lymphocytic foci and calcification. One area of the cyst was compatible with lympho-epithelioma (Fig. 11).

Comment A cyst was discovered after an episode of pneumonia. The histological picture was similar to that of case 4, but in this patient there was more lympho-epitheliomatous tissue present and the cyst was obviously situated in the thymus.

CASE 6 A woman aged 57 had for many years suffered from right shoulder pain, epigastric pain, flatulent dyspepsia, and palpitations. More recently, she had noticed breathlessness. Following a fall she developed lower chest pain, and radiography showed a large opacity in the right middle lobe with an adjacent effusion. Physical examination revealed diminished vocal fremitus, percussion note, and breath sounds over the right lower zone anterolaterally, and crepitations posteriorly. Chest movements were equal and the mediastinum was central. Haemoglobin, white cell count, E.S.R., E.C.G., and bronchoscopy were normal and sputum examination for Mycobacterium tuberculosis and malignant cells was negative.

In 1948 the chest was aspirated anteriorly via the fourth intercostal space and 500 ml. of clear watery fluid was removed; it contained 1 white blood cell per c.mm., 100 mg./100 ml. protein, and no cholesterol crystals, hooklets, or malignant cells. A further radiograph showed almost complete disappearance of the density. At first her breathlessness was much improved, but it gradually returned together with mild right chest pain during the next two and a half years. Radiography showed that the cyst had refilled. Physical examination was normal apart from an impaired percussion note in the right axilla. The vital capacity was 2.2 litres.

Thoracotomy on 6 March 1950 revealed a bluish thin-walled cyst lying between the lung, diaphragm, and pericardium and partly adherent to the latter. It was attached superiorly to a pedicle originating in the region of the thymus. The cyst was aspirated and excised. Recovery was uneventful and there was no recurrence.

The collapsed cyst measured 6 cm. in diameter with a smooth wall 0.1 cm. thick. Microscopy (Fig. 12) showed a single layer of lining epithelium, which was mostly of flattened cells but became more cuboidal in some areas and was heaped up in others. The wall consisted of fibrous tissue, fat, and blood vessels with normal thymic tissue, which showed some differentiation into cortex and medulla. Hassall’s corpuscles were prominent.

Comment This simple thymic cyst enlarged to give rise to pressure symptoms. It was situated low in the thorax in the position of a pericardial cyst, but retained its thymic connexion.

DISCUSSION

During the nineteenth century there were reports of multiple small cysts, ‘Dubois’ abscesses’, which were found at necropsy in the thymus gland of infants suffering from congenital syphilis. Most authors regarded them as syphilitic in origin, but there was some argument about the part played by tuberculosis in their pathogenesis. Such cysts have been described very infrequently in the past 60 years. During the first half of the present century there were occasional reports of larger cysts containing thymic tissue in their walls. These cases showed no evidence of syphilis and the cysts were regarded as congenital. They were described at necropsy or after unsuccessful attempts at excision. Speer (1938) reported a sponge-like multicystic thymus and in a lengthy discussion suggested many possible methods of development (Table IV). The first successful surgical excisions of thymic cysts of the neck (Hyde, Sellers, and Owen, 1944) and of the mediastinum (Bradford, Mahon, and Grow, 1947; Smart, 1947) have been followed by a number of case reports and small series of ‘congenital’ cysts, so that 35 cases had been described by 1960 (Podolsky, Ehrlich, and Howard, 1962). Meanwhile in 1939 Blalock,
Mason, Morgan, and Riven had reported the first thymectomy in the treatment of myasthenia gravis. The tumour had been treated by radiotherapy pre-operatively and was found to be a large cyst that could not be positively diagnosed as thymic in origin, but the myasthenia remitted. In 1940 Ewing subdivided thymic cysts into (1) epithelial (embryonal origin), (2) dermoid, (3) from Hassall’s corpuscles, and (4) cystic lymphangioma. Thymoma was not included. In a comprehensive review of cysts of the mediastinum, Laipply (1945) did not include thymic cysts but mentioned that cystic degeneration could occur in solid tumours. It was against this background that Krech, Storey, and Umiker (1954) proposed that thymic cysts should be classified as (1) congenital, (2) inflammatory, and (3) neoplastic.

This simple classification ignored the cystic teratoma (dermoid cyst), which is included in some definitions of thymic cyst (Ewing, 1940; Williot, Delporte, and Depré, 1964). The origin of cystic teratoma is not settled. Most authors have regarded it as occurring in areas adjacent to the thymus, probably from remnants of the branchial cleft, and subsequently becoming attached to the gland (Rusby, 1944). However, Schlumberger (1946) believed that it arose in the thymus and, if this view is accepted, teratoma should be grouped with thymic cysts. Certainly cystic teratoma can occasionally occur in the thymus (Heuer and Andrus, 1940; O’Gara, Horn, and Enterline, 1958; Videbaek and Thomsen, 1959), but in the restricted space of the anterior mediastinum.

**TABLE IV**

**SPEER’S HYPOTHESES FOR THE PATHOGENESIS OF THYMIC CYSTS**

1. Embryological remnants:
   (a) Branchial clefts
   (b) Thymic tubules
   (c) Thymo-pharyngeal ducts
2. Sequestration products in pathological involution of the thymus
   (a) Lymphoid tissue
   (b) Cytoreticular tissue
   (c) Connective tissue
3. Neoplastic processes in:
   (a) Lymphatic tissue
   (b) Blood vessels
   (c) Connective tissue
4. Degeneration of Hassall’s corpuscles
5. From mesenchymal elements:
   (a) Lymphatics
   (b) Blood vessels
   (c) Connective tissue

In various stages of thymic:
(i) Development
(ii) Hyperplasia
(iii) Involution

**FIG. 12.** Case 6. Simple thymic cyst. H. and E. (left) × 125; (right) × 400.
Cystic thymomas and thymic cysts

Cystic thymomas and thymic cysts

Cysts, whereas Effler any stinum and cystic teratomata all found. These excluded multicystic degeneration Liebow, is origin. May cystic brought lymphatic cysts thymic dermoid Schlumberger may have been flattened thymus. In 1956, these authors lesions. Davis and Pugh, 1956 restricted the definition of thymoma when multicystic degeneration Bernatz, Harrison, and Clagett, 1961. These rare tumours are lined by a single layer of flattened cells and contain smooth muscle in their walls. It is possible that confusion with thymoma of lymphangiomaticous structure (Hubbell and Liebow, 1952) or spindle-cell thymoma with multicystic degeneration (Bernatz et al., 1961) may have resulted in the misdiagnosis of some thymic lymphangioma in the past; but as the thymus has a rich lymphatic supply, true lymphatic cysts could arise here. In the present series no case of intrathymic lymphatic cyst was found.

Inflammatory cysts imply association with congenital syphilis in the older literature, and such cysts are not encountered nowadays. In order to give some group of such cysts a name, the rare hydatid cysts of the thymus may be mentioned (Giraud, Nègre, Thévenet, and Beraud, 1963). Although approximately 2% of hydatid cysts occur in the mediastinum, the parasites lodge in the thymus only in very exceptional cases. A positive Casoni test does not prove the diagnosis, which should be confirmed by thoracotomy.

There have been many reports of thymus glands containing single or multiple minute cysts (Crellin, Pugh, and Janton, 1950). Consequently Pachter and Lattes (1963) restricted the definition of thymic cyst to grossly visible cavities whose capsule contained thymic tissue but no smooth muscle. These authors specifically excluded lymphangioma, teratoma, and bronchogenic cyst as did Abell (1956) and Ringer and Lidholm (1956). These large non-neoplastic cysts are best termed 'simple' as their origin is not settled. Krech et al. (1954) and Willis (1958) believed that they are not related to branchial cysts or fistulae. Most authors think that they are derived from (1) thymic duct remnants which subsequently enlarge due to haemorrhage or fluid accumulation or (2) cystic degeneration in Hassall's corpuscles (Bettega, Tramujo, Da Costa, and Jamur, 1957). The latter are regarded as acquired and not developmental lesions. Willis (1958) described a case in which the cyst developed in later life, and Schlumberger (1951) referred to work on the thymus of dogs and cats in which cysts developed after birth. Ross and Korenchevsky (1941) produced multiple small epithelial-lined cysts in the thymuses of rats by injecting oestrogens, and it is likely that these cysts originated in Hassall's corpuscles. The actual cause of distension was not known but trauma and infection are not responsible (Krech et al., 1954). Both Bradford et al. (1947) and Krech et al. (1954) favoured the theory expressed by Kopač (1939) in which degeneration of the medulla and blood vessels is followed by fluid accumulation and compression of the remaining medullary tissue except for a single layer of reticulum cells which remains as a pavement epithelium. At the same time the Strandberg layer thickens to form a capsule with the compressed thymic cortex remaining externally.

On section the cysts may be unilocular or multilocular and the contents vary. Histological examination reveals many different types of lining cell and includes flattened, cuboidal, columnar, ciliated columnar, and squamous epithelium. The lining may also have degenerated or have been replaced by granulation tissue. The squamous epithelium is usually accepted as being derived from Hassall's corpuscles, but the part played by metaplasia is uncertain. Willis (1958) suggested that in some cases the ciliated columnar epithelium may be derived from squamous epithelium and does not indicate origin in a primary developmental cyst. Multiple minute cysts are sometimes present in the wall and indicate that one has enlarged at the expense of the others. Chronic inflammation with foamy microphages, cholesterol clefts, foreign body giant cells, and haemosiderin pigment occurs in some. The presence of normal thymic tissue is essential for diagnosis, and thymoma should be excluded from the group.

Thymic cyst of the neck is a very uncommon lesion. Behring and Bergman (1963) could collect only 19 cases from the literature. All occurred in infants or children. They were unilateral and
situated along a line from the angle of the jaw to the sternal notch. They were unilocular or multilocular. The lining was variable but squamous cells occurred more frequently than in the mediastinal variety. The walls usually showed chronic inflammatory changes with cholesterol clefts. Cystic swelling following inflammation in an embryological remnant is usually suggested as the cause.

Most reviews indicate that visible cyst formation is a characteristic feature of thymoma. This has been suggested as a sign in its differentiation from malignant lymphoma (O’Gara et al., 1958). Castleman (1955) stated that ‘degeneration with haemorrhage within a thymoma can be so extensive that only a fibrous shell with small remnants of thymoma clinging to its surface is seen’. Examination of the inner wall of such a cyst will be necessary in order to differentiate it from other types of cyst. The proportion of thymomas that contain cysts is not easy to assess and the results of a study of the literature are indicated in Table V. The actual number of true thymomas in different reports is difficult to evaluate because of the confusion in the definition of this tumour (Ringertz and Lidholm, 1956). Moreover, as some papers include lymphoma, teratoma, and thymic hyperplasia with thymoma, the proportion showing cystic change may be meaningless.

The cystic spaces are interpreted as degenerative, probably resulting from liquefactive necrosis or fluid accumulation secondary to haemorrhage. Seybold et al. (1950) have suggested that some may also result from secretory activity, but this is not accepted as a cause of large cysts. Hubbell and Liebow (1952) have postulated that proliferation of lymphatics with infiltration of the gland stroma and subsequent distension occurs. However, O’Gara et al. (1958) demonstrated that the cysts do not arise from blood vessels or lymphatics.

Yamakawa, Tsuchiya, Naito, and Kawaguchi (1961) suggested that neoplastic change could occur in a simple thymic cyst. They described a case in which a thymoma was present but did not line all areas of the cyst wall and was thus thought to arise in the cyst. Their tumour appears to be a thymoma undergoing typical degeneration with cholesterol clefts and lymphocytic foci. The concept of malignancy secondary to thymic cysts has been introduced by Iversen (1956), who reported that some seminomas arise in a cystic thymus.

Cystic degeneration is a feature of the larger thymoma (Bernatz et al., 1961; Lattes, 1962). Few would now accept that it is associated with the more malignant tumours (Bradford et al., 1947). Bernatz et al. (1961) reported that 24% of their non-invasive tumours were almost completely cystic, and O’Gara et al. (1958) found cysts in both encapsulated and non-encapsulated tumours. Unfortunately, complete cystic degeneration is not a guarantee of a good prognosis, as Effer and McCormack (1956) reported a cyst in which a definite histological diagnosis could not be made and which recurred after three years with local and pericardial secondaries showing the histological features of thymic carcinoma. O’Gara et al. (1958) recorded one cystic tumour which developed secondaries and another which was infiltrating locally.

The contents of the cyst are variable, and diagnosis should not be influenced by their appearances. Grumous material may resemble dermoid butter, but hairs will not be present. Serous fluid may suggest a congenital cyst. White putty-like

### Table V

Cystic Changes in Thymomas

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<th>Author</th>
<th>Total No. of Thymomas</th>
<th>No. Cystic</th>
<th>Other Cysts</th>
<th>Comment</th>
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<tbody>
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<td>Not stated</td>
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<td>1 cervical cyst included</td>
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<tr>
<td>Bernatz et al., (1961)</td>
<td>138</td>
<td>41</td>
<td>—</td>
<td>2 dermoids included</td>
</tr>
<tr>
<td>Davis (1956)</td>
<td>17*</td>
<td>—</td>
<td>5</td>
<td>1 necrotic tumour excluded</td>
</tr>
<tr>
<td>Effer and McCormack (1956)</td>
<td>19</td>
<td>2</td>
<td>—</td>
<td>Minor cysts only</td>
</tr>
<tr>
<td>Hasner and Westengärd (1963)</td>
<td>42</td>
<td>2</td>
<td>—</td>
<td>Includes only large cysts</td>
</tr>
<tr>
<td>Herlitzka and Gale (1958)</td>
<td>13</td>
<td>Not stated</td>
<td>2</td>
<td>5 large</td>
</tr>
<tr>
<td>Kemp Harper and Guyer (1965)</td>
<td>40*</td>
<td>1</td>
<td>—</td>
<td>1 thymic cyst is a thymoma</td>
</tr>
<tr>
<td>Larmi (1960)</td>
<td>14*</td>
<td>3</td>
<td>—</td>
<td>‘So-called thymic cysts’</td>
</tr>
<tr>
<td>Legg and Brady (1965)</td>
<td>51</td>
<td>14</td>
<td>—</td>
<td>Only large cysts included</td>
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<td>Le Roux (1961)</td>
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<td>Lowenhaupt (1948)</td>
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<td>Morrison (1958)</td>
<td>42</td>
<td>Not stated</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>O’Gara et al. (1958)</td>
<td>19</td>
<td>5</td>
<td>1</td>
<td></td>
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<tr>
<td>Peabody et al. (1954)</td>
<td>9</td>
<td>2</td>
<td>—</td>
<td></td>
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<tr>
<td>Ringertz and Lidholm (1956)</td>
<td>19</td>
<td>33%</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Seybold et al. (1950)</td>
<td>45</td>
<td>3</td>
<td>—</td>
<td></td>
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<tr>
<td>Shields et al. (1966)</td>
<td>13</td>
<td>—</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Videbaek and Thomsen (1959)</td>
<td>20</td>
<td>2</td>
<td>3</td>
<td></td>
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<tr>
<td>Wilkins et al. (1966)</td>
<td>63</td>
<td>4</td>
<td>—</td>
<td></td>
</tr>
</tbody>
</table>

* Includes tumours which are probably not true thymomas.
material will be confused with tuberculoma. Lindskog (1954) reviewed a number of cases of
tuberculoma of the anterior mediastinum and con-
cluded that they were cystic thymomas and that
tuberculosis should not be diagnosed unless
tubercle bacilli are demonstrated. However, the
cyst he described in more detail might have been
described as non-specific rather than thymoma.

Pallisading of cells surrounding a cavity can occur (Seybold et al., 1950; O'Gara et al., 1958),
and true epithelial-lined cysts have been reported,
in which the lining may be squamoid, flat, or low
columnar (Andritsakis and Sommers, 1959; Lattes, 1962; Legg and Brady, 1965). In true
thymomas, cystic change is probably not
influenced by the histological variant, since
Bernatz et al. (1961) recorded cysts in all four of
their histological groups. Differences in termin-
ology have resulted in apparently contradictory
statements and confusion. For instance, Thom-
son and Thackray (1957) reported that cyst
formation was a feature of their epithelial group
which includes all varieties of true thymoma,
whereas Effler and McCormack (1956) found no
cysts in their epithelial variant, which refers to a
specialized subgroup of thymoma. Iverson (1956)
associated cysts with tumours showing stromal,
endothelial or vascular proliferation, and conse-
quently with the absence of myasthenia gravis.
The latter statement would be disputed by most
authorities, and myasthenia occurred in 50% of
cystic tumours (Bernatz et al., 1961). Most reports
note that cholesterol clefts, foam cells, foreign
body giant cells, haemosiderin pigment, and
calciun deposits are related to cysts.

Cystic change in thymoma has no effect on the
development of associated clinical syndromes.
Cystic tumours are associated with myasthenia
gravis (Castleman, 1955; Bernatz et al., 1961),
red blood cell aplasia, L.E. cells, and antinuclear
factor (Kough and Barnes, 1964); anaemia,
neutopenic and hypogammaglobulinaemia
(Ramos, 1956); granulomatous myocarditis and
myositis (Langston, Wagman, and Dickenman,
1959); hyperglobulinaemic purpura, Sjögren's
syndrome, and Raynaud's phenomenon (Birch,
Cooke, Drew, London, Mackenzie, and Milne,
1964); and pancytopenia (Radojević and Hahn,
1935), although in this case the tumour had been
treated by radiotherapy. The only well-documented
complication that is not associated with
cystic thymic tumour is Cushing's syndrome
(Scholz and Bahn, 1959), but the histological
description and clinical course of these tumours
indicate that they are not thymomas. The
leukaemogenic thymoma (Adams, 1963) contained
areas of haemorrhagic necrosis and cavitation but
was not a true thymoma.

Some cysts of the mediastinum defy diagnosis
even after histological studies, and these are
usually classified as non-specific or indeterminate.
They formed 3-4% of the tumours in 16 series
(Peabody, Strug, and Rives, 1954). It is hardly
surprising that there is no agreement on their
origin. In two out of the three larger cystic
tumours described by Seybold et al. (1950) absolute
diagnosis was impossible, but the authors felt by
inference that they should be included as
thymomas. Similar cases are recorded by Lindskog
(1954) and Williot et al. (1964). Some weight is
given to this argument by the recovery of the
myasthenia gravis after resection of a nondescript
cyst (Blaロック et al., 1939) and the appearance of
local secondaries after the resection of an undiag-
nosable cyst (Effler and McCormack, 1956). Non-
specific cysts have also been found after irradi-
ation of presumed thymomas associated with blood
dyscrasias (Radojević and Hahn, 1935; Havard
and Bodley Scott, 1960).

If the non-specific cysts are situated in the
anterior mediastinum, origin from thymic tumour
or cysts should be considered. Four out of five
non-specific cysts occurred in this position
(Sabiston and Scott, 1952), but the differential
diagnosis given included only dermoid cysts,
necrotic lymph nodes, mesothelial cysts, and
bronchogenic cysts. Morrison (1958) described six
non-specific cysts, which were lined by either
granulation tissue or columnar epithelium, and
added lymphatic cyst to the differential diagnosis
but did not mention thymic lesions. Of the four
cysts included by Pachter and Lattes (1963), how-
ever, three were situated in the posterior media-
stinum and so a thymic origin is ruled out. Cyst
contents varied (Sabiston and Scott, 1952) and
were of no help in diagnosis. Ringertz and
Lidholm (1956) included four non-specific cysts,
one of which was really a 'burnt-out thymoma'.
Two others consisted of a thick fibrous wall con-
taining cholesterol granulomata, and it was
suggested that they originated in dermoid cysts.
A similar picture was present in one of two
anterior mediastinal cysts (O'Gara et al., 1958).
These cysts are very similar to those of cases 4
and 5 in this series, and in view of the tendency
for thymoma to degenerate in this way, such an
origin must be considered. However, Castleman
(1955) describes similar cysts which are usually
small but occasionally large, and attributes them
to degeneration in Hassall's corpuscles.
The differential diagnosis of mediastinal lesions is listed by Schlumberger (1951), but few investigations are helpful. Location in the anterior mediastinum reduces the number of possibilities, but a thymic tumour is not restricted to the superior half and may occur as a paracardiac shadow or at the cardiophrenic angle (Larmi, 1960; Perera and Wilson, 1962; Williot et al., 1964) as in cases 1, 2, and 6. The differentiation from pericardial cyst may be very difficult whether the latter occurs in its normal site (Le Roux, 1961) or in the antero-superior mediastinum (Pachter and Lattes, 1963). If radiography shows linear calcification peripherally, it is likely to be present in the wall of a non-invasive cyst or the fibrous capsule of a solid tumour (Bernatz et al., 1961). However, Kemp Harper and Gayer (1965) stress that rim calcification may occur in many lesions. Artificial pneumothorax and thoracoscopy can be useful (Yamakawa et al., 1961). The performance of the Valsalva manœuvre is sometimes helpful but tomography has proved disappointing. Thus separation of cysts from solid tumours is rarely achieved and the precise diagnosis is seldom made before operation.

Most authors agree with Heuer and Andrus (1940) that surgical excision is the only method of treatment since it provides a positive diagnosis, and malignant or locally invasive tumours are removed. The place of post-operative radiotherapy is not agreed. Some authorities are less enthusiastic about the removal of an asymptomatic calcified cyst, but even grossly degenerate thymomas have shown malignant tendencies. Myasthenia gravis can occasionally have its onset after thymectomy (Ehrenreich and Allen, 1958; Maldonado, Bayrd, and Kiely, 1964), and systemic lupus erythematous (Alarc'on-Segovia, Galbraith, Maldonado, and Howard, 1963) and erythroid aplasia (River, 1966) have also occurred in similar circumstances. Thus, it appears that operative interference with the thymus may occasionally provoke these complications.

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REFERENCES


Cystic thymomas and thymic cysts


ADDENDUM

Since this paper was prepared, Bieger and McAdams (1966) have examined 12 simple thymic cysts and concluded that they arose from persistent thymopharyngeal ducts rather than from cystic Hassall's bodies. They commented on the frequent occurrence of cholesterol granulomata, which they attributed to haemorrhage into the cysts. Linhartova (1965) has also reviewed the histology and pathogenesis of cavity formation in the thymus and has included a useful bibliography.

REFERENCES
